MANAGEMENT OF SKULL BASE PARAGANGLIOMAS

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DISCLOSURES

- No relevant financial disclosures
- On Pheo Para Alliance Medical Advisory Board

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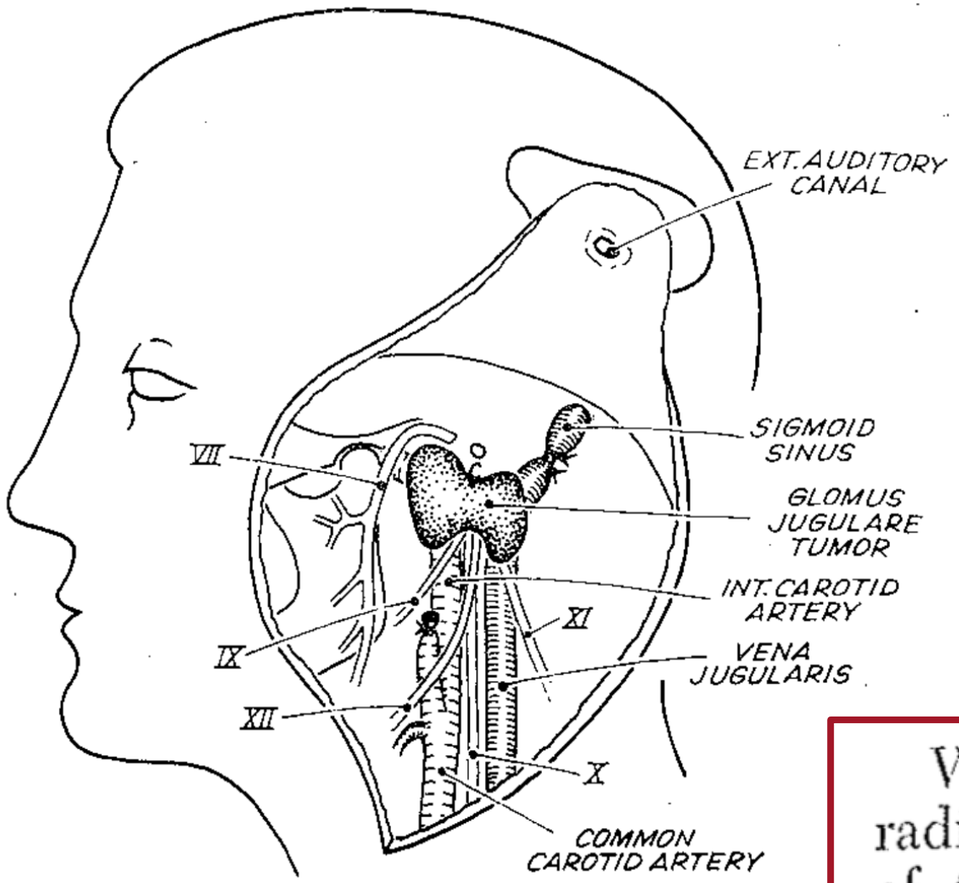
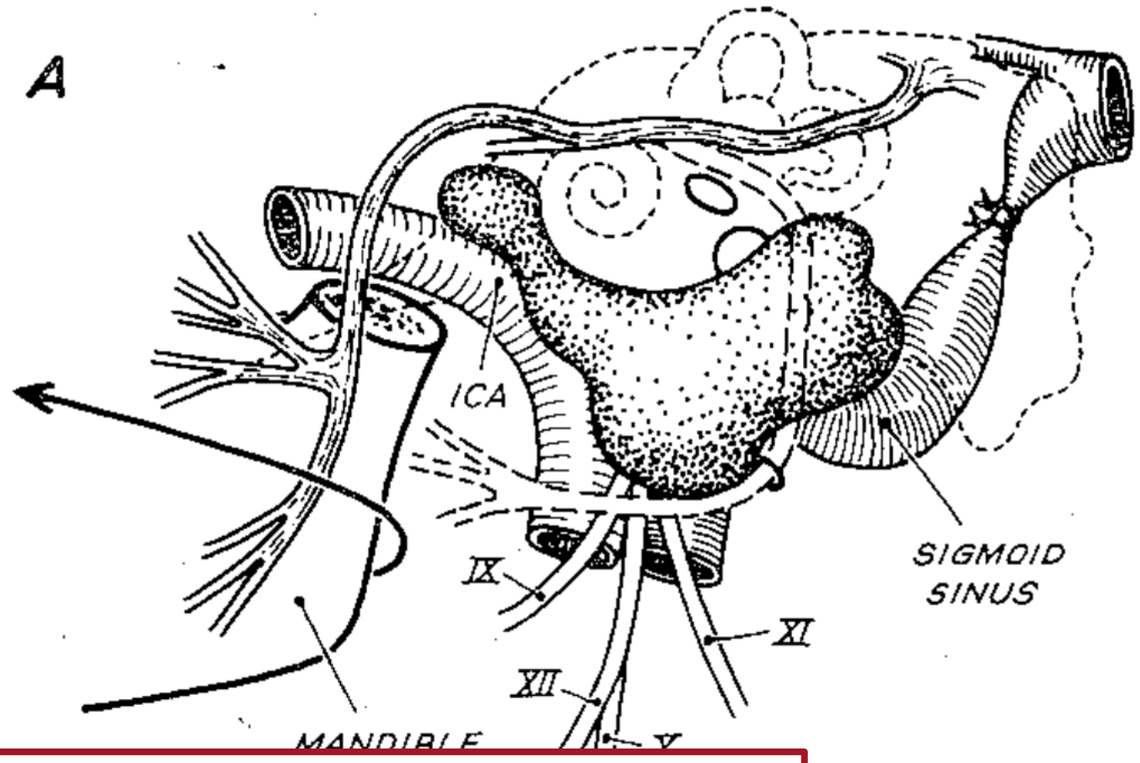
Classic Approach

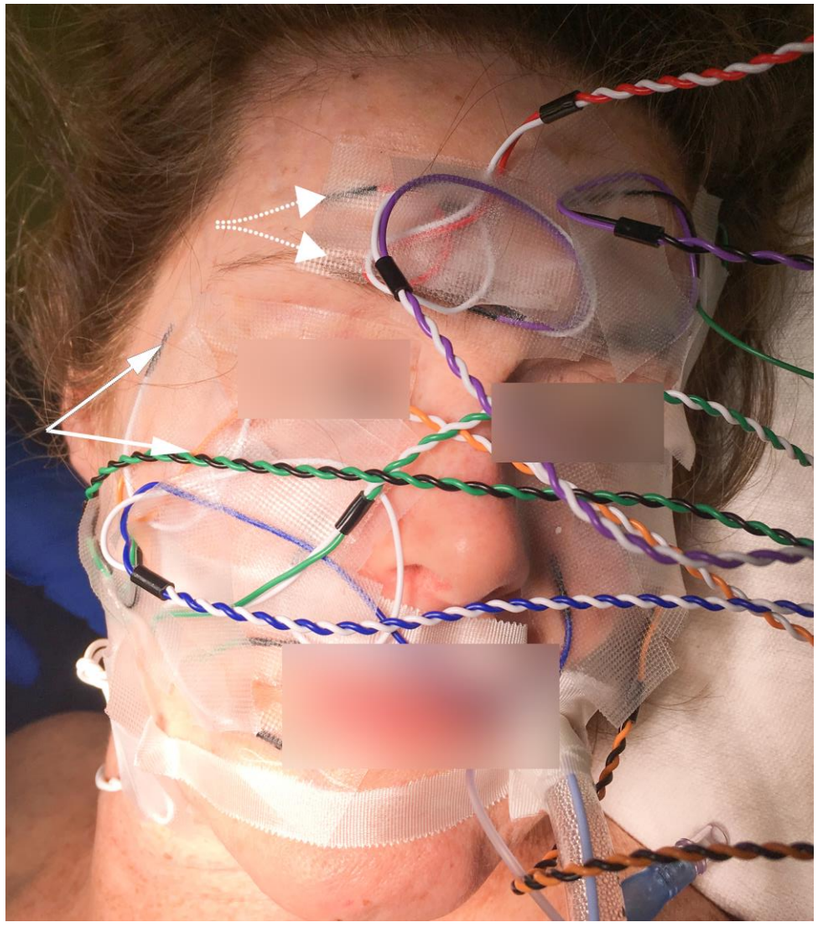




While there is clinical support for radiotherapy as the primary modality of treatment, we do not now believe that such a position has a firm histologic basis. A comparison of the pre-

