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Radiotherapy for vestibular schwannoma: Review of recent literature results

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ABSTRACT

Background: The management of vestibular schwannoma is still a quite controversial issue and can include wait and see policy, surgery and radiotherapy, mainly with stereotactic technique. The purpose of this study is to review the results of recent clinical series treated by radiotherapy.

Materials and methods: Literature search was performed by Pubmed and Scopus by using the words vestibular schwannoma, acoustic neuroma, radiotherapy, radiosurgery.

Results: Management options of VS include wait and see, surgery and radiotherapy. In case of small lesions, literature data report local control rates higher than 90% after radiosurgery (SRS) similar those of surgical techniques. Recent literature reviews show favourable functional outcome by using SRS. Several literature data support the use of fractionated stereotactic radiotherapy (FSRT) in case of large inoperable lesions.

Conclusion: Radiotherapy plays a relevant role in the treatment of VS. In small-size lesions, SRS can guarantee similar local control and potentially better function outcome compared to surgery. In case of large and irregularly shaped lesions, FSRT can be the used when surgery is not feasible.

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1. Background

Vestibular schwannoma (VS), or acoustic neuroma, is the most common tumour of the cerebellopontine angle.[1] It is a benign slow growing tumour with an incidence of about 10–20/million per year.[2] Symptoms at diagnosis commonly include hearing deficiency or loss, tinnitus, loss of balance and, more rarely, change in facial sensation and headache. Diagnosis is performed by magnetic resonance imaging showing a typical gadolinium-enhanced lesion.

The principal management options for VS are watchful waiting, surgery and radiotherapy.[3] The chance of tumour control and optimal functional outcome are very high, so a tailored clinical approach, based on tumour and patients' characteristics is often possible.

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Radiotherapy can be performed by various technical approaches, including in particular stereotactic radiosurgery (SRS) in a single shot and fractionated stereotactic radiotherapy (FSRT) with hypofractionation or conventional fractionation.

The present article aims at reviewing the most recent literature data of radiotherapy to describe the results in terms of local control and side effects in order to define the indication to radiation treatment and the optimal technical approach.

2. Materials and methods

Literature search was performed by using the databases of Pubmed and Scopus and the following keywords: vestibular schwannoma, acoustic neuroma, radiotherapy, radiosurgery. The time period was from 2009 to 2015. Most relevant historical articles from previous years were also included. Case reports were in principle excluded from the analysis. The relevance was assessed on the basis of the numerousness of the series, the length of follow-up and the completeness of analysis of technical data, outcome results in terms of local control and early and late side effects.

3. Results

In total, 324 articles were found and 32 were selected for the analysis. The most relevant clinical studies using radiotherapy and analyzing large series with adequate follow-up are summarized in Tables 1 and 2.

The different radiation therapy approaches can be divided into two principal modalities, according to the fractionation schedule: single fraction stereotactic radio-surgery (SRS) and fractionated stereotactic radiotherapy (FSRT), the latter with standard (1.8–2 Gy/fraction) or hypo-fractionated modality.

3.1. *Stereotactic radio-surgery (SRS)*

Historically, the first radiotherapy experience for VS was conducted by Leksell in 1969 at Karolinska Hospital.[4] He used gamma-knife irradiation by ^{60}Co photons, reporting encouraging results, with local control rates higher than 80% at 3.7 years and only 14% facial nerve impairment. Initially, indications for SRS included: elderly patients, medically inoperable, bilateral tumours and recurrence after previous surgery. After a few decades experience, many centres adopted SRS for treatment of primary VS as a valid alternative to surgery. However, no randomized studies have been conducted in order to compare outcomes from surgery and SRS. However, a recent meta-analysis reported a better hearing function (70.2% vs. 50.3%, $p < 0.001$) and a similar tumour control rate (96.2% vs. 98.7%, $p = 0.122$) comparing stereotactic radiation with microsurgery for treating small (<3 cm) VS.[2] Similar data come from recent reviews.[5,6]

The very first reports on SRS for VS used quite high dose schedules, ranging from 10 up to 25 Gy delivered in single fraction. Local control with this approach was high (90–100%) but a significant number of adverse effects were observed, first of all hearing loss.[7–10] Foote et al. treated 36 patients with acoustic neuromas with SRS using a gamma knife at a dose of 16–20 Gy to the tumour margin. No tumour progression was observed, but the 2-year actuarial rate of preservation of useful hearing was only 41.7%, and the 2-year actuarial incidence of facial or trigeminal neuropathy was 81.7%.[7] In a cohort of 29 patients treated with median marginal dose of 16 Gy, Suh et al. reported hearing deterioration in 74% of patients who had useful hearing prior to treatment and new or progressive trigeminal and facial nerve deficits with estimated 5-year incidence of 15% and 32%, respectively.[8] Kondziolka et al. reported on 162 consecutive patients treated with gamma knife to an average tumour margin dose of 16 Gy achieving 98% local control, but 49% deterioration in hearing ability after 5 years of follow-up. Normal facial function was preserved in 79% of the patients and normal trigeminal function was preserved in 73%.[10]

More recent experiences were published reporting better long term results after SRS for VS. In a retrospective analysis, a dosimetric evaluation was performed by Jacob et al. in order to identify the safe threshold for cochlear maximum tolerated dose.[11] Fifty-nine out of 105 patients treated with SRS (12–13 Gy) for VS were analyzed. A statistically significant association was found between pre-treatment hearing and marginal dose, and mean dose to the cochlear volume. However, in a multivariable model, only pre-treatment pure tone average was significantly associated with non-serviceable hearing after treatment, with serviceable hearing loss of 36% at a mean of 2.2 years after SRS. The authors suggested caution against undertreating the tumour in the distal fundus or further reducing the marginal prescription dose to achieve lower cochlear doses.

A large Italian experience was recently published by Boari et al.[12] They reported outcomes in 523 patients treated between 2001 and 2010. Gamma-knife SRS was delivered with a median margin dose of 13 Gy (range 11–15 Gy). Local control was 97.1% with 82.7% of the patients having a tumour volume downsizing after mean follow-up of 75.7 months. Treatment related complications were only a transient worsening of pre-existing symptoms. The overall rate of preservation of functional hearing at the long term follow-up was 49%.

A substantial analysis was recently published from Japan analyzing safety and effectiveness of Gamma Knife SRS after more than 10 years.[13] Three hundred forty-seven patients were treated with median tumour volume of 2.8 cc to a median marginal dose of 12.8 Gy. The actuarial 5 and ≥10 year progression-free survival rates were 93% and 92%, respectively. No patient developed treatment failure more than 10 years after treatment. The actuarial 10-year facial nerve preservation rate was 97% in the high marginal dose group (>13 Gy) and 100% in the low marginal dose group (≤13 Gy).

An interesting study was recently reported on tumour growth rate, hearing loss and quality of life of 237 patients with unilateral VS receiving either gamma knife SRS (12 Gy, 113 patients) or just observation (124 patients).[14] In this prospective study, Breivik et al. reported no significant difference in hearing preservation between the two approaches: hearing was lost in 76% of conservative management patients and 64% of SRS patients. There was a significant reduction in tumour volume over time in the SRS group. The need for treatment following initial SRS or observation differed at highly significant levels ($p < 0.001$). Development of symptoms and quality

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