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Mikhail F. Chernov
Motohiro Hayashi
Clark C. Chen
Ian E. McCutcheon *Editors*

Gamma Knife Neurosurgery in the Management of Intracranial Disorders II

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Editors

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Editors
Mikhail F. Chernov
Faculty of Advanced Techno-Surgery
and Department of Neurosurgery
Tokyo Women's Medical University
Tokyo
Japan

Motohiro Hayashi
Faculty of Advanced Techno-Surgery
and Department of Neurosurgery
Tokyo Women's Medical University
Tokyo
Japan

Clark C. Chen
Department of Neurosurgery
University of Minnesota Medical School
Minneapolis, MN
USA

Ian E. McCutcheon
Department of Neurosurgery
The University of Texas MD Anderson Cancer Center
Houston, TX
USA

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Sponsors of the Seventh Meeting of the Asian Gamma Knife Academy (October 31–November 1, 2016; Honolulu, HI, USA) and Publication of Its Proceedings

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To the inventors, providers, and practitioners of radiosurgery worldwide, who are giving real hope to so many patients.

M. F. Chernov

To all colleagues working in the field of radiosurgery; and in memory of Professor Kintomo Takakura, MD—an outstanding neurosurgeon, exceptional leader, great mentor, and phenomenal person—who pioneered the Gamma Knife in Japan and Asia, and devoted his lifelong efforts to developing this neurosurgical technique worldwide.

M. Hayashi

To a better world, where tears are not shed because of cancer.

C. C. Chen

To my teachers at the Montreal Neurological Institute and the National Institutes of Health—Drs. Gilles Bertrand, André Olivier, and Edward Oldfield—who exemplified caring, thoughtfulness, integrity, and creativity in caring for patients.

I. E. McCutcheon

Preface

The Asian Gamma Knife Training Program (AGKTP) was established in 2007 as the first and, at that time, the only international professional organization in southeast Asia that was specifically dedicated to intracranial radiosurgery. Its main goals included facilitation of the exchange of ideas and skills among practitioners in the field, continuing education of young neurosurgeons and their training in Gamma Knife surgery (GKS), and dissemination of knowledge about advances in contemporary Gamma Knife techniques to the medical communities in Asian countries. The first AGKTP Meeting was held in the same year at the Saitama Gamma Knife Center at the Sanai Hospital (Saitama, Japan), with subsequent events organized in Tokyo, Japan (in 2008); Busan, Korea (in 2009); Taipei, Taiwan (in 2010); St. Petersburg, Russia (in 2011); and Shanghai, China (in 2014). The unique features of these meetings, which made them somewhat different from typical professional conferences, comprised in-depth, up-to-date, and practice-oriented coverage of all main topics in modern GKS by educational lectures (instead of the usual scientific reports) followed by wide and open critical discussions, and hands-on workshops with demonstration of real-time radiosurgical treatment planning. To better reflect its educational and scientific objectives, the AGKTP was renamed as the Asian Gamma Knife Academy (AGKA) in 2009, although its activities have extended beyond the borders of Asia.

On October 31–November 1, 2016, the seventh AGKA Meeting was conducted at the Hawaii Advanced Imaging Institute (Honolulu, HI, USA) under the leadership of Dr. Stephen Holmes. Reflecting the specific geographical location of the venue, this event was attended mainly by experts from the USA and Japan. The highly advanced level of presentations and general success of this conference led to the decision to report its program in these proceedings under the title *Gamma Knife Neurosurgery in the Management of Intracranial Disorders II*, following the tradition of a similar volume published after the fifth AGKA Meeting held in St. Petersburg in 2011 (*Acta Neurochirurgica Supplement Volume 116*). After the preparation, collection, and thorough editing of all submitted manuscripts, herein you can see the results of our work.

The articles included in this book are dedicated to the management of benign tumors (with a special emphasis on the optimal combination of microneurosurgery and radiosurgery for attaining the best functional results in patients with vestibular schwannomas, craniopharyngiomas, and pituitary adenomas), intracranial malignancies (e.g., pituitary carcinoma and brain metastases from solid cancers), symptomatic cavernous malformations, medically refractory tremors, and intractable pain syndromes, as well as to the specific aspects of radiosurgical treatment planning and dosimetry, medical physics, neuroimaging, anesthetic support, and the history of psychosurgery. We hope that readers will find the materials presented herein scientifically interesting and practically useful, and that our work will contribute to further progress in radiosurgery worldwide for the greatest benefit of all patients.

Mikhail F. Chernov — Tokyo, Japan
Motohiro Hayashi — Tokyo, Japan
Clark C. Chen — Minneapolis, MN, USA
Ian E. McCutcheon — Houston, TX, USA

Contents

Subtotal Resection Followed by Adjuvant Radiosurgery for Large Vestibular Schwannomas: Outcomes with Regard to the Timing and Regimen of Irradiation

Hesham Radwan, Tarek Elserry, Mark B. Eisenberg, Jonathan P. S. Knisely, Maged M. Ghaly, and Michael Schulder

Abstract *Objective:* To evaluate the results of combined management of large vestibular schwannomas (VS) with initial subtotal resection (STR) followed by adjuvant stereotactic radiosurgery (SRS), with a particular emphasis on the timing and regimen of irradiation.

