Vestibular Schwannoma

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Case

- 67 year old F presented with a ringing sensation in her ears for the past few years as well as progressive left sided hearing loss.
- For the past month she noted progressive vertigo causing her to be unable to drive.
- She also endorsed a posterior headache that felt like an earache.

Common presentations

- Symptoms are due to cranial nerve involvement and tumor progression:
- **Acoustic Nerve (VIII): 95% → hearing loss (only 2/3 realize it)**
- **Vestibular nerve (VIII): 61% → unsteadiness**
- **Facial nerve (VII):** 6% → facial paresis and taste disturbances
- **Trigeminal nerve (V):** 17% → facial numbness / pain.
- **Posterior fossa**: rare → compression on cerebellum or brainstem, results in ataxia / hydrocephalus

Differential Diagnoses

- Vestibular schwannoma
- Meningioma (4-10%)
- Facial nerve schwannoma
- Glioma
- Cholesteatoma
- Epidermoid inclusion cyst
- Glomus jugulare
- Lymphoma
- Hemangioblastoma (VHL)
- Brain metastases
- Ependymoma
- Arachnoid cyst
- Lipoma

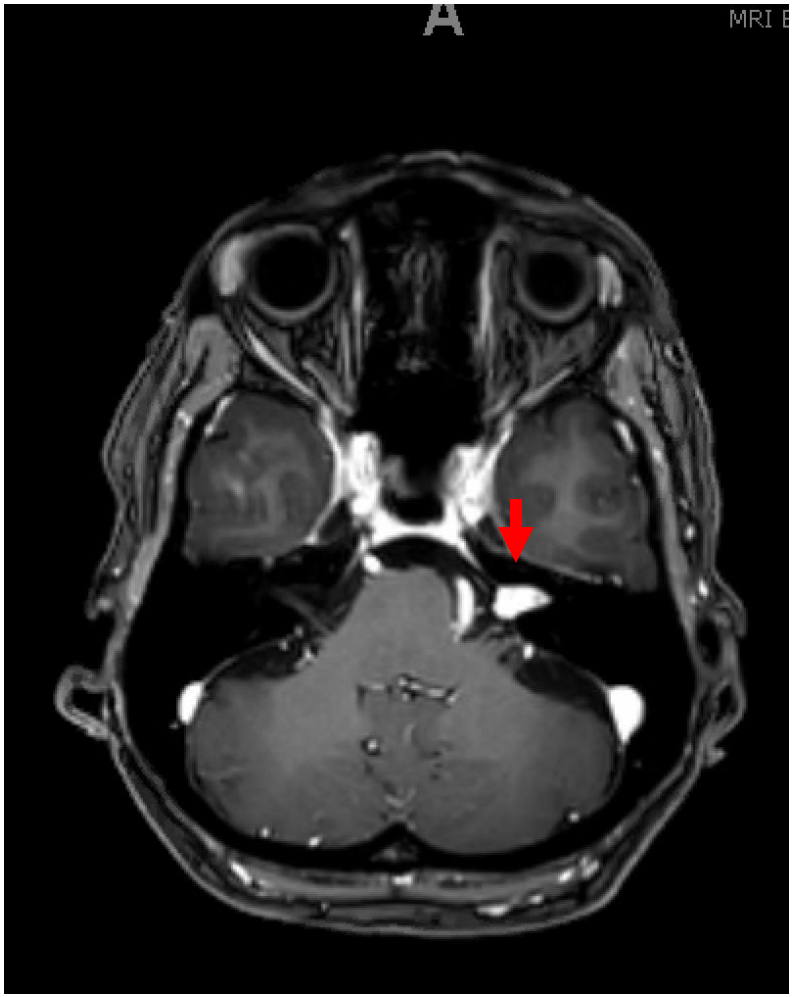
Non-oncologic: hemangioma, aneurysm, basilar artery ectasia

