Aim of the study: One of the alternative methods of surgical treatment of vestibular schwannoma is Gamma Knife radiosurgery. The purpose of this metaanalysis was to analyze the progress in treatment of vestibular schwannoma using Gamma Knife radiosurgery based on data in the literature of the last five years.

Material and methods: In the collected English-language literature from the years 2007–2011, contained in 20 scientific journals, clinical articles of many years study at a single center were extracted and also review papers and case reports. The main criteria of our own analysis were: patient age, tumor size, the dose in Gy, the time from surgery to follow-up, the degree of tumor growth inhibition, and hearing preservation. For statistical calculations comparing series of studies we used nonparametric analysis of variance and tests at the significance level of \( p > 0.05 \).

Results: The 46 evaluated clinical articles show the results of studies over many years. A comparison of the results of the analysis made on the basis of papers published in the period 1998–2007 with the results of the current series from the period 2007–2011 allowed us to establish that the average dose applied to the periphery of the tumor was lower (12.4 Gy) than in the earlier series of 1998–2007 (14.2 Gy), and hearing preservation was higher (66.45% vs. 51.0%).

Conclusions: Clinical findings widely documented in the literature over the past five years indicate the progress in treatment of vestibular schwannoma using Gamma Knife radiosurgery.

Key words: acoustic neuroma, Gamma Knife, hearing preservation, radiosurgery, vestibular schwannoma.

A meta-analysis of treatment of vestibular schwannoma using Gamma Knife radiosurgery

Bartosz Rykaczewski1, Miroslaw Zabek2
1Mazovia Regional Hospital, Warsaw, Poland
2Department of Neurosurgery, Postgraduate Medical Center, Brodno Mazovia Hospital, Warsaw, Poland

Introduction

Vestibular schwannoma (VS), also called acoustic neuroma, is a benign tumor arising from Schwann cells of the vestibular portion of the eighth cranial nerve inside the internal auditory canal. With tumor growth it fills the internal auditory canal and extends beyond it, reaching the cerebellopontine angle region. The most common symptoms of VS occurrence are progressive deterioration of hearing, dizziness and headache. The progression of the tumor to nerve V leads to facial paresthesia. When the tumor reaches nerves IX, X, and XI there are difficulties in swallowing. Compression of the brain stem by the tumor leads to an imbalance and sometimes hydrocephalus. The incidence of these tumors is estimated at one in 100 000 people a year, but recently in connection with the frequent use of magnetic resonance imaging (MRI) detection of VS is twice as high [1, 2].

One of the alternative methods of surgical treatment of VS is Gamma Knife radiosurgery (GKRS). Clinical experience with proton beam irradiation to the central part of the brain was initiated in the 1960s by Professor Lars Lexell at the Gustaf Werner Institute in Uppsala (Sweden) [3]. In 1967, when this therapeutic tool was used for the first time, the name “Gamma Knife” (GK) was coined. The basic concept of GK was that extremely well-collimated beams from a large number of Cobalt-60 sources, distributed around a half-spherical collimator helmet, would allow a circumscribed focus of beam to be produced in the central part of the patient’s skull. The initial goal was to offer the use of GK surgery, the traditional non-surgical removal of only some of the lesions, but later it was found that precise irradiation of small intracranial tumors located even in the pituitary gland was possible. Currently, the number of patients treated using the Gamma Knife is estimated at 50 000 a year [4].

Worldwide, there are four models using the Gamma Knife: U/A, B, C/4-C and LGK Perfexion [5, 6]. The last model was introduced in 2006. It allows the range of operation to be extended and is equipped with advanced dose planning software, for precise and dynamic beam shaping.

Based on a population of 40 000 000 in Poland it is estimated that about 500 vestibular schwannomas are newly diagnosed each year and most of them are treated by a retrosigmoid approach in general anesthesia in neurosurgery departments. In Poland, the Leksell Gamma Knife Perfexion was installed in 2010 in only one center in Warsaw. To date it has been used for the operation of 320 patients with VS. Due to the relatively short time that has elapsed since the application of GK, there are no data about the effects of this method of treatment over time. The purpose of this study was to analyze the progress in treatment of vestibular schwannoma using Gamma Knife radiosurgery based on data in the literature from the last five years.
**Material and methods**

Articles published in 2007–2011 were searched using PubMed and Medline search engines and publishers Springer, Elsevier and Kluwer, the database in English, using the keywords “gamma knife”, “vestibular schwannoma” and “acoustic neuroma”. With over 700 abstracts, to continue the search full texts of the various items of literature that contain all the keywords “gamma knife” and “vestibular schwannoma” and “gamma knife” and “acoustic neuroma” were selected. The collected material, located in 20 scientific journals, comprised case studies, analyses of the work of many years of study at a single center, and review papers. Interesting was the use of new models of Leksell Gamma Knife in the various medical centers. The main criteria for the analysis were patient age, tumor size, dose (Gy), the period from radiosurgery to control, the degree of inhibition of tumor growth, and hearing preservation. Correlations between the investigated characteristics were determined using Microsoft Excel. For statistical calculations comparing the series, nonparametric analysis of variance was used and the following tests: Kruskal-Wallis, Van der Waerden, Kolmogorov-Smirnov test, and median one-way analysis. The level of significance was $p < 0.05$.