Methods: Seventeen patients underwent STR of a VS followed by SRS, whereas five others were observed after STR. Early SRS (<6 months after surgery) and late SRS (>6 months after surgery) were done in 8 and 9 patients, respectively. Single- and multisession SRS treatments were administered in 10 and 7 patients, respectively. The mean follow-up durations after surgery and SRS were 40 and 28 months, respectively.

Results: The rates of radiological and oncological tumor control after SRS were 82% and 100%, respectively. The tumor volume at the last follow-up and its relative changes after SRS did not differ significantly on the basis of the irradiation timing (early versus late) or on the basis of the irradiation regimen (single-session versus multisession). In no patient who was observed after STR of a VS was tumor regrowth noted during a mean follow-up period of 49 months. At 12 months after surgery, motor function of the ipsilateral facial nerve corresponded to House–Brackmann grades I, II, III, and IV in 16 patients (73%), 3 patients (14%), 1 patient (5%), and 2 patients (9%), respectively. Facial nerve function at the last follow-up did not differ significantly on the basis of the irradiation timing (early versus late) or on the basis of the irradiation regimen (single-session versus multisession).

Conclusion: The combination of initial STR followed by adjuvant SRS is an effective treatment strategy for patients with a large VS. Although the optimal timing and regimen of postoperative irradiation of the residual lesion should be defined further, our preliminary data suggest that either early or late SRS after surgery may provide good tumor control and optimal functional results.

Keywords Combined treatment · Facial nerve function Gamma Knife radiosurgery · Linear accelerator · Multisession radiosurgery · Stereotactic radiosurgery · Subtotal removal Surgery · Vestibular schwannoma

H. Radwan
Department of Neurosurgery, Zucker School of Medicine at Hofstra/Northwell, Hempstead, NY, USA

Department of Neurosurgery, Ain Shams University, Cairo, Egypt

T. Elserry
Department of Neurosurgery, Ain Shams University, Cairo, Egypt

M. B. Eisenberg
Department of Neurosurgery, Zucker School of Medicine at Hofstra/Northwell, Hempstead, NY, USA

J. P. S. Knisely
Department of Radiation Oncology, Weill Cornell Medicine, New York, NY, USA

M. M. Ghaly
Department of Radiation Medicine, Zucker School of Medicine at Hofstra/Northwell, Lake Success, NY, USA

M. Schulder (✉)
Department of Neurosurgery, Zucker School of Medicine at Hofstra/Northwell, Hempstead, NY, USA

Brain Tumor Center, Northwell Neurosciences Insitute, Lake Success, NY, USA
e-mail: mschulder@northwell.edu

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Introduction

Vestibular schwannomas (VS) are encountered with an incidence of 1 per 100,000 person-years and comprise 75–90% of all cerebellopontine angle tumors [1, 2]. Management options include observation, microsurgical resection, stereotactic radiosurgery (SRS), and fractionated stereotactic radiotherapy (SRT). In particular, over the last 30 years, SRS has become a standard treatment option for patients with small or medium-sized VS, and there is strong evidence that it not only provides effective tumor control but also allows more favorable results of facial nerve function preservation than microsurgical resection of the lesion. For example, in a prospective study performed by Pollock et al. [3], normal facial movements at follow-up were noted significantly more often in patients treated with SRS than in those who underwent surgery (100% versus 61% at 3 months, $P < 0.001$; 100% versus 69% at 12 months, $P < 0.001$; and 96% versus 75% at the last follow-up visit, $P < 0.01$). However, SRS in patients with a large VS results in lower tumor control rates (of around 82–88%) and is associated with a higher risk of complications (mainly, cranial neuropathy) and a more frequent need for subsequent additional treatment [4–7]. On the other hand, surgery in patients with a large VS is rather challenging as well and often results in suboptimal functional outcomes [1, 8, 9]. Considering these limitations, our group has, during the last decade, adopted a novel combined treatment approach in cases of a large VS, comprising initial subtotal resection (STR) of the tumor, followed by SRS of its remnants. Our initial results with application of such a technique have been reported previously [10]. Herein, we present an additional analysis of the same clinical series directed at evaluation of tumor control and facial nerve function with regard to the timing and regimen of adjuvant irradiation, and discuss provisional advantages of clinical application of such a treatment strategy in cases of a large VS.

Patients and Methods

Demographic details of our study cohort have been presented before [10]. Briefly, our series comprised 7 men and 15 women (mean age 56 years) who were diagnosed with a large VS (maximum diameter >4 cm) corresponding to Koos stage III or IV [11, 12]. All patients underwent STR of the tumor, which in 17 cases (77%) was followed by adjuvant SRS; five other patients (23%) declined postoperative irradiation and preferred to be observed pending any evidence of tumor regrowth.

