

# Facial Nerve Schwannoma Treatment with Stereotactic Radiosurgery (SRS) versus Resection followed by SRS: Outcomes and a Management Protocol

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## Abstract

**Background** Stereotactic radiosurgery (SRS) and resection are treatment options for patients with facial nerve schwannomas without mass effect.

**Objective** This article evaluates outcomes of patients treated with SRS versus resection + SRS.

**Method** We retrospectively compared 43 patients treated with SRS to 12 patients treated with resection + SRS. The primary study outcome was unfavorable combined endpoint, defined as worsening or new clinical symptoms, and/or tumor radiological progression. SRS ( $38.81 \pm 5.3$ ) and resection + SRS ( $67.14 \pm 11.8$ ) groups had similar clinical follow-ups.

**Results** At the time of SRS, the tumor volumes of SRS (mean  $\pm$  standard error;  $1.83 \pm 0.35$  mL) and resection + SRS ( $2.51 \pm 0.75$  mL) groups were similar. SRS ( $12.15 \pm 0.08$  Gy) and resection + SRS ( $12.16 \pm 0.14$  Gy) groups received similar radiation doses. SRS group (42/43, 98%) had better local tumor control than the resection + SRS group (10/12, 83%,  $p = 0.04$ ). Most of SRS (32/43, 74%) and resection + SRS (10/12, 83%) group patients reached a favorable combined endpoint following

## Keywords

- ▶ facial nerve
- ▶ schwannoma
- ▶ stereotactic radiosurgery
- ▶ internal auditory canal

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SRS ( $p = 0.52$ ). Considering surgical associated side effects, only 2/10 patients of the resection + SRS group reached a favorable endpoint ( $p < 0.001$ ).

Patients of SRS group, who are  $> 34$  years old ( $p = 0.02$ ), have larger tumors ( $> 4$  mL,  $0.04$ ), internal auditory canal (IAC) segment tumor involvement ( $p = 0.01$ ) were more likely to reach an unfavorable endpoint. Resection + SRS group patients did not show such a difference.

**Conclusion** While resection is still needed for larger tumors, SRS offers better clinical and radiological outcomes compared to resection followed by SRS for facial schwannomas. Younger age, smaller tumors, and non-IAC situated tumors are factors that portend a favorable outcome.

## Introduction

The facial nerve is a mixed nerve with a complex anatomic course that can be divided into seven segments.<sup>1</sup> Other functionally important structures, such as the cochlear nucleus and the vestibular nerve, also exist in its vicinity.<sup>2</sup> Thus, it is not surprising that facial nerve pathologies and their treatments can adversely affect its function or that of other, adjacent neural structures.

Vestibular nerve schwannomas are the most common cranial nerve (CN) schwannomas, followed by trigeminal nerve and facial nerve schwannomas, respectively.<sup>3</sup> Patients with facial nerve schwannomas may present with a diverse clinical picture, making diagnosis based on imaging and clinical findings alone difficult. Due to their rarity, a well-defined management protocol for facial nerve schwannomas particularly those not requiring urgent decompressive surgery has not been fully defined. Management options include stereotactic radiosurgery (SRS), resection, and active surveillance. All three approaches have their own set of advantages and disadvantages.<sup>4</sup>

Recent studies recommended active surveillance for patients with small facial nerve schwannomas and without facial nerve deficits.<sup>5</sup> SRS has been recommended for small ( $< 1$  cm diameter) facial nerve schwannomas presenting with facial nerve dysfunction, while resection is usually favored for large ( $> 1$  cm diameter) facial nerve schwannomas with poor facial function.<sup>5</sup> Two recent, retrospective multicenter studies showed favorable results (tumor stability/regression) in patients with facial nerve schwannomas following SRS.<sup>1,5</sup>

In this study, we detail our observations on the clinical presentations of a large cohort of facial schwannoma patients. Also, we compare the cohorts treated with primary SRS versus resection + SRS.

## Methods

### Patient Population

Data of patients with facial nerve schwannomas treated with SRS between 1998 and 2020 were retrospectively collected from 11 centers participating in the International Radiosurgery Research Foundation.<sup>1</sup> All participating center received

institutional review board approval to participate in the study.

A different cohort with a distinctly different analytic approach was presented in a prior study.<sup>1</sup> Of the 63 patients included in that study, 8 patients managed with decompressive (8/55, 14.5%) surgery and/or multisession radiosurgery were excluded. In the current study, a retrospective analysis was performed on 55 patients, treated with SRS alone (43 patients) or resection followed by SRS (12 patients), either because of tumor progression or as an adjuvant. Specific analytic emphasis was placed on comparing SRS alone versus resection + SRS in this study.

