CLINICAL REVIEW

Gamma Knife Radiosurgery for Vestibular Schwannomas

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ABSTRACT

The current gamma knife radiosurgery technique involves the use of magnetic resonance imaging for targeting, the application of a low marginal dose (usually between 12 and 13 Gy) and highly conformal treatment planning using multiple small isocenters. This technique achieves an average tumor control rate of 95% and open surgery is needed in fewer than 2 to 3% of patients treated by gamma knife. Facial nerve function preservation is achieved in up to 99% of cases and chance of preserving serviceable hearing is usually between a 70 to 80%. The introduction of ventriculoperitoneal drainage after radiosurgery is required for 1 to 8% of patients. Gamma knife radiosurgery can be treatment of choice for the patients, where the diameter of the tumor is less than 3 cm.

**Keywords:** Vestibular schwannoma, Radiosurgery, Gamma knife, Results, Complications.

INTRODUCTION

Vestibular schwannoma is a benign tumor arising from the Schwann cells in the vestibular division of the eighth cranial nerve. Vestibular schwannomas constitute 7 to 8% of intracranial tumors and 75 to 90% of tumors in the pontocerebellar angle. They most commonly occur between the 3rd and 6th decade with a predominance found in women.[1,35,47] The annual incidence of vestibular schwanommas is reported to be 9.4 to 17.4 per million, a realistic estimate is 13 per million of the population.[52]

The history of gamma knife surgery of vestibular schwannomas goes back more than 40 years.[19] Over this period, it has evolved into a standard therapy, where the highest conformity of focused radiation applied in a single session produces the most significant therapeutic results for the patient, while minimizing the treatment risks. To date, more than 50,000 patients with vestibular schwannomas have been treated worldwide using the Leksell gamma knife and the number of patients treated by this method each year is continually increasing. In certain regions, where this technique is available and patients have the advantage of choice, more than half of those suffering from vestibular schwannomas are currently treated by gamma knife surgery.
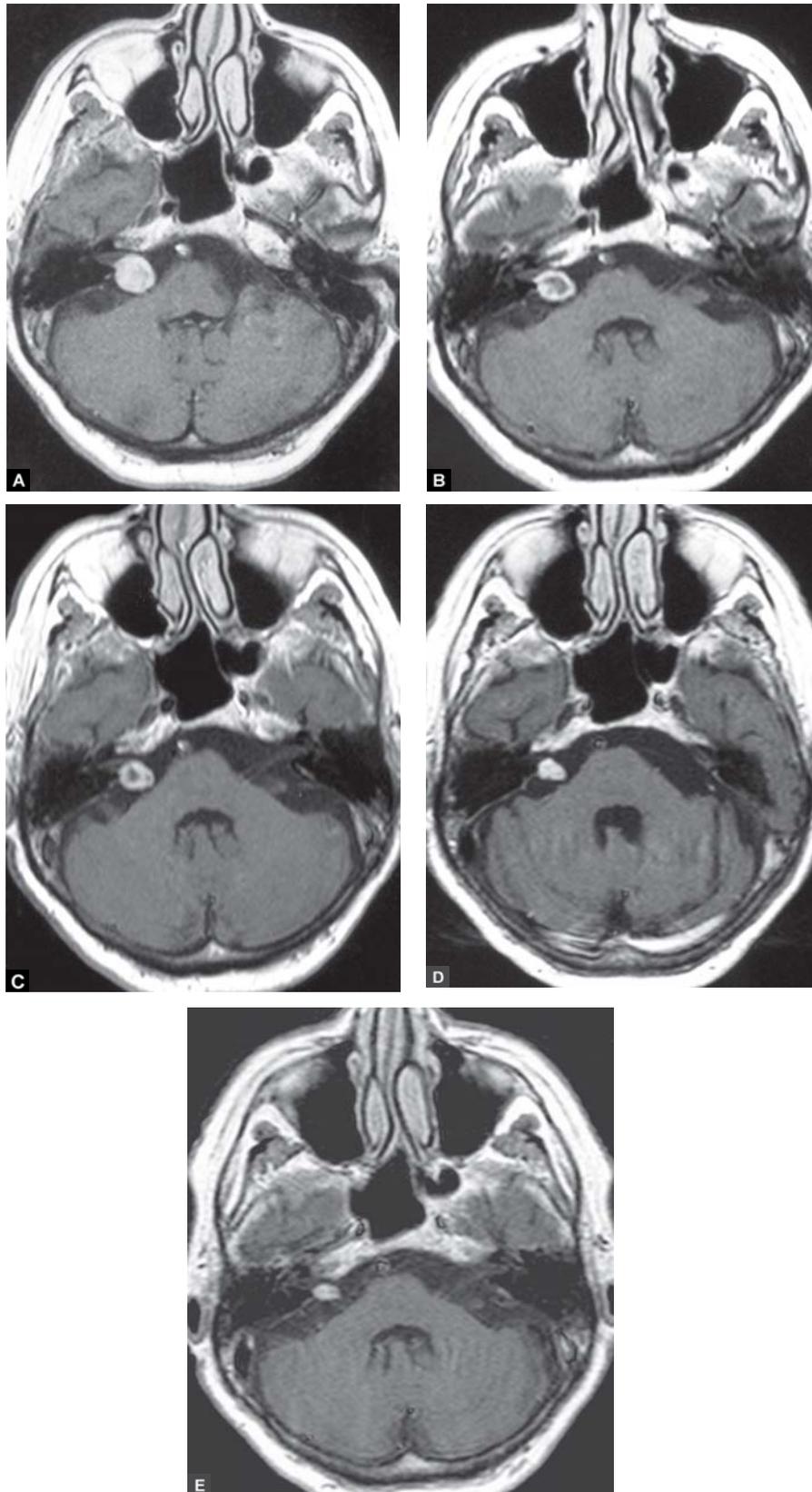
RESULTS OF GAMMA KNIFE RADIOSURGERY

