

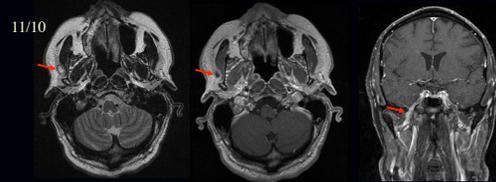
Imaging of Perineural Tumor Spread in Head and Neck Cancer



Lawrence E. Ginsberg, MD
 Departments of Diagnostic Radiology and Head and Neck Surgery
 University of Texas M.D. Anderson Cancer Center
 Houston, Texas

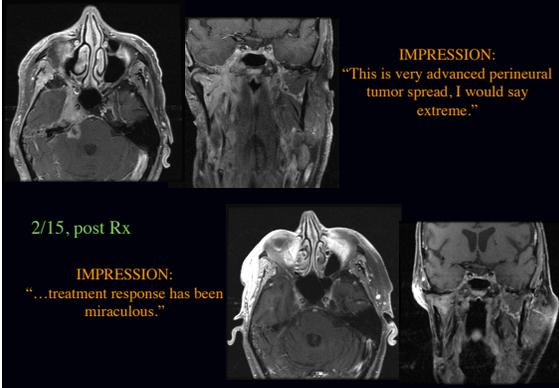
PNS bad, but not universally deadly, as in this typical scenario

66-y/o man with Hx/o right cheek SCCa, disappeared with topical 5FU, subsequent paresthesias dismissed by ENT because scope was neg. Ultimately developed parotid met, resected, XRT, but had progressive multiple cranial neuropathies



Outside report: "Worrisome for right parotid met, no facial PNS."

Fast forward, admission to MDACC 7/12



Perineural Tumor Spread (PNS)

- Definition: dissemination of tumor from the primary site along tissue planes of the neural sheath
- Small vs. large nerve PNS
- Clinical settings:
 - salivary gland-parotid, minor salivary gland (palate)
 - mucosal (SCCa)-palate/RMT, nasopharynx (via MS, PPF)
 - skin (SCCa, desmoplastic melanoma)
 - occasionally lymphoma or other cancer
 - previously treated/forgotten disease*
- Symptoms: pain, paresthesias, motor denervation, but up to 40% may be asymptomatic
- Implications: serious finding associated with decreased survival. Detection will often affect treatment

Perineural Tumor Spread (PNS)

- Failure to recognize PNS (big problem)
 - common pitfall in head and neck imaging
 - good way to get sued
 - guarantees disease recurrence/progression
- Because may be asymptomatic, up to radiologist to think of PNS and detect it
- Rarely, site to which tumor spreads perineurally may present prior to detection of primary cancer. Therefore, must consider PNS whenever lesion is seen in Meckel's cave, pterygopalatine fossa, or cavernous sinus

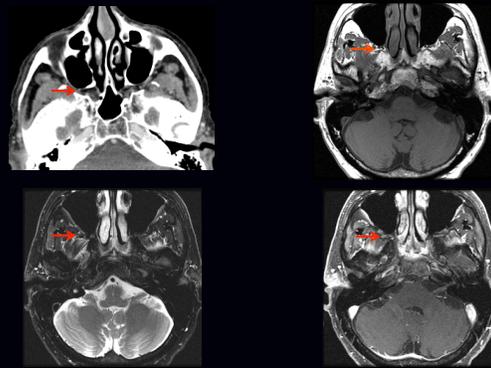
PNS Anatomic Considerations

- Trigeminal nerve V
 - V₁ ophthalmic
 - V₂ maxillary
 - V₃ mandibular
- Facial nerve VII
- Connections between V and VII
- Uncommon routes