Fisch 1978 and Brackmann

Modern Microsurgery



Radiosurgery: Over 600 patients reported

TABLE 4. Radiosurgical series for primary and recurrent treatment of JP

Authors & Year	No. of Pts	Delivery Method	Marginal Dose (Gy)	Tumor Control Rate (%)	FU (mos)	Definition of Progression	Comments
Dobberpuhl et al., 2016	12	GKRS	Median 15	100.0	27.6	Growth	
Ibrahim et al., 2017	75	GKRS	Median 18	93.4	51.5	Volumetric growth using Gamma-Plan software or linear growth >2 mm in any dimension	
Schuster et al., 2016	14	LINAC	NA	92.9	31.7	Growth	
El Majdoub et al., 2015	27	LINAC	Median 15	100.0	129.2	Growth	
Gandía-González et al., 2014	58	GKRS	Mean 13.6	94.8	76.6	Growth	
Liscak et al., 2014	44	GKRS	Median 20	97.8	118	Growth	6 glomus tympanicum
Hurmuz et al., 2013	14	CyberKnife	25 Gy in 5 Fx	100.0	39	Growth	
Sheehan et al., 2012	132	GKRS	Median 15	93.0	50.5	Growth (varied)	
Lee et al., 2011	14	GKRS	NA	100.0	40.3	Growth	3 glomus tympanicum
Chen et al., 2010	15	GKRS	Mean 14.6	80.0	43.2	15% increase in vol	
Genç et al., 2010	18	GKRS	Median 15	94.4	41.5	Volumetric growth using radial ellipse approximation ($V = 4\pi/3 \times r_1 \times r_2 \times r_3$)*	
Ganz & Abdelkarim, 2009	14	GKRS	Mean 13.6	100.0	28	Growth	
Miller et al., 2009	5	GKRS	Mean 15	100.0	29	Growth	
Sharma et al., 2008	10	GKRS	Mean 16.4	100.0	25.4	Growth	
Bitaraf et al., 2006	14	GKRS	Median 18	100.0	18.5	Growth	
Feigl & Horstmann, 2006	10	GKRS	Mean 17	100.0	33	Vol reduction >10%	
Gerosa et al., 2006	20	GKRS	Mean 17.5	100.0	50.85	Volumetric growth using Gamma-Plan software	
Poznanovic et al., 2006	8	LINAC	Median 15	100.0	15.6	Growth	
Varma et al., 2006	17	GKRS	Median 15	76.0	48	Volumetric growth using proprietary software	
Sheehan et al., 2005	8	GKRS	Median 15	100.0	28	Growth	
Eustacchio et al., 2002	19	GKRS	Median 14	94.7	86.4	Growth	
Saringer et al., 2001	13	GKRS	NA	100.0	50.4	Growth	
Jordan et al., 2000	7	GKRS	Mean 16.3	100.0	27	Growth	
Present study	60	GKRS	Median 16	91.7	66	Volumetric growth by serial tumor segmentation >15%	

FU = follow-up; NA = not applicable; pts = patients.
* r = radius of lesion in each plane.

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SKULL BASE PARAGANGLIOMAS

- Jugular paraganglioma (glomus jugulare)
- Vagal paraganglioma (glomus vagale)
- Carotid body tumor (glomus caroticum)

WORKUP AND DIAGNOSIS

1. History and examination with neurotologist (GJT) or head and neck surgeon (GV, CBT)
2. MRI +/- CT of temporal bones
3. Laboratory tests
    1. Catecholamines
    2. Genetics
4. Whole-body imaging if hypersecretion or SDH mutation identified
5. Shared decision-making model for treatment decision

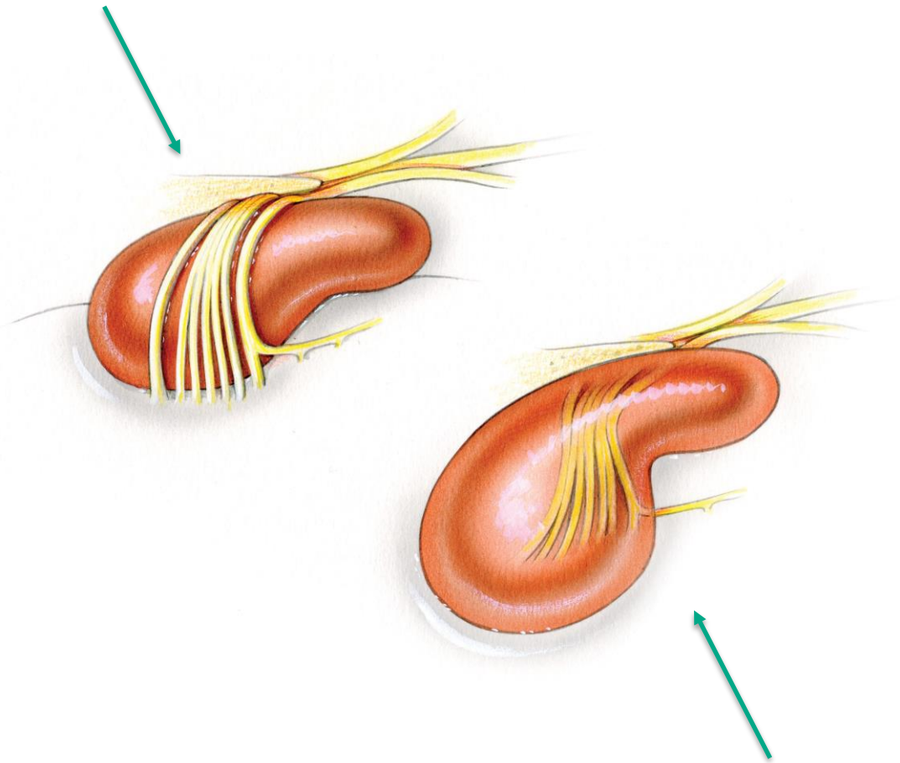
KEY ELEMENTS OF SURGERY FOR GJT

1. Angiography and tumor embolization: recommended for all HNPGLs
2. Cranial nerve monitoring: facial and lower cranial nerves
3. Multi-surgeon team: neurotologist, head and neck surgical oncologist, neurosurgeon, vascular surgeon
4. Transjugular and transcervical approach
5. Observation in neurosurgical ICU or surgical floor depending on extent of surgery (1-4 nights)