The current technique of using gamma knife radiosurgery to treat vestibular schwannoma offers a high rate of successful treatment and patient satisfaction with a short treatment time, no need for convalescence and a low risk of complications. The current gamma knife radiosurgery technique involves the use of magnetic resonance imaging
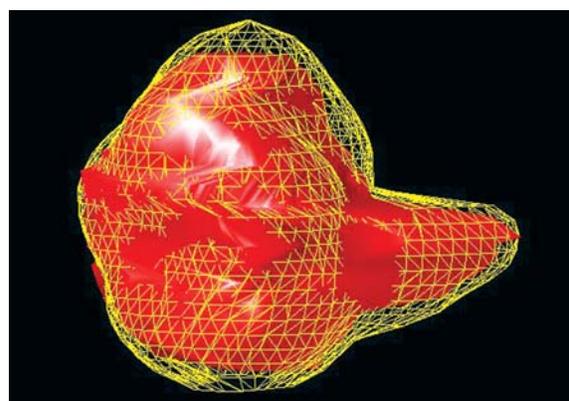

Fig. 1: Radiosurgery using Leksell gamma knife is characterized by the high conformity of the planning, when the spatial distribution of minimal peripheral radiation dose applied most frequently to the 50% isodose (yellow mesh) accurately reproduces the shape of the tumor (red)
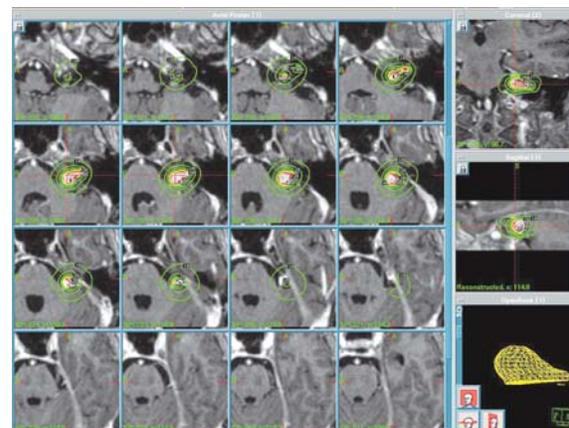

