Fractionated Stereotactic Radiotherapy for Facial Nerve Schwannomas

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Abstract

Purpose Data on the clinical course of irradiated facial nerve schwannomas (FNS) are lacking. We evaluated fractionated stereotactic radiotherapy (FSRT) for FNS.

Methods Eight consecutive patients with FNS treated at our institution between 1998 and 2011 were included. Patients were treated with FSRT to a median dose of 50.4 Gy (range: 46.8–54 Gy) in 1.8 or 2.0 Gy fractions. We report the radiographic response, symptom control, and toxicity associated with FSRT for FNS.

Results The median follow-up time was 43 months (range: 10–75 months). All patients presented with symptoms including pain, tinnitus, facial asymmetry, diplopia, and hearing loss. The median tumor volume was 1.57 cc. On the most recent follow-up imaging, five patients were noted to have stable tumor size; three patients had a net reduction in tumor volume. Additionally, six patients had improvement in clinical symptoms, one patient had stable clinical findings, and one patient had worsened House-Brackmann grade due to cystic degeneration.

Conclusion FSRT treatment of FNS results in excellent control of growth and symptoms with a small rate of radiation toxicity. Given the importance of maintaining facial nerve function, FSRT could be considered as a primary management modality for enlarging or symptomatic FNS.

Keywords

- stereotactic radiotherapy
- facial nerve schwannoma

Introduction

Facial nerve schwannomas (FNS) are benign slow-growing tumors arising from Schwann cells surrounding the seventh cranial nerve (facial nerve). Even though they can involve any

segment of the nerve, they tend to occur most frequently in the perigeniculate area, tympanic segment, or mastoid segments.¹ Variations exist, and so-called skip lesions, or involvement of multiple segments, have been described. Reported symptoms are numerous but frequently depend

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on the size and location of the tumor. Facial weakness, tinnitus, hearing loss, pain, and vestibular symptoms are typically evident on diagnosis.² The House-Brackmann (H-B) scale has been widely used as an objective tool to quantify the degree of facial nerve dysfunction.

Surgical excision with nerve grafting was traditionally considered the primary treatment.³ This approach was notable for a period of ipsilateral facial palsy with gradual partial improvement in function. The level of recovery observed was often no better than H-B grade III (moderate dysfunction). In some cases partial removal with the goal of peeling or “stripping” tumoral cells off the functional nerve was advocated.⁴ Even with this approach, a significant potential for worsened facial function was witnessed.

Observation is normally recommended for patients with preserved facial function.⁵ It is not uncommon for tumors to be followed for several years without intervention. Growing tumors may be managed with bony decompression or surgical resection with or without adjuvant radiation depending on the status of hearing or facial function.³

Recently, stereotactic radiosurgery (SRS) has been advocated for the treatment of FNS. SRS has already been shown to be an effective therapeutic modality for patients with vestibular schwannomas.⁶ However, data on the clinical course of irradiated FNS is lacking, and long-term follow-up studies are few. Available retrospective studies suggest good tumor control with preservation of facial nerve function,^{7–9} although the incidence and potential risk of morbidity has been difficult to ascertain. In this article, we hypothesize fractionated stereotactic radiotherapy (FSRT) for FNS would result in similar reported clinical outcomes as SRS with minimal associated toxicity.

Materials and Methods

Patients

After obtaining institutional review board approval, we identified eight consecutive patients with FNS treated with fractionated radiotherapy at Thomas Jefferson University Hospitals between 1998 and 2011. Medical records for these patients were reviewed including in-patient hospital notes, magnetic resonance imaging (MRI) scans, radiation treatment records, and follow-up notes. The tumor was determined to be FNS by radiographic characteristics based on typical findings of pathologic enhancement and enlargement along the labyrinthine segment of the facial nerve and geniculate ganglion as well as the cerebellopontine angle (CPA) component. The tumor was noted to arise from the facial nerve at the time of surgery in one patient whose preoperative diagnosis was vestibular schwannoma.

Radiation Treatment

All the patients were evaluated and discussed by a multidisciplinary tumor board consisting of neurosurgeons, radiation oncologists, neuroradiologists, neuro-oncologists, and pathologists. FSRT was recommended for patients with normal or good facial nerve function, with the goal of preservation. All patients were treated on a Varian (Palo Alto, California, United

States)/Brainlab Novalis (Feldkirchen, Germany) stereotactic system, including Brainlab masks for immobilization, dynamic arc plans with Brainlab iPlan treatment planning system, and daily ExacTrac Image Guidance. The patients were treated with FSRT to a median dose of 50.4 Gy (range: 46.8–54 Gy) in 1.8- or 2.0-Gy fractions (►Fig. 1).