Stereotactic Radiosurgery

The mean interval between STR of a VS and SRS of the residual tumor was 9.5 months (median 7 months, range 2–50 months). Eight patients were treated within 6 months after surgery (early SRS), and 9 were treated later on (late SRS). Overall, 9 patients underwent single-session Gamma Knife surgery (GKS) with a marginal dose of 12–14 Gy delivered at the 50% prescription isodose line. Seven other patients who had either a prolonged (>3-month) postoperative recovery from cranial neuropathy or a large residual tumor (volume >3 cc) received multisession SRS with a linear accelerator (LINAC); in 6 of them, the total dose at the 80% prescription isodose line was 25 Gy, being delivered in five fractions (5 Gy per fraction), and in one, it was 21 Gy in three fractions (7 Gy per fraction). One additional patient underwent single-session LINAC-based SRS with a marginal dose of 12 Gy.

Follow-Up, Tumor Volumetry, and Outcome Measures

The mean lengths of follow-up after surgery and SRS were 40 months (median 20 months, range 20–128 months) and 28 months (median 22 months, range 17–77 months), respectively. The lesion volumes both before and after treatment were calculated with the use of iPlan® Net (Brainlab AG; Munich, Germany), and decreases or increases of ≥1 cc during follow-up were considered tumor shrinkage and tumor enlargement, respectively. Facial nerve function was assessed according to the House–Brackmann grading system [13]. In addition, trigeminal nerve function, lower cranial nerve function, vestibular function, and hearing were evaluated.

Statistics

The Mann–Whitney test and Spearman correlation were used for data analysis. P values <0.05 were considered statistically significant.

Results

The mean VS volumes before surgery, at the time of SRS after STR, and at the last follow-up after SRS were 13.1, 2.9, and 2.8 cc, respectively. The mean extent of resection (EOR) was 77%. The tumor volume at the time of SRS did not differ significantly on the basis of the irradiation timing (early versus late: mean 4.0 versus 2.0 cc, $P > 0.05$) or on the basis of the irradiation regimen (single-session versus multisession: mean 3.4 versus 2.2 cc, $P > 0.1$). In patients who declined SRS and were observed after STR, the mean postoperative tumor volume was 0.35 cc.

Tumor Control and Volumetric Response to Radiosurgery

Tumor shrinkage, stabilization, and enlargement after SRS were noted in 1 case (6%), 13 cases (76%), and 3 cases (18%), respectively. No patient required additional treatment during follow-up. Thus, the radiological and oncological tumor control rates after SRS were 82% and 100%, respectively.

The mean lengths of follow-up in the groups of patients who underwent early and late SRS were 24 and 42 months, respectively. The tumor volume at the last follow-up did not differ significantly on the basis of the irradiation timing (early versus late: mean 3.6 versus 2.0 cc, $P > 0.1$) or on the basis of the irradiation regimen (single-session versus multisession: mean 3.3 versus 2.0 cc, $P > 0.1$). The relative changes in the tumor volume after SRS varied from −83% to +193% (mean +9%, median 0%), did not demonstrate any correlation with the preradiosurgery tumor volume ($R_s = -0.224$, $P = 0.3681$) or the time interval between STR and SRS ($R_s = 0.330$, $P = 0.1868$), and did not differ significantly on the basis of the irradiation timing (early versus late: mean −3% versus +20%, $P > 0.1$) or on the basis of the irradiation regimen (single-session versus multisession: mean +10% versus +7%, $P > 0.1$).

The mean length of follow-up in the group of patients who were observed after STR of a VS was 49 months, and in none of them was tumor regrowth noted.

Preservation of Facial Nerve Function

Anatomical preservation of the facial nerve during surgery was attained in all patients. Immediately after STR of a VS, excellent-to-moderate (House–Brackmann grades I–III) motor function of the ipsilateral facial nerve was noted in 15 of 22 patients (68%), whereas in 5 others (23%), disfiguring facial weakness was obvious (House–Brackmann grades IV–V), and 2 patients (9%) had complete facial paralysis (House–Brackmann grade VI). The postoperative House–Brackmann grade inversely correlated with the volume of the residual VS after STR ($R_s = -0.63$, $P = 0.0039$), and the best outcome was generally attained in cases with a residual tumor volume >3 cc [10].

Nevertheless, at 12-month follow-up after surgery, excellent motor function (House–Brackmann grade I), good motor function (House–Brackmann grade II), and moderate motor function (House–Brackmann grade III) of the ipsilateral facial nerve were noted in 16 patients (73%), 3 patients (14%), and 1 patient (5%), respectively, whereas in 2 others (9%), it corresponded to House–Brackmann grade IV. It was found that in patients with motor function of the ipsilateral facial nerve that corresponded to House–Brackmann grades III–V immediately after surgery, the probabilities of recovery to an excellent-to-good level (House–Brackmann grades I–II) within 6 and 18 months were >50% and approximately 80%, respectively [10].