Workup

- **Physical exam:**
  - **Rinne test** (tuning fork on mastoid bone, air conduction > bone conduction is normal, with sensorineural both are depreciated)
    - In **conductive** hearing loss, bone conduction > air conduction
  - **Weber test** (assessed sensorineural hearing loss; vibratory sound louder on "good" side);
  - Cranial nerve test (facial weakness, facial numbness, corneal reflex)
  - Vestibular testing: May see decreased or absent caloric response on affected side.
  - Romberg, Dix Hall-Pike, and balance are typically normal
- **Audiometry:** Best initial screening test, since **only 5% will have normal initial test**.
  - Look for asymmetrical high frequency hearing loss.
  - Speech discrimination loss is often out of proportion to measured hearing loss

Imaging

MRI demonstrated a 14 x 7 mm left cerebellopontine angle cistern mass most likely representing an acoustic neuroma



Typical imaging findings

- well circumscribed T1-gad enhancing lesions arising near porus acusticus. T2 isointense
  - "Ice cream on a cone" or "Dumbbell" in IAC
- CPA angle tumors: **80% are vestibular schwannomas**. Of remaining 20%, majority are meningiomas, cholesteatoma, etc.
- MRI sensitivity: 98% (miss some due to small size)
- MRI specificity – approaches 100%

	Vestibular Schwannoma	Meningioma	Cholesteatoma
CT scan	Usually iso intense and contrast enhancing	Greater contrast than VS	**Hypodense with irregular, lobulated margins. No contrast enhancement**
MRI T1	Isointense (compared to pons)	Iso- or minimally hyper-	**Hypo, ~CSF-like**
MRI T2	"filling defect" – heterogeneously hyperintense	Usually hypointense	**hyperintense**
MRI post contrast	Enhancing: may be homogeneous (50%), hetero (30%), or cystic (5-15%)	Strongly enhancing	
Other		**Obtuse angle with petrous ridge vs acute for VS**	**Keratinizing squamous epithelium, erosive (best seen on CT)**

Audiometry

- Non-serviceable≥50dB audiogram and <50% speech discrimination
- Gardner-Robertson scale used

Gardner-Robertson scale	Grade	Description	Pure-tone Average (decibels)	Speech-discrimination Score (percent)
	1	Good to excellent	0-30	70-100
	2	Serviceable	31-50	50-69
	3	Non-serviceable	51-90	5-49
	4	Poor	91-100 (maximum)	1-4
	5	None	Not testable	0

Epidemiology

- Overall incidence: 1-2/100,000 (increased over past the 30-40 years with improved non-invasive diagnostic studies)
- 3000 cases in US per year
- Size has decreased as incidence has increased
- Autopsy results have shown that subclinical acoustic neuromas are present in up to 1% of people
- Account for 8% of intracranial tumors and 80-90% of CPA tumors
- Age at presentation: 30 to 50
- Almost always unilateral, with exception of NF-2

Risk Factors

- **Acoustic trauma** - OR of 2.2 if 10 years exposure to extremely loud noise. OR 13.1 if 20 or more years of exposure but subject to RECALL BIAS (studies looking at occupational exposure negative)
- **Parathyroid adenoma-** OR of 3.4 for acoustic neuroma (cause/association is unknown)
- **Childhood radiation exposure-** 20x higher compared to normal population
- **NF-2 (bilateral)-** Accounts for 10% of patients with acoustic neuroma
- **Cell phone use (controversial)-** ipsilateral use >1640 hr – OR 2.55 (1.5-4.4)

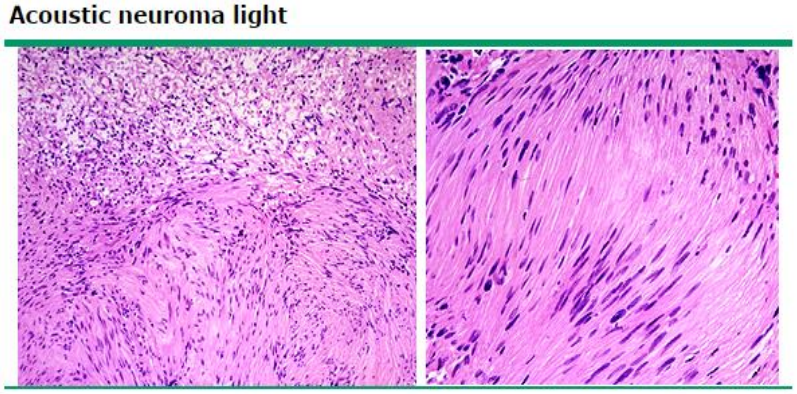
Neurofibromatosis (NF1 and NF2)

