Chapter 6
Vestibular Schwannoma

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Stereotactic radiosurgery and conventionally fractionated radiotherapy have well-established track records with high local control rates and robust long-term follow-up data; recent studies utilizing FSRT in patients with large tumors or those abutting critical OARs have emerged. This chapter summarizes hypofractionated radiotherapy techniques, including SRS and FSRT, for vestibular schwannomas.

6.1 Pearls

- Incidence is estimated at 0.6–0.8 per 100,000 person-years and is increasing over time.
- Increased incidence is due (at least in part) to incidental diagnosis in asymptomatic patients in the setting of widespread MRI and CT imaging—as vestibular schwannomas are identified on 0.2% of MRIs in asymptomatic patients.
- Comprise 8% of adult intracranial tumors, 80–90% arise within the cerebellopontine angle, with more than 90% being sporadic and unilateral.
- The median age of diagnosis is 50 years; rare in children with the exception of patients with NF2.
- Both sporadic and NF2-associated vestibular schwannomas are routinely associated with biallelic inactivating mutations of the tumor-suppressor gene *NF2* (located on 22q12).

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  - Bilateral vestibular schwannomas are pathognomonic for NF2 and patients with NF2 commonly manifest symptoms by 20–30 years of age.

- For sporadic lesions, the estimated average growth rate is 1–2 mm per year, while for NF2-associated lesions it is 3 mm per year.
- The cystic schwannoma subtype displays a more aggressive growth pattern, but malignant transformation is rare.
- When tumors are symptomatic, the most common symptoms include hearing loss (95% objective, 66% subjective; usually gradual in tempo—but a subset present with sudden hearing loss), tinnitus (63%), imbalance or vertigo (61%, generally mild-to-moderate unsteadiness with ambulation, tilting, or veering, with true spinning vertigo unusual), facial paresthesias or pain (17%, typical onset more than 2 years since presence of hearing loss), facial paresis or taste disturbance (6%), and less commonly cerebellar symptoms or lower cranial nerve deficits.
- Local anatomy:
  - The cerebellopontine angle is bounded by the temporal bone laterally, the brainstem medially, the cerebellum superiorly and posteriorly, and the inferior cranial nerves inferiorly (CN IX-XI).

    Additional structures within the cerebellopontine angle include CN VII and the anterior inferior cerebellar artery.

  - The vestibular and cochlear nerve roots arise from the vestibular and cochlear apparatus, respectively, which together form the vestibulocochlear nerve, which travels through the internal auditory canal to the cerebellopontine angle.
  - The majorities of vestibular schwannomas arise within the internal auditory canal from the superior or inferior branches of the vestibular nerve, and rarely arise from the cochlear nerve.
  - The natural history is characterized by progressive growth within the internal auditory canal, extending to the cerebellopontine angle with associated compression of nearby cranial nerves—most notably the facial and trigeminal nerves—as well as the brainstem.

- Medical workup:
  - History and physical, including assessment of performance status, with emphasis on preceding neurological symptoms (e.g., hearing loss, tinnitus, imbalance, facial paresthesias, or weakness) and thorough neurologic examination including detailed examination of cranial nerves, balance, and ambulation.

    Weber and Rinne testing may suggest asymmetric sensorineural hearing loss. Romberg and Hall-Pike maneuvers are typically normal.

  - Audiometry: Initial screening test of choice, as 95% of patients will have an abnormal test, most commonly revealing asymmetric sensorineural hearing

loss, preferentially at higher frequencies with impaired speech discrimination scores out of proportion to the degree of hearing loss.
  - Vestibular testing: Not commonly performed as a screening modality given decreased sensitivity, but may show decreased or absent caloric response on the involved side.
  - Brainstem-evoked response audiometry is less commonly performed.

- Imaging workup:
  - CT: Appear as a well-defined isodense, contrast-enhancing mass within the internal auditory canal with variable extension into the cerebellopontine angle, and rarely harbor calcifications (as opposed to meningiomas).
  - MRI: Gold standard imaging modality; typically appear iso- or hypointense to the pons on T1-weighted images, heterogeneously hyperintense on T2-weighted images, and strongly and homogenously contrast enhancing.

    Purely intracanalicular vestibular schwannomas are usually round or oval in shape, while those extending into the cistern have a spherical extra-internal auditory canal component with a taillike taper into the internal auditory canal.

    Post-contrast T1-weighted images with thin (1 mm) sectioning through the internal auditory canal are ideal. High-resolution constructive interference in steady state (CISS) or 3D fast imaging employing steady-state acquisition (FIESTA) sequences can show enhanced visualization of structures surrounded by CSF, thereby assisting in delineation of the tumor and cranial nerves.