**Results**

In total, 46 long-term clinical studies covering a period from 3 to 22 years were included [7–52] (Table 1). The longest observations took place in the following medical centers: Pittsburgh (USA), Marseille (France), Komaki (Japan) and Seoul (Korea). The works used different models of Gamma Knife, depending on the period of study and institutions. The latest model, PFX Leksell Gamma Knife, was used in studies at the University of Verona [34] and Marseille [42], and the 4-C model in the study at the University of Pittsburgh [12, 17, 25, 35], Nijmegen [31, 41], Philadelphia [43] and Maastricht [46, 47].

For further analysis the literature was selected according to data required for the analysis of own studies (Table 2). The total number of patients meeting the criteria for the work selected in 28 articles was 3233 [7, 9, 12, 15–17, 22, 23, 25–27, 29, 30, 33, 34, 36–41, 43, 45, 47–50, 52]. The described groups of patients ranged from 21 to 444 in size depending on location and duration of the study [33, 36]. Average age was 52.6 years. The lowest was 29, and the highest was 68 years [40, 38]. Tumor volume varied from 0.17 to 12.6 cm$^3$ and on average was 3.9 cm$^3$. The Gamma Knife surgery (GKS) radiation dose to the periphery of the tumor was on average 12.4 Gy, but was greater than 13.0 Gy only in one publication [12]. The resulting tumor growth control was achieved in 92.7%, and the preservation of serviceable hearing was on average 66.45% with a mean follow-up of 51.24 months. There was no significant correlation between radiation dose and GKS tumor growth inhibition and hearing preservation. In the overall analysis case studies are not included due to the small database [53–58].

The efficacy of radiosurgery using the Gamma Knife in the comprehensive analysis of data from 28 papers (Table 2) was compared with several meta-analyses contained in the scientific literature [1, 59–66] (Table 3). Age of patients ranged on average from 51.8 to 57 years [64, 60]. Tumor size presented in units of volume ranged from 2.7 to 4.0 cm$^3$. With an observation period from 16 to over 60 months, tumor growth inhibition was achieved in an average of 81 to 100% of patients, and the preservation of serviceable hearing from 20 to 57% of such patients.

A comparison of the results of the analysis made on the basis of papers published in the period 1998–2007 [64] with the analysis of the current series of works from the period 2007–2011 shows that both of these series combine the highest similarity in the type of data obtained. Based on surveys, it was found that data on patient age, tumor size and tumor growth control are not significantly different between the several sets of analyses (Table 4). There was, however, a highly significant difference in the size of the dose and in the degree of serviceable hearing preservation, and quite significant in the follow-up (Fig. 1, 2 and 3). In the current series of studies, the dose applied to the periphery of the tumor was lower, the hearing preservation was higher, and the follow-up was longer than in previous series [64].

**Discussion**

The most important goal in treating patients with vestibular schwannoma is the control of tumor growth and maintaining the quality of life (QOL), while minimizing the side effects of treatment. Gamma Knife generally meets these criteria and is used successfully worldwide as an alternative method of treatment of VS [50]. The use of the Gamma Knife in radiosurgery of vestibular schwannoma is a breakthrough for patients suffering from this disease. In most cases, it does not create a need for hospitalization [63, 64]. The results of many years of experience, gained in leading medical institutions, have led to improvements of GK [5, 6]. The latest model, LGK PFX, is more widely used, most recently in Russia and Ukraine [4]. Implementation of a quantitative comparison of radiosurgical treatment of VS using the Leksell Gamma Knife Perfexion and Model C has shown that the most important new features of PFX lead to improvement of dosimetric parameters, especially for large tumors [42]. Optimizing the dose planning can improve results of treatment, but a fully comprehensive assessment of the benefits to patients requires long-term clinical observations.