	NF1	NF2
Inheritance	Autosomal dominant	Autosomal dominant
Incidence	1:3000	1:40,000
Chromosome	17q11.2	22q12.2
Gene product	Neurofibromin	Merin
Presentation	Café-au-lait macules, axillary/inguinal freckling, cutaneous neurofibromas, subcutaneous neurofibromas	Hearing loss or vestibular dysfunction at young age, cataracts, juvenile posterior subcapsular lenticular opacity cutaneous schwannomas
Intracranial tumors	Optic path gliomas, other astrocytomas/gliomas	Vestibular schwannomas, meningiomas
Cognitive	IQ mildly decreased	Normal
Other tumors	CML, pheochromocytoma	None

Diagnosis of NF2: 1.Bilateral eighth nerve masses with imaging OR 2. A first degree relative with NF2 with either a unilateral eight nerve mass or 2 of the following: glioma, meningioma, schwannoma, neurofibroma, or juvenile posterior subcapsular lenticular opacity

Pathology

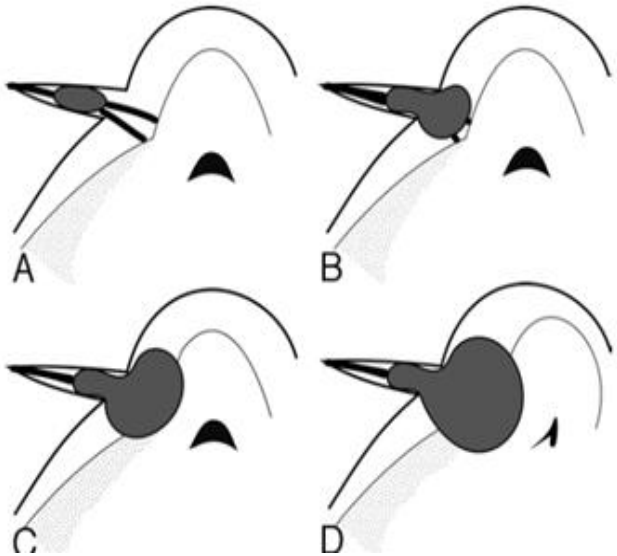
- Arise from the **Schwann cell:** perineural elements of the affected nerve
- Occur with equal frequency on the superior and inferior branches of the vestibular nerve (rarely affect cochlear portion CN VIII)
- **Obersteiner-Redlich zone**: Arise at junction of central myelin produced by glial cells and peripheral myelin from Schwann cells
  - This zone is where the CNS meets the PNS so change from oligodendrocyte myelin to Schwann cell myelin
- **Antoni A and B areas**: Microscopically, zones of alternately **dense (A) and sparse (B) cellularity** are characteristic of AN's.
- Stain positive for **S100**



Acoustic neuroma. Low and high power magnification of acoustic neuroma with zones of alternately dense and sparse cellularity.