    High-resolution CT with and without contrast can be used as an alternative in patients who cannot tolerate MRI.

- Management options include surveillance, surgical resection, SRS, FSRT, or conventionally fractionated radiotherapy.
- Goals of therapy are to maximize local tumor and preservation of function (i.e., minimizing hearing loss and other cranial nerve deficits such as facial or trigeminal nerve dysfunction).
- Surgical resection is performed via a suboccipital (retrosigmoid), middle fossa, or translabyrinthine approach. Hearing preservation rates for suboccipital and middle fossa approaches range from 20 to 71% with smaller tumor size and extent of preoperative hearing level of variable prediction for hearing preservation; the general indications and limitations for each are as follows [1–3]:
  - Suboccipital (retrosigmoid):

    Indications: Any tumor size, can attempt hearing preservation, lower risk of facial nerve injury.

    Limitations: Increased incidence of headache and CSF leak, incomplete visualization of the internal auditory canal fundus.

  - Middle fossa:

Table 6.1 Koos Grading System for Vestibular Schwannomas

Koos grading system for vestibular schwannomas[a]	
Grade	Tumor localization/extension
I	Purely intracanalicular
II IIA IIB	Extension into the CPA (without contacting the brainstem): ≤ 10 mm from the porus acusticus 11–18 mm from the porus acusticus
III	Large tumor extending to the CPA cistern without brainstem displacement
IV	Very large tumor with displacement of brainstem and/or cranial nerves

[a]Modified from Koos et al. [4]. *CPA* cerebellopontine angle

Indications: Small tumors ≤1.5–2 cm and hearing preservation can be attempted (highest rates of hearing preservation among surgical approaches).

Limitations: Increased risk of facial nerve damage, incomplete visualization of the internal auditory canal fundus.

– Translabyrinthine:

Indications: Non-serviceable hearing in affected ear, any tumor size, and complete visualization of the internal auditory canal.

Limitations: Hearing is inevitably sacrificed.

6.2 Staging, Grading, and Other Classifications

Vestibular schwannomas are divided into four grades based on size and location according to the Koos grading system (Table 6.1, [4]).

6.3 Patient Selection for SRS or FSRT

- Factors influencing treatment recommendations include patient age, medical comorbidities, cranial nerve deficits, tumor size and/or growth rate, presenting symptoms, competing symptoms (i.e., contralateral hearing loss), and proximity to critical organs at risk (OAR, such as brainstem, cochlea).
- For single-fraction SRS, targets should generally be <3 cm.
- For FSRT, tumors may be larger (>3–4 cm), in closer proximity to or involving OARs.
- Patients with non-serviceable hearing (typically <50% speech discrimination at >50 dB) may not benefit from therapeutic approaches to preserve hearing [5].

6.4 Treatment Planning Considerations (Table 6.2)

Table 6.2 Treatment planning considerations

Simulation instructions	**Position**: Supine, arms at sides, head and neck neutral. **Immobilization**: A rigid (frame or frameless) stereotactic immobilization system[a]. – GaK: Head frame in conjunction with a metal collimator helmet. – Linac based: Various, including rigid frame with external skull fixation, noninvasive modified GTC frame (noninvasive fixation by use of a dental plate), or a three-point thermoplastic mask with a modified stereotactic frame (see Fig. 3.1). **CT**: Thin-cut CT images (1.0–3.0 mm slice thickness) ideally with IV contrast spanning from vertex to mid-cervical spine. **Diagnostic imaging**: Co-registration of planning CT with the appropriate diagnostic imaging (contrast-enhanced MRI or CT) for target and OAR delineation. MRI sequences should include pre- and post-contrast T1-weighted, pre-contrast T2-weighted and FLAIR, and multi-planar (axial, sagittal, and coronal) post-contrast T1-weighted images. Post-contrast T1-weighted images with thin (1 mm) sectioning should be obtained. High-resolution series, such as MP-RAGE, should be obtained for contrast-enhancing targets. Cranial nerves may be more readily visualized on a CISS or 3D FIESTA series [6].
Image guidance	Imaging options include CBCT, orthogonal KV X-rays; misalignment corrections via positional systems with four or six rotational axes of the patient couch/platform.
Target delineation	The tumor bed/GTV is defined as the enhancing lesion on the post-gadolinium T1-weighted MRI ([6], and see Fig. 6.1a).
Margins	GTV = CTV. PTV = CTV plus 0–5 mm uniform expansion (depending on institutional setup error, including accuracy and reproducibility of immobilization). Generally CTV plus 3–5 mm uniform expansion for standard thermoplastic mask or CTV plus 0–2 mm uniform expansion for a stereotactic frame.
Tumor/target coverage considerations	≥98% of the GTV/CTV should receive the prescription dose. ≥95% of the PTV should receive the prescription dose.
Treatment modality	Linac, GaK, CyK, proton beam
Planning strategies/ assessment	Steep PTV to OAR dose gradients are generated using multiple beam arrangements or non-coplanar arcs together with dose prescription to the steepest portion of the beam profile (often the 50% IDL for GaK or the 80–90% IDL for linac based). For linac-based SRS, the standard beam profile is shaped by collimation with cones or MLCs. An example treatment plan is depicted in Fig. 6.1b. Notably, as target size increases, the dosimetric advantages of SRS tend to decline—as the sharp dose falloff becomes shallower and the higher doses to adjacent normal tissue become prohibitive, thereby generally precluding safe and effective SRS delivery to targets >3 cm in diameter. The following indices should be generated [7]: **Conformality index**: Prescription isodose volume/target volume (ideally ≤2). **Heterogeneity index**: Maximum dose to target volume/prescription dose (ideally ≤2). **Gradient index**: Volume receiving half the prescription isodose/volume receiving the full prescription isodose (ideally ≥3).

