Safety and Efficacy of Hypo Fractionated Stereotactic Radiosurgery in Facial Nerve Schwannoma: a Single Institution Retrospective Case Series

Nida Fatima (fnida99@yahoo.com)
Massachusetts General Hospital https://orcid.org/0000-0002-0976-888X

Anna La Dine
Department of Neurosurgery, House Institute, Los Angeles

Zachary R Barnard
Department of Neurosurgery, House Institute, Los Angeles

Katherine Ko
Department of Neurosurgery, House Institute, Los Angeles

Kevin Peng
Department of Otolaryngology, House Institute

William H Slattery
Department of Otolaryngology, House Institute

Gregory P Lekovic
Department of Neurosurgery, House Institute, Los Angeles

Research Article

Keywords: facial nerve, schwannoma, tumor control, stereotactic radiosurgery

Posted Date: December 15th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-1153892/v1

Abstract

Background: In the current era of modern neurosurgery, the treatment strategies have been shifted to “nerve-preservation approaches” for achieving a higher facial and hearing function preservation rate following facial nerve tumors.

Objective: We have conducted this novel report on determining the outcome of patients with facial nerve schwannomas (FNS) treated with hypo fractionated stereotactic radiosurgery (hfSRS).

Methods: Retrospective chart review of a prospectively maintained database search was conducted. Patients who underwent hfSRS CyberKnife (Accuray Inc, Sunnyvale, California., USA) for FNS were included. Outcomes consisted of tumor control, facial and hearing nerve function as graded by House-Brackmann (HB) and Gardner-Robertson scale, and adverse radiation effects. SPSS 23 was used to perform statistical analysis.

Results: With an institutional board review approval, we retrospectively identified 5 patients with FNS [4 intracranial (80%) and 1 extracranial (20%)] treated with hfSRS (2011-2019). Patients received definitive SRS in 3 patients (60.0%) wile adjuvant to surgical resection in 2 patients (40.0%). A median tumor volume of 7.5 cm^3 (range, 1.5-19.6 cm^3) received a median prescription dose of 23.2 Gy (range, 21-25 Gy) administered in median of 3 fractions (range, 3-5 session). With a median radiographic follow-up of 31.4 months (range, 13.0-71.0 months) and clinical follow-up of 32.6 months (range, 15.1-72.0 months), the local tumor control was 100.0%. At last clinical follow-up, the facial nerve function improved or remained unchanged HB I-II in 80.0% of the patients, while the hearing nerve function improved or remained stable in 100.0% (Gardner-Robertson I-II) of the patients. Temporary clinical toxicity was seen in 3 patients (60.0%) which resolved. None of the patient developed adverse radiation effect.

Conclusion: From our case series, hfSRS in FNS seems to be safe and efficacious in terms of local tumor control, and improved facial and hearing nerve function.

Introduction:

The treatment strategy for facial nerve schwannomas (FNS) has evolved from microsurgical resection to facial nerve preservation approaches [1]. However, the standard management in terms of weighting the normal or near-normal facial nerve function [House-Brackmann (HB) I-II] over tumor size is still controversial [2]. Stereotactic radiosurgery (SRS) is now considered as a safe and alternative treatment to surgery with excellent tumor control and very low risk of treatment associated facial nerve morbidity [3–5]. Although the studies have established the role of hypo fractionated SRS (hfSRS) on vestibular schwannoma [6], there are has not been previously reported safety and efficacy of hfSRS on intra- and/or extracranial FNS. Given that the FNS constitutes 0.15%-0.8% of all intracranial tumors, it is understandable that very few institutions have large treatment series with respect to SRS [7].

This study determined the impact of hfSRS on facial nerve and hearing function outcomes of intra and extra-cranial FNS. We have conducted this research in order to better inform future-treatment, physician decision making options and patient counselling when discussing about the SRS as treatment options.

Patients And Methods:

Patient Demographics:

The charts of all the patients who were treated with hfSRS were retrospectively reviewed between 2011-2019 in accordance with the institutional IRS policies. Patients were included if they had a histological or radiologically diagnosed FNS and hfSRS was provided as a definitive treatment. In total, 5 patients with facial nerve schwannoma had evaluable imaging follow-up, 2 were females (40.0%). The median age was 41.0 years (range, 37-60 years). Baseline characteristics are described in Table 1.