In numerous studies on the use of Gamma Knife radiosurgery for vestibular schwannomas, there are many factors that have been frequently studied in detail [7–52]. These include patient age, tumor size, dose to the tumor periphery, tumor growth control, the preservation of hearing and facial nerve function, and the quality of life after radiosurgery. To analyze the preservation of hearing, most neuro-otology reports use the classification of AAO-HNS and the majority of neurosurgical publications apply the GR classification [17]. Differences between pre- and postoperative hearing class are presented differently in each survey. A common strategy is, however, the use of the concept of serviceable hearing (GR grade I or II or the
| First author, year | Institution* | Years of the study | Model of GK** |
|-------------------|--------------|--------------------|--------------|
| Chopra, 2007      | University of Pittsburgh, USA | 1992–2000 | B, C, U |
| Iwai, 2007        | Osaka City General Hospital, Japan | 1994–2004 | DN |
| Kim, 2007         | Seoul National University, Korea | 1997–2001 | DN |
| Litre, 2007       | Timone University, Marseille, France | 1992–2003 | DN |
| Massager, 2007    | University of Brussels, Belgium | 2000–2004 | C |
| Mathieu, 2007     | University of Pittsburgh, USA | 1987–2005 | U, B, C, 4-C |
| Delsanti, 2008    | Gamma Knife Center, Marseille, France | 1992–2004 | DN |
| Dewan, 2008       | Brown University, USA | 1994–2007 | DN |
| Iwai, 2008        | Osaka City General Hospital, Japan | 1994–2003 | DN |
| Nagano, 2008      | Chiba University, Japan | 1998–2006 | DN |
| Niranjan, 2008    | University of Pittsburgh, USA | 1987–2003 | B, C, 4-C |
| Lasak, 2008       | Kansas University, USA | 2003–2007 | C |
| Shuto, 2008       | Yokohama Rosai Hospital, Japan | 1992–2005 | B |
| Wackym, 2008      | Medical College of Wisconsin, USA | 2000–2008 | B |
| Yang, 2008        | University Hospital of Goyang, Korea | 1998–2004 | B, C |
| Franzin, 2009     | IRCCS San Raffaele, Italy | 2001–2007 | C |
| Fukuoka, 2009     | Hospital of Sapporo, Japan | 1991–2003 | DN |
| Ganz, 2009        | Nasser Institute Shobra, Egypt | DN | DN |
| Kano, 2009        | University of Pittsburgh, USA | 2004–2007 | C, 4-C |
| Liscak, 2009      | Na Homolce Hospital, Prague, Czech Republic | 1992–2001 | B |
| Lobatto-Polo, 2009| University of Pittsburgh, USA | 1987–2003 | U, B, C, |
| Mysret, 2009      | Haukeland University Hospital, Norway | 2001–2006 | C |
| Pollock, 2009     | Mayo Clinic, Rochester, USA | 1990–2004 | DN |
| Tamura, 2009      | Timone University, Marseille, France | 1992–2003 | B, C |
| Timmer, 2009      | Radbout University, Nijmegen, The Netherlands | 2003–2007 | 4-C |
| Yomo, 2009        | Timone University, Marseille, France | 1992–2007 | B, C |
| Chung, 2010       | Taipei Veterans General Hospital, Taiwan | 1993–2009 | B, C |
| Gerosa, 2010      | University of Verona, Italy | 2003–2009 | C, PFX |
| Kano, 2010        | University of Pittsburgh, USA | 1987–2008 | U, B, C, 4-C |
| Lee, 2010         | Taipei Veterans General Hospital, Taiwan | 1993–2008 | B, C |
| Nagano, 2010      | Chiba Center, Tokyo, Japan | 1998–2004 | B, C |
| Nakaya, 2010      | University of Pittsburgh, USA | 1987–1991 | U, B, C |
| Regis, 2010       | Timone University, Marseille, France | 1981–1999 | B |
| Sharma, 2010      | All India Medical Institute, India | 1997–2008 | B |
| Timmer, 2010      | Radbout University, Nijmegen, The Netherlands | 2003–2007 | 4-C |
| Yomo, 2010        | Timone University, Marseille, France | 2006–2008 | 4-C, PFX |
| Brown, 2011       | University of Pennsylvania, USA | 2006–2009 | 4-C |
| Haque, 2011       | Columbia University, New York, USA | 1998–2009 | DN |
| Hasegawa, 2011    | Komaki City Hospital, Japan | 1991–2009 | DN |
| Langenberg, 2011a | Maastricht University, The Netherlands | 2002–2009 | 4-C |
| Langenberg, 2011b | Maastricht University, The Netherlands | 2002–2009 | 4-C |
| Massager, 2011    | Gamma Knife Center, Brussels, Belgium | DN | C |
| Milligan, 2011    | Mayo Clinic, Rochester, USA | 1997–2006 | DN |
| Murphy, 2011a     | Cleveland Clinic, USA | 1997–2003 | B, C |
| Park, 2011        | Kyung University of Seoul, Korea | 1994–2009 | DN |
| Yang, 2011        | University of Pittsburgh, USA | 1994–2008 | DN |

* short name

**Leksell Gamma Knife, Elekta Instruments, Stockholm, Sweden

DN – data not available
A meta-analysis of treatment of vestibular schwannoma using Gamma Knife radiosurgery

AAO-HNS class A or B). Such a strategy was adopted in this work.

