ORIGINAL ARTICLE

Non surgical Treatment of Vestibular Schwannoma

Leoncio Arribas, a,f,* María L. Chust, a Antonio Menéndez, b Estanislao Arana, c Juan B. Vendrell, d Vicente Crispín, c Carmen Pesudo, a José L. Mengual, a Alejandro Mut, a Mar Arribas, g José L. Guinot a

a Servicio de Oncología Radioterápica, Hospital Fundación IVO, Valencia, Spain
b Servicio de Neurocirugía, Hospital Universitario La Fe, Valencia, Spain
c Servicio de Radiología, Hospital Fundación IVO, Valencia, Spain
d Servicio de ORL, Hospital Fundación IVO, Valencia, Spain
e Servicio de Radiofísica, Hospital Fundación IVO, Valencia, Spain
f Facultad de Medicina, Universidad Católica de Valencia San Vicente Mártir, Valencia, Spain
g Servicio de ORL, Hospital General de Valencia, Valencia, Spain

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KEYWORDS
Vestibular schwannoma; Acoustic neuroma; Radiosurgery; Fractionated stereotactic radiotherapy; Observation

Abstract
Introduction and objectives: To evaluate the results of local control and complications in the treatment of vestibular schwannoma treated with radiation.
Methods: A retrospective study of 194 patients diagnosed with vestibular schwannoma, treated consecutively with radiation (either stereotactic radiosurgery or fractionated radiotherapy) from 1997 to 2012. We analyse the local control of tumours, as well as secondary complications to treatment with radiation.
Results: A total of 132 (68%) tumours, 68% are grade I-II tumours of the Koos classification, 40 (19%) are grade III, and 22 (13%) are grade IV. The tumours associated with neurofibromatosis (NF2) are 3.6% (6 tumours in 4 patients). The tumour control for the overall series is 97% at 5 years, with a median follow-up of 80.4 months. For large tumours the local control is 91% at 5 years. Free survival of chronic complications is 89% at 5 years. Additionally, 50 tumours were subjected to regular follow-up with MRI without treatment, and 28 (58%) did not experience tumour growth.
Conclusions: Radiation and follow-up with MRI are alternatives to surgery in the treatment of vestibular schwannoma, with a low level of complications in a multidisciplinary approach.

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* Corresponding author.
E-mail address: larribas@fivo.org (L. Arribas).

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Introducción y Objetivos: Valorar los resultados de control local y complicaciones en el tratamiento del schwannoma vestibular tratado con radiaciones.

Métodos: Estudio retrospectivo de 194 pacientes diagnosticados de schwannoma vestibular, tratados de manera consecutiva bien con observación o bien con radiaciones (bien radiocirugía o radioterapia esterotáctica fraccionada) de 1997 a 2012. Analizamos el control local de los tumores, así como de las complicaciones secundarias al tratamiento con radiocirugía.

Resultados: El 68% (132 tumores) son inferiores a 2 cm es decir grado i de la clasificación de Koos, 22 pacientes (13%) con tumores grandes grado iv, el resto (40 pacientes) son grado m. Los tumores relacionados con la neurofibromatosis (NF2) representan el 3,6% (6 tumores en 4 pacientes). El control tumoral para los pacientes tratados con radiaciones es del 97% a 5 años, con un seguimiento mediano de 80,4 meses. Para los tumores grandes el control local es del 91% a 5 años. La supervivencia libre de complicaciones crónicas es del 89% a 5 años. De los 50 tumores a los que se realizó seguimiento, 28 (58%) continuían en seguimiento al no haberse objetivado crecimiento alguno.

Conclusiones: La radiación y el seguimiento con RM, dentro de un enfoque multidisciplinar, es una alternativa a la cirugía en el tratamiento del schwannoma vestibular, con un bajo nivel de complicaciones.