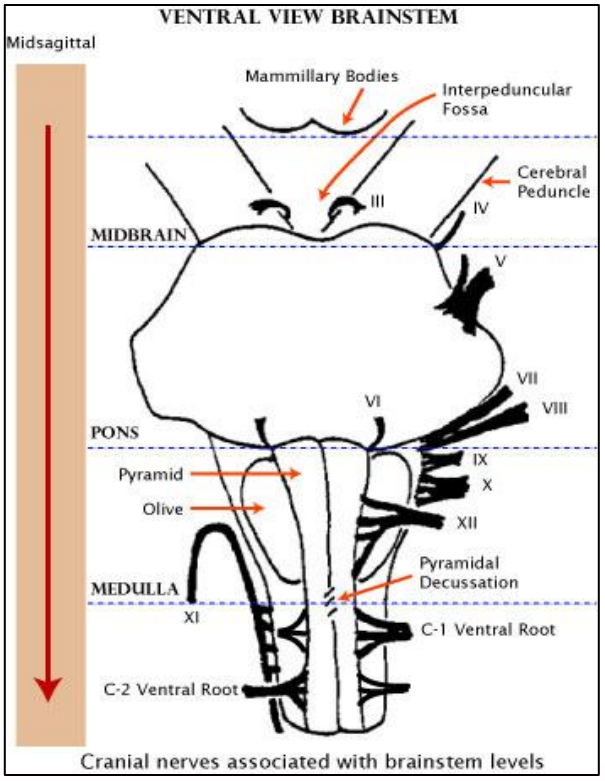
Koos grading system

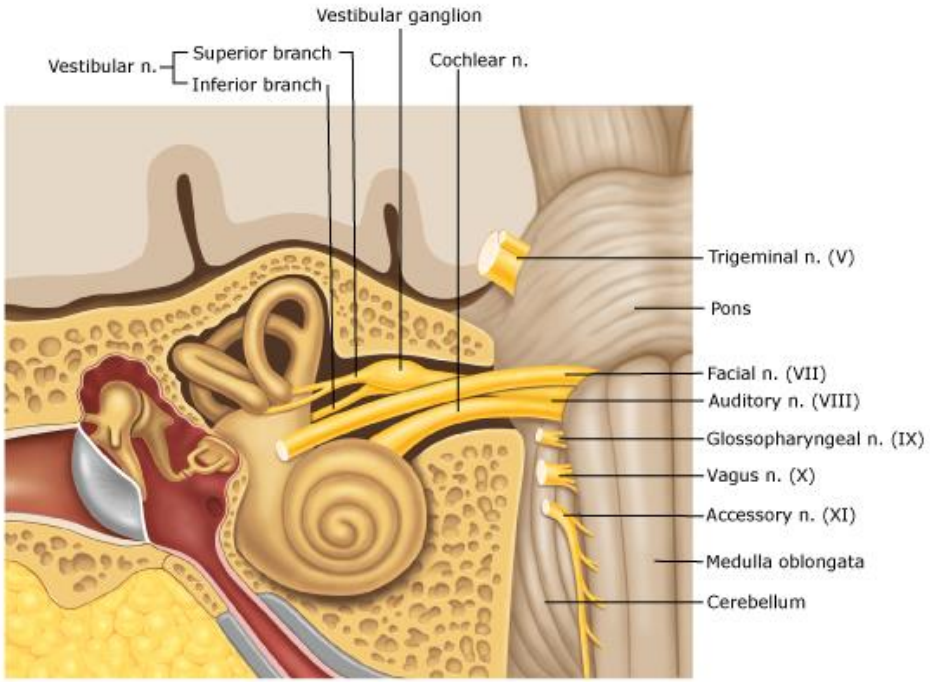
- Grade I: small intracanalicular tumor
- Grade II: small tumor with protrusion into the cerebellopontine angle
- Grade III: Tumor occupying the cerebellopontine cistern with no brainstem displacement
- Grade IV: Large tumor with brainstem and nerve displacement



Anatomy

- Common to have CN deficits in CN V, VII and VIII





House-Brackmann Score

- Scores the degree of facial nerve palsy
- Measurement determined by measuring the upwards (superior) movement of the mid-portion of the top of the eyebrow, and the outward (lateral) movement of the angle of the mount
- 1 point per 0.25 cm movement, up to a max. of 1 cm. Scores added together to give a number out of 8

Grade	Description	Measurement	Function %	Est. Function %
I	Normal	8/8	100	100
II	Slight	7/8	76-99	80
III	Moderate	5/8-6/8	51-75	60
IV	Moderately Severe	3/8-4/8	26-50	40
V	Severe	1/8-2/8	1-25	20
VI	Total	0/8	0	0