The results of a systematic study by Yang and colleagues show that the radiation dose is an important and critical prognostic factor for hearing preservation regardless of tumor size or age of patients with VS treated with GKRS [63]. Patients treated with doses ≤ 13 Gy had better hearing compared to patients treated with high doses. Results of treatment of hearing loss in older patients were comparable to the results of younger patients. Similarly, patients with large tumors had clinical indicators of serviceable hearing loss compared to patients with small tumors. This suggests that patient age and tumor size may not be critical prognostic factors in predicting the preservation of hearing after GKRS. The analysis presented in this study, conducted on the basis of the results documented in the literature of the last five years, points to the patients’ age and tumor size being less critical in predicting preservation of hearing. Highly important, however, was the application of the lower radiation dose to the periphery of the tumor used in recent years, thanks to the introduction into medical centers of the new models of GK and greater possibilities of precise planning.

The results of a comprehensive analysis of facial nerve preservation after radiosurgery of VS using GK confirmed the importance of medium doses of radiation as an important and critical prognostic factor [62]. In this case, however, the patient’s age played a significant role. In patients treated with 13 Gy or less, with tumors smaller than 1.5 cm³ in volume, results of treatment in young pa-

| First author, year | Number of patients | Age (yrs) | Tumor volume (cm³) | Margin dose (Gy) | Mean follow-up (months) | Tumor control (%) | Hearing preservation (%)* |
|--------------------|--------------------|----------|-------------------|-----------------|------------------------|------------------|--------------------------|
| Chopra, 2007       | 216                | 56.5     | 1.3               | 13              | 68                     | 98.3             | 70.0                     |
| Kim, 2007          | 59                 | 48       | 3.41              | 12              | 73                     | 97               | 33.3                     |
| Mathieu, 2007      | 62                 | 36       | 5.7               | 14.0            | 53                     | 85               | 48                       |
| Iwai, 2008         | 25                 | 48       | 0.27              | 12              | 89                     | 96               | 64                       |
| Nagano, 2008       | 100                | 59.1     | 2.7               | 12.2            | 66                     | 91               | 60                       |
| Niranjan, 2008     | 96                 | 54       | 1.12              | 13              | 28                     | 99               | 77.5                     |
| Franzin, 2009      | 50                 | 54       | 0.73              | 13              | 36                     | 96               | 68                       |
| Fukuda, 2009       | 152                | 54       | 2.0               | 12              | 60                     | 94               | 71                       |
| Kano, 2009         | 77                 | 52       | 0.75              | 12.5            | 20                     | 94.7             | 71                       |
| Liscak, 2009       | 351                | 56       | 1.9               | 12.5            | 43                     | 91               | 50                       |
| Lobato-Polo, 2009  | 55                 | 35       | 0.17              | 13              | 64                     | 96               | 93                       |
| Pollock, 2009      | 293                | 58       |                   | 13              | 84                     | 94               |                          |
| Tamura, 2009       | 74                 | 47.5     | 1.35              | 12              | 48                     | 93               | 78.4                     |
| Chung, 2010        | 21                 | 49.5     | 17.3              | 11.9            | 66                     | 90.5             |                          |
| Gerosa, 2010       | 74                 | 59       | 2.7               | 12.4            | 50                     | 96               | 72                       |
| Lee, 2010          | 444                | 51.0     | 4.4               | 12.0            | 35.7                   | 79.1             |                          |
| Nagano, 2010       | 87                 | 58.6     | 2.5               | 12.0            | 90                     | 89.7             |                          |
| Nakaya, 2010       | 202                | 68       | 3.9               | 13              | 65                     | 97               | 79                       |
| Regis, 2010        | 47                 | 54.4     | 11.2              | 12.0            | 34.7                   | 97               | 79                       |
| Sharma, 2010       | 30                 | 29       | 3.7               | 12.0            | 26.6                   | 87.5             | 66.7                     |
| Timmer, 2010       | 108                | 56       | 2.721             | 11.1            |                       |                  | 78                       |
| Brown, 2011        | 53                 | 56       | 1.12              | 12.5            | 16                     | 96               | 79                       |
| Hasegawa, 2011     | 117                | 52       | 1.9               | 12              | 56                     | 97.5             | 43                       |
| Langenberg, 2011b  | 33                 | 54.8     | 8.8               | 12.6            | 30.0                   | 88               | 58                       |
| Massager, 2011     | 203                | 53       |                   | 12              | 42                     | 89.7             | 41.8                     |
| Milligan, 2011     | 22                 | 61.0     | 9.4               | 12              | 66                     | 86               | 47                       |
| Murphy, 2011a      | 117                | 60.9     | 1.95              | 12.8            | 37.5                   | 91.8             | 85                       |
| Yang, 2011         | 65                 | 51       | 9                 | 36              | 93                     | 93               | 82                       |
| **Total**          | **3233**           |          |                   |                 |                        |                  |                          |

