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REVIEW

An update on the treatment of vestibular schwannoma

Luis Lassaletta* and Javier Gavilán

Servicio de Otorrinolaringología, Hospital Universitario La Paz, Madrid, Spain

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Abstract
The increase in the diagnosis of ever smaller vestibular schwannomas (VS), the fact that many tumours can be observed with serial MRI, and the development of radiosurgery as an alternative to microsurgery have led the neurotologic surgeon to a new global approach to patients with VS. On the other hand, the spread of internet-based information sources, often with biased or incomplete information, makes counselling patients with VS a challenging task. This study provides an overview of the natural history of these tumours and the main therapeutic options: observation, surgery, and radiosurgery, with comments on their indications, advantages and disadvantages. Due to the completely different approach and peculiar features of bilateral VS in patients with type II neurofibromatosis, these are excluded.

PALABRAS CLAVES
Schwannoma vestibular;
Neurinoma del acústico;
Tratamiento;
Historia natural;
Comportamiento;
Observación;
Cirugía;
Radiocirugía

Actualización en el tratamiento del schwannoma vestibular

Resumen
El incremento en el diagnóstico de schwannomas vestibulares (SV) cada vez más pequeños, la constatación de que muchos tumores pueden ser observados con resonancia magnética seriada y el desarrollo de la radiocirugía como modalidad de tratamiento alternativa a la cirugía son las causas del cambio en el planteamiento del otoneurocirujano ante el paciente con un SV. Por otro lado, la enorme difusión de fuentes de información médica en internet, con información muchas veces incompleta y sesgada, dificulta aún más el planteamiento terapéutico del paciente con SV. En este artículo repasamos el comportamiento de estos tumores y las principales opciones de tratamiento: observación, cirugía y radiocirugía, y comentamos sus indicaciones, ventajas e inconvenientes. Por sus peculiaridades y planteamiento totalmente diferentes, se excluyen los casos de SV bilaterales en pacientes con neurofibromatosis tipo 2.

*Corresponding author.
E-mail address: luikilassa@yahoo.com (L. Lassaletta).

Figure 1 View of a vestibular schwannoma in the cerebellopontine angle by left retrosigmoidal route. The tumour, originating from the vestibular portion of the VIII cranial nerve contacts the V nerve cranially and the anteroinferior cerebellar artery caudally.

Incidence of vestibular schwannoma

In recent years, the systematic use of magnetic resonance imaging (MRI) has increased the number of patients diagnosed with vestibular schwannoma (VS). Thus, in Denmark, a country with a comprehensive database of VS, the number of cases has increased from 9.4 per million to 13 per million inhabitants.[1] In the United States, the incidence of VS is 10 cases per million inhabitants.[2] Despite this increase, the percentage of VS over total brain tumours remains at around 6%-10%. Since many patients with VS are never diagnosed, we have to distinguish 3 groups of patients or 3 types of incidence. The clinical incidence corresponds to symptomatic patients who are diagnosed with VS through image testing, with an incidence of around 10 cases per million inhabitants (1:100 000). The radiological incidence would be the percentage of patients for whom an MRI is requested for other reasons and where VS is found incidentally. Lin et al[3] found 9 cases of VS in 46 414 MRI. In last place would be the incidence in autopsies, for which the work of Leonard et al[4] is often cited, as they found 0.8% of tumours in systematically performed autopsies. The disparity in the figures is striking, as it can be summarized as 1 tumour/100 000 inhabitants, 1 tumour/5000 MRI performed for other reasons or 1 tumour/100 autopsies. The true incidence of VS would be somewhere between these 3 values.

Natural history and speed of growth

Growth pattern

VS is a benign tumour originating in the vestibular portion of cranial nerve VIII. Most of the tumours originate in the internal auditory canal (IAC). From there they grow toward the cerebellopontine angle (CPA) where they initially compress cranial nerves VII and VIII and the anteroinferior cerebellar artery (AICA) (Figure 1). They then compress the brainstem, cranial nerve V, and if growth continues, they collapse ventricle IV causing hydrocephalus and eventually death of the patient. For a similar size of tumour, the fact that the greater diameter is anteroposterior or lateromedial makes a tumour with the same volume compress the stem more or less.