Toxicity Evaluation and Follow-Up

Patients were initially seen in follow-up 3 months after treatment. Patients were then followed yearly with detailed clinical examination and MRIs for a scheduled period of 10 years. At 10 years, if there was no sign of progression or treatment failure, patients followed up on an as-needed basis only. Tumor control was defined as stable or decreased tumor size on MRIs. Treatment failure was defined as sustained tumor growth on two consecutive follow-up MRIs. Acute toxicity was defined as any event within 3 months from the initiation of FSRT. Nonacute symptomatology was defined as events beyond 3 months. Toxicity was quantified via usage of the Common Terminology Criteria for Adverse Events v.4.0. Trigeminal nerve function was assessed according to the patient's perception of pain and sensation (normal, decreased, or lack of) and by corneal reflex. If no deficit was observed on examination, but the patient subjectively reported one, this was included as a cranial nerve neuropathy. Facial strength and nerve function was assessed according to the H-B grading system.

Results

►Table 1 lists patients and tumor characteristics. The median age of patients at the time of diagnosis was 39 years (range: 19–68 years). There were two men and six women. None of the patients had a prior history of radiation treatment. One patient underwent a suboccipital craniectomy for treatment of a CPA lesion. Intraoperatively it was discovered to arise from the facial nerve. Partial debulking of the tumor was undertaken to preserve nerve function. The remainder of the cohort did not undergo any surgical intervention. All patients except one presented with facial nerve symptoms including weakness, pain, twitching, or diplopia. Five patients presented with symptoms of hearing loss and tinnitus. At the time of radiation treatment, H-B facial function grades were grade I ($n = 2$), grade II ($n = 2$), grade III ($n = 2$), and grade IV ($n = 2$). In one of the patients with H-B grade I, the lesion was localized to the parotid gland. The median tumor volume was 1.57 cc, although three of the tumors had volumes < 1 cc, and one was 12.38 cc.

Efficacy and Toxicity

The median clinical follow-up time was 43 months (range: 10–75 months). On the most recent follow-up imaging, five patients were noted to have stable tumor size; three patients had a net reduction in tumor volume (►Table 2). For the patients who had regression, the respective reductions in volumes were 30%, 70%, and 10%, respectively. Additionally, six patients had improvement in clinical symptoms, one patient had stable clinical findings, and one patient had a

Fig. 1 Sample radiation plan for a patient with facial nerve schwannoma.

Table 1 Pretreatment summary of patient characteristics

Patient no.	Age (sex)	Location	Presenting symptoms	Resection	Hearing impairment	H-B grade before FSRT	KPS score
1	30 (F)	L ear canal	Facial pain, tinnitus	No	Yes	IV	90
2	37 (F)	L temporal with involvement of geniculate ganglion	Diplopia, facial asymmetry	No	No	II	80
3	53 (F)	L CPA	Tinnitus, ear fullness	No	Yes	III	80
4	41 (M)	L 7th nerve	Tinnitus	Partial debulking	Yes	I	90
5	19 (M)	L 7th nerve	Facial pain	No	No	I	90
6	23 (F)	Distal L IAC, with involvement of geniculate ganglion	Facial asymmetry	No	No	IV	90
7	46 (F)	L petrous apex, genu of facial nerve	Ear fullness, facial weakness	No	Yes	II	90
8	68 (F)	L IAC, extending to geniculate region, tympanic segment of VII	Facial spasms and weakness, imbalance	No	Yes	III	50

Abbreviations: CPA, cerebellopontine angle; F, female; FSRT, fractionated stereotactic radiotherapy; HB, House-Brackmann; IAC, internal auditory canal; KPS, Karnofsky Performance Status; L, left; M, male.

Table 2 Results following treatment with fractionated stereotactic radiotherapy

Patient no.	Dose per fraction/Total dose, Gy	Tumor volume, cc	Facial function before/after	Hearing	Size on follow-up	Total follow-up time, mo
1	1.8/52.2	4.17	IV/II	Mild improvement	Stable	10
2	1.8/50.4	1.17	II/IIsubjective improvement	Stable	Markedly decreased/Diminished	75
3	2/54	0.51	IV/I	Stable	Stable	50
4	1.8/46.8	0.56	I/I	Stable	Stable	12
5	2/50	12.38	I/I	Stable	Decreased	51
6	1.8/50.4	1.96	IV/II	Stable	Decrease	51
7	1.8/50.4	4.098	II/VI	Worsened	Increased	36
8	1.8/50.4	0.246	III/II	Mild improvement	Stable	21

worsened H-B grade. One patient developed acute worsening of facial nerve palsy within 2 months of completing treatment, with improvement of symptoms at 10-month follow-up. There was no grade II or high acute or late toxicities.

Discussion

Facial schwannomas are rare benign tumors. They have been associated with neurofibromatosis, but unlike vestibular schwannomas, no genetic locus has been identified in afflicted individuals.¹⁰ Location, rather than size, generally dictates their clinical presentation. Interestingly, Lipkin et al noted no correlation between tumor size and clinical symptoms.² Rather, intracranial and intratemporal lesions tended to present with worse clinical manifestations than extracranial ones.¹¹

The most common symptom noted at diagnosis, in the literature as well as our patient population, was facial weakness and hearing loss. Facial weakness may present acutely, gradually, or even with a fluctuating course. Associated spasms are frequently seen secondary to irritation of motor fibers. Hearing loss may be conductive (e.g., secondary to mass effect within the middle/external auditory canal or ossicular erosion) or sensorineural (e.g., secondary to cochlear erosion or compression of the cochlear nerve). Other symptoms like otalgia and otorrhea are not unusual and can occur if the tumor is within the middle or external ear canal. Xerophthalmia and dysgeusia may occur if fibers of the chorda tympani are affected. Similarly, hyperacusis can occur if there is stapedius fibers involvement.