Fig. 2: In addition to a high conformity of planning, radiosurgery is characterized by a steep gradient decrease outside the target volume. The tumor is covered by 50% isodose (yellow), the next lines (green) represent the dose decreased by 10%
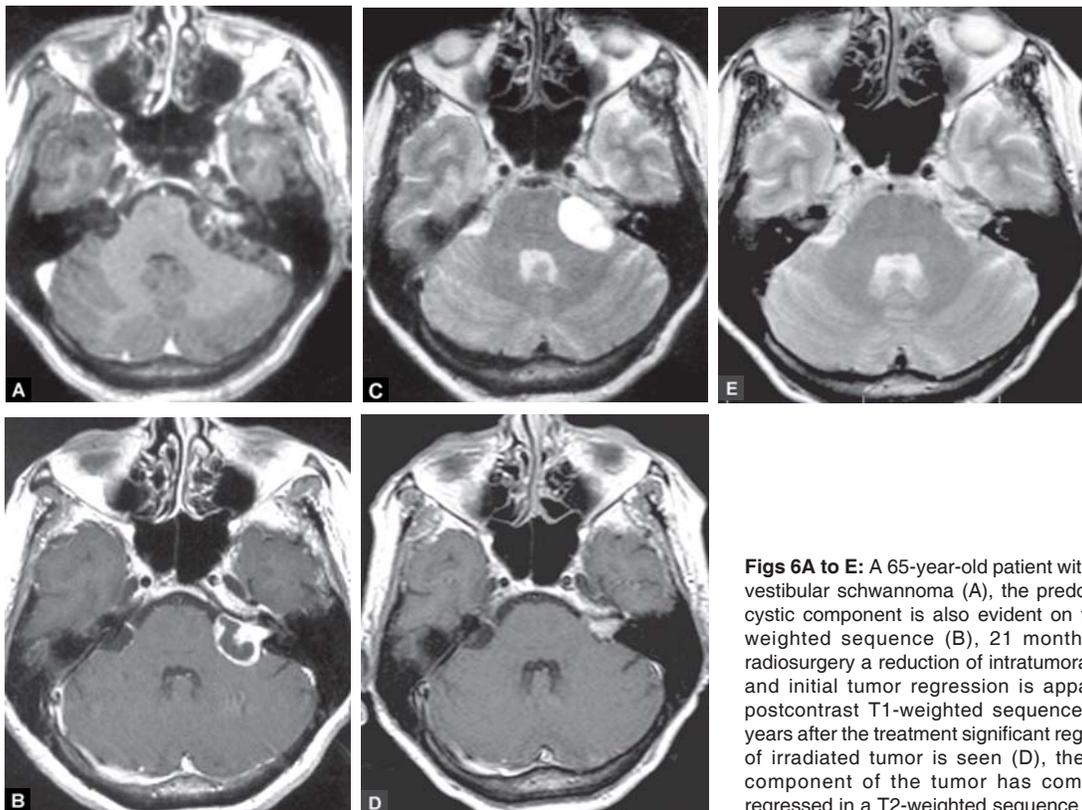
Figs 3A to E: A 65-year-old patient with vestibular schwannoma before radiosurgery (A), one year after the gamma knife treatment a central hypodensity is present after administration of the paramagnetic contrast agent with incipient regression of the tumor (B), continued tumor regression after 3 years (C), 6 (D) and 10 years (E) after treatment
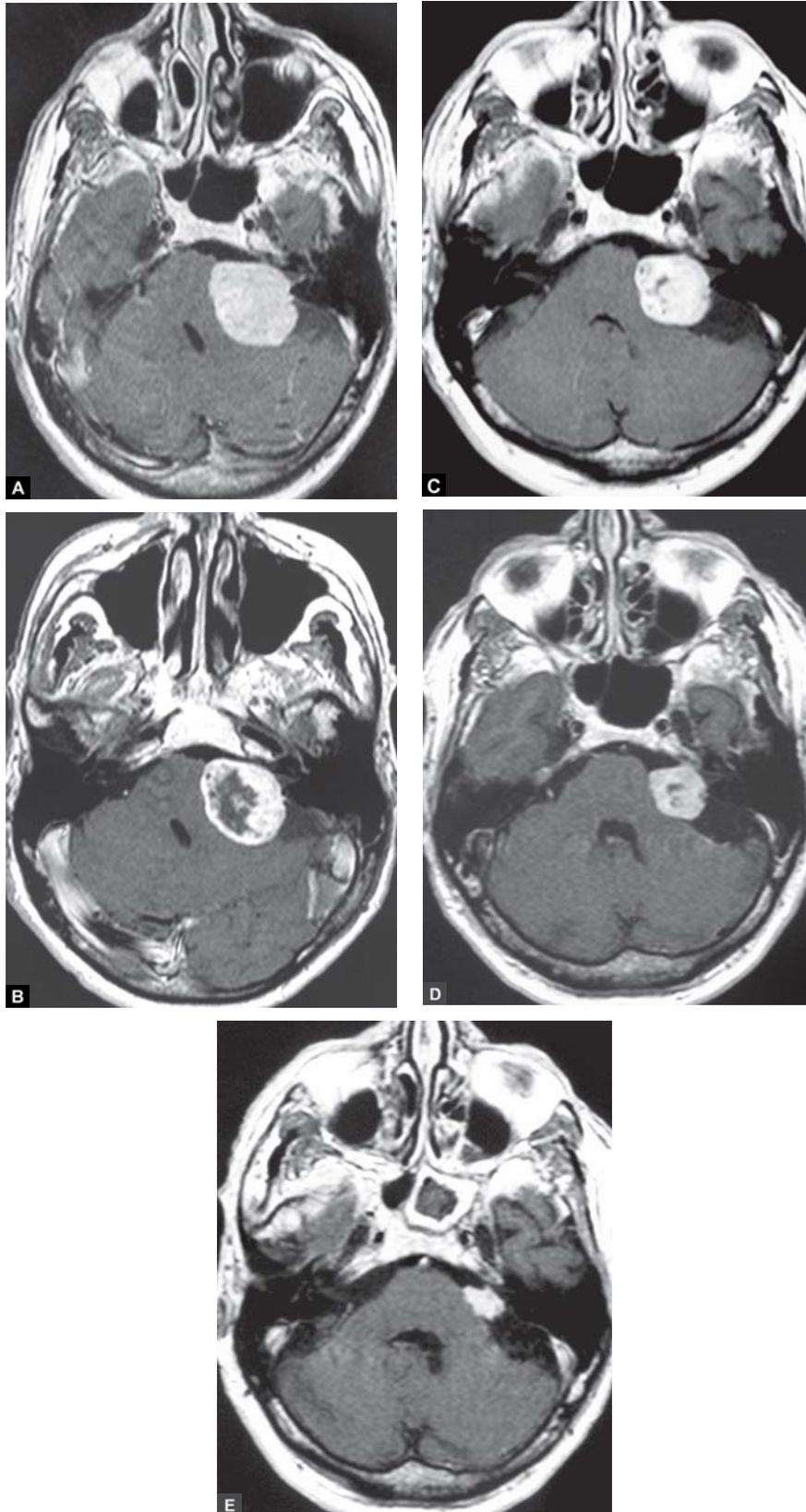
Figs 4A to E: A 63-year-old patient with a large vestibular schwannoma (diameter 39 mm), an open operation was not indicated because of a blood