Speed of growth

While the pattern of growth of VS is fairly predictable, one of the biggest questions about VS is its speed of growth. The generally accepted average is 1-2 mm per year, although there are tumours in which no growth at all is observed and others which grow more than 1 cm per year. As for volume, the accepted average growth is 1 mm^3 per year. In most of those with faster growth, this is a result of intratumoural haemorrhage or an increase in their cystic component, which occurs in approximately 2% of VS cases. If, instead of the growth rate of a specific tumour, we consider the percentage of tumours that grow, the answer is highly dependent on the monitoring time and the variability of results is enormous. In the classic study by Selesnik et al,[5] approximately 55% of the tumours grew after an average follow-up of 3 years. However, by increasing the follow-up time, almost all the tumours grow. Thus, Charabi et al[6] observed growth in 82% of cases. Depending on the length of monitoring time and variations in the design of the study, the percentage of growing tumours lies between 23% and 82%.[6-9]

Problems with the trials analyzing growth

The enormous variability in the results of studies examining the growth of VS is due to several factors. Apart from the small number of patients included and variability in the observation periods, it is common to find different imaging tests (computerized tomography, MRI with and without contrast) and measurements employed (maximum diameter, maximum diameter of the component in the CPA, volume calculated in different ways). While it would be necessary to measure the size of VS in order to make comparisons between different methods of diagnosis and treatment, there is no universally accepted way of doing so. Two features of these tumours complicate their measurement: their irregular geometry and the non-linear relationship between a tumour's diameter and its volume. If it were a spherical lesion, it would be sufficient to measure the diameter in one plane in order to obtain the volume; however, if the measure includes the intracanalicular portion of the tumour, then the volume obtained is larger than the real volume. Therefore, many authors consider only the extrameatal portion and take into account diameters on 3 axes: parallel to the axis of the petrous bone, perpendicular to the axis of the petrous bone, and vertical. The first 2 can be measured in an axial MRI and the third in a coronal MRI. In practice, often the maximum diameter in the axial plane is used. There is controversy about whether or not to include the intracanalicular portion. If excluded, the intracanalicular tumours would be considered separately. Regardless of the method of measurement used, it should be noted that a small

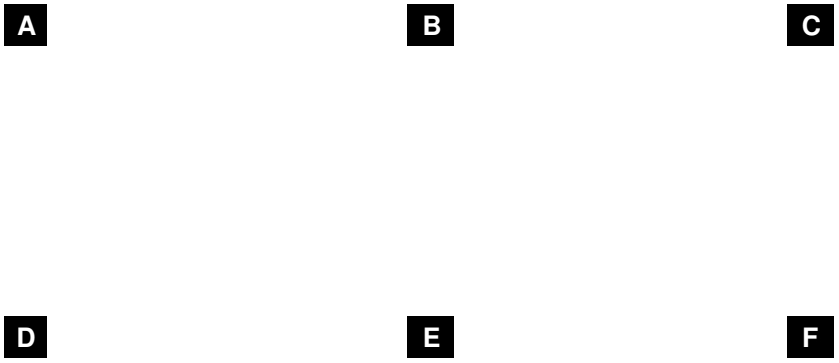

Figure 2 Examples of different-sized vestibular schwannomas. A. Three mm tumour in the medial area of the internal auditory canal (IAC). B. Intracanalicular tumour. C. Ten mm tumour in the IAC and 10 mm at the cerebellopontine angle (CPA) with cystic centre. D. Ten mm tumour within the IAC and 15 mm in the CPA. The maximum diameter considering the intracanalicular portion would be 22 mm. E. Thirty-two mm tumour in the CPA and partial occupation of the IAC. As the maximum diameter is parallel to the petrous bone, in this case the inclusion or exclusion of the part in the IAC does not affect the maximum diameter. F. Forty-five mm tumour at the CPA with occupation and destruction of the IAC walls. Major displacement of the brainstem.

increase in the diameter of the tumour represents a much larger increase in its volume. Various classifications have been proposed, depending on the maximum diameter, but none is universally accepted, and there is little agreement on the concept of small, medium, or large tumours. Figure 2 shows tumours of different sizes.