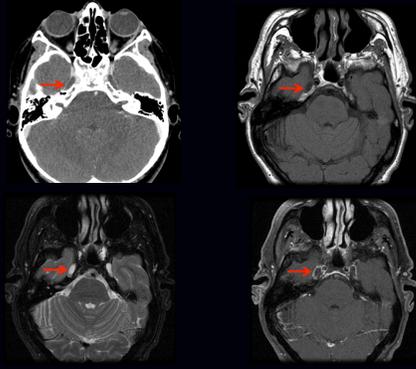
Perineural Tumor Spread-Imaging

- Widening/destruction of or excessive enhancement within neural foramina (ovale, rotundum, palatine, stylomastoid foramen/ descending facial canal, vidian canal)
 - CT better for bone destruction (late finding)
- Loss of normal fat density (CT)/T1 signal intensity (MR) or excessive enhancement/ widening of the pterygopalatine fossa
- Enlargement/excessive enhancement within cavernous sinus or Meckel's cave
- MR technique: 16-18 cm FOV, 3 mm slices, fat-suppressed, post contrast T1-weighted images

What should a normal pterygopalatine fossa look like?

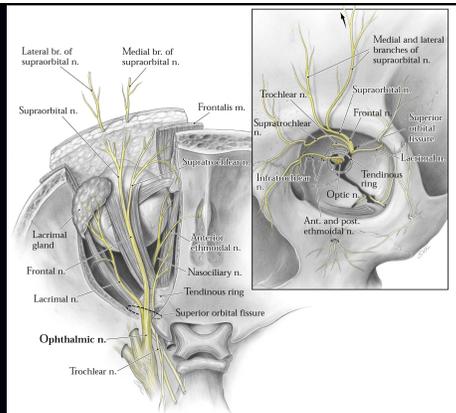


What should a normal Meckel's Cave look like?

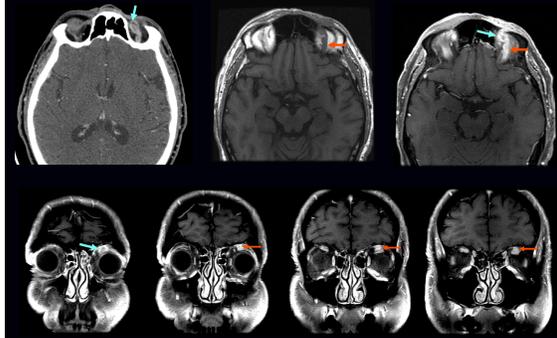


Ophthalmic Nerve V₁

- Provides sensory innervation to the eye, lacrimal gland, conjunctiva, and skin of the nose, supraorbital region, and frontal scalp
- Course-cavernous sinus to SOF, orbit, divides into branches-lacrimal, nasociliary, frontal
- Lacrimal branch also carries parasympathetic innervation originating in the facial nerve, via the GSPN and ultimately a small twig from the zygomaticotemporal branch of V₂
- Main nerve involved in PNS is frontal nerve, which divides into (or is formed by the joining of) the supratrochlear and supraorbital branches



58-y/o man, s/p resection SCCa left medial forehead, locally recurrent 5 months later, with PNS on supratrochlear branch V₁, extending to frontal nerve

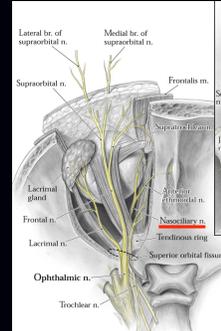
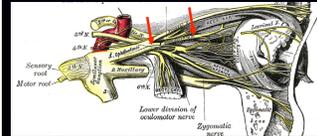


57-y/o man with neglected chronic, bleeding left forehead wound. Spread along **frontal nerve** and through **superior orbital fissure**.