Facial nerve schwannomas were differentiated from vestibular nerve schwannomas by intraoperative findings or by neurological features and radiologic characteristics.<sup>1,3</sup> Facial nerve schwannoma patients had more facial nerve function deficits along with tumor involvement of the temporal bone or extratemporal segments.<sup>3</sup> All imaging was reviewed by experienced neuroradiologists, as well as radiosurgical teams practicing at tertiary or quaternary referral centers. If there is any doubt about the diagnosis of a facial schwannoma, the patient was excluded from the study. Patients with less than 3 months of imaging or clinical follow-up were excluded from the analysis.

Clinical factors recorded included patient age, gender, preoperative signs and symptoms, facial nerve segment involvement, and tumor size. Anatomic facial nerve segments were defined as previously described.<sup>1</sup>

### Stereotactic Radiosurgery Procedure

Single-session SRS was performed using Gamma Knife (Elekta AB, Stockholm, Sweden) and the Leksell model G frame (Elekta AB).<sup>6</sup> SRS planning was performed using thin-sliced, T1 brain magnetic resonance imaging (MRI) with and without contrast. Gamma Knife radiosurgery was performed by a multidisciplinary team including a neurosurgeon, a radiation oncologist, and a radiation physicist. Treatment characteristics recorded included margin (prescription) and maximum dose, isodose line, and treatment volume.

### Follow-Up

Clinical and imaging follow-up was performed by each contributing center as per the local protocol. Typically, patients were followed at 3- to 6-month intervals for the first 1 to

2 years after SRS and then yearly thereafter. All included patients were followed with contrast-enhanced brain MRI.

Post-SRS tumor progression and regression were defined as a change in volume greater than or equal to 20%.<sup>1</sup> Clinical presentation and outcomes following SRS including facial nerve outcome, other CN function, and the occurrence of adverse radiation effects were analyzed. Facial nerve function was quantified using the House–Brackmann grading scale. Pre- and posttreatment audiograms were not routinely performed across all centers.

Adverse radiation effects were recorded and graded according to the criteria devised by the Radiation Therapy Oncology Group and the European Organization for Research and Treatment of Cancer.<sup>7</sup>

### Definition of Combined “Endpoint”

Based on the clinical and radiological outcome, a combined endpoint was defined. If any single unfavorable event (worsening or new clinical symptoms related to the tumor) or tumor growth was noted, the patient was considered to have reached an “unfavorable combined endpoint.” Patients who had tumor control/shrinkage and neurological stability or improvement were defined to have a “favorable combined endpoint.”

### Statistical Analysis

Statistics were done using SPSS (2021 version) software (IBM, Chicago, Illinois, United States). A *p*-value less than 0.05 was deemed statistically significant.

Ordinal variables were compared using chi-square analysis. The *p*-value was adjusted using the Bonferroni method. Nominal variables were compared using *t*-test.

## Results

Forty-three (43/55, 78%) patients were managed with primary SRS, while 12 (12/55, 22%) had resection initially and subsequently SRS, either due to residual tumors (8/12, 66%) or tumor recurrences (4/12, 34%).

### Patient and Tumor Characteristics

Age, gender, and mean tumor sizes of both groups are detailed in ▶Table 1 and were not statistically different between the groups. At the time of SRS, the primary SRS group and resection + SRS group had comparably sized tumors ( $1.83 \pm 0.35$  vs.  $2.51 \pm 0.75$  mL, *p* = 0.76). Preresection tumor sizes and growth rates were not recorded.

The resection + SRS (3/9, 25%) group had fewer patients with tumors involving the geniculate ganglion region relative to the SRS group (29/43, 67%, *p* = 0.01). Also, the resection + SRS group had more patients involving the cisternal location (8/12, 66%) compared to the primary SRS group (12/43, 30%, ▶Table 2, *p* = 0.01). Tumors involving the cisternal segment in the primary SRS group had larger mean tumor volume ( $3.41 \pm 0.92$  vs.  $1.36 \pm 0.23$  mL, *p* = 0.01) compared to tumors involving other segments. Most (38/55, 69%) of the patients of both groups had schwannomas involving

**Table 1** Baseline patient and tumor characteristics and SRS treatment parameters

	Primary SRS	Resection + SRS	<i>p</i> -Value
Patient number	43	12	
Sex	20 (47%) male 23 (53%) female	8 (67%) male 4 (33%) female	0.217
Mean age (SE), y	46.58 ± 2.7	53.86 ± 4.6	0.63
Mean tumor volume (SE), mL	1.83 ± 0.35	2.51 ± 0.75	0.76
SRS parameters			
Mean margin dose (SE), Gy	12.15 ± 0.08	12.16 ± 0.14	0.93
Mean maximum dose (SE), Gy	22.80 ± 0.45	23.35 ± 0.76	0.55
Mean isodose line (SE), %	54.44 ± 1.49	52.58 ± 1.54	0.53

Abbreviations: SE, standard error; SRS, Stereotactic radiosurgery.