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**Table 1** Koos Classification of Vestibular Schwannomas.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Description</th>
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<tbody>
<tr>
<td>I</td>
<td>Intracanalicular tumour</td>
</tr>
<tr>
<td>II</td>
<td>Small tumour protruding at cerebelloptine angle, up to 2 cm</td>
</tr>
<tr>
<td>III</td>
<td>Tumour which occupies the cerebelloptine angle cistern, with no displacement of the cerebral trunk, up to 3 cm</td>
</tr>
<tr>
<td>IV</td>
<td>Large tumour, with displacement of the trunk or cranial nerves, &gt;3 cm</td>
</tr>
</tbody>
</table>

Source: Gonzalez-Darder et al.
Hearing was assessed using the House and Brackman (HB) classification. Those patients with intracanalicular tumours or with a minimum extracanalicular component, i.e. Koos grade I–II, who were oligo- or pauci-symptomatic, were offered the option of surveillance, observation, or follow-up. Initial control 9 months after diagnosis in the radiological examination, audiometry, and MRI, with subsequent annual examinations up to year 5; thereafter examinations were to be performed every 2 years, or every 5 years depending on patient characteristics.

Treatment is shown in Table 2. 86% (145 tumours) were treated exclusively with radiation, 133 with RS and 12 with FSRT. The remaining 14% (22 tumours) received RS as rescue treatment after surgery.

We used RS in all tumours ≤25 mm; the procedure is currently outpatient. The dose used was 12 Gy at the margin of the lesion marked by the MRI imaging in the T1 sequence contrast enhancer and in CISS T2 sequence, with no additional margin; we applied several dose limits to the trigeminal nerve level of <9 Gy; the dose of the cochlea and the ependymal wall (ependyma) had to be as low as possible, trying not to go above 5 Gy at the cochlear (marked in the CISS T2 sequence or the bony window) or above 10-12 Gy in the ependymal wall (a volume below 0.1 cc). Initially we used the stereotactic frameworks of Prof. Bervia Salorio and Leksell; since 2005 we have been using the Brainlab AG (Feldkirchen, Germany) framework. In lesions over 25 mm we used FSRT, with a dose range between 30 and 50.4 Gy with fractioning of either 3 or 5 Gy per day if we administered 30 Gy or 1.8 Gy per fraction per day if we administered 50.4 Gy. This dose was administered to the marked lesion as it was with RS, increasing the irradiated volume between 2 and 3 mm to compensate for possible positioning errors. The procedure was performed with repositionable masks, made for each patient.

Until 2005, conical collimators and dynamic RS therapy were used; from then onwards we carried out the treatments with a multilamine microcollimator, BrainLAB AG plan, with dynamic conformal arc therapy technique. This plan creates automatic fusion of the cerebral MRI imaging of the gadolinium enhanced sequences in T1 and CISS T2 sequences with the brain CAT scan with the inserted stereotactic framework/repositionable mask on the patient.

Follow-up after treatment involved clinical examination of the fifth, seventh and eighth cranial homolateral nerve, audiometry, and MRI after 9 months. This examination was then annual for 5 years and bi-annual afterwards up to 10 years; after this period, follow-up was every 3–5 years, depending on patient characteristics.

The absence of the need to administer any other treatment was considered as the local clinical control (LCC). A criterion of local radiological failure was a >2 mm increase in any dimension, present in at least 2 cerebral MRIs. Severe complications were those appearing during the first 3 months after treatment. Chronic complications were those appearing from the 6th month after treatment.

Estimation of survival was performed using the Kaplan–Meier method. For analysis of those factors which could potentially affect survival, the Cox Regression model was used. A value of P<.05 was used as a statistically significant difference. For the creation of the database and statistical analysis, the STATA 12.0 statistical package was used. For the different survival analysis, multivariate studies were performed using the Cox model of proportional risks.