Treatment Options

- Observation
- Surgical resection
- Radiotherapy (EBRT, FSRT, SRS)

Observation

- MRI recommended every 6 to 12 months in patients without baseline hearing loss and stable or slow growth rates, especially elderly patients
  - Beware 15-30% are lost to follow-up.
- **Growth rate of 2.9 mm/year** per UCSF lit review (others say 1.2-1.9mm/yr)
- **30%-50% of tumors show no growth or regression** on serial imaging studies
- Growth rate is highest for those that grow in first year. Progressive decrease in rate of growth if growth starts later.
- No predictive relationship between growth rate and tumor size at presentation

Surgical Resection

- Typically performed by ENTs and neurosurgeons. Learning curve is steep → 20 to 60 cases.
- Often recommended for tumors > 3-4 cm or for salvage after RT.
- CN VII, VIII damage is significant
- French series also shows good CN VII function (preservation not correlated with surgical approach used), but 1/3 pts had disabling vestibular symptoms at 1 year.

Surgical Resection

Approaches (based on size, location, and consideration of hearing preservation):

- **Retromastoid suboccipital (retrosigmoid)**: An incision is made behind the ear and mastoid bone and some inner ear structures are removed. **Often best hearing preservation**
  - Advantages: decreased risk of facial nerve damage, ability to attempt hearing preservation, any size tumors, good visualization of CPA
  - Disadvantage: If tumor extends distally into IAC, complete resection may not be possible; long term postop headaches; cerebellar retraction may increase rates of ataxia
- **Middle cranial fossa (transtemporal)**: Incision anterior to the ear with removal of the underlying bone to expose the area of interest; used primarily for small tumors confined to IAC (allows for complete exposure of IAC)
  - Advantage: Hearing preservation attempted (preservation of inner ear structures), only approach for IAC fundus
  - Disadvantage: complete tumor removal may not be feasible due to poor visualization of CPA; risk of facial nerve palsies due to increased manipulation of nerve within the auditory canal (puts facial nerve between surgeon and tumor). Need to be less than 1.5 - 2 cm.
- **Translabyrinthine**: This approach goes directly through the inner ear and **invariably sacrifices hearing**, but preserves CN VII
  - Recommended for large vestibular schwannomas (> 3 cm) in young pts without serviceable hearing
  - Can be used for smaller tumors if hearing preservation is not important.
  - Associated with better post operate gait stability because there is minimal retraction of the cerebellum, lowest incidence of postoperative headaches
- **Retrolabyrinthine:**
  - Allows excision from both the CPA and the IAM, regardless of the histological nature of the tumor and size

SRS Data

- First used by Leksell at Karolinska institute in Sweden to treat vestibular schwannoma in 1969.
  - Tumor control 81% at 3.7y med f/u.
  - Transient CN V and VII in 18% and 14% of pts, respectively.
- Initially used for older patients, recurrence after surgery, bilateral tumors, and medically inoperable pts.
- Early Gamma Knife data (Pitt, Mayo) had significant CN toxicity (33-80% preservation). Prescribed to higher dose than given now.
- Initial **Linac** results (Florida, Cleveland Clinic) showed better toxicity profile. Likely because prescribing a lower dose (~12 Gy).

Modern SRS series:

- lower doses 12-13Gy, MRI-based planning, improved conformality in plans (multiple isocenters, improved planning systems)
- **PFS: 92-100%**
- **CN V preservation: 92-100%**
- **CN VII preservation: 94-100%**
- **Hearing preservation: 60-68%**

SRS Data

- **Flickinger Pittsburgh** (Gamma Knife)- 6 year follow-up after 12-13 Gy
  - Tumor control= 98.6%
  - Facial nerve function preservation=100%
  - Normal trigeminal function=95.6%
  - Unchanged hearing level- 70.3%
  - Useful hearing preservation=78.6%