Another source of confusion in observational studies is the lack of consensus on the definition of tumour growth. It is not well established by how many millimetres the maximum diameter or volume of a tumour should increase in order to consider that it has grown. Nor is it clear in what period of time this increase should occur. And there is even less agreement on defining what would be the minimum tumour growth that would imply that a patient initially under observation should start to undergo treatment. But perhaps one of the largest biases occurs because the observational studies do not include large tumours which require more or less urgent surgery, and which probably present high rates of growth but of course do not allow MRI monitoring.[10]

Dissociation between clinical presentation and tumour size

Most patients with VS complain of tinnitus and hearing loss. Other less common symptoms are dizziness, vertigo, headache, and impairment of facial function or sensitivity. It is common for patients with a small or medium sized VS to ask about symptoms potentially indicating that the tumour is growing. Except for possible signs of intracranial hypertension in cases of giant tumours, we cannot answer their questions. This is due to the well-known dissociation between clinical presentation and the VS tumour size. Thus, we see both intracanalicular tumours in patients with acute vertigo or severe tinnitus and patients with large tumours with only mild hearing loss as a symptom.[11] Similarly, there could be a clinical worsening, for example a sharp rise in the hearing loss and instability, without tumour growth.

Prediction of tumour growth. Clinical and radiological data. Experimental data

Apart from knowing the average speed of growth of tumours or the percentage of tumours that grow, the question we face in clinical practice is how fast the tumours of specific patients will grow, and whether this will be life-threatening and thus force consideration of whether or not they should be treated. There are currently no clinical or radiological data at the time of diagnosis that allow us to predict the rate of growth of VS.[10] Herwadker et al[12] studied 50 patients with VS monitored by serial MRI. They found no relationship between gender, age, laterality of the tumour, tumour volume, and speed of growth.

Since the information available at the time of diagnosis does not allow us to predict the behaviour of the VS and in particular its growth, the genetic and molecular studies become crucially important. Collaboration between basic and clinical researchers allows the combination of genetic and molecular information with clinical and radiological data; this is the only way that the experimental data can have a practical application. The molecular changes involved in the pathogenesis of VS are not precisely known. Most studies have focused on the *NF2* gene, located on chromosome 22 (22q12). The inactivation of the merlin protein, the product of the *NF2* tumour suppressor gene, is involved in the development of VS, both in sporadic and bilateral cases.[13] A loss of chromosome 22 is found in up

to 50% of schwannomas, whatever their location; mutation and deletion are the main alterations found. It has also been shown that there are other regions of the genome, apart from chromosome 22, that are frequently altered in schwannomas. These regions (7p, 9q, 10q, 13q, 11q, and 17q) could be the location of other genes involved in the development of these tumours.[14,15] Epigenetic changes in the development of VS have recently been studied. While genetics refers to the information transmitted by a sequence of genes, epigenetic alterations are those that result in changes in gene expression without affecting the sequence of genes. The main epigenetic modification in humans is methylation of the cytosine located within the CpG dinucleotide. When the related transcription factors exist and the CpG island remains in a non-methylated state, there is transcription of a specific gene.[16] By contrast, the methylation of CpG promoter regions is associated with a compact chromatin structure, resulting in the transcriptional silence of the gene involved. Thus the hypermethylation of regulatory regions represents an alternative mechanism to deletion and mutation for the silencing of tumour suppressor genes. In a recent study by our group, variable methylation values (between 9% and 27%) were found in 12 out of 16 genes analyzed, including *RASSF1A, VHL, PTEN, TP16, CASP8, TIMP3, MGMT, DAPK, THBS1, hMLH1, TP73,* and *GSTP1*, in a series of 22 samples of VS. Methylation of the *RASSF1A* gene was associated with tumour growth.[17] Other lines of investigation other than gene inactivation have focused on angiogenesis factors and expression of genes regulating growth. Some studies have linked the most potent mediator of angiogenesis and best-known cell mitogen, the *VEGF* gene, with the growth pattern of VS. Caye-Thomas et al[18] found a relationship between the concentration of VEGF and VEGFR1 in tumour samples with tumour growth in 27 patients undergoing surgical treatment. Lassaletta et al[19] found immunohistochemical expression of cyclin D1, a product of the *cyclin D1* proto-oncogene, over-expression of which has been linked with various tumours, in 52% of 21 VS. The lack of expression of cyclin D1 was associated with longer duration of deafness and higher hearing thresholds at 2000 Hz. In a subsequent study,[20] we found an association between hypermethylation of the *RASSF1A* gene and the negative expression of cyclin D1.