### Results

Baseline patient characteristics are included in Table 3. Mean age is 58.4, with a range between 19 and 87 years. Median follow-up is 80.4 months (12–175 months). Median tumour volume is 0.98 cc. Using Koos classification, 17% are grade i, 51% grade ii, 21% grade iii and 12% grade iv. 22 patients (13%) with large tumours were treated. Neurofibromatosis (NF2) tumours represented 3.6% (6 tumours in 4 patients).

LCC is 97% at 5 years and 95% at 10 years. Local clinical failure is 3%. In large tumours, a 91% LCC is obtained at 5 and 10 years. Local control was obtained in 6 cases of VS related to NF2.

Of the 5 local failures, resection was performed in 2, and patients are currently tumour free. The other 3 patients were referred for treatment and received repeated cyst punctures, and died due to secondary surgical complications. They were all treated with RS. No Koos grade i patient relapsed; 2/84 (2.3%) with grade ii relapsed, 1/34 (2.9%) with grade iii relapsed, and did 2/22 (9%) with level iv (Table 4).

Of those patients who were under observation or follow-up (34 were Koos grade I and 14 grade II), 14 from the first group had tumour growth and 7 from the second group, i.e. growth was 42% and 58% remained stable.

Severe complications appeared in 15 patients (9%). These included increased instability in 10 cases, facial and eyelid oedema the day after treatment, in one case, increased tinnitus with sudden deafness in another, homolateral trigeminal pain in 2 cases, and infection in a stereotactic frame attachment point, in another case. All cases were rapidly resolved with medical treatment.

89% of patients had chronic complication-free survival after 5 years, and 85% after 10 years. Neuropathy of the facial nerve appeared in 9 patients with a 5% probability to appear after 5 years and 7% after 10 years. 4 patients presented with sensory-motor impairment, and 5 with facial myokymias. Of these, 3 presented simultaneously with trigeminal neuropathy. Permanent paralysis (always Grade HB I–II) occurred in 1.1%. They were more frequent in men, with a 2:1 ratio and if the dose was above 13 Gy, at a 2:2:1 proportion, they appeared with greater frequency between 60 and 69 years of age, and also increased with tumour size. None of these conditions were statistically significant.
Neuropathy of the trigeminal nerve presented in 11 patients (8% to 5 and 10 years). They were related to a dose >13 Gy (P=.05). They presented more frequently in women and with a ratio of 2.69:1. They may present with clinical symptoms which are sensitive to changes in facial sensitivity in the form of hypoesthesia, disesthesias or paresthesias, or as trigeminal neuralgia, mainly in V2–V3. All chronic complications appeared in patients treated with RS.

With regard to hearing preservation, only 19% of our patients had useful hearing prior to diagnosis, after RS hearing was preserved in 68.7% of the overall sample.

The rate of overall hydrocephalus was 5% after 5 and 10 years, and all the patients had tumours larger than 2 cm treated with RS.

We observed no radiation-induced secondary brain tumours. In 2 patients with NFZ standard meningiomas were associated and schwannomas of the trigeminal nerve, synchronous with V5.

Fourteen patients (8.3% of the sample) presented with an extracerebral cancer during their lives, synchronous in 3 cases and metachronic in 11 cases (over 6 months before or after V5 was diagnosed). If the overall cancer rate is 241.1 cases per 100 000 inhabitants and year, for the mean follow-up of 6.7 years they should have presented 3.27 cases of cancer for the 165 patients of the sample treated, which is why the incidence of presented extracerebral malignant tumours is 4.27 times higher.

Discussion

Regarding symptomology, as with other works, we found no relationship between the clinical symptoms presented by the patient and tumour size; thus intracanalicular tumours which maintain useful hearing below the mean were 16.8% compared with the 19% overall.

LCC of 97% after 5 years and 95% after 10 years is found between the rates of tumour control described, as between 93% and 100%.