All 8 patients (100%) who underwent early adjuvant SRS after STR had excellent (House–Brackmann grade I) motor function of the ipsilateral facial nerve at the last follow-up, in comparison with 5 of 9 patients (56%) in the late SRS group. However, statistical analysis showed that the House–Brackmann grade at the time of the last follow-up did not differ significantly on the basis of the irradiation timing (early versus late: $P > 0.1$) or on the basis of the irradiation regimen (single-session versus multisession: $P > 0.1$).

Other Outcome Measures

Temporary trigeminal neuropathy and dysphagia/dysarthria after surgery were noted in 4 patients (18%) and 2 patients (9%), respectively. Out of 7 patients who demonstrated vestibular dysfunction preoperatively, slight symptomatic improvement during follow-up after STR of the tumor was marked in 3, whereas in 4 others, pre-existing symptoms remained stable.

Temporary trigeminal neuropathy after SRS was noted in 1 patient (6%). Out of 8 patients with serviceable hearing before SRS, only one demonstrated a decline (from Gardner–Robertson class II to class IV) after irradiation. No patient showed deterioration of vestibular function after SRS.

Discussion

From the dawn of neurological surgery as a medical specialty, and for nearly a century thereafter, surgical tumor removal was the only treatment option available for patients with a VS. Novel technologies and technical developments introduced over the decades resulted in significant improvements in surgical results and declines in morbidity and mortality [14]. Nevertheless, even today, gross total resection (GTR) of a VS is a highly challenging goal, and postoperative complications in such cases are not uncommon [1, 8, 9]. This is particularly true in patients with large tumors, in whom the prevalence of excellent-to-good (House–Brackmann grades I–II) facial nerve function after surgery averages only 54%, although it has ranged widely from 44% to 94% [4]. Schwartz et al. [8] reported that better facial nerve function preservation and a lower incidence of complete facial paralysis (House–Brackmann grade VI) may be achieved after near-total resection (NTR) (78% and 2%, respectively) or STR (71% and 10%, respectively) of a large VS in comparison with GTR (53% and 24%, respectively). Although the impact of the EOR on postoperative facial nerve function remains debatable, it is evident that conservative (i.e., less aggressive) surgery is associated with reduced intraoperative mechanical stress on adjacent anatomical structures, including cranial nerves. In concordance, in our series, the House–Brackmann grade immediately after STR of a VS inversely correlated with the volume of the residual lesion [10]. The problem is that incomplete surgical removal is accompanied by high rates of tumor regrowth, which were 22%, 21%, and 3% after STR, NTR, and GTR, respectively [8]. The optimal solution in such cases may be a combined treatment strategy, as was advocated in several previous reports [6, 10, 15–21] and has been presented herein.

Initial STR is directed at reduction of the VS volume and decompression of the brainstem, cerebellum, and cranial nerves, and it limits the risk of their anatomical injury so as to decrease the chance of permanent postoperative neurological deficits. The main question is when to stop resection. It should be emphasized that we are not advocating leaving large tumor remnants. Nevertheless, since the primary objective of conservative surgery in such cases is preservation of neurological function, a larger residual lesion volume (if it is small enough to allow postoperative SRS) may be considered an appropriate price for optimal functional outcome. In particular, anatomical preservation of the facial nerve is of paramount importance, but it is hardly possible to predict when it may be injured during tumor removal [22, 23]. In our experience, some patients developed postoperative facial palsy despite the absence of significant changes during intraoperative electrical stimulation of the nerve. On the other hand, the results indicate that better facial nerve function after surgery may be observed in cases with a residual tumor volume >3 cc [10]. Thus, we recommend that the volume of a residual VS should be in the range of 3 cc if this can be achieved safely.

Subsequent adjuvant SRS of a residual tumor prevents its regrowth in the same way as occurs with a smaller VS. The questions are when to perform postoperative irradiation and whether it should be done for the management of a residual lesion or at the time of its progression. This issue clearly remains controversial. It is well recognized that a residual VS may be stable after surgery for a more or less prolonged period of time. None of the patients we observed after STR demonstrated tumor regrowth during a mean follow-up duration of 49 months, while other researchers have reported that progression of an incompletely resected VS usually occurs 2–3 years after the intervention [1, 8, 22, 24, 25]. Although in the present series, early SRS was associated with the most prominent volumetric tumor response and better facial nerve function at the last follow-up, the statistical analysis did not reveal significant differences in comparison with delayed irradiation, which, however, was still done for a residual (i.e., nonprogressing) VS. Similarly, we did not find any advantages of multisession SRS, which was arbitrarily selected for patients with prolonged postoperative recovery from cranial neuropathy or in cases of a relatively large residual lesion. It should be underlined, however, that our study was retrospective and based on a limited number of cases, and the short length of follow-up did not allow differentiation between true progression of a VS and pseudoprogression, which is typically observed between 6 and 18 months after SRS. Therefore, the optimal timing and regimen of adjuvant SRS after STR of a VS should be evaluated further. A randomized, controlled trial could clarify these important issues but would be very difficult to complete, whereas use of registry-based data seems more achievable and could provide equally robust information.