**Table 2** Tumor location based on the involved segment(s) of the tumor

Location	Primary SRS	Resection + SRS	<i>p</i> -Value
Cisternal	12/43 (28%)	8/12 (67%)	0.01
Internal auditory canal	25/43 (58%)	10/12 (83%)	0.11
Labyrinthine	20/43 (47%)	5/12 (42%)	0.77
Geniculate	29/43 (67%)	3/12 (25%)	0.01
Tympanic	14/43 (33%)	4/12 (33%)	0.96
Mastoid	5/43 (12%)	1/12 (8%)	0.75
Extratemporal	1/43 (2%)	0/12 (0%)	0.59

Abbreviation: SRS, Stereotactic radiosurgery.

**Table 3** Preoperative presentation features for facial schwannoma patients

Preop presentation	Primary SRS	Resection + SRS	p-Value
Facial weakness	Tumor related 33/43 (77%)	Tumor related 4/12 (34%) Surgery related 7/12 (58%)	< 0.001
HBS I	10/43 (23%)	1/12 (8%)	0.185
HBS II	9/43 (21%)	4/12 (34%)	
HBS III	7/43 (16%)	2/12 (17%)	
HBS IV	10/43 (23%)	2/12 (17%)	
HBS V	5/43 (12%)	0 (0%)	
HBS VI	2/43 (5%)	3/12 (25%)	
Hearing loss	26/43 (60%)	Tumor related - 4/12 (33.3%) Prior treatment related - 4/12 (33.3%)	< 0.001
Tinnitus	11/43 (26%)	Tumor related 2/12 - (17%) Prior treatment related - 3/12 (25%)	0.03
Headache	4/43 (9%)	0/12 (0%)	0.27
Other neurological deficits	16/43 (37%)	Tumor related - 4/12 (34%) Prior treatment related - 2/12 (16%)	0.024

Abbreviations: HBS, House–Brackmann score; SRS, Stereotactic radiosurgery.

multiple segments. These schwannomas always involved the internal auditory canal (IAC), geniculate, or tympanic segment combinations.

### Initial Presentation

Both groups had similar pre-SRS clinical presentations, if only tumor-related symptoms were considered ( $p > 0.05$ ). If resection-attributed complications were included, the resection + SRS group had more patients with preexisting facial deficits ( $p < 0.001$ ), hearing loss ( $p < 0.001$ ), tinnitus ( $p = 0.03$ ), and other neurological deficits ( $p = 0.024$ , ►Table 3).

### SRS Treatment Parameters

Treatment parameters of both groups are listed in ►Table 1, and they were similar in both groups. Margin dose with an isodose line of primary SRS group were  $12.15 \pm 0.08$  Gy with  $54.44 \pm 1.49\%$  and for the resection + SRS groups were  $12.16 \pm 0.14$  Gy with  $52.58 \pm 1.54\%$  ( $p = 0.93$  and  $p = 0.53$ , respectively). Maximum doses were  $22.80 + 0.45$  Gy for SRS alone and  $23.35 + 0.76$  Gy for resection followed by SRS ( $p = 0.55$ ).

### Radiological Outcome

At a mean follow-up of  $38.81 \pm 5.3$  months, radiological tumor control was significantly higher in the primary SRS group ( $p = 0.04$ ). Specifically, tumor stability was documented in 25/43 patients (58%) in the primary SRS group and 3/12 patients (25%) in the resection + SRS group, regression in 17/43 patients (40%) in the primary SRS group and 7/12 patients (58%) in the resection + SRS group, and progression in 1/43 patients (2%) in the primary SRS group and 2/12 (17%) of patients in the resection + SRS group, respectively (►Table 3).

### Clinical Outcome

Facial weakness, hearing loss, tinnitus, and other neurological deficits showed an improvement following SRS in both

groups except for headaches in the resection + SRS group (►Table 4). In both groups, facial nerve function improved following SRS ( $p < 0.001$ ) when preop and postop states were compared. The time to improvement was similar in both groups ( $11.88 \pm 2.4$  vs.  $10.20 \pm 1.5$  months,  $p = 0.8$ ).