Therapeutic options

General approach. Goals of treatment. Quality of life

There are 3 treatment options for patients with VS: observation with serial MRI, surgery, and radiotherapy. In recent years, the wide diffusion of the Internet has meant that many patients come to consultation with prior knowledge about the various treatment options, which far from making matters clearer, often mislead patients due to incomplete and biased information. It is very important for all patients to be informed of the 3 treatment modalities. We must explain the possible side effects, risks, advantages, and disadvantages of each. Once in possession of all the information, it is the patient who must make the decision. With the exception of some situations where the choice of treatment is clear, for example observation for a 90-year-old patient with a 3 mm tumour or surgery for a 30-year-old patient with a 5 cm tumour, the decision on the best therapeutic option for patients with VS is very difficult to take. The lack of randomized prospective studies which include observation, surgery, and radiotherapy means that are no evidence-based clinical practice guidelines for patients with VS. Therefore, the recommendation to a patient with VS relies heavily on the experience of the otoneurology surgeon. The ideal situation is for a patient to consult a multidisciplinary team in a centre with experience. In any case, we must explain to patients the benign nature of their lesion, convey to them that the vast majority of cases do not require urgent treatment, which means that they have time to decide the most appropriate therapeutic option, and especially the purpose of treatment must be made very clear. As discussed previously, most patients with VS present only hearing loss and/or tinnitus at the time of diagnosis, and disabling symptoms are rare. This means that the vast majority of patients have very good quality of life despite having a tumour. After the chosen treatment, even if there are no serious or unforeseen complications, this quality of life worsens.[21] This is because no matter how few sequelae there are after surgery or radiotherapy, as a rule the patient will be worse than before treatment.[22] Obviously, this situation is exacerbated if severe complications or sequelae appear. Therefore, the patient must understand that the goal of VS treatment is to avoid problems derived from the growth of the tumour, which by its nature and location can lead to intracranial hypertension and death. But these problems can appear after many years, so the treatment involves, at the present time, a reduction in the quality of life to avoid serious complications in an uncertain future. An exception to this rule are patients with large and symptomatic tumours, in which treatment is imperative, and patients with severe vertigo. In these cases, quality of life may improve after treatment.

Observation. Wait-and-scan

An observation or "wait and scan" approach consists in performing serial MRI, the first one generally 6 months after diagnosis and, if there are no significant changes, every year. The possible changes in the symptoms of the patient are assessed at each review and an audiometry is carried out. In older patients with small tumours where the expected growth of the tumour is not life-threatening in the years they presumably have left to live, this attitude would be the treatment indicated. In these cases, as long as no significant changes are observed in the symptoms, an annual MRI is carried out (Figure 3). Advanced age, deterioration of general condition, absence of relevant symptoms, long-standing clinical condition indicating slow growth, are all factors in favour of this wait-and-scan treatment.

While the combination of advanced age and small tumour size is hardly questioned as an indicator for observation, there are other situations which may also indicate the same treatment. One of the most controversial is the case of a young patient with a small tumour and good hearing. In this case, all 3 therapeutic options could be considered: microsurgery to resect the tumour and preserve hearing while the tumour is still small; radiosurgery to control the

Figure 3 Growth of a vestibular schwannoma after one and a half years of observation.

growth of the tumour, thus avoiding the potential morbidity of surgery, relying on preserving hearing; and observation, as the rate of tumour growth is not initially known and the possibility exists that it may not grow or it does so at a normal rate, in which case the injury will not become life-threatening for many years. And lastly, the slow rate of growth of most tumours makes observation a valid option as an initial approach in almost all tumours, except in very large ones which may become life-threatening in the short or medium term.

The main advantage of observation is that it avoids the morbidity of surgery or radiation. A theoretical disadvantage of this wait-and-scan approach is the delay in providing definitive treatment if the growth of the tumour is established, although it has not shown that this delay has a negative impact on the quality of life. Other drawbacks are the need for lifelong imaging tests and the psychological factor, due to knowing that there is an untreated intracranial tumour. When observation is chosen as a therapeutic option, we must warn the patient that it is likely that the hearing loss will increase, even if the tumour does not grow.[23]