PRIORITIES: JUGULAR PARAGANGLIOMA

LOWER CRANIAL NERVES

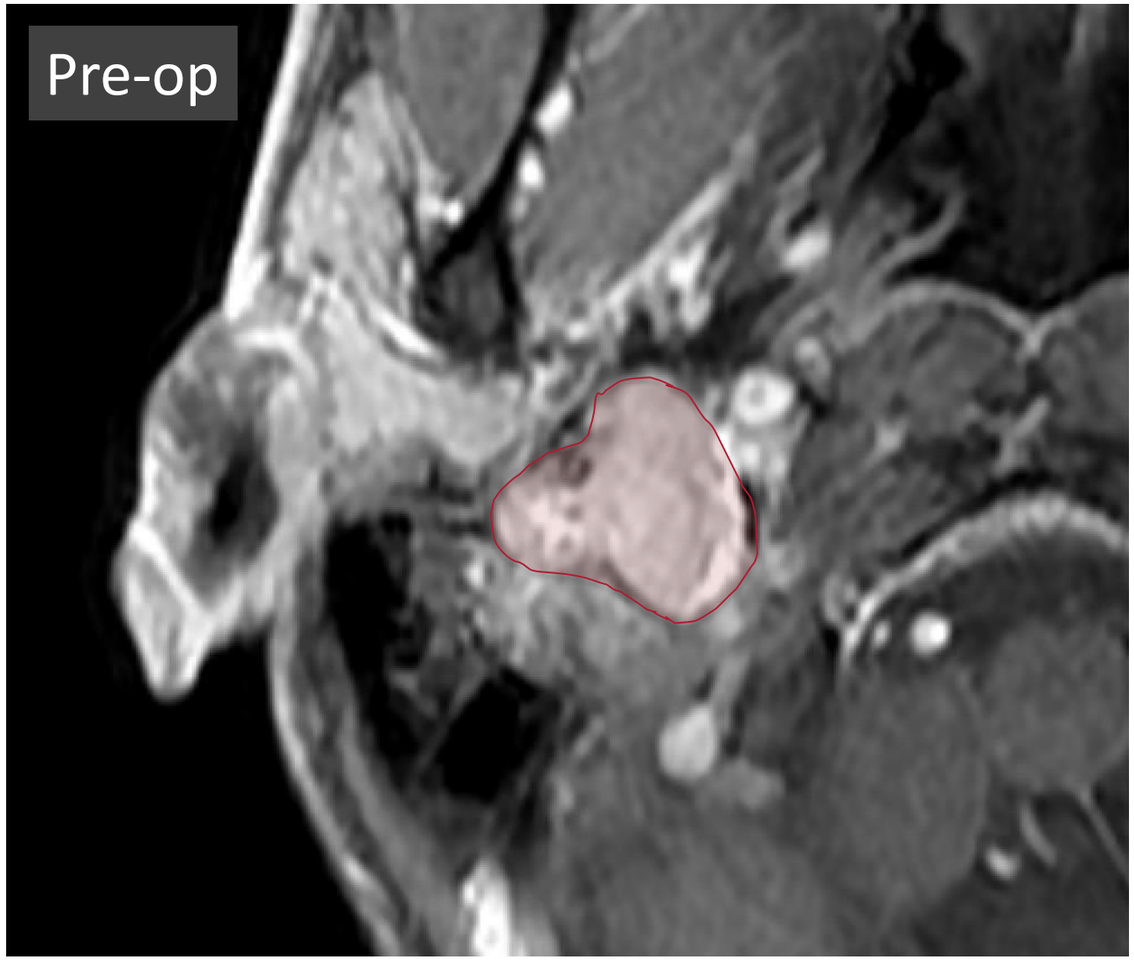
Nerves between surgeon and tumor

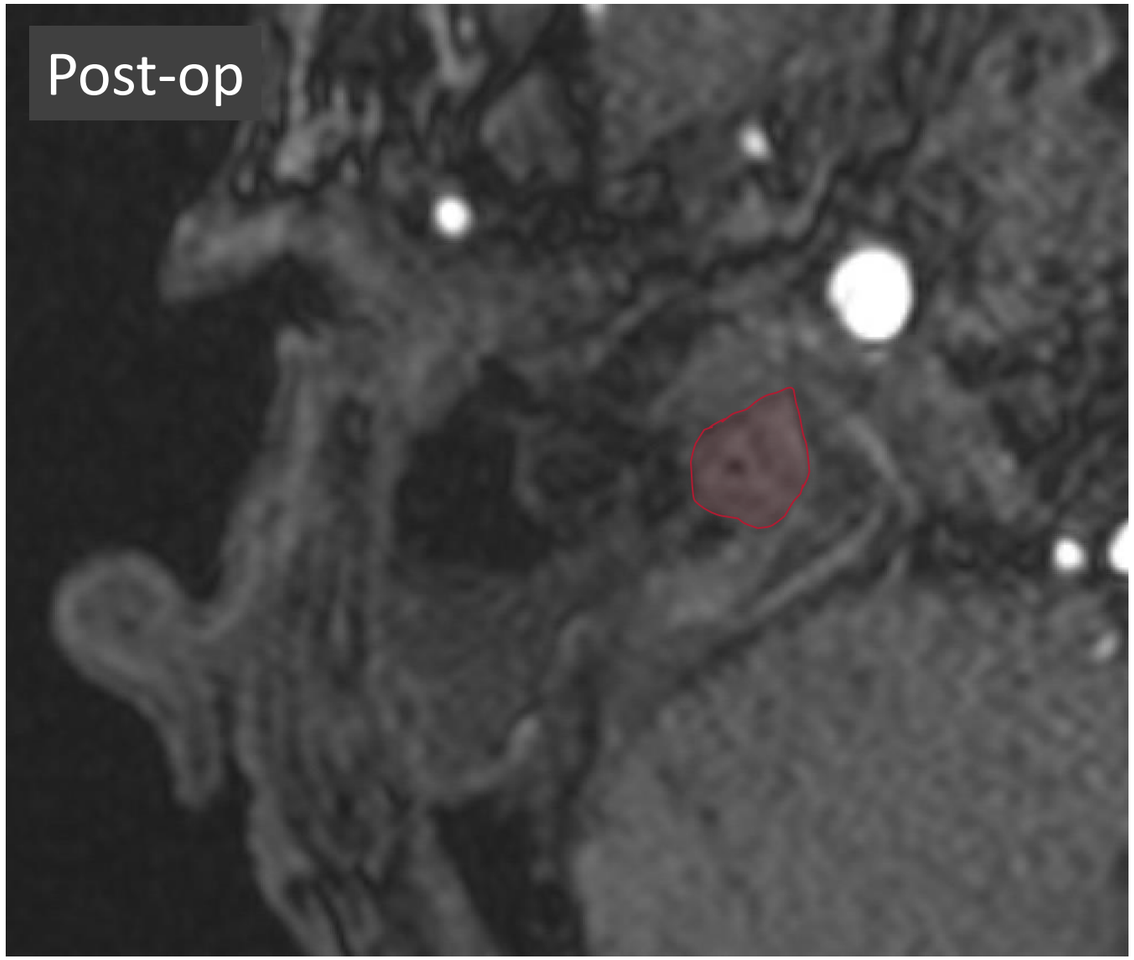


Tumor between surgeon and nerves

- Voice, articulation, swallowing
- Tumor location and size influence surgical outcome
- Major difference between pre-treatment vocal cord paralysis and post-treatment “high vagal” neuropathy