clotting disorder and therefore gamma knife treatment was performed (A), 9 months after the radiosurgery a change in the uptake of paramagnetic contrast agent is present (B), 1.5 years after the treatment uptake of the contrast substance is again more homogeneous, and an initial reduction of the tumor volume is aparent (C), which continues 3 (D) and 8 years (E) after the gamma knife treatment
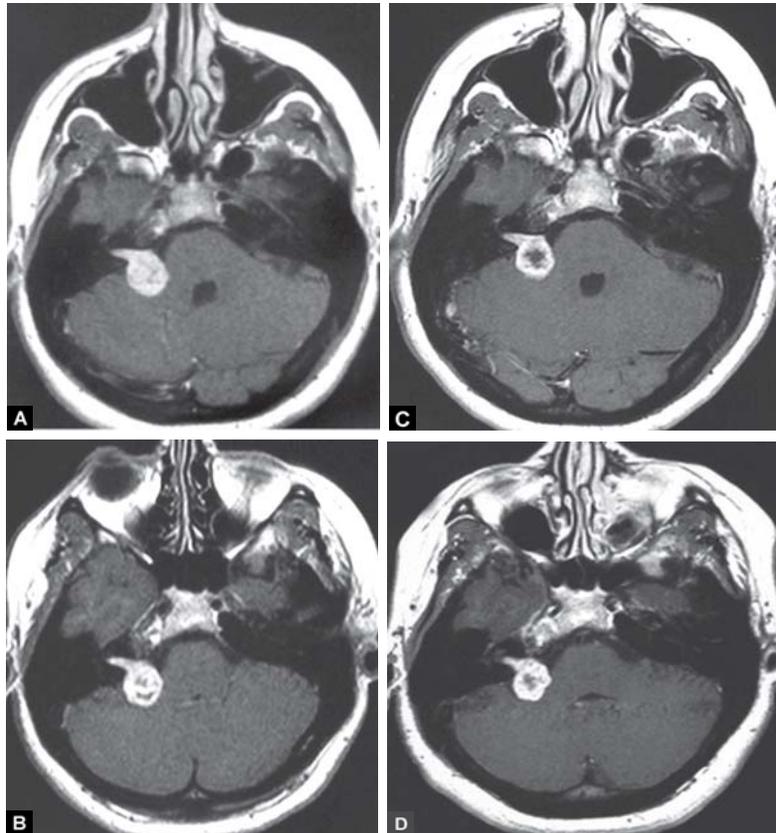
Figs 5A to D: A 48-year-old patient with a vestibular schwannoma before radiosurgery (A), one year after treatment a central hypodensity is evident after administration of the paramagnetic contrast agent (B), 3 years after treatment, the tumor enhancement is again more homogeneous (C), 9 years after treatment there is no evidence of tumor growth and regressive changes are present (D)