[a]Based on delivery system and institutional protocol. *GTC* Gill-Thomas-Cosman, *FLAIR* fluid-attenuated inversion recovery, *MP-RAGE* magnetization-prepared rapid gradient echo, *CISS* constructive interference in steady state, *FIESTA* 3D fast imaging employing steady-state acquisition

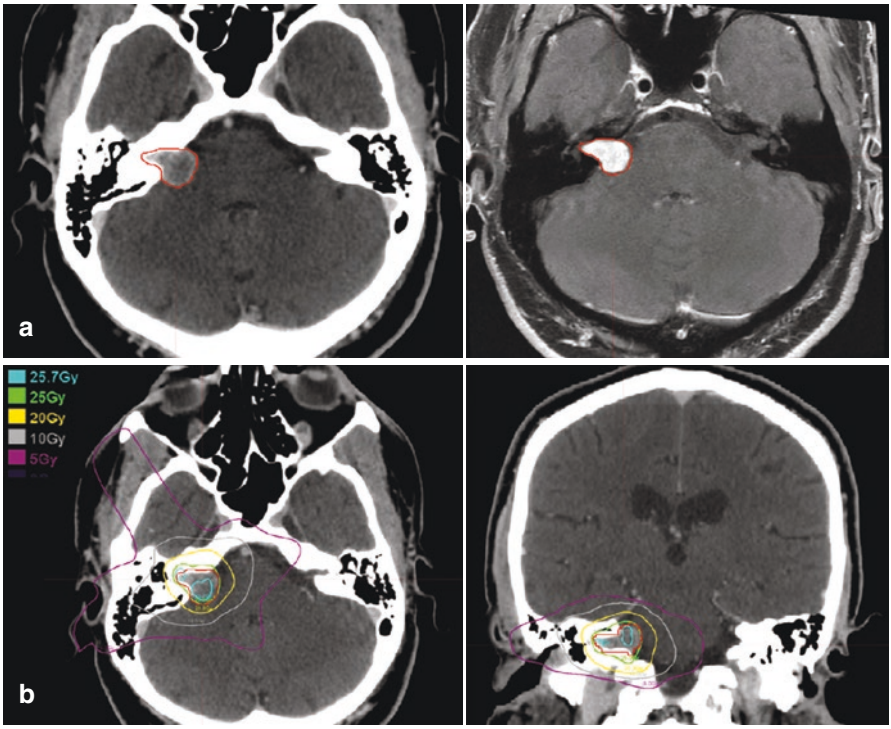

Fig. 6.1 A 1.9 cc right vestibular schwannoma; GTV target delineation in red. (**a**) Simulation CT (left), post-contrast T1-weighted MRI (right). (**b**) Treatment plans with prescription IDL in green, effective normalization 97%. HSRT, 5 Gy × 5 fx (25 Gy total) with 6 MV photon using VMAT. Simulation CT axial (left) and coronal (right). *IDL* isodose line

6.5 Commonly Used Dose/Fractionation Schemes

Commonly utilized dose/fractionation schemes for SRS and FSRT are described in Table 6.3.

6.6 Normal Tissue Tolerances

Improved serviceable hearing preservation has been reported in patients with vestibular schwannomas treated with GammaKnife SRS who received a central cochlea dose <4.2 Gy [10] (Table 6.4).