In our opinion, the challenge of GTR for a large VS is an idea whose time has passed, given the benign nature of these slow-growing tumors, the high risks of facial nerve palsy and other cranial neuropathies after aggressive surgery, and the established role of SRS as a safe and effective treatment option. Several reports in the literature [6, 15–21], as well as our own results [10], indicate that in such cases, STR followed by adjuvant SRS may be quite effective and provides local tumor control rates similar to those observed after GTR, but with much more favorable functional outcomes. An important issue is that such a clinical strategy, and thus conservative surgery, should be preplanned, since it provides a 95–100% rate of preservation of facial nerve function (and even hearing in some cases) in comparison with a 35–40% rate when the decision to perform combined treatment is done intraoperatively because of an inability to attain GTR of the tumor [5, 20].

Conclusion

Patients with a large VS may be treated effectively with a combination of initial preplanned STR of the tumor followed by adjuvant SRS of its remnants. In such cases, the goal of conservative surgery is reduction of the mass lesion volume and decompression of adjacent anatomical structures without an excessive risk of injuring them, in order to prevent a permanent postoperative neurological deficit. The optimal timing (early versus late) and regimen (single-session versus multisession) of postoperative SRS should be defined in further studies involving large numbers of patients, but our preliminary data suggest that either option may result in good tumor control and an optimal outcome—in particular, providing high rates of ipsilateral facial nerve function preservation.

Conflict of Interest The authors have no conflict of interest concerning the reported materials or methods.

References

1. Arlt F, Trantakis C, Seifert V, Bootz F, Strauss G, Meixensberger J. Recurrence rate, time to progression and facial nerve function in microsurgery of vestibular schwannoma. Neurol Res. 2011;33:1032–7.
2. Propp JM, McCarthy BJ, Davis FG, Preston-Martin S. Descriptive epidemiology of vestibular schwannomas. Neuro Oncol. 2006;8:1–11.
3. Pollock BE, Driscoll CL, Foote RL, Link MJ, Gorman DA, Bauch CD, Mandrekar JN, Krecke KN, Johnson CH. Patient outcomes after vestibular schwannoma management: a prospective comparison of microsurgical resection and stereotactic radiosurgery. Neurosurgery. 2006;59:77–85.
4. Flickinger JC, Kondziolka D, Niranjan A, Maitz A, Voynov G, Lunsford LD. Acoustic neuroma radiosurgery with marginal tumor doses of 12 to 13 Gy. Int J Radiat Oncol Biol Phys. 2004;60:225–30.
5. Milligan BD, Pollock BE, Foote RL, Link MJ. Long-term tumor control and cranial nerve outcomes following Gamma Knife surgery for larger-volume vestibular schwannomas. J Neurosurg. 2012;116:598–604.
6. van de Langenberg R, Hanssens PE, van Overbeeke JJ, Verheul JB, Nelemans PJ, de Bondt BJ, Stokroos RJ. Management of large vestibular schwannoma. Part I: planned subtotal resection followed by Gamma Knife surgery: radiological and clinical aspects. J Neurosurg. 2011;115:875–84.
7. Yang HC, Kano H, Awan NR, Lunsford LD, Niranjan A, Flickinger JC, Novotny J Jr, Bhatnagar JP, Kondziolka D. Gamma Knife radiosurgery for larger-volume vestibular schwannomas. J Neurosurg. 2011;114:801–7.
8. Schwartz MS, Kari E, Strickland BM, Berliner K, Brackmann DE, House JW, Friedman RA. Evaluation of the increased use of partial resection of large vestibular schwanommas: facial nerve outcomes and recurrence/regrowth rates. Otol Neurotol. 2013;34: 1456–64.
9. Talfer S, Dutertre G, Conessa C, Desgeorges M, Poncet JL. Surgical treatment of large vestibular schwannomas (stages III and IV). Eur Ann Otorhinolaryngol Head Neck Dis. 2010;127:63–9.
10. Radwan H, Eisenberg MB, Knisely JPS, Ghaly MM, Schulder M. Outcomes in patients with vestibular schwannoma after subtotal resection and adjuvant radiosurgery. Stereotact Funct Neurosurg. 2016;94:216–24.
11. Koos WT. Criteria for preservation of vestibulocochlear nerve function during microsurgical removal of acoustic neurinomas. Acta Neurochir (Wien). 1988;92:55–66.
12. Koos WT, Day JD, Matula C, Levy DI. Neurotopographic considerations in the microsurgical treatment of small acoustic neurinomas. J Neurosurg. 1998;88:506–12.
13. House JW, Brackmann DE. Facial nerve grading system. Otolaryngol Head Neck Surg. 1985;93:146–7.
14. Arthurs BJ, Fairbanks RK, Demakas JJ, Lamoreaux WT, Giddings NA, Mackay AR, Cooke BS, Elaimy AL, Lee CM. A review of treatment modalities for vestibular schwannoma. Neurosurg Rev. 2011;34:265–79.
15. Daniel R, Tuleasca C, George M, Schiappacasse L, Zeverino M, Maire R, Levivier M. Combined approach for the management of large vestibular schwannomas: planned subtotal resection followed by Gamma Knife surgery in a series of 20 consecutive cases. Neurochirurgie. 2014;60:331–2.
16. Daniel RT, Tuleasca C, Rocca A, George M, Pralong E, Schiappacasse L, Zeverino M, Maire R, Messerer M, Levivier M. The changing paradigm for the surgical treatment of large vestibular schwannomas. J Neurol Surg B Skull Base. 2018;79(Suppl 4):S362–70.
17. Fuentes S, Arkha Y, Pech-Gourg G, Grisoli F, Dufour H, Régis J. Management of large vestibular schwannomas by combined surgical resection and Gamma Knife radiosurgery. Prog Neurol Surg. 2008;21:79–82.
18. Iwai Y, Yamanaka K, Ishiguro T. Surgery combined with radiosurgery for large acoustic neuromas. Surg Neurol. 2003;59:283–91.
19. Iwai Y, Ishibashi K, Watanabe Y, Uemura G, Yamanaka K. Functional preservation after planned partial resection followed by Gamma Knife radiosurgery for large vestibular schwannomas. World Neurosurg. 2015;84:292–300.
20. Pan HC, Sheehan J, Sheu ML, Chiu WT, Yang DY. Intracapsular decompression or radical resection followed by Gamma Knife surgery for patients harboring a large vestibular schwannoma. J Neurosurg. 2012;117(Suppl):69–77.
21. Yang SY, Kim DG, Chung HT, Park SH, Paek SH, Jung HW. Evaluation of tumour response after Gamma Knife radiosurgery for residual vestibular schwannomas based on MRI morphological features. J Neurol Neurosurg Psychiatry. 2008;79:431–6.
22. Bloch DC, Oghalai JS, Jackler RK, Osofsky M, Pitts LH. The fate of the tumor remnant after less-than-complete acoustic neuroma resection. Otolaryngol Head Neck Surg. 2004;130:104–12.
23. Nonaka Y, Fukushima T, Watanabe K, Friedman AH, Sampson JH, Mcelveen JT Jr, Cunningham CD 3rd, Zomorodi AR (2013) Contemporary surgical management of vestibular schwannomas: analysis of complications and lessons learned over the past decade. Neurosurgery 72 (2 Suppl Operative): ONS103–15.
24. Boari N, Bailo M, Gagliardi F, Franzin A, Gemma M, del Vecchio A, Bolognesi A, Picozzi P, Mortini P. Gamma Knife radiosurgery for vestibular schwannoma: clinical results at long-term follow-up in a series of 379 patients. J Neurosurg. 2014;121(Suppl):123–42.
25. Lownie SP, Drake CG. Radical intracapsular removal of acoustic neurinomas: long-term follow-up review of 11 patients. J Neurosurg. 1991;74:422–5.