Figs 6A to E: A 65-year-old patient with cystic vestibular schwannoma (A), the predominant cystic component is also evident on the T2-weighted sequence (B), 21 months after radiosurgery a reduction of intratumoral septs and initial tumor regression is apparent—postcontrast T1-weighted sequence (C), 5 years after the treatment significant regression of irradiated tumor is seen (D), the cystic component of the tumor has completely regressed in a T2-weighted sequence (E)
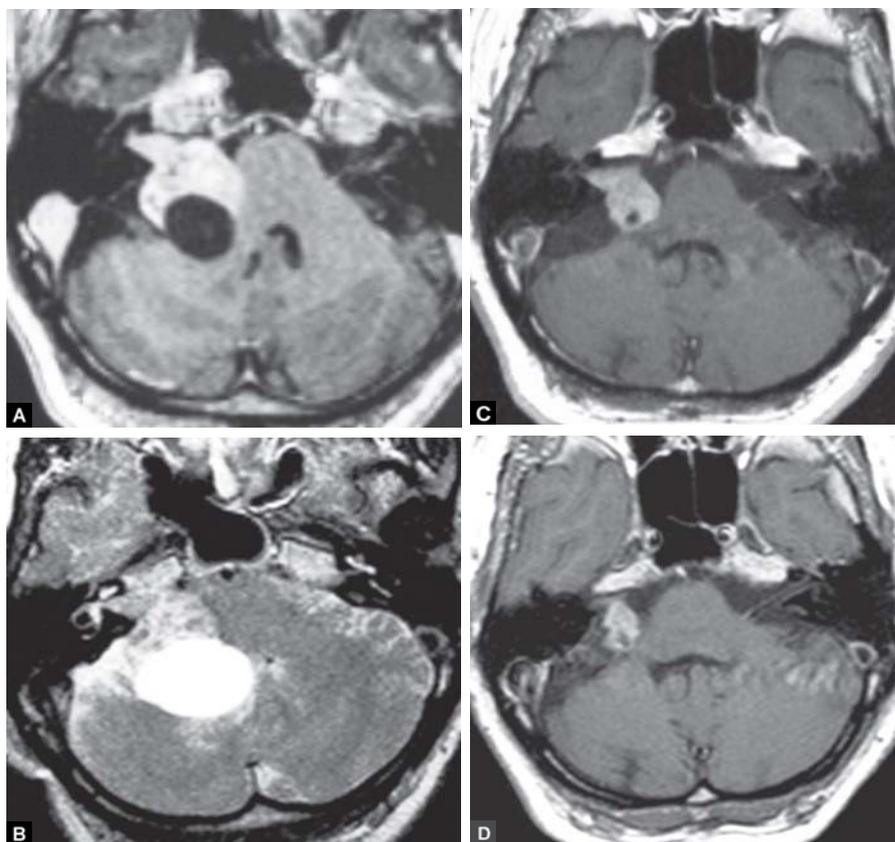
Figs 7A to D: A 59-year-old patient with a cystic vestibular schwannoma, who refused open surgery and would only agree to gamma knife treatment (A). One month after radiosurgery stereotactic aspiration of the cyst was carried out, which then refilled, and 9 months after radiosurgery Rickham drainage was inserted into the cyst (B). The further course of disease has been without complications, 3 years after the treatment the cystic part of the tumor completely regressed and the drainage was removed (C), 5 years after treatment a significant regression of the tumor was recorded (D)