Surgery

Goals of surgery. Who should perform the VS surgery. Importance of experience. Since Sir Charles Balance carried out the first extirpation of a VS in 1894 by inserting a finger between the brainstem and the tumour, there has been a remarkable evolution in the resection of these tumours. The introduction of the microscope, microsurgical techniques, monitoring of the facial nerve, the refinement of anaesthesia and the experience acquired at some centres have helped to generate new targets in neurinoma surgery. These days, the goal is not just excision of the tumour with minimal mortality, but also the preservation of facial function and, where possible, hearing. While mortality has fallen to values below 1%2% at experienced centres, and preservation of facial function is achieved in most cases, the preservation of hearing is achieved in only a select few. As in other areas of otolaryngology falling between different specialities, there is controversy about which specialist should carry out VS surgery. The answer, in our view, that it should be performed by the person with most experience in it. In theory, any otoneurology surgeon or neurology surgeon with enough experience can carry out the complete surgery, although it is rare for a neurosurgeon to have experience in the milling of the IAC. At our centre, the otolaryngology department has performed VS surgery since the nineteen-eighties. However, since 2000, cooperation between otolaryngology specialists and neurosurgeons has been enriching and brought several advantages: each specialist provides their expertise in different fields, allowing for shifts to be set up so that, in patients with large tumours, dissection of the cranial pairs can be performed more restfully, and all approaches can be used, some of which are not accessible to certain specialists (eg, the translabyrinthine route for a neurosurgeon). Regardless of who performs the surgery, there is unanimous agreement on the importance of expertise in performing VS surgery. Only at experienced centres where skull base surgery is a routine procedure (daily or weekly) is it possible to achieve the best results.

Approaches: indications, advantages, and disadvantages. The approaches for VS surgery are translabyrinthine, retrosigmoidal, and medial fossa or transtemporal. The main factors in choosing one route or another are the size of the tumour, hearing levels, and the age of the patient. While each approach route has its advantages and disadvantages, one of the aspects most pondered in selecting one or another is the surgeon's expertise. The ideal situation is to master all 3 routes and thus decide in the light of the characteristics of the tumour and the patient. In general, the translabyrinthine route is used when the patient has no useful hearing (maximum discrimination <50% and tonal threshold >50 dB, class C or D) (Table 1)[24] or when the characteristics of the tumour (invasion of the bottom of the IAC or size >2 cm) make conservation of hearing highly unlikely. When there is a chance to preserve hearing, then one of the other 2 approaches is generally used. If the patient has useful hearing and the tumour does not invade the lateral third of the IAC the retrosigmoidal route can be used providing the tumour component in the CPA is >5-10

Table 1 Classification of hearing into 4 classes according to the American Academy of Otolaryngology

Class	Average tone threshold (conversational frequencies)	Maximum discrimination
A	0-30 dB	70%-100%
B	31-50 dB	50%-100%
C	51-100 dB	50%-100%
D	Any figure	0%-49%

mm, or else the medial fossa route if the tumour is purely intracanalicular or its extension into the CPA is <5-10 mm. The main advantages of the translabyrinthine route are the possibility of resecting tumours of any size and avoiding the need to retract the cerebellum; its most important drawback is the cophosis inherent to the approach. The main advantages of the retrosigmoidal route are its fast, direct access to the CPA allowing good control of the nervous and vascular structures (Figure 1), the possibility of preserving hearing and the more favourable position of the facial nerve when compared with the transtemporal route. On the other hand, its main disadvantages are post-operative headache, the need to retract the cerebellum and the difficulty to access the bottom of the IAC. The main advantage of the approach through the medial fossa is the possibility of preserving hearing, while among its disadvantages are the technical difficulty and the more superficial position of the facial nerve.