INTENTIONAL SUBTOTAL RESECTION FOR LOWER CRANIAL NERVE PRESERVATION





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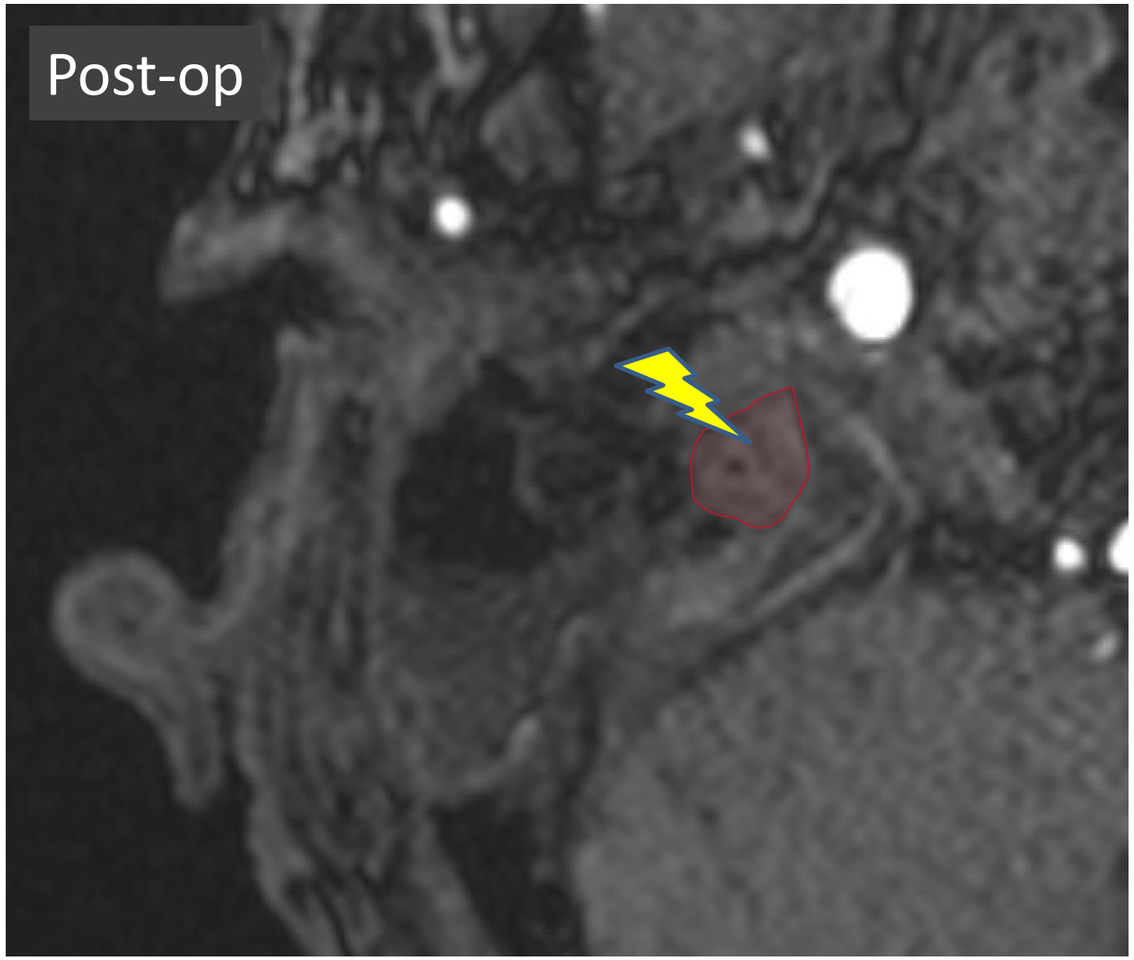
MANAGEMENT OF RESIDUAL TUMOR



- Intentional subtotal resection
- Post-operative staged stereotactic radiosurgery (SRS) 3-6 months later or observation: controversial

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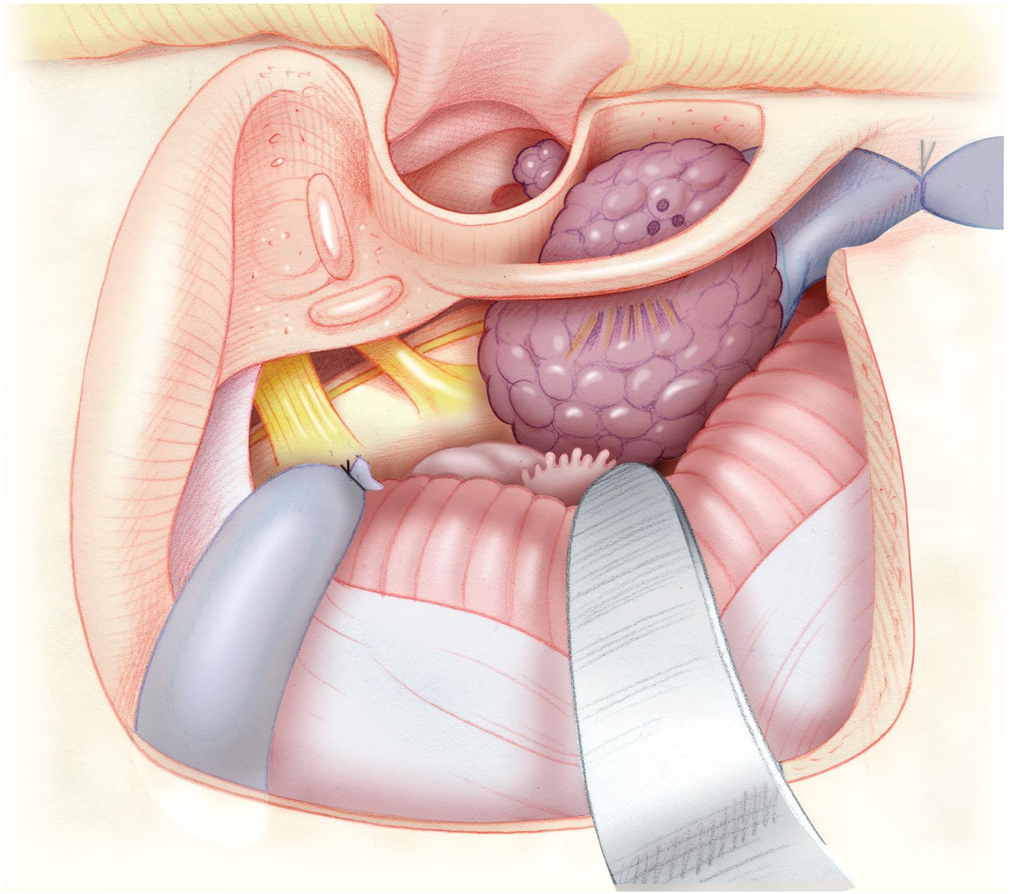
FACIAL NERVE

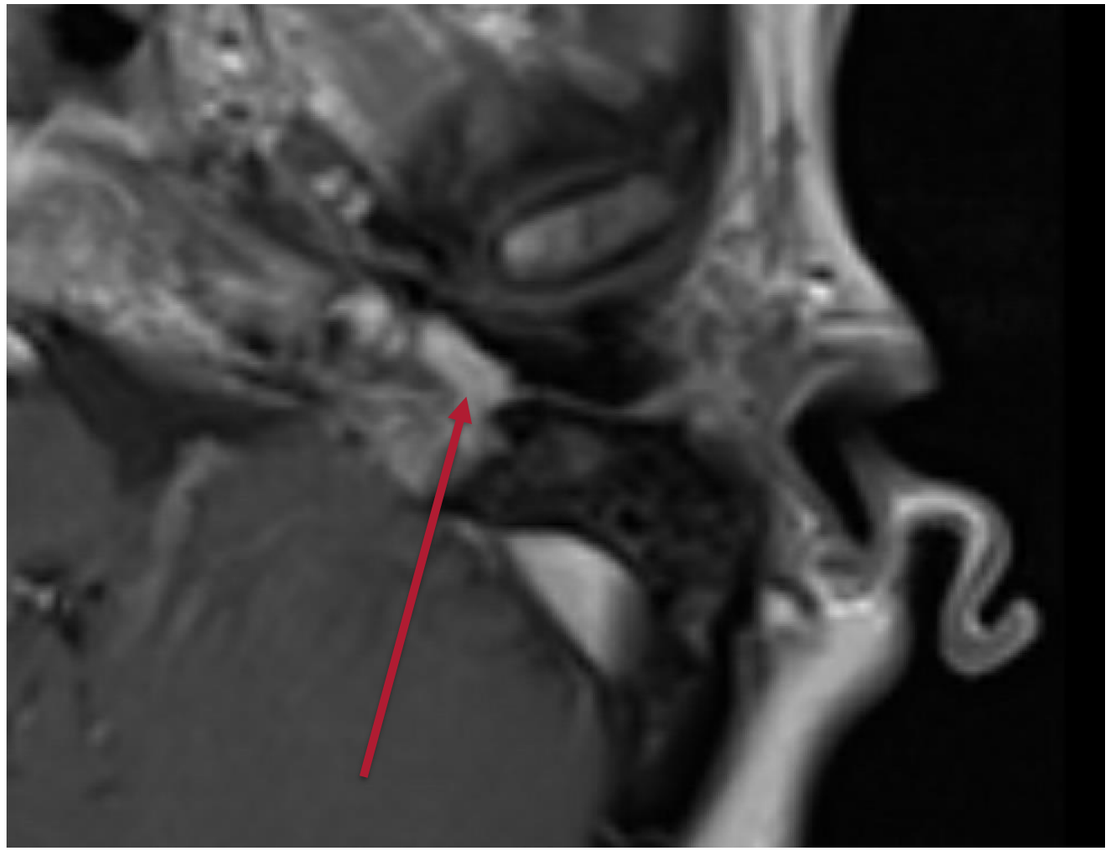


- Continuous neuromonitoring with dedicated team
- Fallopian bridge technique
- Avoid nerve transposition