Preplanned Partial Surgical Removal Followed by Low-Dose Gamma Knife Radiosurgery for Large Vestibular Schwannomas

Yoshiyasu Iwai, Kenichi Ishibashi, and Kazuhiro Yamanaka

Abstract *Objective:* The present study evaluated outcomes after preplanned partial surgical removal of a large vestibular schwannoma (VS) followed by low-dose Gamma Knife surgery (GKS).

Methods: Between January 2000 and May 2015, 47 patients with a unilateral VS (median maximum diameter 32 mm) underwent preplanned partial tumor removal at our clinic. GKS for a residual lesion was done within a median time interval of 3 months. The median prescription dose was 12 Gy. The median length of subsequent follow-up was 74 months.

Results: The actuarial tumor growth control rates without a need for additional management at 3, 5, and 15 years after GKS were 92%, 86%, and 86%, respectively. At the time of the last follow-up, the function of the ipsilateral facial nerve corresponded to House–Brackmann grade I in 92% of patients. Significant improvement of ipsilateral hearing was noted in two patients after partial tumor removal and in one after GKS. Among 16 patients who presented with ipsilateral serviceable hearing, it was preserved immediately after surgery in 81% of cases and at the time of the last follow-up in 44%. Salvage surgical treatment was required in 9% of patients.

Conclusion: Preplanned partial surgical removal followed by low-dose GKS provides a high level of functional preservation in patients with a large VS.