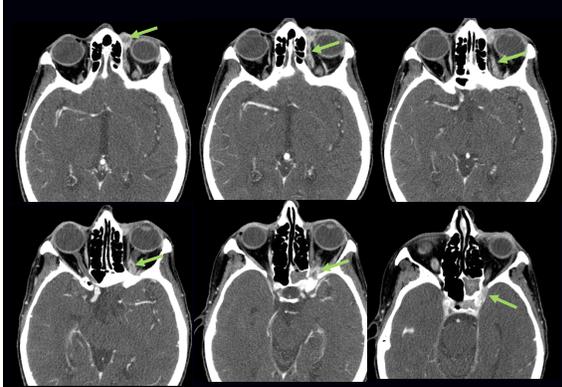
Nasociliary Nerve

- Branch of V1
- Provides cutaneous sensory fibers to skin of lateral nose, and sensory innervation from the frontal dura, sphenoid and ethmoid sinus mucosa, nasal mucosa, and medial canthus



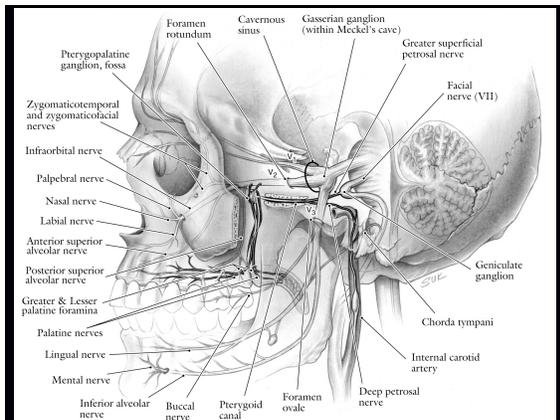
Shah K, Esmaili B, Ginsberg LE. Perineural tumor spread along the nasociliary branch of the ophthalmic nerve: imaging findings. J Comput Assist Tomogr. 37(2):282-5. Mar-Apr. 3/2013.

77-year old woman with recurrent SCCa, left medial canthal region

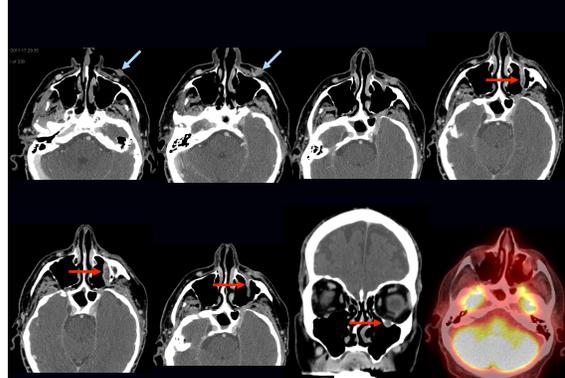


(PNS) Anatomic Considerations

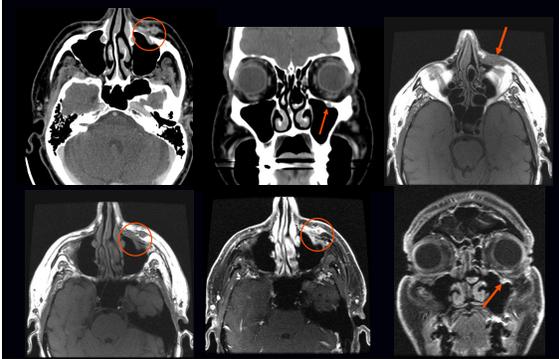
- Maxillary nerve, V₂-sensory to the mid-face, palate, sinonasal region, upper oral cavity. Common pathway to PPF, foramen rotundum, cavernous sinus, Meckel's cave
- Mandibular nerve, V₃-sensory to lower face and oral cavity, motor innervation to muscles of mastication. Common pathway to foramen ovale, Meckel's cave
- Antegrade PNS-Meckel's cave to cavernous sinus or downward along V₃, Cavernous sinus anteriorly along V₂, PPF along palatine or infraorbital nerves
- Facial nerve, generally from primary parotid lesions or lesions that secondarily extend into the parotid



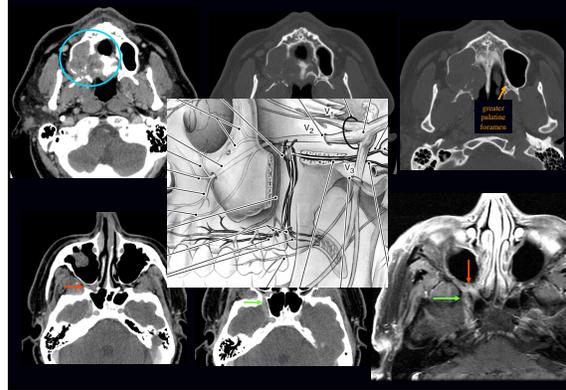
Fair-skinned 74-y/o male with left cheek melanoma, and V₂ hypesthesia