HEARING

- Tumor location, not just size, influences type of hearing loss and prognosis
  - Sensorineural (inner ear) hearing loss generally not recoverable
  - Conductive hearing loss may improve, unless surgical approach requires sacrifice of the ear canal
- Radiation has low chance of worsening hearing
- Pulsatile tinnitus treated primarily with surgery, but may improve with radiation (about 60% chance)
- Bone conduction hearing devices

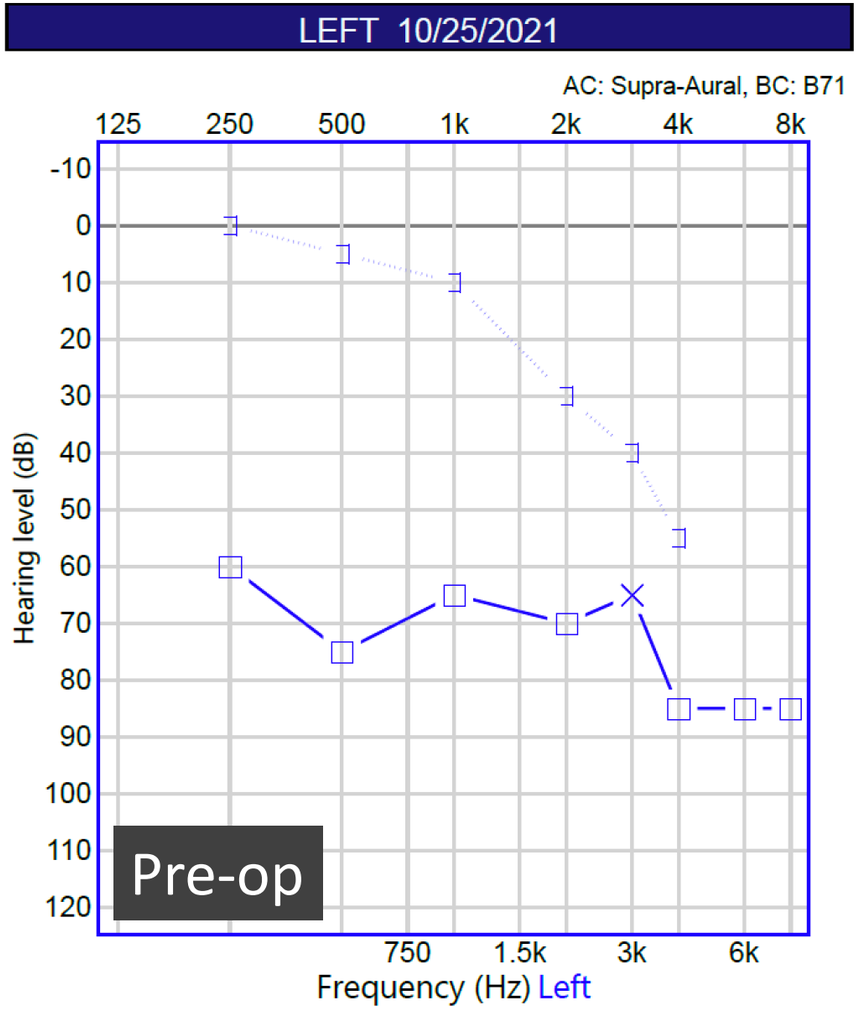
HEARING

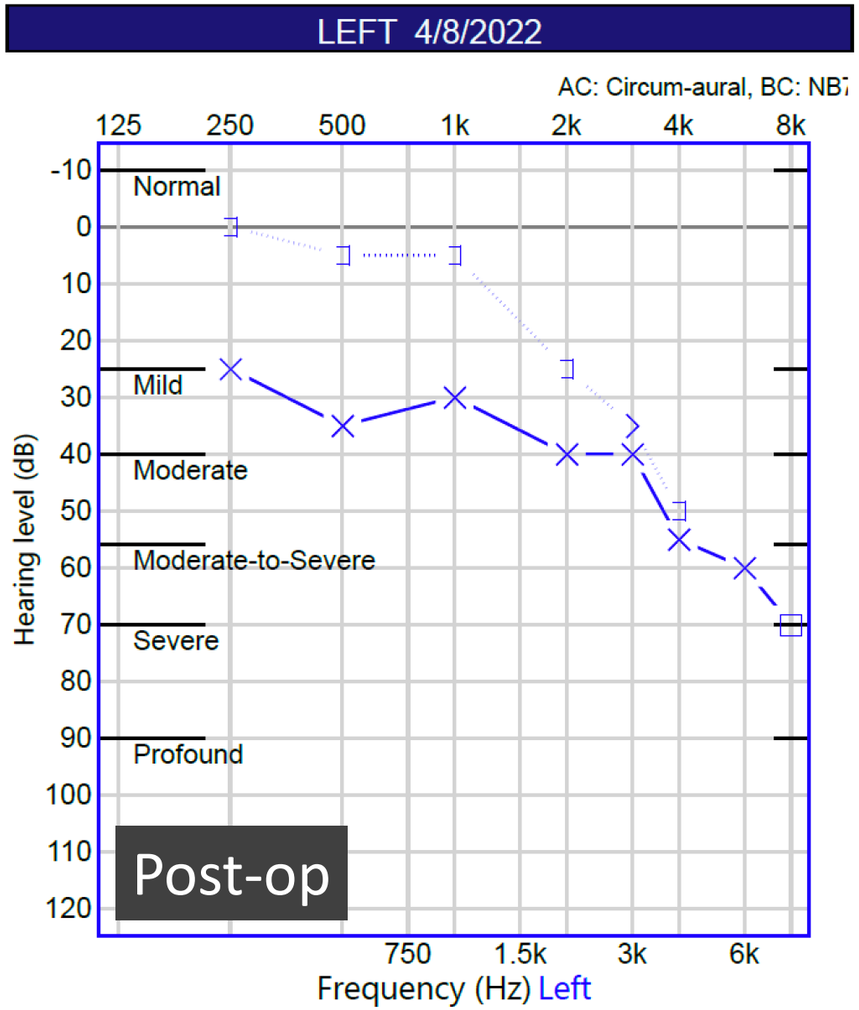


- Tumor in middle ear space
  - Pulsatile tinnitus
  - Marked conductive hearing loss
  - Ear fullness, pain

→ Surgery with CN preservation
Postoperative SRS for residual

HEARING





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PRIMARY RADIOSURGERY

JNS CLINICAL ARTICLE

Long-term tumor control following stereotactic radiosurgery for jugular paraganglioma using 3D volumetric segmentation