Keywords Combined treatment · Facial nerve function Gamma Knife radiosurgery · Hearing preservation · Partial removal · Retrosigmoid approach · Surgery · Vestibular schwannoma

Introduction

Gamma Knife surgery (GKS) has become a mainstream treatment option for patients with a small-to-medium-sized vestibular schwannoma (VS) because it offers minimal invasiveness, optimal tumor growth control, and beneficial long-term functional results—in particular, with regard to preservation of facial nerve function and hearing [1–3]. Nevertheless, in cases of large tumors, surgical resection is clearly indicated to relieve increased intracranial pressure and cerebellar dysfunction [4, 5]. A meticulous microsurgical technique and advanced intraoperative neurophysiological monitoring allow good facial nerve preservation rates, but maintenance of serviceable hearing after tumor removal is still a significant challenge [6]. Since 1994, we have performed preplanned partial surgical tumor removal followed by GKS to improve functional outcomes in patients with a large VS [4]. Steady gains in our clinical experience have allowed this management strategy to be upgraded and optimized, and have clearly demonstrated its benefits and efficacy [7]. The objective of the present study was evaluation of the results of such combined treatment in a recent cohort of patients.

Patients and Methods

Between January 2000 and May 2015, 47 patients with a large unilateral VS (maximum diameter ≥25 mm) underwent preplanned partial tumor removal followed by low-dose GKS at our clinic (Table 1). This cohort comprised 22

Y. Iwai (✉)
Department of Neurosurgery, Tominaga Hospital, Osaka, Japan
e-mail: y-iwai@rc5.so-net.ne.jp

K. Ishibashi · K. Yamanaka
Department of Neurosurgery, Osaka City General Hospital, Osaka, Japan

Table 1 Clinical characteristics at presentation in 47 patients who underwent preplanned partial surgical removal of a large unilateral vestibular schwannoma followed by low-dose Gamma Knife radiosurgery

Clinical characteristic	Values
Sex (*N*)	
Male	22 (47%)
Female	25 (53%)
Age (years)	
Range	30–82
Median	60
Symptoms and signs (*N*)	
Hearing impairment	43 (91%)
Cerebellar ataxia	37 (79%)
Trigeminal neuropathy	36 (77%)
Facial weakness	14 (30%)
Headache caused by increased intracranial pressure	6 (13%)
Hydrocephalus	2 (4%)
Pure tone average (*N*)	
0–30 dB	8 (17%)
31–50 dB	8 (17%)
51–80 dB	14 (30%)
81–110 dB	5 (10%)
>110 dB	12 (26%)
Maximum tumor diameter (*N*)	
25–29 mm	11 (23%)
30–39 mm	27 (57%)
40–49 mm	4 (9%)
50–52 mm	5 (11%)

men and 25 women aged from 30 to 82 years (median age 60 years). The most common preoperative symptoms and signs were hearing impairment (in 43 patients; 91%), cerebellar ataxia (in 37 patients; 79%), and trigeminal neuropathy (in 36 patients; 77%), including 1 patient with trigeminal neuralgia. Ipsilateral facial weakness was noted in 14 cases (30%) and corresponded to House–Brackmann grades II and III [8] in 12 and 2 patients, respectively. Before surgery, 16 patients (34%) had ipsilateral serviceable hearing (pure tone average (PTA) ≤50 dB), 19 (40%) showed some preservation of ipsilateral hearing (PTA >50 to ≤110 dB), and 12 (26%) were considered deaf (PTA >110 dB). The median maximum diameter of the tumor was 32 mm (range 25–52 mm). Eleven patients with smaller tumors (maximum diameter 25–29 mm) underwent initial surgical resection instead of primary GKS because of the presence of cerebellar ataxia and/or trigeminal neuropathy.

Surgical Technique

Our surgical technique for partial removal of a large VS and reduction of its size to make the mass suitable for GKS was described in detail previously [4]. In brief, the retrosigmoid approach was used in all cases, and the portion of the mass adjacent to the cerebellum was resected as much as possible, but the ventral and intracanalicular parts of the tumor were intentionally left in situ. Opening of the internal auditory canal (IAC) was avoided. Spinal or ventricular drainages were never used either intra- or postoperatively.

Radiosurgical Technique

The median interval between partial removal of a VS and GKS was 3 months (range 1–12 months). In cases of cystic tumors, GKS was done earlier (usually at 1 month after surgery) to prevent re-expansion of the cyst. The median preradiosurgery lesion volume was 2.7 cc (range 0.4–10.4 cc). Treatment planning and radiation dosimetry were done with Leksell GammaPlan® (Elekta AB; Stockholm, Sweden). The median prescription dose was 12 Gy (range 10–12 Gy). Of note, a prescription dose of 10 Gy was applied only once, for irradiation of the largest tumor in the present series, which had a volume of 10.4 cc.

Follow-Up

All patients underwent clinical evaluations, PTA measurements, and magnetic resonance imaging (MRI) examinations every 6 months during the first 3 years after GKS and, in cases of tumor growth control, yearly thereafter. The median length of follow-up after irradiation was 74 months (range 24–180 months).