### Overall Combined Endpoint

At a mean follow-up of  $38.81 \pm 5.3$  months, 32/43 patients (74%) of the primary SRS group reached a favorable combined endpoint outcome. The remaining of 11 patients (26%) had an unfavorable outcome—due to clinical deterioration despite tumor stability in 5/43 patients (12%), due to worsening of existing clinical symptoms despite tumor regression in 5/43 patients (12%), and due to asymptomatic radiological tumor progression in one patient (2%).

At a similar ( $p = 0.42$ ) mean follow-up of  $67.14 \pm 11.8$  months, the resection + SRS group had 2/12 patients (17%) with treatment-related side effects. However, if prior resection-related side effects were considered, 10/12 (83%) had treatment-related effects. Out of these, 9/12 (75%) were due to resection-related adverse effects, and 2/12 (17%) was due to SRS-related adverse effects. From their new baseline following resection, 10/12 patients (83%) reached a favorable combined endpoint. Excluding resection-related side effects, combined endpoints for the two groups were not different ( $p = 0.52$ ), but they were significantly different including resection-related side effects ( $p < 0.01$ ).

### Factors Affecting Outcomes

In the primary SRS group, a favorable combined endpoint was more likely to be achieved in patients exhibiting tumor volume  $< 4$  mL ( $< 4$  mL [ $n = 36/43$ , 84%] vs.  $> 4$  mL [ $n = 7/43$ , 16%],  $p = 0.04$ ), or no IAC involvement of the tumor (17/18 [94%] vs. with IAC involvement [1/18, 6%],  $p = 0.011$ ), or age  $< 34$  years old at time of SRS (11/43, 26%) and more than 34 years old (32/43, 74%),  $p = 0.024$ .

**Table 4** Postoperative presentation features for facial schwannoma patients

Postop presentation	Primary SRS	Resection + SRS	p-Value
Facial weakness	Stable - 8/43 (19%) Improved - 13/43 (30%) Worsened - 18/43 (42%) New deficit - 4/43 (9%)	Stable - 1/12 (8%) Improved - 2/12 (17%) Worsened - 8/12 (67%) New deficit - 1/12 (8%)	0.48
HBS I	13/43 (30%)	2/12 (17%)	0.41
HBS II	11/43 (26%)	3/12 (25%)	
HBS III	8/43 (19%)	2/12 (17%)	
HBS IV	4/43 (9%)	2/12 (17%)	
HBS V	4/43 (9%)	0/12 (0%)	
HBS VI	3/43 (7%)	3/12 (25%)	
Hearing loss	No - 15/43 (35%), Improved - 6/43 (14%) Stable - 19/43 (44%) Worsened - 1/43 (2%) New - 2/43 (5%)	No - 4/12 (33%) Improved - 3/12 (25%) Stable - 5/12 (42%) Worsened - 0/12 (0%) New deficit - (0%)	0.82
Tinnitus	No - 31/43 (72%) Improved - 4/43 (9%) Stable - 7/43 (16%) New deficit - 1/43 (2%)	No - 7/12 (58%) Improved - 3/12 (25%) Stable - 2/12 (17%) Worsened - 0/12 (0%) New deficit - 0/12 (0%)	0.5
Headache	No - 38/43 (88%) Improved - 3/43 (7%) Stable - 1/43 (2%) Worsened - 1/43 (2%) New deficit - 0/12 (0%)	No - 10/12 (84%) Improved - 0/12 (0%) Stable - 1/12 (8%) Worsened - 1/12 (8%) New deficit - 0/12 (0%)	0.44
Other neurological deficits	No - 30/43 (70%) Improved - 4/43 (9%) Stable - 6/43 (14%) Worsened - 1/43 (2%) New deficit - 2/43 (5%)	No - 7/12 (58%) Improved - 2/12 (17%) Stable - 2/12 (17%) Worsened - 1/12 (8%) New deficit - 0/12 (0%)	0.7
Combined endpoint 1 excluding prior resection	Favorable - 32/43 (74%) Unfavorable - 11/43 (26%)	Favorable - 10/12 (83%) Unfavorable - 2/12 (17%)	0.520
Combined end point including prior resection	Favorable - 32/43 (74%) Unfavorable - 11/43 (26%)	Favorable - 2/12 (17%) Unfavorable - 10/12 (83%)	< 0.001
Clinical result	Stable - 21/41 (51%) Improved - 16/41 (39%) Worsened - 4/41 (10%)	Stable - 6/12 (50%) Improved - 5/12 (42%) Worsened - 1/12 (8%)	0.981
Radiology result	Stable - 25/43 (58%) Regression - 17/43 (40%) Progression - 1/43 (2%)	Stable - 3/12 (25%) Regression - 7/12 (58%) Progression - 2/12 (16%)	0.04

Abbreviations: HBS, House–Brackmann score; SRS, Stereotactic radiosurgery.