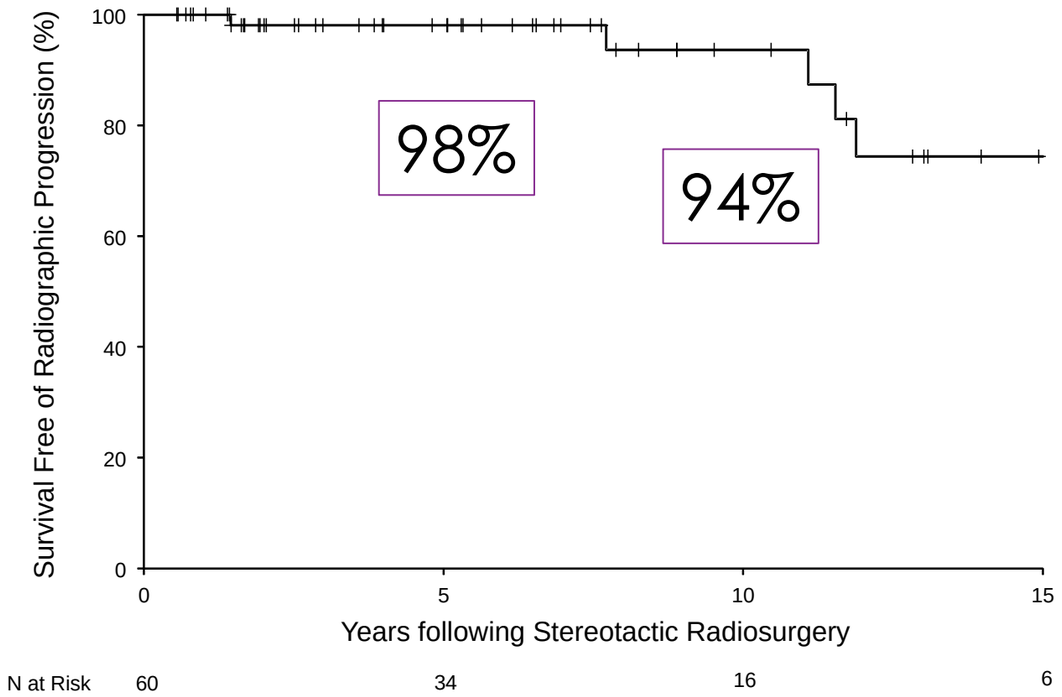
Neil S. Patel, MD,[1] Matthew L. Carlson, MD,[1,2] Bruce E. Pollock, MD,[2,3] Colin L. W. Driscoll, MD,[1,2] Brian A. Neff, MD,[1] Robert L. Foote, MD,[3] Christine M. Lohse, MS,[4] and Michael J. Link, MD[1,2]

Departments of [1]Otorhinolaryngology, [2]Neurologic Surgery, [3]Radiation Oncology, and [4]Health Sciences Research, Mayo Clinic, Rochester, Minnesota

Median follow up 5.5 yrs

5 Radiographic Progression

1 Clinical Failure



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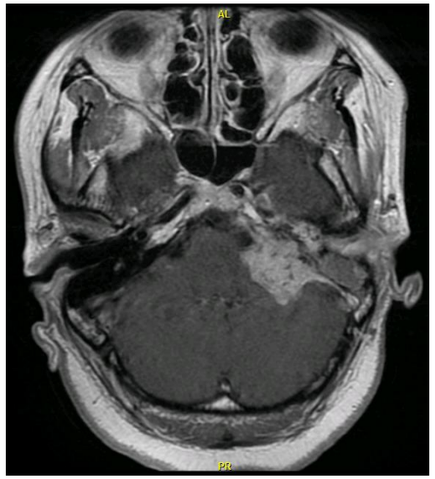
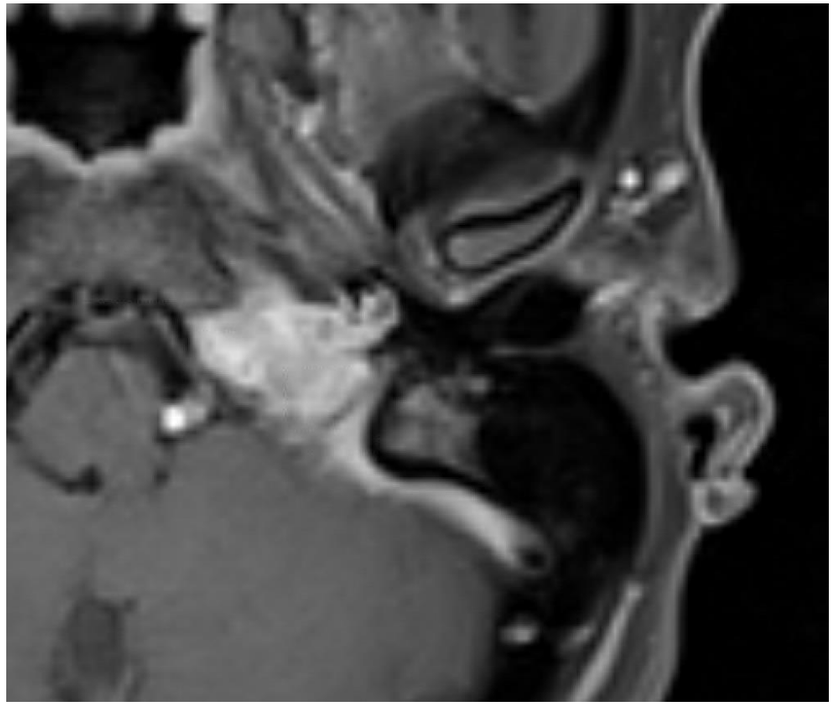
SURGERY VERSUS RADIATION?

1. Symptoms and pre-treatment cranial nerve function
2. Presence of intracranial disease
3. Tumor overall size and location
4. Growth rate (if initially observed)
5. Patient age and overall health
6. Sporadic or familial





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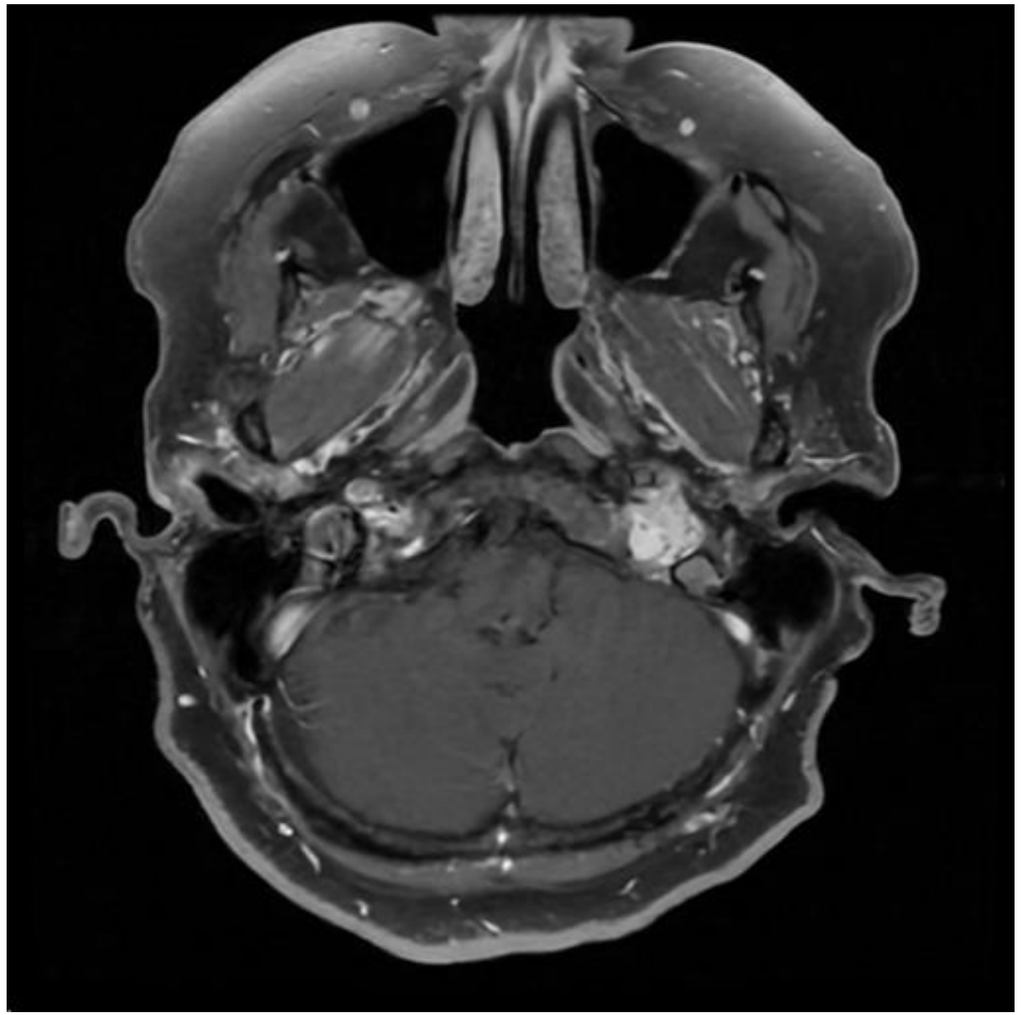
OBSERVATION: WHAT IS THE NATURAL HISTORY