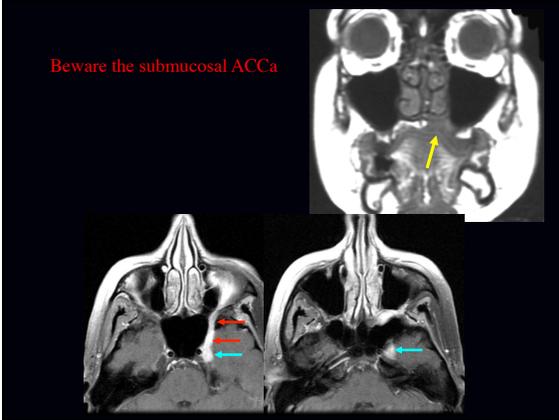
62-y/o man, now with left V₂ paresthesias following Mohs surgery for left cheek SCCa. Recurrence with infraorbital nerve PNS



Palatal/maxillary alveolar ridge ACCa, PNS to PPF, rotundum



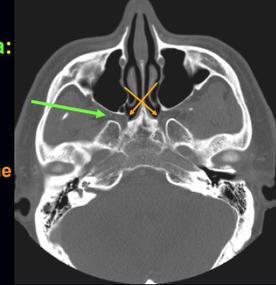
Beware the submucosal ACCa



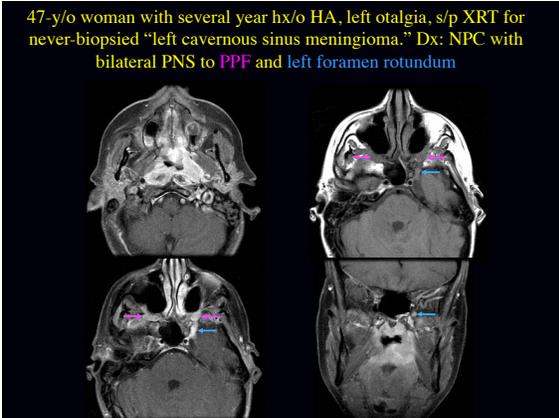
V₂ PNS in Nasopharyngeal Carcinoma

Requires extension into the pterygopalatine fossa:

- direct extension through pterygoid plates
- anterior extension into nasal cavity and laterally through the sphenopalatine foramen
- both