Table 1
Baseline Characteristics of the Patients

Parameter	N (%)
Gender	
Male	3 (60.0)
Female	2 (40.0)
Age, median (range) years	41.0 (37-60)
Prior surgery	2 (40.0)
Tumor Volume, median (range) cm^3	7.5 (1.5-19.6)
Prescription dose, median (range) Gy	23.2 (21-25)
Isodose, median (range) %	81.0 (80.0-82.0)
Follow-up, median (range) months	
Radiological	31.4 (13.0-71.0)
Clinic	32.6 (15.1-72.0)

The indication of hfSRS was definitive treatment in 3 patients (60.0%), while adjuvant to surgical resection in 2 patients (40.0%). None of the patients had prior irradiation. 2 patients (40.0%) presented initially with hemifacial spasm, 1 patient (20.0%) with facial mass, and 2 patients (40.0%) had progression of tumor on their CT-scan or MRI following surgery. The clinical and radiographic characteristics of the patients are included in Table 2.

Table 2

Overview of the included patients

Pt	Age (years)	Gender	Prior Treatment	Tumor Volume cc	Prescription Dose (Gy)	No. fractions (n)	Isodose %	Facial Nerve Segments Involved	Pre-op HB	HB at last follow up	Pre-tx hearing status (PTA/SDS)	Post tx hearing status
1	45	M	N	7.5	22.5	3	80%	CPA/IAC/GEN	1/6	2/6	78dB/ DNT	DNT
2	41	F	N	8.38	25	5	81%	IAC/GEN	2/6	1/6	46dB/ 68%	60dB/ 96%
3	37	M	N	19.6	25	5	82%	GEN/MAST/EXTRA	1/6	1/6	20dB/ 100%	DNT
4	41	F	Y (s/p MFC for AN 2000)	4.8	22.5	3	80%	IAC/GEN	2/6	2/6	deaf (NF2)	deaf (NF2)
5	60	M	Y (s/p MFC decompression 2012)	1.5	21	3	81%	CPA/IAC	1/6	1/6	25dB/96%	DNT

M=Male, F= Female, N= No, Y= Yes, MFC: Middle Fossa Craniotomy, s/p: status post operative, CPA: cerebellopontine angle, IAC: Internal auditory meatus, Gen: geniculate ganglion, MAST: Mastoid, EXTRA: extracranial, HB: House-Brackman, DNT: Didn't evaluate, PTA: Pure Tone Average, SDS: Speech Discrimination Score.

Following anatomical facial nerve segments were involved: (i) labyrinthine segment-internal auditory canal (IAC) to geniculate ganglion (n=3), meatal segment (n=1), and geniculate ganglion to extratemporal segment (n=1).

The median pre-operative HB among the patients was 1 (range, 1-2). The preoperative hearing status consisted of median pure tone average of 35.5 dB (range, 20.0-78 dB) and speech discrimination of 96.0% (range, 68.0-100.0%).

SRS Planning and Characteristic:

SRS planning and treatments were delivered with CyberKnife robotic radiosurgery system (Accuray Inc, Sunnyvale, California., USA). The median SRS target volume was 7.5 cm^3 (range, 1.5-19.6 cm^3). The median prescription dose was 23.2 Gy (range, 21-25 Gy) administered in a median of 3 fractions (range, 3-5 session). The most common dose/fractionation schemes were median of 25 Gy in 5 fraction, 22.5 Gy in 3 fractions. The median isodose line was 81.0% (range, 80.0-82.0%) with a median coverage of 98.9% (range, 98.5-99.9%). (Figure 1 and 2)

Clinical and Radiological Outcome Assessment:

After receiving SRS, patients were evaluated for 6-month and 1-year interval and annually thereafter. The patient's postoperative neurological status (unchanged, improved or worsened) and radiographic tumor control were compared with their baseline status prior to SRS treatment. The House-Brackmann Classification was used for grading facial nerve outcome and Gardner-Robertson Hearing scale was used for grading VIII nerve.