SRS vs. FSRT

- **Jefferson (Andrews) (Gamma Knife)** =
  - 12 Gy SRS vs. 50 Gy in 2 Gy fractions
  - Tumor control: 98% SRS vs 97% SRT
  - Hearing preservation was significantly higher in FSRT=81 % vs SRS=33%
  - Criticized for short follow-up time and worse patients in SRS group
- **Heidelberg (Combs) (Linac)** = both safe/effective
  - FSRT= 57.6 Gy/1.8 Gy fractions vs. median SRS of 13 Gy
  - SRS ≤ 13 Gy for smaller lesions (< 3cm), FSRT for larger lesions.
  - Local control: SRS=90% vs. FSRT=95% (NS)
  - Hearing at 5 years SRS=60% vs. FSRT 78% (p=0.02)
- **BC (Chung) (Linac)**= FSRT gives comparable tumor control, good rates of hearing preservation (all SRS patients were already had non-serviceable hearing)
  - 12 Gy SRS vs. 45 Gy/1.8 Gy fractions
  - Local control 100% in both groups

Meijer Netherlands IJROBP 2003	Tumor Control	CN V Preservation	CN VII Preservation	Hearing Preservation
SRS	100%	92%	93%	75%
FSRT	94%	98%	97%	61%

Surgery vs. SRS

Regis JNS France 2002	**Facial motor disturbance**	**CN V disturbance**	**Preserved Hearing**	**Overall functional disturbance**	**Hospital Stay (Days)**	**Mean days missed from work**
Surgery	37%	29%	37.5%	39%	23	130
Gamma Knife	0%	4%	70%	9%	3	7