Of the 11 patients in the primary SRS group who reached an unfavorable outcome, 10/11 (90%) had IAC involvement. Out of those 10 patients with IAC involvement, 2 had worsening hearing loss, 1 had worsening facial weakness, 1 had new facial weakness, 1 developed new facial twitching, 3 developed other neurological deficits, 1 had increasing headaches, and 1 had progression of the tumor following SRS.

Nine of 12 (75%) patients in the resection + SRS group had surgery-related side effects. In 8/9 (89%), those facial schwannomas involved the IAC. Following both treatments 10/12 (83%) patients had treatment-related side effects.

**Adverse Radiation Effects**

Four patients out of 43 (9%) of the primary SRS group developed adverse radiation effects within 2 to 9 months from SRS; these included facial spasms, facial nerve palsy (1/43, 2%), twitching (1/43, 2%), hypoesthesia (1/43, 2%), and vertigo (1/43, 2%). The symptoms improved in three patients under conservative management, while one patient improved following facial nerve anastomosis surgery.

A single patient from the resection + SRS group experienced symptomatic tumor progression caused by cyst formation compressing the brainstem.

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## Discussion

Facial nerve schwannomas are rare tumors that typically demonstrate a reasonable response to SRS alone or SRS combined with prior resection.<sup>8</sup> However, if the patient presents with appreciable mass effect, resection would be the preferred option. In our study, tumor control was achieved in 98% of patients treated with SRS alone and 84% of patients managed by resection + SRS. However, the combined endpoint of clinical and radiologic stability and/or improvement was more likely to be achieved in those treated with SRS alone. In the overall cohort, schwannomas involving the cisternal segment tended to be larger than schwannomas involving other segments of the facial nerve. Our data showed that in the SRS-only group, patients with a schwannoma volume less than 4 mL or patients younger than 34 years old showed more favorable outcome following SRS. These results are comparable to those from an earlier study stating that patients with facial schwannoma of diameter less than 1 cm were more likely to show a favorable outcome following SRS.<sup>5</sup>

The IAC is the longest segment of the facial canal. It includes the vestibulocochlear nerve (CN VIII), facial nerve (CN VII), nervus intermedius, labyrinthine artery, and the vestibular ganglion. Due to the close proximity to the above-mentioned structures, an IAC-located facial schwannoma may increase the likelihood of an unfavorable outcome. In the current study, the SRS group patients with schwannomas involving the IAC segment were more likely to show an unfavorable outcome following SRS alone. Sixteen out of 19 (84%) patients who had an unfavorable outcome of both groups had tumors involving the IAC segment. Hypofractionated SRS may be an option to consider for facial schwannomas involving the IAC,<sup>9</sup> but its impact in reducing post-SRS complications warrants further study.

An earlier proposed protocol recommended active surveillance until deterioration of facial nerve function to initiate treatment.<sup>5</sup> A lower rate of side effects has been observed following SRS seems compared to other more invasive interventions.<sup>1</sup> In our series, younger patients fared better than older patients irrespective of schwannoma volume. Therefore, active surveillance should be an option to carefully consider in the presence of progressive growth and even in the absence of facial nerve function deterioration. We recommend considering younger age (< 34 years old) and smaller tumor volume (< 4 mL) as predictive factors for a favorable outcomes after SRS. However, patients with schwannomas involving the IAC should be approached with caution for SRS and even more so if resection is to be considered.

## Study Limitations

This study is limited by the retrospective nature of its design and the limited statistical power secondary to the rarity of this tumor type. Also, there were likely biases in the selection of SRS alone versus resection + SRS originating from provider and patient preferences. The two cohorts were not equally matched at baseline in terms of number of patients, patient attributes, or all tumor features.

## Conclusion

While resection for large facial schwannomas may help to alleviate mass effect and associated symptoms, SRS treatment alone provided a more favorable outcome than those treated with resection followed by SRS. Younger patients, those with tumor volumes less than 4 mL, and tumors not involving the IAC segment of the facial nerve were more likely to have favorable outcomes with SRS.

## Conflict of Interest

None declared.

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