If image-defined adverse radiation effect (ARE) were seen, clinical symptoms were graded according to Common Terminology Criteria for Adverse Events (CTCAE) as Grade1=asymptomatic, Grade 2=steroids, Grade 3=hospitalization or need for bevacizumab, Grade 4=surgery, and Grade 5= death.

Statistical Analysis:

Categorical variables were evaluated through frequencies and percentages, median and range were used for continuous variables.

Results:

Tumor Control:

The median radiological follow-up was 31.4.0 months (range, 13.0-71.0 months). The crude incidence of local tumor control was 100.0%, with tumor size unchanged in 3 patients (60.0%) and regression in tumor size in 2 patients (40.0%).

Clinical Outcome and Toxicity:

The median clinical follow-up for our study was 32.6 months (range, 15.1-72 months). At last follow-up, the postoperative HB grade remained unchanged or improved (HB grade I-II) in 4 patients (80.0%), while it worsened by 1-grade (HB Grade II) in 1 patient (20.0%). The patient in which HB grade was worsened had initial degradation of HB grade from 1 to 5 within first 8 months following SRS, and then improved to Grade 2 at last follow up of 71 months. The postoperative SDS and PTA improved (Gardener-Robertson grade I-II) among all the patients (80.0%), except in 1 patient (20.0%) which remained unchanged.

Following SRS 3 patients had temporary clinical toxicity symptoms 3 months to 12 months after SRS which resolved over the ensuing 6 weeks which included: 1 patient had facial nerve weakness of 5/6 which improve to 2/5 within a week, 1-patient had moderate ear pain which improved with gabapentin in a few days, and 1-patient had diplopia due to VI nerve paresis which improved with resolved on its own. None of the patients had ARE.

Discussion:

FNS treatment is challenging due to critical function of the parent nerve as well as the morbidity associated with the growth and mass effect on the surrounding neurovascular structure. The incidence of FNS is 3.0% of all cerebellopontine angle schwannomas [8], therefore the outcome of these tumors remain uncertain due to infrequency. The current case series is the first study reporting the facial nerve and hearing function outcome after hfSRS for patients with FNS. This study is conducted for better decision making among the patients with this rare tumor. Based on the findings of our series, hfSRS significantly benefit more patients in terms of preservation and/or improvement of facial nerve and hearing function outcome. These findings will help the physician and patients alike in understanding the risks and benefits of hfSRS for treatment of FNS.

The treatment of FNSs is difficult because the surgical options are limited. Usually, the surgery is offered when the patient becomes symptomatic, typically as facial nerve paralysis. With respect to surgery, the options are limited to FN decompression or debulking versus resection and FN graft. Total surgical resection with graft is typically performed when patients are HB grade III or worse. Subtotal resections have been described with variable clinical outcomes. Limited surgical options create opportunity for SRS as a treatment modality for FNS [9].

hfSRS has proven to have comparable outcomes with respect to tumor control while also lowering the risk of collateral damage to surrounding tissue as that of SRS [10,11]. In our study, hfSRS has demonstrated its safety and efficacy in terms of preservation of nerve function and perifocal critical tissue. Based on our findings, hfSRS appears to be significantly associated with stable to improved facial and hearing nerve function outcome with no complications. This is however, in contrast to the previous studies with vestibular schwannoma in which the authors did not detect significant difference between SRS and hfSRS [12].

Preoperative facial nerve function is also an important determinant in decision-making in FNS, hence surgeons recommend observation to patients with minimal degradation in facial function; SRS for moderate reduction in facial function; and surgery with or without grafting for poor facial nerve function (HB IV or worse) or for significant mass effect [13–15]. Studies have suggested that with a treatment goal of preventing the tumor growth while preserving function of facial nerve in FNS, surgery poses a higher risk of facial palsy compared to SRS for facial nerve function [16]. Further, multi-institutional studies have demonstrated that SRS can result in durable tumor control 87.2–92% and facial nerve functional preservation of approximately 90–94% [17–19]. No study to date has assessed the relationship of hfSRS to radiological and functional outcome in FNS.