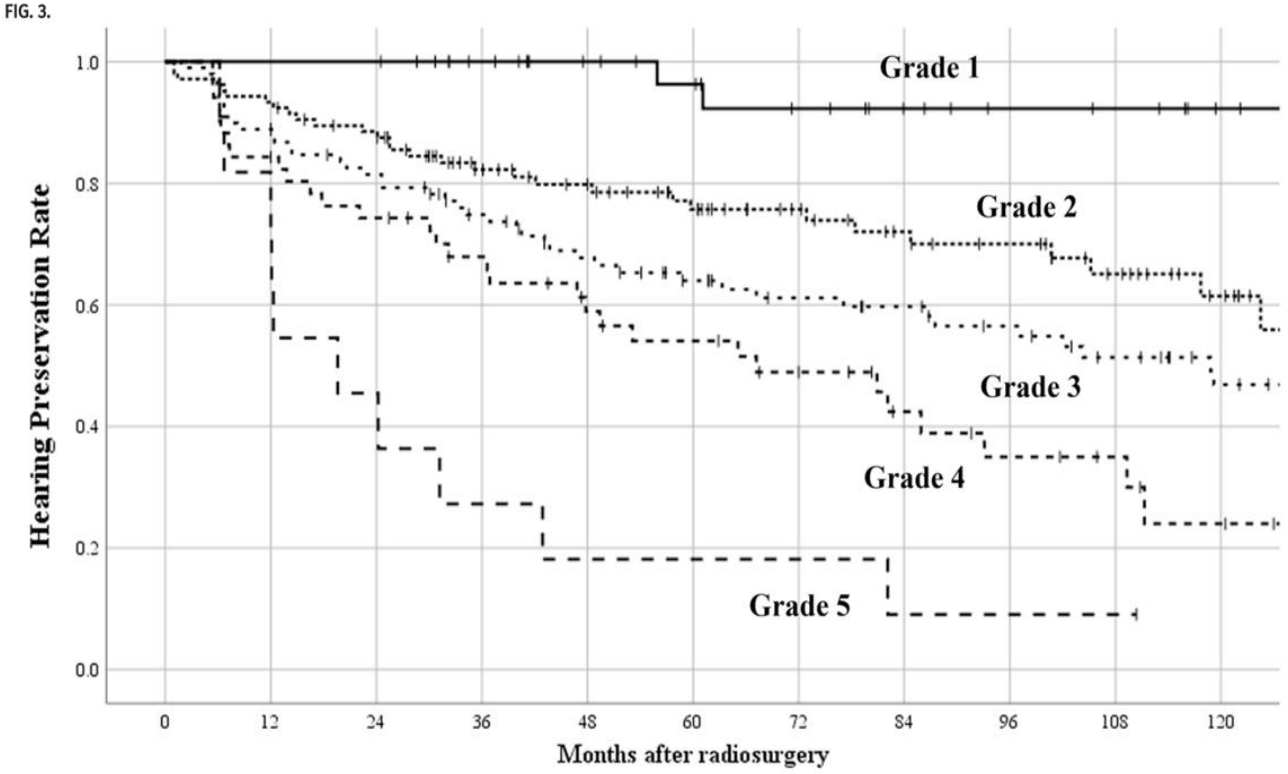
Observation vs. FSRS

- **Shirato Japan IJROBP**– Observation vs. FSRT as Initial Management for Vestibular Schwannoma
  - No permanent facial or trigeminal neuropathy observed in the SRT group
  - SRT: **Transient VII** in 5%, **Transient V** in 12%
  - Obs: 4% permanent facial palsy (after salvage surgery) and 4% w/transient V palsy (after salvage surgery)
  - **Hearing:** No SS difference in G & R class preservation rates for patients with measurable hearing
    - Hearing preservation: **60.9% (3yr) and 31% (5yr) observation vs 53% SRT (at 3yr and 5yr)**
    - Analysis of Hearing preservation excludes/censors patients in observation group at time of salvage.
    - In reality **4/6 sx salvaged pts and 1/4 RT salvaged pts** became DEAF but were **NOT** included in actuarial curve!
    - In **FSRT group**, 1 pt (3%) became deaf

Hearing Preservation after SRS

Johnson et al. Pittsburgh. J Neurosurg. Predicting hearing outcomes before primary radiosurgery for vestibular schwannomas.

- Retrospective study of 307 patients with serviceable hearing at time of SRS



Dose and CN Toxicity

- **CN V and VII:** tumor size and prescription dose correlate with toxicity.
  - Friedman UF JNS 2006 (p.24)→ CN VII tox: 1cc increase in tumor = 17% increase, 2.5Gy increase in dose = 8.1x increase
  - Boegle UF JNS 2007 → Dosimetric variables: Conformity and dose gradient: no effect on outcomes
  - Generally no SRS if >3cm tumors
- **CN VIII:** Fukuoka Japan Prog Neurol Surg 2009 17% transient dizziness/gait imbalance post SRS, 2% persistent dizziness post SRS
- **Hearing:** Range of hearing preservation 32-71%. Hearing can decline long-term (>10yrs) after SRS. Dose matters.
  - **Prasad UVa JNS 2000** – no decline in first 2 years, then progressive decline
  - **Chopra Pitt IJROBP 2007** – 3y 75% G-R I/II, 10y 44%
  - **Combs Heidelberg RadOnc 2013** –@10yr, 72% if ≤13Gy (if >13Gy, 36%)
  - **Yang UCSF J NSGY 2010** – Review: N=4234, Preservation of hearing about 50% overall, but can be increased to 60% if <13 Gy