| Mean               | 52.6               | 3.90     | 12.40            | 51.24           | 92.73                  | 66.45            |

Empty data fields are from data that were not reported, not accessible, or could not be disaggregated for analysis in this study.

*Hearing preservation in grade I-II according to Gardner-Robertson scale (good-serviceable, pure tone average 0-50 dB, speech discrimination 50-100%)
patients were better than in older patients. According to Kim et al. [6] to reduce the radiation dose, however, does not adequately protect the hearing, and therefore it is believed that this is a more complicated problem and requires further study. Common hypotheses for hearing deterioration after irradiation include damage to cochlear primary sensory cells, injury to the cochlear nerve by the tumor, injury to the cochlear nerve by radiation, and compression or vascular thrombosis, leading to ischemic injury of the cochlea [25]. Franzin [22] believes that due to the high frequency of hearing loss in patients prior to radiosurgery, it is difficult to determine whether hearing loss is caused by the surgery or the natural course of the disease. The exact mechanism of delayed hearing loss is still unclear.

Preservation of hearing in patients is associated with the overall quality of life (QOL). Whitmore et al. [65] compared the quality of life in patients after 5 years of radiosurgical and surgical treatment. Overall QOL was better

| First author, year [references] | Years of cited publications | Number of patients | Age of patients | Tumor volume (cm³) | Marginal dose (Gy) | Mean follow-up (months) | Tumor control (%) | Hearing preservation (%) |
|--------------------------------|----------------------------|--------------------|----------------|-------------------|-------------------|------------------------|------------------|-------------------------|
| Myrseth, 2007 [37]            | 1989–2006                  | 300                |                |                   |                   |                        |                  |                         |
| Rowe, 2007 [50]               | 1984–2005                  | 856                | 57             | 2.8               | 13.0              | 45.0                   |                  |                         |
| Sughrue, 2009 [53]            | 1979–2007                  | 50 000             |                | < 25 mm           | > 13; < 13        |                        |                  |                         |
| Yang, 2009 [62]               | 1990–2007                  | 1908               | 55.3           | 3.2               | 13.1              | 54.1                   | 82.5             |                         |
| Yang, 2009 [61]               | 1988–2007                  | 2083               | 53.6           | 4.05              | 16                | 41.2                   | 94               | 57                      |
| Yang, 2010 [63]               | 1998–2007                  | 4 234              | 51.8           | 3.9               | 14.2              | 44.4                   | 92.0             | 51.0                    |
| Arthurs, 2011 [2]             | 2004–2009                  | 397–5825           | 2.7–4.0        | 13.7–17.3         | 25–60             | 91–94.6                | 44–57            |                         |
| Murphy, 2011 [36]             | 1992–2010                  | 29–162             | < 3–3.14       | 8–25              | 16– > 60          | 81–100                 | 20–51            |                         |

Empty data fields are from data that were not reported.

### Table 4. Comparison of data from earlier studies [63] and current series – results of variance analysis – p-value*

| Kind of statistical test       | Number of patients | Age of patients | Tumor volume | Marginal dose (Gy) | Follow-up | Tumor control rate | Hearing preservation |
|--------------------------------|--------------------|-----------------|--------------|--------------------|-----------|--------------------|----------------------|
| Kruskal-Wallis Test Pr > χ²    | 0.2480             | 0.5462          | 0.3461       | 0.0009             | 0.0398    | 0.2614             | 0.0166               |
| Median One-Way Analysis Pr > χ²| 0.3369             | 0.1662          | 0.1055       | 0.0006             | 0.0906    | 0.7078             | 0.0157               |
| Van der Waerden One-Way Analysis Pr > χ² | 0.1980 | 0.5976 | 0.4688 | 0.0010 | 0.0736 | 0.2099 | 0.0259 |
| Kolmogorov-Smirnov Two-Sample Test Pr > KSa | 0.4509 | 0.7154 | 0.1312 | 0.0086 | 0.0889 | 0.6079 | 0.0382 |

*p Significance at p < 0.05

**Fig. 1.** Marginal dose in the earlier (1) [63] and current (2) series of studies – significance of differentiation in Table 4

**Fig. 2.** Hearing preservation in the earlier (1) [63] and current (2) series of studies – significance of differentiation in Table 4
when patients were treated with radiosurgery, but too little information on QOL after 10 years did not allow this thesis to be proved in the long run. There is a need for further research in this field [59].