65 years old

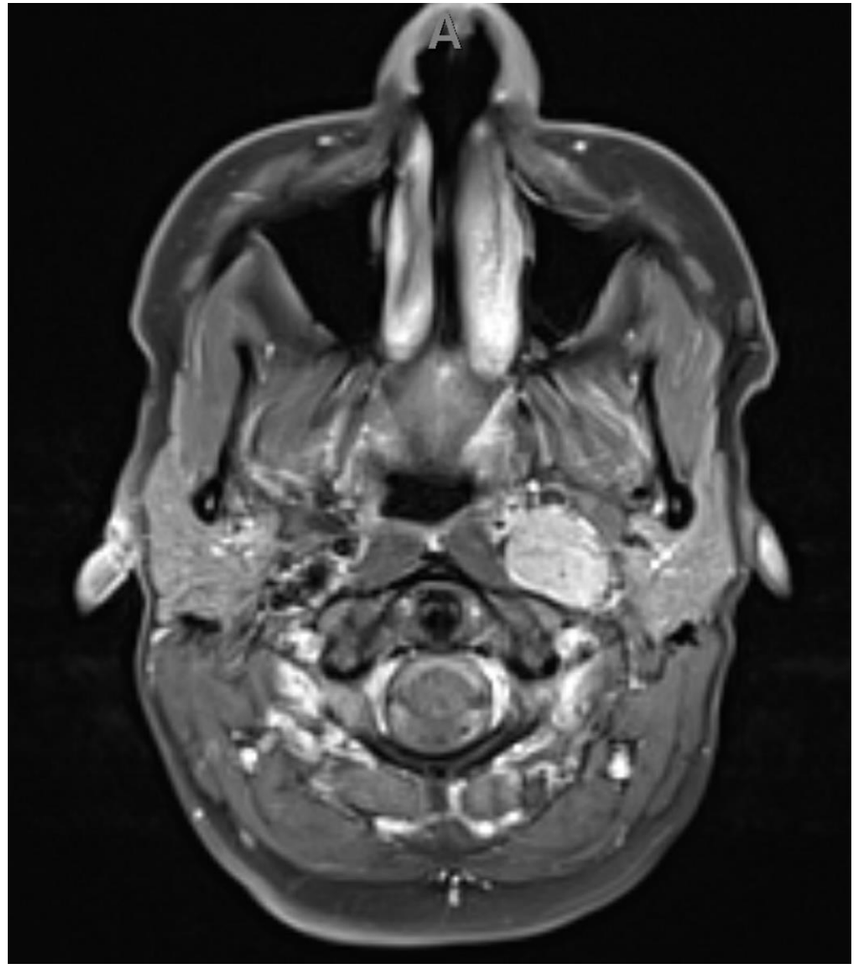
Normal CN function

Profound HL L ear x 20 years

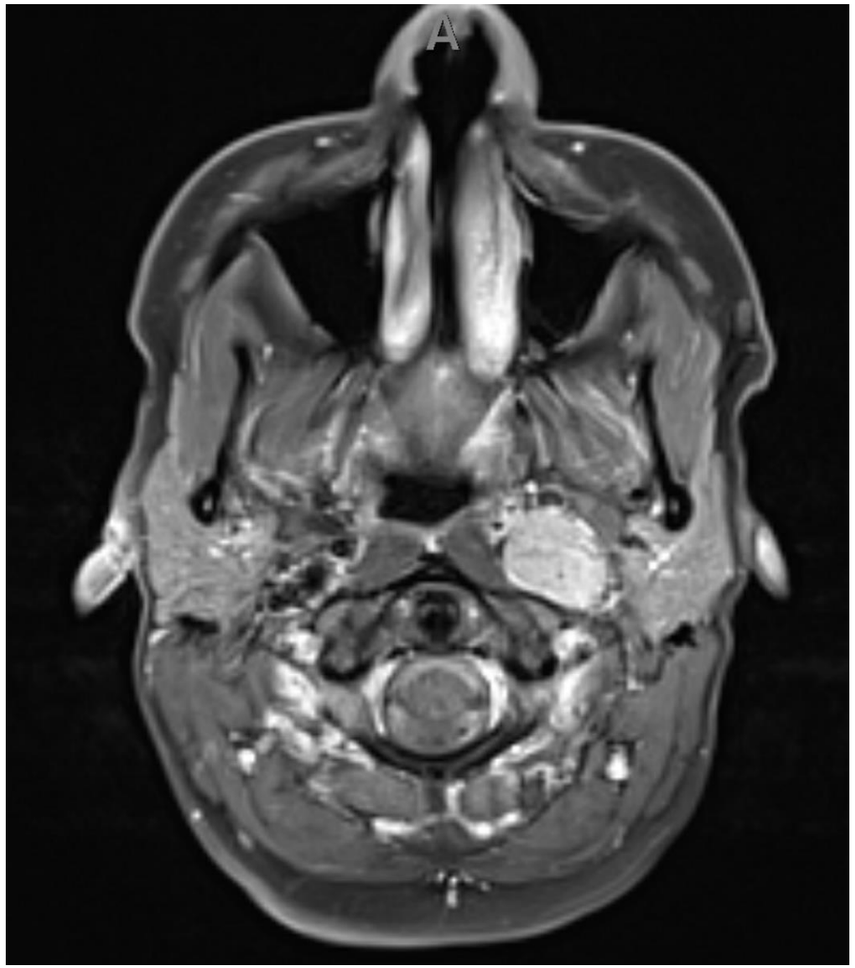
What will happen?

VAGAL PARAGANGLIOMA

Because the excision of these tumors is a formidable undertaking, the surgeon should have at his or her disposal surgical approaches that provide cranial base exposure and allow for carotid artery control. In addition, a "skull base operative team" consisting of an otologist, head and neck surgeon, vascular surgeon, and neurosurgeon should be assembled, and be available should it become necessary.