(MRI) for targeting, the application of a low marginal dose (usually between 12 and 13 Gy) and highly conformal treatment planning using multiple small isocenters. The level of conformal treatment planning and the precision of the treatment is enhanced using the model C, Leksell gamma knife with APS (automatic positioning system) or with the Perfexion fully robotic version, allowing the use of dynamic shaping and hybrid shots (Figs 1 and 2). This technique achieves an average tumor control rate of 95%, facial nerve function preservation in up to 99% of cases and usually between 70 and 80% chance of preserving serviceable hearing[3,12,16,18,21-25,32,36,41,42,46,53,57] (Figs 3A to 7D).

COMPLICATIONS OF RADIOSURGERY

The Risk of Facial Nerve Palsy

Up until the beginning of the 1990s, the treatment strategy was to apply as high as possible a marginal dose in order to guarantee the tumor control rate, but a side effect was the significant risk of facial nerve palsy.[26,34] A gradual reduction of the marginal dose to values of 12 to 13 Gy has greatly reduced this risk, usually to below 1%, without decreasing the tumor control rate.

The Risk of Hearing Deterioration

The deterioration of useful hearing, where this occurs after radiosurgery, can be expected in 21 to 29% of cases up to 2 years, usually not later.[26,31] For intracanalicular tumors this risk is lower—about 10%.[26]

The Risk of Trigeminal Nerve Neuropathy

Postirradiation trigeminal nerve neuropathy (paresthesia or hypesthesia) is observed in between 3 and 8% of cases.[21,26,31] Complete anesthesia or neuropathic pain is not observed.

Tumor Volume Increase after Radiosurgery

In most patients, the control CT or MRI, 6 to 12 months after radiosurgery, can detect a typical image when, after the administration of a contrast or paramagnetic substance, the neurinoma is hypointensive in its center with a hyperintensive annular margin. After, further 6 to 12 months the contrast substance filling may again become more homogeneous. The loss of contrast filling may be followed by a transitional increase in the tumor volume in 17 to 39% of all patients as a result of intratumoral swelling, but this

does not indicate treatment failure.[10,57] This enlargement can be detected between 3 and 9 months after radiosurgery (an average of 1-2 mm). Over the course of several months, intratumoral swelling is resolved, followed by tumor volume shrinkage.[26,57] At least 2 years of follow-up is usually required to avoid misinterpreting any temporary swelling and growth of the tumor. Any tumor volume increase observed 2 years or more after treatment can indicate continued growth, however open surgery is needed in fewer than 2 to 3% of patients treated by gamma knife.[23,26,40,57] Repeated radiosurgery is performed in up to 7% of intitially treated patients without increased risks of complications and it is chosen in smaller tumors.[23]

Hyporesorptive Hydrocephalus

An increase of proteins in the cerebrospinal fluid can be detected in two-thirds of patients with vestibular schwannoma (the Schwann cells have the ability to synthesize and secrete polypeptides and glycoproteins, which are precursors of collagen, contributing to the formation of an extracellular matrix).[1,47] If the protein increase exceeds the compensation options of cerebrospinal fluid absorption, hyporesorptive hydrocephalus may develop and up to 14% of patients have developed hydrocephalus before starting treatment,[37] in elderly patients this is up to 29%.[51] The introduction of ventriculoperitoneal drainage after radiosurgery is required for 1.1 to 8% of patients.[7,8,22,27,43]

Secondary Malignant Tumors

The hypothetical risk of secondary malignancy after radiosurgery does not exceed one per mille, a realistic estimation is 1:20,000.[26,45] To date, our experience has not registered an excess incidence of malignancies after radiosurgery compared to their incidence in the normal population.[45] Therefore, the risk of oncogenesis does not impose any major restrictions in the practical application of radiosurgery.