In conclusion, clinical findings widely documented in the literature over the past five years indicate the progress in treatment of vestibular schwannoma using Gamma Knife radiosurgery. In a new series of studies, published in 2007–2011, the average dose applied to the periphery of the tumor was lower (12.4 Gy) than in the earlier series from the years 1998 to 2007 (14.2 Gy), and hearing preservation was higher (66.45% vs. 51.0%). This was confirmed statistically, and the differences were highly significant.

Authors declare no conflict of interest.

References

1. Arthurs BJ, Fairbanks RK, Demakas JJ, et al: A review of treatment modalities for vestibular schwannoma. Neurosurg Rev 2011; 34: 265-79.
2. Forthum H, O’Neill C, Taylor R, et al: The role of magnetic resonance imaging in the identification of suspected acoustic neuroma: a systematic review of clinical and cost effectiveness and natural history. Health Technol Assess 2009; 13: iii-iv, ix-xi, 1-154.
3. Backlund EO. Gamma knife – the early story: memoires of a privileged man. In: Radiosurgery and Pathological Fundamentals. Prog Neurol Surg 2007; 20: XXI-XXIII.
4. Elekta Instruments, Sztokholm (electa.org).
5. Niranjan A, Matz AH, Lunsford A, Gerszten PC, Flickinger JC, Kondziolka D, Lunsford LD. Radiosurgery techniques and current devices. Prog Neurol Surg 2007; 20: 50-67.
6. Régis J, Roche PH, Delsanti C, Thomassin JM, Ouaknine M, Gabert K, Pellet W. Modern management of vestibular schwannomas. Prog Neurol Surg 2007; 20: 129-41.
7. Chopra R, Kondziolka D, Niranjan A, Lunsford LD, Flickinger JC. Long-term follow-up of acoustic schwannoma radiosurgery with marginal tumor doses of 12 to 13 Gy. Int J Radiat Oncol Biol Phys 2007; 68: 845-51.
8. Iwai Y, Yamanaka K, Yamagata K, Yasui T. Surgery after radiosurgery for acoustic neurinomas: Surgical strategy and histological findings. Neurosurgery 2007; 60 (2 Suppl 1): ONS75-82.
9. Kim KM, Park CK, Chung HT, Paek SH, Jung HW, Kim DG. Long-term outcomes of gamma knife stereotactic radiosurgery of vestibular schwannomas. J Korean Neurosurg Soc 2007; 42: 286-92.
10. Litre CF, Goung GP, Tamura M, Mdarhi D, Touzani A, Roche PH, Régis J. Gamma Knife surgery for facial nerve schwannomas. Neurosurgery 2007; 60: 853-9.
11. Massager N, Nissim O, Delbrouck C, et al. Irradiation of cochlear structures during vestibular schwannoma radiosurgery and associated hearing outcome. J Neurosurg 2007; 107: 733-9.
12. Mathieu D, Kondziolka D, Flickinger JC, Niranjan A, Williamson R, Martin JJ, Lunsford LD. Stereotactic radiosurgery for vestibular schwannomas in patients with neurofibromatosis type 2: an analysis of tumor control, complications, and hearing preservation rates. Neurosurgery 2007; 60: 460-8.
13. Delsanti C, Roche PH, Thomassin JM, Régis J. Morphological changes of vestibular schwannomas after radiosurgical treatment: pitfalls and diagnosis of failure. Prog Neurol Surg 2008; 21: 93-7.
14. Dewan S, Norén G. Retreatment of vestibular schwannomas with Gamma Knife surgery. J Neurosurg 2008; 109 Suppl: 144-8.
15. Iwai Y, Yamanaka K, Kubo T, Aiba T. Gamma knife radiosurgery for intracanalicular acoustic neurinomas. J Clin Neurosci 2008; 15: 993-7.
16. Nagano O, Higuchi Y, Seizawa T, Ono I, Matsuda S, Yamakami I, Saeki N. Transient expansion of vestibular schwannoma following stereotactic radiosurgery. J Neurosurg 2008; 109: 811-6.
17. Niranjan A, Mathieu D, Flickinger JC, Kondziolka D, Lunsford LD. Hearing preservation after intracanalicular vestibular schwannoma radiosurgery. Neurosurgery 2008; 63: 1054-62.