Results

The rates of actuarial tumor growth control without a need for additional management at 3, 5, 10, and 15 years after GKS were 92%, 86%, 86%, and 86%, respectively (Fig. 1). Treatment failure was significantly associated with the lesion volume before irradiation (37.5% versus 3% in VS with preradiosurgery volumes of ≥6 cc versus <6 cc, $P = 0.01$) and showed a statistically nonsignificant trend toward a higher incidence in younger patients (33% versus 6% in patients aged <50 years versus ≥50 years, $P = 0.076$). The sex of the

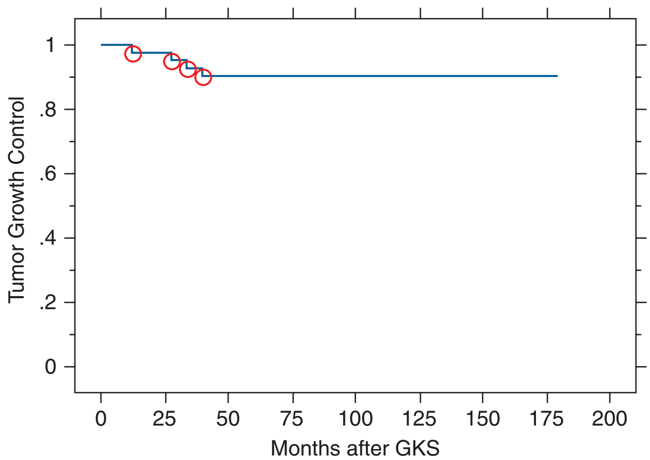

Fig. 1 Kaplan–Meier curve demonstrating tumor growth control without a need for additional management in 47 patients with a large unilateral vestibular schwannoma after preplanned partial surgical removal followed by low-dose Gamma Knife surgery (GKS)

Table 2 Preservation of motor function of the ipsilateral facial nerve in 47 patients who underwent preplanned partial surgical removal of a large unilateral vestibular schwannoma followed by low-dose Gamma Knife radiosurgery (GKS)

	Preservation of motor function (*N*)		
House–Brackmann grade	Before surgery	After surgery	At last follow-up after GKS
I	33 (70%)	37 (79%)	43 (92%)
II	12 (26%)	7 (15%)	1 (2%)
III	2 (4%)	0	0
IV	0	1 (2%)	2 (4%)
V	0	2 (4%)	1 (2%)

patient and the presence of a tumor cyst were not associated with growth control of a VS after low-dose GKS.

Preservation of Facial Nerve Function

Two weeks after partial surgical tumor removal, the motor function of the ipsilateral facial nerve corresponded to House–Brackmann grade I in 37 patients (79%) and to grade II in 7 (15%), but in 1 patient (2%), it deteriorated to grade IV and in 2 (4%), it deteriorated to grade V (Table 2). At the time of the last follow-up after GKS, the motor function of the ipsilateral facial nerve corresponded to House–Brackmann grade I in 43 patients (92%), to grade II in 1 (2%), to grade IV in 2 (4%), and to grade V in 1 (2%); in the latter patient, no substantial functional improvement was noted during the entire follow-up period after partial surgical tumor removal.

Preservation of Hearing

After partial tumor removal, two patients (6%) experienced a significant improvement in their ipsilateral hearing, with changes in PTA from 115 dB to 59 dB in one case and from 115 dB to 12.5 dB in another (Fig. 2). In addition, in one patient, a significant improvement in ipsilateral hearing with a change in PTA from 115 dB to 35 dB was noted 1.5 years after GKS.

Overall, out of 16 patients with ipsilateral serviceable hearing (PTA ≤50 dB) at presentation, 13 (81%) showed its preservation after partial tumor removal and 7 of them maintained the same level of serviceable hearing at the time of the last follow-up after GKS. Out of 35 patients with any degree of ipsilateral hearing preservation (PTA ≤110 dB) at presentation, 25 (71%) showed the same level of hearing after partial tumor removal (PTA changes within 20 dB but not exceeding 110 dB) and 11 of them maintained the same level of hearing at the time of the last follow-up after GKS.

Salvage Surgery

Following preplanned partial surgical removal and subsequent GKS, 4 patients (9%) suffered from cerebellar or truncal ataxia, which necessitated salvage surgery performed within a median interval of 31 months (range 12–42 months) after irradiation. In this group, the median VS volume before GKS was 6.6 cc (range 3.5–10.4 cc). In all cases, salvage surgery was directed at partial tumor removal with the purpose of functional preservation. During subsequent follow-up (median 84 months, range 60–96 months), two VS demonstrated gradual shrinkage; one was stable, and in the other case, enlargement of the tumor cyst necessitated stereotactic aspiration of its content via the transcerebellar approach 54 months after salvage surgery.

Complications

There were no deaths in the present series. Four patients experienced complications after partial removal of a large VS: a lung abscess due to aspiration pneumonia, aseptic meningitis necessitating steroid therapy, a pulmonary embolism, and venous infarction of the cerebellum requiring surgery directed at external decompression of the posterior cranial fossa were each noted once. In none of these cases did the development of a complication affect the overall treatment strategy.