VAGAL PARAGANGLIOMA



- When to intervene: vagus nerve status, tumor size, and whether unilateral or bilateral
- Surgery almost always results in complete vagal neuropathy
- Radiation is effective but location can require a different treatment schedule

KEY ELEMENTS OF SURGERY FOR GV

1. Angiography and tumor embolization: not always done, but I recommend it
2. Cranial nerve monitoring: facial and lower cranial nerves
3. Multi-surgeon team: head and neck surgical oncologist, neurotologist, vascular surgeon
4. Transcervical and transmastoid approach
5. Observation in neurosurgical ICU or surgical floor depending on extent of surgery (1-4 nights)
6. Speech and swallowing evaluation

PRIORITIES: VAGAL PARAGANGLIOMA

Cranial Nerves

Tumor Control

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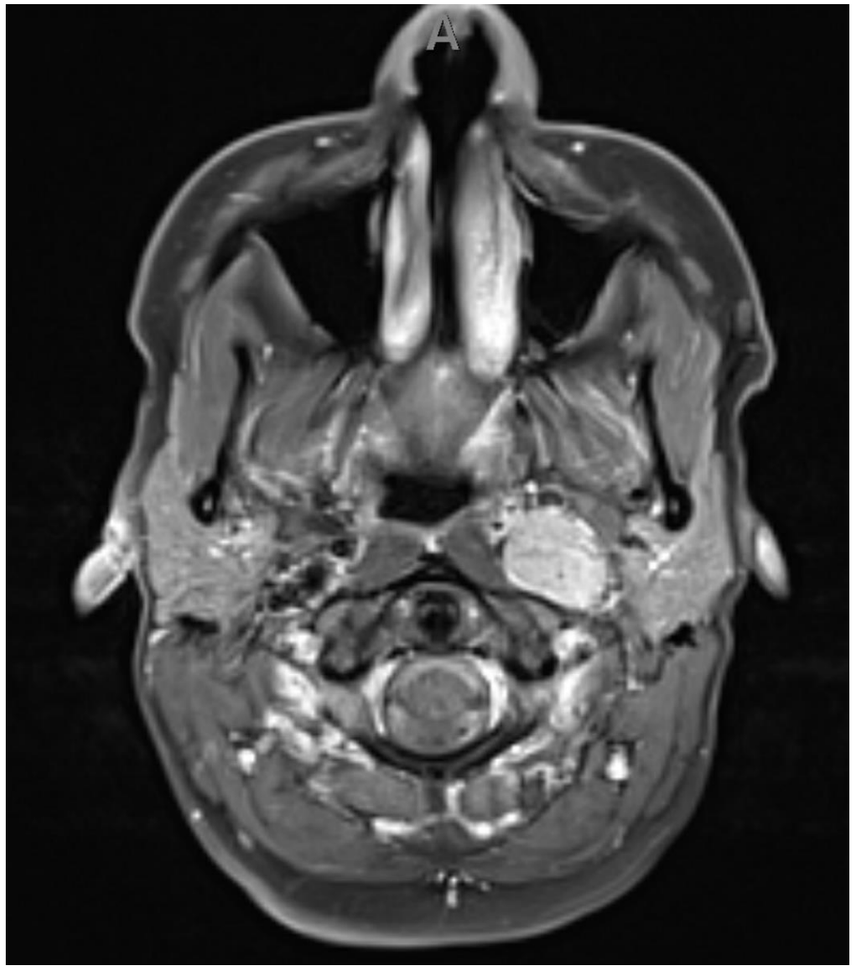
VAGAL PARAGANGLIOMA



- Approach determined by location and size
- Netterville classification
  - A: neck only
  - B: in contact with jugular foramen
  - C: into or beyond jugular foramen (+/- intracranial extension)
- Transcervical for A and some B
- Transcervical and transmastoid for most B and all C

INFLUENCE OF SDH MUTATION

Table 1. Most Common Clinical Presentations of *SDHx*-Related HNPGLs and Malignancy Risks[a]

Gene	Inheritance	Family History	Tumor Number in Head and Neck	Concomitant Sympathetic PGLs, %	Malignancy Risk, %[b]	Related Conditions
SDHA	AD	Low	Single	None reported[c]	10[c]	GIST
SDHB	AD	Low	Multiple	<5	20–30	GISTs, RCCs
SDHC	AD	Low	Single	Rare	Rare	GISTs
SDHD	AD (paternal)	High	Multiple	10–15	<5	GISTs, pituitary adenomas
SDHAF2	AD (paternal)	High	Multiple	None reported	None reported	None reported

Abbreviations: AD, autosomal dominant; RCC, renal cell carcinoma.

[a] *SDHD* and *SDHAF2* mutation carriers develop tumors only when the mutation is inherited from the father; the latter is found very rarely and only in young adults. Non-*KIT/PDGFRA* GIST may be caused by mutations in one of the *SDH* genes and can be associated with PGL in Carney-Stratakis syndrome. Renal cell carcinoma has been mainly described as a component of *SDHB*-associated syndromes but may also occur in the presence of other *SDHx* mutations. Pituitary adenomas have been mainly reported in PGL patients with *SDHD* germline mutations but may also occur in the presence of other *SDHx* mutations.

[b] All primary sites pooled.

[c] Further study needed.

Taïeb et al, 2014

RISK OF MALIGNANCY

- Biochemical and histopathologic features
- Size doesn't matter in HNPGL (does in PHEO)
- Highly infiltrative tumors may predict malignant potential (anecdotal)
- Sample lymph nodes in neck at time of surgery even if negative on imaging
- Favor early intervention for SDHB patients

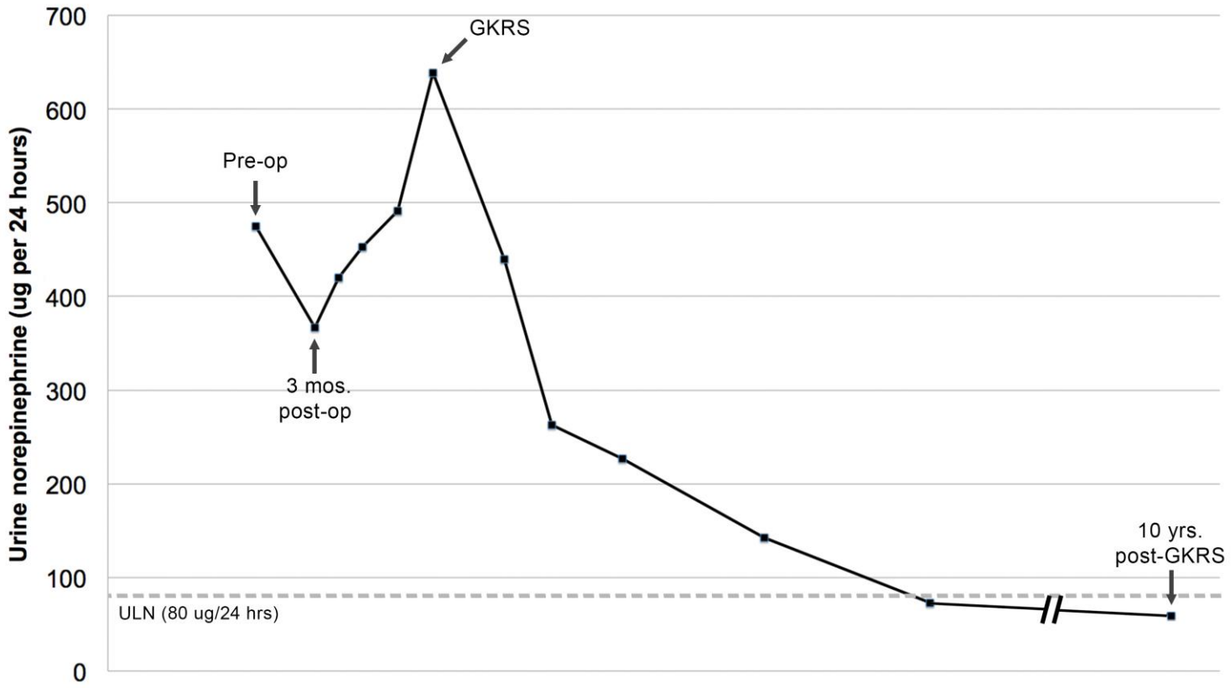
Taïeb et al, 2014

HYPERSECRETION

- Catecholamine excess best measured using 24 hour urine collection
- Generally favor surgery but radiosurgery can be effective
- Vital to involve endocrinologist for periop management
- Look for occult PHEO

Salvage Radiosurgery After Subtotal Resection for Catecholamine-secreting Jugular Paragangliomas: Report of Two Cases and Review of the Literature

Chweya, Cynthia M.*; Patel, Neil S.†; Young, William F. Jr‡; Pollock, Bruce E.||; Link, Michael J.||; Carlson, Matthew L.|| Author Information



THANK YOU!

Q&A