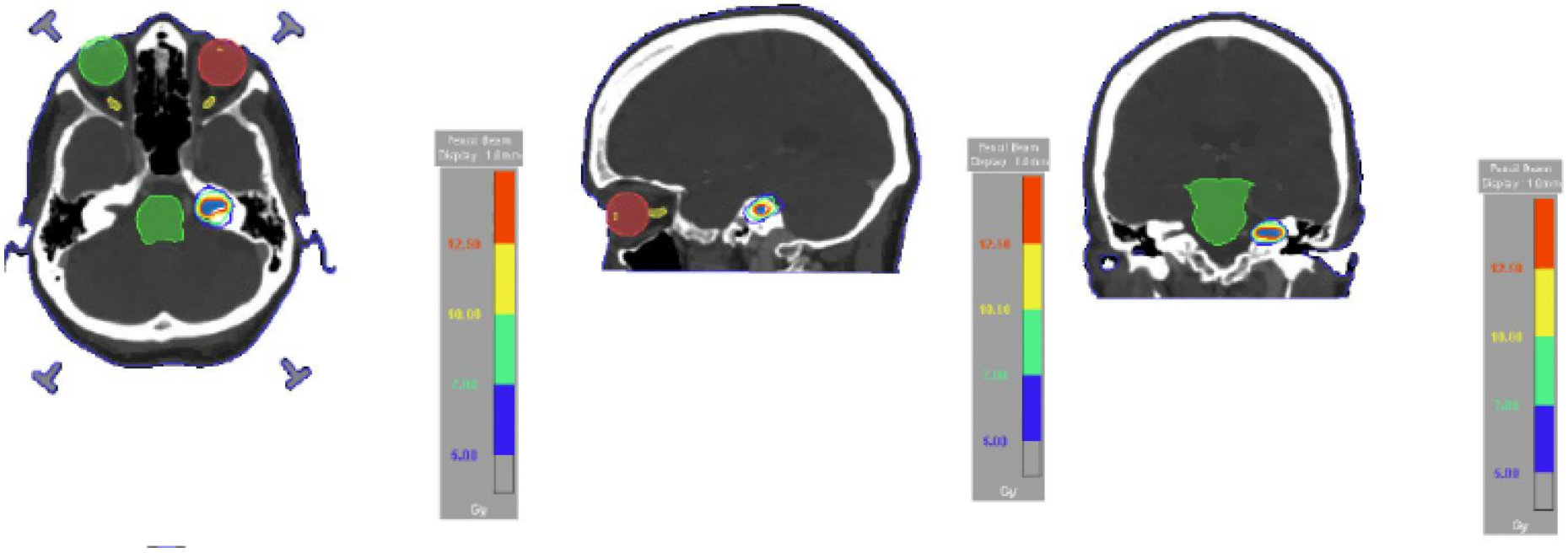
Treatment

- **Sim**: Scan vertex to C2, 1mm thickness
- With IV contrast, upper alpha cradle, and stereotactic frame
- **Contour:** Contour GTV=PTV (in this case due to frame)
  - PTV expansion based on immobilization
    - Framed cases may use 0 mm expansion, while frameless SRS cases may use 2-3 mm expansion

Treatment

- Linac based framed SRS to L-sided vestibular schwannoma 12.5 Gy to 80% isodose line using 6 MV photons, FFF

Representative Isodose lines



OAR Constraints

- Brainstem: 12.5 Gy (<5% neuropathy or necrosis)
- Chiasm: 8 Gy (<10% optic neuropathy)
- Cochlea: 14 Gy (<25% sensory-neural hearing loss), Ideally keep cochlea/modiolus <5.3 Gy (possibly <4.2 Gy)
- Spinal cord: 13 Gy (1% myelopathy)
- Brain: V12 <5-10 cc (<20% symptomatic necrosis)

- **Conformality index:** (Rx isodose volume)/(tumor volume) should be ≤ 2
- **Homogeneity index:** (maximum dose)/(peripheral dose) should be ≤ 2

- **Gamma-knife:** Rx to 50% IDL
- **Linac:** Rx to 80% IDL

Follow-up

- ~ 30% vestibular schwannomas will show a transient increase in volume after SRS (mean time to max tumor is roughly 13 months)
- Hearing may continue to decline long term after SRS (even >10 years)
- 36% of tumors shrink, 58% remain unchanged after SRS
- Imaging can be performed at 3-6 months followed by yearly or if changes in symptoms

Summary

- SRS is a good treatment option for vestibular schwannoma with excellent control rates
- SRS has decreased rates of CN toxicities and increased rates of hearing preservation when compared to surgery
- Surgery may be a better option if there is brain stem compression, due to minimal change in size of tumor after SRS or transient increase in tumor size
- Observation with imaging every 6-12 months may be appropriate for some patients due to many vestibular schwannomas remaining stable or regressing without treatment

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