Local clinical failure is 3%, similar to the rate of local clinical failure of published series for RS with Gamma knife, with linear accelerator (LA) or with FSRT, which ranges between 1.4% and 9%. The 5 tumorigeneses after RS of our series occurred during the first 2 years. The different authors state them as appearing within the first 3 years although they are described sporadically 3, 4 and 18 years after treatment.

Local radiological control of the 167 tumours 5 years after treatment is 93%, descending to 90% after 10 years. These results are similar to those published which range from 85.4% to 93%.

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**Table 3 Base Patient Characteristics.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Measurement</th>
<th>Total (n=167)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up</td>
<td>Months</td>
<td>80.4 (12–175)</td>
</tr>
<tr>
<td>Gender</td>
<td>Female</td>
<td>93 (56%)</td>
</tr>
<tr>
<td>Side</td>
<td>Left</td>
<td>88 (53%)</td>
</tr>
<tr>
<td>Age</td>
<td>Mean (years)</td>
<td>58.4 (19–87)</td>
</tr>
<tr>
<td></td>
<td>Median (years)</td>
<td>60</td>
</tr>
<tr>
<td>Image</td>
<td>Intracanalicular</td>
<td>30 (18%)</td>
</tr>
<tr>
<td></td>
<td>Extracanalicular</td>
<td>137 (82%)</td>
</tr>
<tr>
<td>Volume (cc)</td>
<td>Mean</td>
<td>2.76 cc</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>0.98 cc</td>
</tr>
<tr>
<td>Permissible dose D (Gy)</td>
<td>Mean</td>
<td>12.4 Gy</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>12.0 Gy</td>
</tr>
<tr>
<td>Hypoacusia prior to treatment</td>
<td>Useful (slight-moderate 0–50 db)</td>
<td>32 (19%)</td>
</tr>
<tr>
<td></td>
<td>Severe (55–80 db)</td>
<td>103 (61%)</td>
</tr>
<tr>
<td></td>
<td>Profound</td>
<td>32 (19%)</td>
</tr>
<tr>
<td>Clinical expressions prior to treatment</td>
<td>Duration of symptoms</td>
<td>34 months</td>
</tr>
<tr>
<td></td>
<td>Hypoacusia</td>
<td>159 (95%)</td>
</tr>
<tr>
<td></td>
<td>Changes in balance</td>
<td>97 (58%)</td>
</tr>
<tr>
<td></td>
<td>Tinnitus</td>
<td>90 (54%)</td>
</tr>
<tr>
<td></td>
<td>Hydrocephalus</td>
<td>19 (11%)</td>
</tr>
<tr>
<td></td>
<td>Trigeminal nerve damage</td>
<td>17 (10%)</td>
</tr>
<tr>
<td></td>
<td>Facial nerve damage</td>
<td>12 (7%)</td>
</tr>
<tr>
<td></td>
<td>Sudden deafness</td>
<td>8 (5%)</td>
</tr>
<tr>
<td>Neurofibromatosis</td>
<td></td>
<td>6 (3.6%)</td>
</tr>
</tbody>
</table>

**Table 4 Recurrence According to Tumour Size (Koos Classification).**

<table>
<thead>
<tr>
<th>Koos Classification</th>
<th>Recurrences, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Koos I intracanalicular</td>
<td>27/167 17%</td>
</tr>
<tr>
<td>Koos I ≤ 2 cm (84/167)</td>
<td>51%</td>
</tr>
<tr>
<td>Koos [\leq] 3 cm (34/167)</td>
<td>21%</td>
</tr>
<tr>
<td>Koos IV &gt; 3 cm (22/167)</td>
<td>13%</td>
</tr>
<tr>
<td>Total 167 patients</td>
<td>5 (3)</td>
</tr>
</tbody>
</table>
In the surgical series the probability of incomplete excision ranges between 2.4% and 6%,31 the possibility of local recurrence between 0.7%,32 6.2%,31 and 10%,31 with a surgical mortality of between 0 and 1.3%.3,31,32,33,34,35