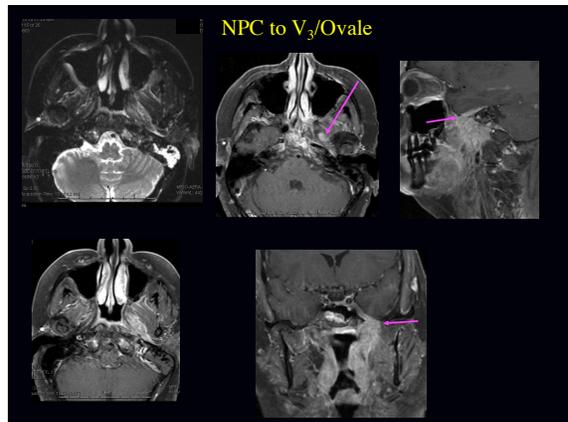
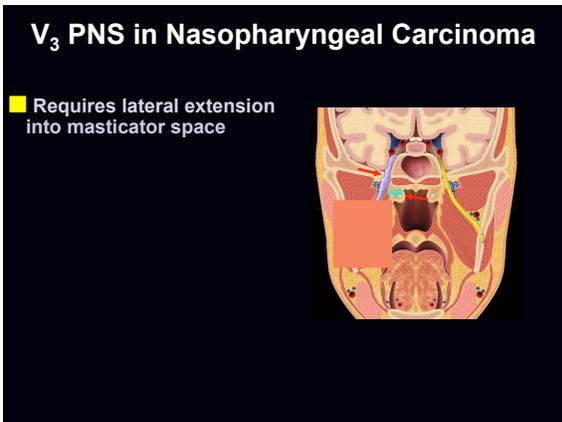
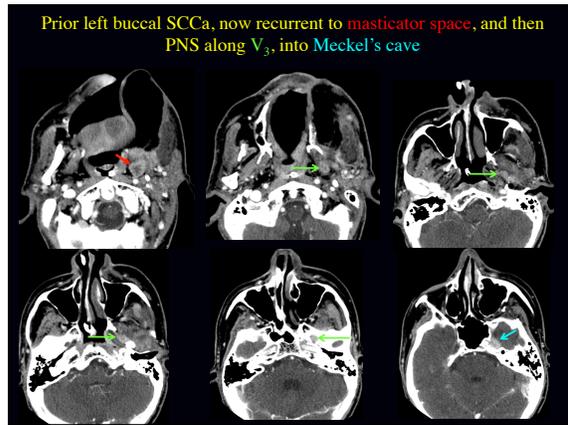
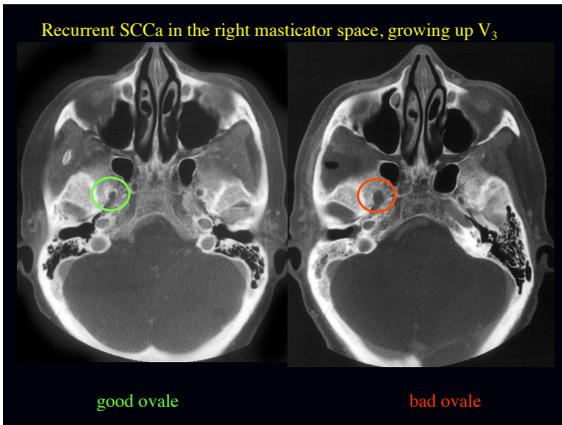
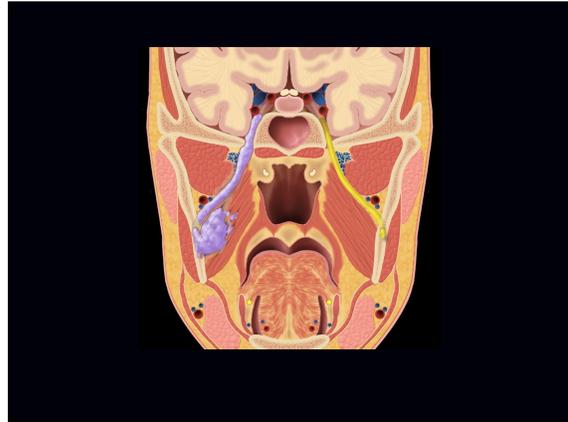
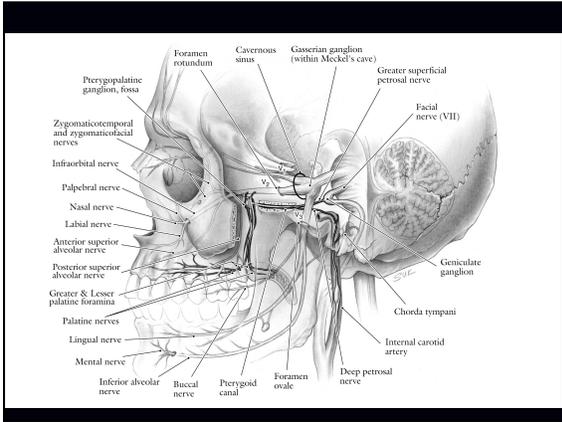


47-y/o woman with several year hx/o HA, left otalgia, s/p XRT for never-biopsied "left cavernous sinus meningioma." Dx: NPC with bilateral PNS to PPF and left foramen rotundum