Table 6.3 Commonly utilized dose/fractionation schemes for SRS and FSRT

	Patient selection considerations	Dose/fractionation
SRS	Small, <3 cm	12–13 Gy
FSRT	Larger, >3–4 cm	5 Gy × 5 fx, 3 Gy × 10 fx [8, 9]

Fx fraction(s)

Table 6.4 Normal tissue tolerances

Dmax[a] (Gy) in critical structures for SRS and FSRT							
Organ	Authors' recommendations			TG101 [11]			QUANTEC [12]
Fractions	One	Three	Five	One	Three	Five	One
Brainstem	≤ 12 Gy	≤ 21 Gy	≤ 30 Gy	15 Gy	23.1 Gy	31 Gy	< 12.5 Gy
Cochlea	< 4.2 Gy	–	–	9 Gy	17.1 Gy	25 Gy	≤ 14 Gy

[a]Maximum point dose

6.7 Patient Management Considerations

- Premedication/prophylactic medication:
  - There is no standard premedication regimen.
  - Consideration of steroids is dependent on severity and tempo of symptoms or neurologic deficit(s), treatment volume, number of fractions, as well as patient age and/or medical comorbidities.
- Acute toxicity: Treatment is generally well tolerated, transient dizziness reported in ~17% [13].
- Late toxicity: Hearing loss (29–68%), CN V/VII neuropathy (<5%), dizziness (2%) [13, 14].

6.8 Follow-Up

- H&P every 6–12 months.
- Yearly imaging (ideally MRI, CT with contrast if non-tolerant, or MRI contraindicated) for 4–5 years, then every 2 years.
- Audiometry and vestibular testing as needed.

6.9 Relevant Literature

- The treatment of vestibular schwannomas with stereotactic radiosurgery and conventionally fractionated radiotherapy is well characterized with excellent local control rates and extensive long-term follow-up.
- In recent years FSRT has emerged as a promising treatment technique in patients with large tumors or those in close proximity to or involving critical OARs. However, more mature data are required for adequate evaluation of long-term local control rates as well as associated toxicity profiles for FSRT compared to SRS or conventionally fractionated radiotherapy (Table 6.5).

Table 6.5 Relevant literature

Study	Patients (*n*)	Median follow-up (year)	Mean tumor vol (cm^3)	Modality, dose, fractionation	PFS	Hearing preservation (%)
Prasad 2000 [15]	153	4.3, (mean)	2.6–2.8	GaK, 13 Gy × 1 fx	93%	58[a]
Hasegawa 2005 [16]	317	7.8	5.6	GaK, 13.2 Gy × 1 fx	– 93% 5 years – 92% 10 years	13(>13 Gy)[a] 68(≤13 Gy)[a]
Friedman 2006 [17]	295	3.3	2.2, (median)	Linac, 12.5 Gy × 1 fx	– 98% 2 years – 90% 5 years	NA
Chopra 2007 [18]	216	5.7	1.3	GaK, 13 Gy × 1 fx	– 98% 10 years	44, 10 years[a]
Fukuoka 2009 [13]	152	>5	2.0	GaK, 12 Gy × 1 fx	– 94% 5 years – 92% 8 years	71
Murphy 2011 [14]	103	3.1	1.95	GaK, 13 Gy × 1 fx	91%	NA
Kalapurakal 1999 [19]	19	5.4	3.5 cm (mean diameter)	Linac, 6 Gy × 6 weekly fx (*n* = −6); 5 Gy × 6 weekly fx (*n* = 13)	100%	100
Williams 2002 [8]	150	1.9	1.5 (≤3 cm), 8.7 (3–4 cm), 26.3 (≥4 cm)	Linac, 5 Gy × 5 fx (≤3 cm, *n* = 131), 3 Gy × 10 fx (3–4 cm, *n* = 18), 2 Gy × 20 fx (>4 cm, *n* = 1)	100%	72[a]
Meijer 2003 [20]	80	2.8	2.5 cm, (mean diameter)	Linac, 4 Gy × 5 fx (1992–1995), 5 Gy × 5 fx (1995–2000)	– 94% 5 years	61

Table 6.5 (continued)

Study	Patients (*n*)	Median follow-up (year)	Mean tumor vol (cm^3)	Modality, dose, fractionation	PFS	Hearing preservation (%)
Kapoor 2011 [9]	385	4.7	2.66, (mean)	Linac, 5 Gy × 5 fx (*n* = 340) or 3 Gy × 10 fx (*n* = 36)	– FFS 97% – FFRP 70% – 7.6 years median time to progression	NA

[a]Gardner-Robertson Class I–II.; *vol* volume, *FFS* freedom from surgery, *FFRP* freedom from radiologic progression

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