The LC obtained in large tumours of 91% after 5 years, with follow-up of 9.3 years, is similar to that presented by other authors with RS between 87%6 and 82%.36 The complication level in this subgroup is lower than the rest of the series; we only found one patient with a transitory trigeminal disease 6 months after RS (4.5%), with no facial nerve damage or postural hydrocephalus after treatment, compared with 2% of facial damage, 6% of trigeminal nerve damage and 5% of hydrocephalus from the Yang et al.6 series, and 29% facial nerve damage and 13% of trigeminal nerve damage from the Mandl et al.36 series. Complications or recurrence appeared with a mean of 16 months.

Surgery on these tumours achieved complete resection which ranges between 100%7 and 87%,34 with morbidity of the facial nerve between 27% and 72%, LCR fistulas between 5.5% and 14%, a meningitis rate of between 5.5% and 9.5%, and no deaths during surgery.1,3,4,37

Although we have controlled the 6 tumours related to NF2, local control in this situation is not normally as good as in sporadic cases,29,38,39 with a need for additional treatment in 21% of patients treated with RS with a marginal dose of 13.4 Gy.

Regarding patients for whom follow-up was indicated, we observed that the number of patients who continued in follow-up was 58%, which is within published findings ranging between 50% and 68%.40-49 It is of note that the growth of these tumours is not affected by the tumour stage at diagnosis, since the percentage of patients with growth is the same in Grade i (41%) as in Grade ii (43%) tumours.

Severe complications, such as sudden deafness and trigeminal pain, are usually reversed with steroid treatment according to published works.9,22

Facial neuroma incidence falls between the ranges described by different authors, between 4.5% and 8%,17-18,46-48 The rate of permanent facial paralysis (1.2%) ranges between 1% and 1.5%,22,48 Occasional spasms of the side of the face, with little clinical repercussions are present in 8%. In other series this is between 2%-4%22 and 8%.49 This low rate of permanent facial nerve damage is due to the mean dose of 12 Gy administered.12 In the surgical series facial damage (> HB iii) ranges between 10% and 40%,3,31,32 depending on the tumour size, the surgical approach route31 and the experience of the medical teams.

The 8% neuropathy of the trigeminal nerve is similar to other series where it ranges between 4%-5%17,48 and 8%-18%.20 Permanent dysfunction in our series is 2.3%, identical to that described by La Roche et al.48 68.7% of patients maintained their hearing levels prior to treatment. At present, it is stated that between 33% and 90% of hearing has been preserved12,50,51 in patients with previous useful hearing.

In the 3 cases who underwent surgery after RS failure, surgery presented greater difficulty, similar to that suggested by other authors.4,52

With regard to a higher incidence of extracerebral cancer being diagnosed, we must remember that the appearance of VS is associated with an alteration of the NF2 tumour suppressor gene and that the majority of diseases linked to the inactivation of the tumour suppressor gene lead to the development of malignant tumours, with this point being the possible focus of connection.41

Conclusions

We would suggest that follow-up is offered for Koos Grade ii tumours when non-surgical treatment of VS is indicated, since almost 60% of them will not grow, nor will the patient be clinically compromised.

The lower aggressiveness of the technique and low level of complications of both RS and FSRT, compared with surgery, makes radiation a clear alternative to the surgical option which up until now was considered the standard treatment in small and intermediate sized tumours. In large tumours where there are surgical contraindications, FSRT may be an alternative, provided there are no neurological symptoms of compression of the encephalon trunk or cranial nerves, nor hydrocephalus, where surgery should continue being first line treatment.

Conflict of Interest

The authors have no conflicts of interest to declare.

References

11. Del Rio L, Lassaletta L, Alfonso C, Sarria MJ, Gavilan J. Disociacion clinica del tamaño tumoral en el neuroma del acústico:


50. Andrews DW, Suarez O, Goldman HW, et al. Stereotactic radiosurgery and fractionated stereotactic radiotherapy for the