Taking into account the fact that the total number of patients with vestibular schwannomas treated by gamma knife surgery exceeds 50,000 worldwide, it is not surprising that malignant variants of the vestibular schwannoma after radiosurgery have been recorded in the literature.[9,48] This undoubtedly reflects the fact that the results of gamma knife radiosurgery are carefully monitored and verified, and each complication is thoroughly analyzed. This, therefore eliminates the phenomenon where only the positive results are published, while the complications are glossed over. However, the incidence of malignant schwannomas does not surpass current expectations based on pathological findings after microsurgical treatment, where repeatedly recurring malignant schwannomas are characterized by increasing anaplasia, although radiation treatment had not been applied.[45,47] The incidence of malignant schwannoma

after radiosurgery or microsurgery is so rare that the few isolated cases do not allow any comparison of patients according to the treatment method.

STEREOTACTIC FRACTIONATED RADIOTHERAPY

Stereotactic radiotherapy applies focused-radiation in several fractions. Fractionation decreases the risk of morbidity in cases of less conformal planning, which is achieved with limited isocenters usually used in linear accelerator therapy (while for the gamma knife treatment 10-30 isocenters are commonly used, most linear accelerator treatments use 2-3 isocenters). However, the biological effect of fractionation on the vestibular schwannoma may be less favorable.[20] Depending on the method used, fractionation treatment takes several days to weeks. The preliminary results are similar to the single session radiosurgery,[2,4] but long-term experience of a larger number of patients is missing.

CONSERVATIVE APPROACH—NATURAL COURSE OF THE DISEASE

The natural course of the disease has been followed by several authors.[5,11,13,17,30,33,49,50,54-56,58] Tumor growth varied significantly in these studies. Annual enlargement of the tumor varied between 1 and 17 mm, averaging between 1 and 4 mm per year. No growth or even spontaneous regression was observed in 0 to 32% or 0 to 16% respectively, depending on follow-up. In cases where the "watch and scan" policy is chosen for individual patients, magnetic resonance should be repeated at least once a year in order not to miss the progression of the tumor.[28] This requires the necessary availability and capacity of investigative methods. Their limited availability may lead to sporadic checks over long intervals, entailing the risk of too much tumor progression. Therefore, waiting tactics in the majority of patients, particularly those younger in age, is considered to unnecessarily delay treatment until the tumor is larger and the chance for uncomplicated course of treatment is lower.[15,21,44] Early radiosurgical treatment for the patient is therefore usually more advantageous than observation and waiting for deterioration in the clinical status.[6]

INDICATIONS FOR GAMMA KNIFE RADIOSURGERY

Patients with vestibular schwannomas have a choice of two comparably effective treatment options—microsurgery and radiosurgical treatment using a gamma knife. In patients with large vestibular schwannomas that cause compression of the brainstem, open surgery must be performed, since tumor growth prevention alone is already insufficient and

decompression of the brainstem is needed. This situation occurs in schwannomas with a diameter of 3 cm or more. In patients with internal diseases that make open surgery and general anesthesia too risky (e.g. myocardial infarction, severe diabetes, etc.) and where the diameter of the tumor is less than 3 cm, gamma knife treatment is more appropriate (Fig. 4). For all other patients, there is a choice between an open surgery and gamma knife treatment. The majority of patients who opt for gamma knife radiosurgery do so for the following reasons—firstly, they are afraid of open surgery and gamma knife radiosurgery represents a minimally invasive and bloodless treatment. Secondly, for social reasons facial nerve palsy is the most feared complication of the treatment and this risk is lower in gamma knife radiosurgery—less than 1%. Thirdly, there is no need of recovery after gamma knife treatment and the patients can either return to work or continue their usual daily activities or pretreatment on the following day. Comparison of clinical outcomes—facial nerve function, hearing, risk of complications and quality of life after microsurgery and gamma knife radiosurgery tends to favor radiosurgery, the risk of disease relapse is statistically similar for both treatments.[14,29,38,39]

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