Results, sequelae, and complications. Sequelae or complications after VS surgery include hearing loss, facial palsy, impaired balance, fistulae of cerebrospinal fluid (CSF), headache, meningitis, and severe complications. Once severe complications are ruled out, the interest of the surgeon is mainly focused on preserving facial function and hearing. The results of hearing conservation after surgical removal of VS are more uncertain than the ultimate results in facial function. Post-operative facial function is more or less predictable with the information obtained by a facial monitor during and, especially, after surgery. If we obtain a response from the monitor at an intensity of 0.05 mA or less after resection of the tumour, the patient is likely to have a normal or nearly normal facial function (House-Brackmann grade I or II, excellent outcome) (Table 2)[25] one year after surgery.[26] At experienced centres, excellent outcomes are achieved in 60%-90% of cases.[27,28] In general, there are no significant differences regarding facial function outcome between the 3 approaches. For a tumour of the same size approached by any of the 3 routes, the probability of facial paralysis would be greater with the medial fossa approach as the facial nerve is more exposed to manipulation. However, the medial fossa approach is mainly used for small tumours, whereas the translabyrinthine and retrosigmoidal routes are used for tumours of any size. This is a fact that must be taken into account when assessing surgical series. Thus, in the review by Backous et al[29] the total of House-Brackmann grades I and II represented 82% for all approaches; 92% by retrosigmoidal, 89% by medial fossa, and 73% by translabyrinthine. The lower percentage of excellent results in the translabyrinthine route is probably due to the larger size of tumours managed using this approach. Although post-operative facial function is the most important factor of success or failure for the surgeon, it not necessarily so for the patient. In a study of our group, we found no difference in perceived quality of life among patients when comparing cases with better or worse post-operative facial function.[30] While facial function conservation is feasible in many cases, the results of hearing conservation are much less consistent.[31] It is relatively frequent to find post-operative cophosis despite anatomically preserving both the inner ear and the cochlear nerve. The main prognostic factors when it comes to preserving hearing are tumour size, the extension into the IAC, and pre-operative hearing levels. Using the medial fossa approach for selected cases, the preservation of hearing reaches 60%-70%.[32,33] In a review of articles on hearing conservation in 618 out of 2034 patients (30%), class A or B hearing was achieved post-operatively (Table 1).[29] As a general rule, the lack of consensus on both the criteria for selecting patients for hearing conservation procedures and the definition of hearing conservation makes us sceptical when interpreting the published studies.[34] This means that the actual likelihood of preserving hearing for a patient may not be as high as indicated by the literature. CSF

Table 2 House-Brackmann scale for facial function

		At rest	Forehead	Eye	Mouth
I 100%	Normal	Normal	Normal	Normal	Normal
II 80%	Slight weakness, possible synkinesis	Normal tone and symmetry	Moderate-good movement	Complete closure with minimal effort	Low asymmetry
III 60%	Obvious, but not disfiguring facial asymmetry. Non-severe synkinesis, contractions, or spasms	Normal tone and symmetry	Slight to moderate movement	Complete closure with effort	Slight weakness with maximum effort
IV 40%	Obvious weakness and/or disfiguring asymmetry	Normal tone and symmetry	No movement	Incomplete closure	Asymmetrical with maximum effort
V 20%	Minimal perception of movement	Asymmetry	No movement	Incomplete closure	Small movement
VI 0%	No function	No function	No movement	No function	No function

fistula is the most common complication after VS surgery. In review studies, fistulae have been described in about 8%-15% of cases, although only in 25% of cases was surgical treatment needed. Apart from prolonging hospital stay, CSF fistulae pose a risk of meningitis, which may appear long after the procedure is performed. No large differences have been described between the different approaches.[35] Alterations in balance after VS surgery depend on each patient's ability to compensate after the cancellation of vestibular function implied by surgery.[36] Most patients can return to daily activities after surgery. Sometimes balance disorders can persist that do not appear well systematized in the literature.[21] Headache is common in post-operative recovery after VS surgery. However, impacts lasting more than 3-6 months are rare and occur in less than 10% of cases. In general, these occur most frequently after the retrosigmoidal route or the medial fossa route and far less often with the translabyrinthine approach.[37] Severe complications such as hydrocephalus, severe neurological sequelae, or death occur in less than 2% of cases in experienced centres.[38,39]

Role of subtotal resection. Since the surgical results on facial function are worse for larger tumours and radiosurgery is ineffectual in these lesions, the possibility of combining both techniques has been raised. Thus, in recent years the idea of performing subtotal resections in tumours larger than 3 cm has been mooted, with the remnant being irradiated if the tumour grows. In our experience, the success of this approach depends on the concept of subtotal resection. If we consider resection of almost all the tumour, leaving a small portion attached to the facial nerve, the result is usually positive, and radiological follow-up of the patient may be enough, leaving radiotherapy as an option if growth is observed. Conversely, if subtotal resection is seen as a mere partial resection, there is often not even any alleviation of the tumour's compression on the brain stem and the outcomes with radiation therapy are often poor, as the size of the tumour is hardly modified; for all these reasons, we do not support this option.