Given the low estimated tumor recurrence rate and significant nerve preservation, we do consider that hfSRS might be a better option for FNS. The data suggest that hfSRS should be considered among the primary treatment options for large or growing FNS associated with some degree of facial nerve function. This study would be beneficial in terms of comparing the risk profiles between different treatment options when counselling patients with FNS. Therefore, hfSRS confers the highest incidence of facial and hearing nerve function, with excellent local tumor control and very low incidence of complications. Our current study would support consideration of hfSRS as the predominant first line treatment therapy for FNS, in hope of reducing the incidence of patients developing more severe clinical symptoms or sufficient tumor growth that mandates microsurgical resection.

Our study has a few limitations, which include (i) retrospective report, (ii) small cohort size and statistical power, however it is difficult to ascertain the safety and efficacy of novel treatment in a huge cohort initially. Therefore, our study would guide in the treatment strategy for FNS worldwide, (iii) although HB grading and Gardner Robertson scale are standardized metric, still there can be inconsistencies inn an inter-rater reliability, and (iv) short follow up of 31.4 months. Further prospective studies using hfSRS on large cohort of FNS are needed.

Conclusion:

In this study, we have demonstrated the safety and efficacy of hfSRS on FNS in terms of local tumor control, and improved facial and hearing nerve function. The results suggest that hfSRS should be considered as a front-line option in patients with FNS in order to preserve their facial and hearing nerve function. Further prospective studies should be conducted to investigate the impact of this treatment in large cohort of patients with FNS.

Abbreviations:

hfSRS: hypo fractionated stereotactic radiosurgery, HB: House-Brackmann, FNS: facial nerve schwannoma, SRS: Stereotactic radiosurgery

Declarations:

Acknowledgments: None

Funding: None.

Conflict of interest/Competing Interest: None

Ethics Approval: IRB Approved House Institute

Availability of data and material: All data generated or analyzed during this study are included in this published article

Consent to Participate: Not Applicable

Consent to Publish: Not Applicable

References:

1. Minovi A, Vosschulte R, Hofmann E, Draf W, Bockmühl U. Facial nerve neuroma: surgical concept and functional results. *Skull Base*. 2004;14(4):195-200; discussion 200-201. doi:10.1055/s-2004-860948
2. Chen MC, Tseng TM, Hung SH, Chen PY. Facial nerve schwannoma: A case report and review of the literature. *Oncology Letters*. 2014;8(6):2787-2789. doi:10.3892/ol.2014.2550
3. Moon JH, Chang WS, Jung HH, Lee KS, Park YG, Chang JH. Gamma Knife surgery for facial nerve schwannomas: Clinical article. *JNS*. 2014;121(Suppl_2):116-122. doi:10.3171/2014.8.GKS141504
4. Litre CF, Gourg GP, Tamura M, et al. Gamma Knife Surgery for Facial Nerve Schwannomas. *Neurosurgery*. 2007;60(5):853-859. doi:10.1227/01.NEU.0000249282.46514.DA
5. Fezeu F, Lee CC, Dodson BK, et al. Stereotactic radiosurgery for facial nerve schwannomas: A preliminary assessment and review of the literature. *British Journal of Neurosurgery*. 2015;29(2):213-218. doi:10.3109/02688697.2014.976173
6. Morimoto M, Yoshioka Y, Kotsuma T, et al. Hypofractionated Stereotactic Radiation Therapy in Three to Five Fractions for Vestibular Schwannoma. *Japanese Journal of Clinical Oncology*. 2013;43(8):805-812. doi:10.1093/jjco/hyt082
7. Saito H, Baxter A. Undiagnosed Intratemporal Facial Nerve Neurilemomas. *Archives of Otolaryngology - Head and Neck Surgery*. 1972;95(5):415-419. doi:10.1001/archotol.1972.00770080651004
8. Liu R, Fagan P. Facial Nerve Schwannoma: Surgical Excision versus Conservative Management. *Ann Otol Rhinol Laryngol*. 2001;110(11):1025-1029. doi:10.1177/000348940111001106
9. McRackan TR, Wilkinson EP, Brackmann DE, Slattery WH. Stereotactic Radiosurgery for Facial Nerve Schwannomas: Meta-analysis and Clinical Review. *Otology & Neurotology*. 2015;36(3):393-398. doi:10.1097/MAO.0000000000000708
10. Nguyen T, Duong C, Sheppard JP, et al. Hypo-fractionated stereotactic radiotherapy of five fractions with linear accelerator for vestibular schwannomas: A systematic review and meta-analysis. *Clinical Neurology and Neurosurgery*. 2018;166:116-123. doi:10.1016/j.clineuro.2018.01.005
11. Fatima N, Meola A, Ding VY, et al. The Stanford stereotactic radiosurgery experience on 7000 patients over 2 decades (1999–2018): looking far beyond the scalpel. *Journal of Neurosurgery*. Published online April 2021:1-17. doi:10.3171/2020.9.JNS201484
12. Söderlund Diaz L, Hallqvist A. LINAC-based stereotactic radiosurgery versus hypofractionated stereotactic radiotherapy delivered in 3 or 5 fractions for vestibular schwannomas: comparative assessment from a single institution. *J Neurooncol*. 2020;147(2):351-359. doi:10.1007/s11060-020-03423-w
13. Rotter J, Lu VM, Graffeo CS, et al. Surgery versus radiosurgery for facial nerve schwannoma: a systematic review and meta-analysis of facial nerve function, postoperative complications, and progression. *Journal of Neurosurgery*. Published online October 2020:1-12. doi:10.3171/2020.6.JNS201548
14. Wilkinson EP, Hoa M, Slattery WH, et al. Evolution in the management of facial nerve schwannoma. *The Laryngoscope*. 2011;121(10):2065-2074. doi:10.1002/lary.22141
15. McRackan TR, Rivas A, Wanna GB, et al. Facial Nerve Outcomes in Facial Nerve Schwannomas. *Otology & Neurotology*. 2012;33(1):78-82. doi:10.1097/MAO.0b013e31823c8ef1
16. Bartindale M, Heiferman J, Joyce C, Anderson D, Leonetti J. Facial Schwannoma Management Outcomes: A Systematic Review of the Literature. *Otolaryngol Head Neck Surg*. 2020;163(2):293-301. doi:10.1177/0194599820913639
17. Mehta GU, Lekovic GP, Slattery WH, et al. Effect of Anatomic Segment Involvement on Stereotactic Radiosurgery for Facial Nerve Schwannomas: An International Multicenter Cohort Study. *Neurosurgery*. 2020;88(1):E91-E98. doi:10.1093/neuros/nyaa313
18. Kondziolka D, Lunsford LD, McLaughlin MR, Flickinger JC. Long-Term Outcomes after Radiosurgery for Acoustic Neuromas. *N Engl J Med*. 1998;339(20):1426-1433. doi:10.1056/NEJM199811123392003
19. Kress B, Griesbeck F, Stippich C, Bähren W, Sartor K. Bell Palsy: Quantitative Analysis of MR Imaging Data as a Method of Predicting Outcome. *Radiology*. 2004;230(2):504-509. doi:10.1148/radiol.2302021353

Figures

Figure 1

CyberKnife radio surgical planning for a hyo fractionated treatment for a large geniculate ganglion facial nerve schwannoma extending extracranially. The plan is displayed on the axial (A) and coronal (B) planes. A 37-year-old man was treated for a large (19.6 cm3) right facial nerve schwannoma (red contour) with a marginal dose of 25 Gy, delivered to the 82% isodose line (green contour) in 5 sessions.

Figure 2

CyberKnife radio surgical planning for a hyo fractionated treatment for an internal auditory canal geniculate ganglion facial nerve schwannoma. The plan is displayed on the axial (A) and coronal (B) planes. A 41-year-old man was treated for a 4.8 cm3 right facial nerve schwannoma (red contour) with a marginal dose of 22.5 Gy, delivered to the 80% isodose line (green contour) in 3 sessions.