Recently, several authors have explored the role of SRS as a safe and efficient alternative to microsurgery (►Table 3). Mabanta et al⁸ reported no decrement of facial motor function in two patients treated with linear accelerator-based radiosurgery. In a separate report, Hasegawa et al¹² reported stabilization in tumor size and improvement of facial function in one of two patients who underwent gamma knife radio-

surgery. A case report by Isono et al documented combined surgery and gamma knife radiosurgery for residual tumor to a marginal dose of 12 Gy. They noted improvement in facial spasms 14 months posttreatment; however, facial weakness remained unchanged.¹³

Several larger case studies have also noted stabilization or improvement in facial function after SRS (►Table 3).^{7,9,14–16} In the largest published series, Kida et al studied 14 subjects for a mean follow-up time of 31.4 months and noted tumor response and control rates of 57% and 100%, respectively.⁷ One patient was noted to develop worsening facial function with subsequent recovery to H-B grade III. Other groups have reported similar findings. Cumulatively, of the 45 patients reported in the literature, local control was achieved in all individuals with 44 experiencing stable or improved facial function.

Fewer studies exist examining the use of FSRT for FNS. In the past, FSRT paradigms were used in patients with vestibular schwannomas. Comparable local control rates were observed versus SRS, with improved rates of hearing and cranial nerve preservation.^{17,18} Because FNS are histologically similar to vestibular schwannomas, it follows that similar results could be extrapolated.

From a radiobiological standpoint, there appears to be an intuitive value to fractionation (i.e., limiting damage to normal structures with smaller treatment doses while potentially allowing for repair between fractions). Data regarding outcomes are still limited, however. A secondary pitfall is the higher total dose of radiation delivered to the area of interest compared with a single fraction (to match equivalent radiobiological dosing).

Hillman et al¹⁹ followed a patient with FNS 3 years after delivery of 25 Gy in 5 fractions. Stable H-B grade and tumor size were noted. Progressive hearing loss, however, was seen on the same side as the tumor. In a larger study from Japan of patients with nonacoustic intracranial schwannomas (NACNS) undergoing FSR (a dose of 50 Gy delivered in 25

Table 3 Review of available literature

Study	No. of patients	Marginal dose, Gy	Tumor size	Facial function	Mean follow-up, mo
Mabanta et al ⁸	2	10–15		2 stable	32
Hasegawa et al ¹²	2	12.6	1 decreased, 1 stable	1 improved, 1 stable	42
Isono et al ¹³	1	12	Decreased	Stable	14
Kida et al ⁷	14	11–16	8 decreased, 6 stable	5 improved, 8 unchanged, 1 worse	31.4
Madhok et al ⁹	6	12–12.5	3 decreased, 3 stable	1 improved, 5 unchanged	46.6
Litre et al ¹⁴	11	10–16	4 decreased, 6 stable	3 improved, 8 unchanged	39
Hillman et al ¹⁹	2	12 FSRT: 25/Fx 5	2 stable	1 improved, 1 unchanged	30
Nishioka et al ¹⁵	4	50 Gy/Fx 2	2 decreased, 2 stable	4 unchanged	67.3
Showalter et al ¹⁶	5	FSRT: 45–54/Fx 1.8–2			28 (median)
Current study	8	FSRT: 46.8–52.2/ Fx 1.8–2	5 stable, 3 decreased	6 improved, 1 unchanged, 1 worsened	38.3

Abbreviations: FSRT, fractionated stereotactic radiotherapy; Fx, dose per fraction.

fractions), 50% of patients noted subjective improvement in facial symptoms, and 50% also experienced regression in tumor size. None of the patients had worsening of their preexisting neurologic symptoms.¹⁵ In yet another case series of patients with NACNS, Showalter et al followed five patients with FNS (after median dose of 50.4 Gy in 1.8- to 2-Gy fractions) and reported 100% tumor control rates and no new cranial nerve deficits.¹⁶

Favorable results were seen in our current case series, save for one patient who experienced delayed progression of symptoms 1 year past treatment. Initially the patient reported subjective improvement in facial functioning 3 and 6 months posttreatment. What factors contributed to her clinical deterioration thereafter is unclear. Patient characteristics are summarized in ► **Tables 1 and 2.**

In this study, we demonstrate that FSRT appears efficacious in the treatment and management of FNS with good tumor control rates. Although radiosurgery is limited to small tumor volumes, FSRT is capable of treating large tumors with minimal risk of late morbidity. Long-term follow-up of FSRT for schwannomas in the similar locations showed a very favorable toxicity profile.^{20–22} Furthermore, FSRT combines the precision of radiosurgery with the potential radiobiological advantage of less normal tissue injury. In this article we present eight additional patients who underwent FSRT for FNS. We show that treatment was generally well tolerated, suggesting that FSRT may be an effective noninvasive alter-

native for patients at higher risk for microsurgery or with residual/recurrent tumors.

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