Radiosurgery

Goals of radiosurgery. In recent years, stereotactic radiosurgery or radiotherapy has become a therapeutic option in high demand for patients with VS. Unlike conventional surgery, radiosurgery aims at controlling tumour growth. The degree of local control achieved with radiosurgery is defined as the percentage of tumours which do not grow in serial imaging studies. Many authors define local control as the percentage of tumours not requiring surgical treatment. This definition is not correct, since many tumours can grow without making surgical intervention necessary.

Techniques, indications, advantages, and disadvantages. Stereotactic radiosurgery was developed by Leksell in 1951 and consists of the application of a single dose of ionizing radiation to an intracranial target with submillimetric precision. The source of radiation can be natural, such as the Gamma Knife, which uses cobalt, or a specific device, such as the linear accelerator. The most widespread technique for radiosurgery is the Gamma Knife, also developed by Leksell in 1969. This is a specialized radiation system which uses 201 sources of cobalt 60 to send high doses of radiation to a tumour. To ensure immobility of the patient and the precise application of radiation, it is necessary to fix a stereotactic frame to the skull under local anaesthesia. In recent years, the radiation dose has been reduced to decrease side effects, while theoretically maintaining the same rates of tumour control. Linear accelerator radiosurgery (LINAC) uses fewer isocentres and the dose reaching the tumour is more homogeneous. It also requires the use of a stereotactic frame. Fractionated stereotactic radiotherapy (FSRT) is the newest form of radiosurgery. Unlike the Gamma Knife or LINAC, the stereotactic frame is not invasive and is therefore more comfortable for the patient. In theory, fractionation reduces the toxic effects of radiosurgery while maintaining tumour control. Initially, radiation therapy arose as an alternative to surgery in patients who declined it or could not be operated on. At present, radiosurgery is offered as an alternative to surgery in patients with VS when the tumour is smaller than 3 cm. Above this size, tumour control is much lower. Below 3 cm, advanced age is the main argument in favour of radiosurgery, since young patients are more vulnerable to the adverse effects of radiosurgery. The main advantages of radiosurgery are the lower initial morbidity of the procedure and the possibility of carrying it out as a day-surgery procedure. On the other hand, it has drawbacks such as the difficulty of performing surgery on irradiated tumours, the possibility of the VS becoming malignant or the formation of other tumours, patients' uncertainty as they will continue to live with a tumour along with the need for lifelong radiological controls. While the radiological characteristics of VS are usually sufficiently clear, the absence of histological confirmation means there is no precise diagnosis. Although unusual, there are some lesions simulating VS that cannot be diagnosed without surgery.[40] Another disadvantage of radiosurgery is that it can generate instability after treatment or aggravate a prior situation of instability.

Results, complications, and sequelae. As the goal of radiosurgery is to control the growth of the tumour instead of eliminating it, the effectiveness of this approach can reach 90%-95%. In a review of studies on tumours treated with radiosurgery between 1994 and 2007, with an average follow-up of at least 2 years, local control ranged between 87% and 100%.[29] The results decline in large tumours, with 33% of growth in this group, as well as in NF-2 where tumour control decreased to 70%.[41] In 50% of irradiated tumours, there was central necrosis which increased the tumour volume in 23% of them. This phenomenon can occur up to 4 years after treatment and may disappear after between 6 months and 5 years. The approximate rate of facial palsy after radiosurgery is <2% and it has been clearly associated with radiation dosage. In the paper by Kondziolca et al[42] on 157 VS in a group of 285 intracranial tumours, the facial function was maintained in 95% of patients who had a prior normal function. In general, with low doses of radiosurgery, the incidence of facial paralysis is very low. However, as in the case of hearing, there is often a lack of accurate data on patients' facial function. The hearing conservation rate is around 60%, but the data on hearing are usually not systematically processed in the literature. Hearing loss after radiosurgery usually appears between 6 and 24 months after treatment, but hearing may worsen years later. Trigeminal neuralgia is a dreaded complication

Figure 4 Major cerebral oedema associated with radiosurgery after partial resection of vestibular schwannoma.

after radiosurgery. It has been reported more frequently after FSRT (8%) than after LINAC (2%).[43] Although the follow-up is increasing in the published series, the complications of radiosurgery may appear more than 20 years after treatment. These include vertigo, tinnitus, headache, hydrocephalus, formation of cysts, oedema (Figure 4), or radiation-induced necrosis, intratumoural haemorrhage, and malignant transformation.