18. Lasak JM, Klisch D, Kryzer TC, Hearn C, Gorecki JP, Rine GP. Gamma Knife radiosurgery for vestibular schwannoma: early hearing outcomes and evaluation of the cochlear dose. Otol Neurotol 2008; 29: 1179-86.
19. Shuto T, Inomori S, Matsunaga S, Fujino H. Microradiosurgery for vestibular schwannoma after Gamma Knife radiosurgery. Acta Neurochir (Wien) 2008; 150: 229-34.
20. Wackym PA, Hanley MT, Rune-Samuelson CL, Jensen J, Zhu YR. Gamma Knife surgery of vestibular schwannomas: longitudinal changes in vestibular function and measurement of the Dizziness Handicap Inventory. J Neurosurg 2008; 109 Suppl: 137-43.
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 Neurosurg Psychiatry 2008; 79: 431-6.
22. Franzin A, Spatola G, Serra C, Picozzi P, Medone M, Milani D, Castellazzi P, Mortini P. Evaluation of hearing function after Gamma Knife surgery of vestibular schwannomas. Neurosurg Focus 2009; 27: E3.
23. Fukuoka S, Takenashi M, Hojo A, Koshima M, Tanaka C, Nakamura H. Gamma knife radiosurgery for vestibular schwannomas. Prog Neurol Surg 2009; 22: 45-62.
24. Ganz JC, Reda WA, Abdelkarim K. Adverse radiation effects after Gamma Knife surgery in relation to dose and volume. Acta Neurochir 2009; 151: 9-19.
25. Kano H, Kondziolka D, Khan A, Flickinger JC, Lunsford LD. Predictors of hearing preservation after stereotactic radiosurgery for acoustic neuroma. J Neurosurg 2009; 111: 863-73.
26. Liscak R, Vladyka V, Urgosik D, Simonova G, Vymazal J. Repeated surgery. Acta Neurochir 2009; 151: 9-19.
27. 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 Neurosurg Psychiatry 2008; 79: 431-6.
28. Myrseth E, Møller P, Pedersen PH, Lund-Johansen M. Evaluation of vestibular schwannoma surgery or Gamma Knife radiosurgery ? A perspective, nonrandomized study. Neurosurgery 2009; 64: 654-63.
29. Pollock BE, Link MJ, Foote RL. Failure rate of contemporary low-dose radiosurgical technique for vestibular schwannoma. J Neurosurg 2009; 111: 840-4.
30. Tamura M, Carron R, Yomo S, et al. Hearing preservation after gamma knife radiosurgery for vestibular schwannomas presenting with high-level hearing. Neurosurgery 2009; 64: 289-96.
31. Timmer FC, Hanssens PE, van Haeren AE, Mulder JJ, Cremers CW, Beynon AJ, van Overbeeke JJ, Graamans K. Gamma Knife radiosurgery for vestibular schwannomas: results of hearing preservation in relation to the cochlear radiation dose. Laryngoscope 2009; 119: 1076-81.
32. Yomo S, Arkha Y, Delsanti C, Roche PH, Thomassin JM, Régis J. Re-peat Gamma Knife surgery for regrowth of vestibular schwanno-mas. Neurosurgery 2009; 64: 128-35.
33. Chung WY, Pan DH, Lee CC, et al. Large vestibular schwannomas treated by Gamma Knife surgery: long-term outcomes. J Neurosurg 2010; 112: 112-21.
34. Gerosa M, Mesiano N, Longhi M, De Simone A, Foroni R, Verlic-chi A, Zanotti B, Nicolato A. Gamma Knife surgery in vestibular schwannomas: impact on the anterior and posterior labyrinth. J Neurosurg 2010; 113: 128-35.
35. Cremers CW, Graamans K. Quality of life associated with hearing preservation after Gamma Knife surgery for vestibular schwannoma. J Neurosurg 2011; 115: 885-93.
36. Wharam DL, Roche PH, et al. Wait-and-see strategy compared with proactive Gamma Knife surgery in patients with intracanalicular vestibular schwannomas. J Neurosurg 2010; 113: 105-11.
37. Gamma Knife surgery for vestibular schwannoma. J Neurooncol 2010; 98: 203-12.
38. Nakaya K, Niranjan A, Kondziolka D, Flannery TJ, Flickinger JC, Roche PH. et al. Comparison of radiosurgical treatment parameters in vestibular schwannomas: the Leksell Gamma Knife Perfexion versus Model 4C. Acta Neurochir 2010; 152: 47-55.