Sequelae and quality of life. Although differences in inclusion criteria, age, and treatment goals do not allow systematic comparisons between operated and irradiated VS patients, in general, the conservation of facial function and quality of life are better in irradiated patients when compared with operated patients.[44,45] However, the quality of life also deteriorates after radiosurgery, and we must not forget that the objectives of the 2 treatments are different, as one resects the tumour and the aim of the other is for it not to grow.[46]

Possibility of malignancy. One of the most fearsome aspects of radiosurgery is the possibility of developing other tumours following radiation, as well as the potential for the VS to become malignant. Both risks are very low, but not negligible. To date, 20 cases have been identified of malignant tumours that have appeared after radiosurgery, all of them with a fatal outcome.[47] The actual number of cases is undoubtedly higher than reported in the literature, and in centres with experience the risk of malignancy after radiosurgery is considered similar to the mortality due to VS surgery.

Unresolved matters on the therapeutic options

Observation is as effective as radiosurgery

One argument used against radiosurgery is that its results in tumour control are similar to those of a wait-and-scan approach. The literature does not enable definitive conclusions to be reached, although the radiosurgery series show tumour control rates of 80%–90% and the percentage of tumours which do not grow or decrease in the observation series is around 61%–77%.[79] According to Jackler,[41] 30% of observed tumours grow in 3 years, whereas only 5%–10% do so after radiosurgery. Battaglia et al[48] studied 164 patients treated with radiosurgery between 1986 and 2004 and compared the rates of growth of their tumours with the results of a meta-analysis of 5 studies of patients treated by observation. No significant differences were observed between the groups. These results indicate that the success of radiosurgery is usually much lower than reflected in the literature.

Surgery is more complicated after radiosurgery

As a general rule, this assertion is correct, as it increases the likelihood of complications, the results in facial function are worse, and the certainty of complete resection is more complicated.[49] In a series of 63 patients operated on following radiosurgery at the House Ear Clinic, the results for post-operative facial function, in addition to increasing surgery time, were worse than in the case of untreated tumours.[41,50]

Radiosurgery is equally effective in an operated tumour as in an untreated tumour

While the contrary is not true, radiosurgery has been shown to be just as effective after a partial resection as in an operated tumour. The main factor for response to radiosurgery is the size of the tumour, meaning that, as discussed previously, the difference lies in the extension of the partial resection.

Otoneurology surgeons indicate excessive surgery and radiosurgeons indicate excessive radiosurgery

One of the main criticisms that can be made of studies on radiosurgery is the inclusion of patients in whom no prior growth of the tumour has been shown. In these cases it is not known whether the "success" of the tumour control corresponds to the treatment option, or to the natural history of the tumour. This bias is particularly evident in the series which include cases with few years of follow-up, a very common fact in the literature. This criticism would also apply to surgery in patients with small tumours, because the consequences of the surgery would be more "justified" if the growth of the tumour were established. If this is not the case, the patient may have enjoyed a better quality of life until then.

Conclusions, how to raise the question of treatment with a VS patient

In view of the points discussed, it seems clear that there is insufficient scientific evidence to allow us to say which therapeutic option is the treatment of choice for patients with VS. At the moment we have no means to determine the speed of growth of a specific tumour, and this is the information that would help us most in selecting an option. The only case in which there is broad consensus is when a patient has a large tumour (>3 cm) in which surgery is the

best option if the patient's general condition allows. For medium and small tumours, an initial observation period of 6 months can be suggested. During that time, the patient can internalize and contrast the information provided by the otoneurology surgeon, who should explain the 3 treatment options in simple language, along with their advantages and disadvantages. It is essential to explain the purpose of each option clearly, so as not to alarm the patient unnecessarily with regard to a benign tumour that will not normally cause major problems in the short to medium term, without omitting either the possible risks of serious complications that can arise after surgery, radiosurgery and, in time, with observation. With a second MRI after 6 months, it is possible to evaluate if the tumour shows growth or not. It is then that the patient, with all the information available, must choose one of the 1 options available.

Conflict of interests

The authors have indicated there is no conflict of interest.

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