39. Yang I, Sughrue ME, Han SJ, Aranda D, Cheung SW, Pitts LH, Parsa AT. A comprehensive analysis of hearing preservation after Gamma Knife surgery. J Neurosurg 2009; 110: 540-2.
40. Yang I, Aranda D, Han SJ, Chennupati S, Sughrue ME, Cheung SW, Pitts LH, Parsa AT. Facial nerve preservation after Gamma Knife surgery: an early report from 2 Canadian centers. J Neu-rosurg 2008; 109: 2-7.
41. Myrseth E, Pedersen PH, Miler P, Lund-Johansen M. Treatment of vestibular schwannoma. Why, when and how? Acta Neurochir (Wien) 2007; 149: 647-60.
42. Yomo S,Tamura M, Carron R, Porcheron D, Régis J. A quantitative comparison of radiosurgical treatment parameters in vestibular schwannomas: the Leksell Gamma Knife Per-fection versus Model 4C. Acta Neurochir 2010; 152: 47-55.
43. Brown M, Ruckenstein M, Bigelow D, Judy K, Wilson V, Alonso-Basanta M, Lee JY. Predictors of hearing loss after Gamma Knife radiosurgery for vestibular schwannomas: age, cochlear dose, and tumor coverage. Neurosurgery 2011; 69: 605-14.
44. Haque R, Wójcieszewicz T, Gigante PR, Atthiah MA, Huang B, Isaac-son SR, Sisti MS. Efficacy of facial nerve-sparing approach in pa-tients with vestibular schwannomas. J Neurosurg 2011; 115: 917-23.
45. Hasegawa T, Kida Y, Kato T, Izuza H, Yamamoto T. Factors assoc-iated with hearing preservation after Gamma Knife surgery for vestibular schwannomas in patients who retain serviceable hear-ing. J Neurosurg 2011; 115: 1078-86.
46. van de Langenberg P, Hanssens PE, Oostendorp R, de Bondt BJ, et al. 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.
47. van de Langenberg P, Hanssens PE, Verheul JB, van Overbeeke JJ, Nelemans PJ, de Bondt BJ, et al. Management of large vestibular schwannoma. Part II. Primary Gamma Knife surgery: radiological and clinical aspects. J Neurosurg 2011; 115: 885-93.
48. Massager N, Lonneville S, Delbrouck C, Benmebarek N, Desmedt F, Devriendt D. Dosimetric and clinical analysis of spatial distribution of the radiation dose in Gamma Knife radiosurgery for vestibular schwannoma. Int J Radiation Oncology Biol Phys 2011; 81: 511-8.
49. Milligan BD, Pollock BE, Foote RL, Link M. Long-term tumor con-trol and cranial nerve outcomes following Gamma Knife surgery for larger-volume vestibular schwannomas. J Neurosurg 2012; 116: 598-604.
50. Murphy ES, Barnett GH, Vogelbaum MA, Neyman G, Stevens GH, Cohen BH, et al: Long-term outcomes of Gamma Knife radiosur-gery in patients with vestibular schwannomas. J Neurosurg 2011; 114: 432-40.
51. Park CE, Park BJ, Lim YJ, Yeo SG. Functional outcomes in retrosigmoid approach microsurgery and Gamma Knife stereotactic ra-diosurgery in vestibular schwannoma. Eur Otolarhinologynol 2011; 268: 955-9.
52. Yang HC, Kano H, Awan NR, et al. Gamma Knife radiosurgery for larger-volume vestibular schwannomas. J Neurosurg 2011; 114: 801-7.
53. Yang I, Sughrue ME, Han SJ, Chennupati S, Parsa AT. Non-audiofacial morbidity after Gamma Knife sur-gery for vestibular schwannoma. Neurosurg Focus 2009; 27: E4.
54. Yang I, Sughrue ME, Han SJ, Fang S, Aranda D, Cheung SW, Pitts LH, Parsa AT. Facial nerve preservation after vestibular schwanno-ma Gamma Knife radiosurgery. J Neurooncol 2009; 95: 41-8.
55. Yang I, Aranda D, Han SJ, Chennupati S, Sughrue ME, Cheung SW, Pitts LH, Parsa AT. Hearing preservation after stereotactic radio-surgery for vestibular schwannoma: a systematic review. J Clin Neurosci 2009; 16: 742-7.
56. Murphy ES, Suh JH. Radiotherapy for vestibular schwannomas: a critical review. Int J Radiation Oncology Biol Phys 2011; 79: 985-97.
57. Whitmore RG, Urban C, Church E, Ruckenstein M, Stein SC, Lee JY. Decision analysis of treatment options for vestibular schwanno-ma. J Neurosurg 2011; 114: 400-13.