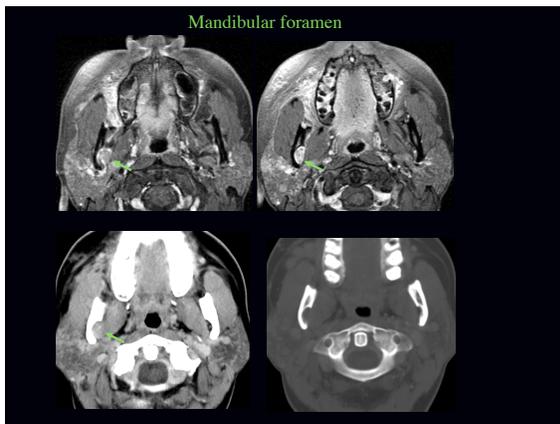
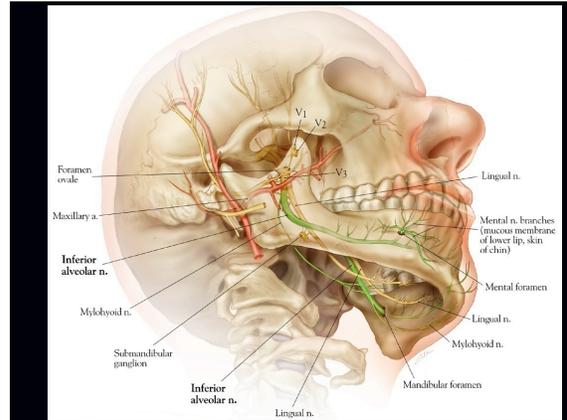
(PNS) Anatomic Considerations

- Maxillary nerve, V₂-sensory to the mid-face, palate, sinonasal region, upper oral cavity. Common pathway to PPF, foramen rotundum, cavernous sinus, Meckel's cave
- Mandibular nerve, V₃-sensory to lower face and oral cavity, motor innervation to muscles of mastication. Common pathway to foramen ovale, Meckel's cave
- Antegrade PNS-Meckel's cave to cavernous sinus or downward along V₃, Cavernous sinus anteriorly along V₂, PPF along palatine or infraorbital nerves
- Facial nerve, generally from primary parotid lesions or lesions that secondarily extend into the parotid

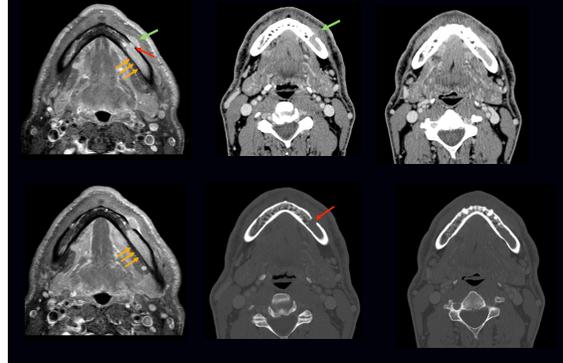


Inferior Alveolar Nerve

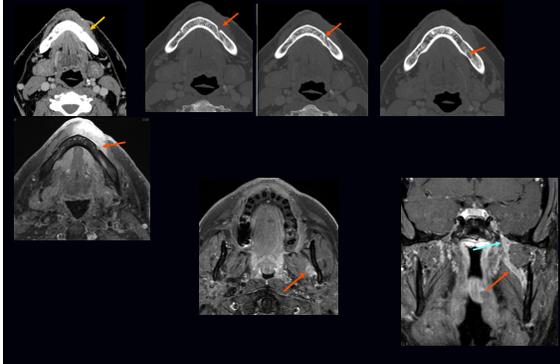
- Branch of mandibular nerve (V₃)
- Provides sensory innervation to lower gingiva and teeth, and cutaneous sensory innervation to the chin via the mental nerve
- Enters the mandible through the mandibular foramen
- At risk for PNS from lower lip primaries or any tumor that invades the mandible
- May be involved in downhill or antegrade PNS



56-y/o man presenting with left "numb chin" syndrome, outside radiologist interpreted MR as osteomyelitis. Dx: lymphoma

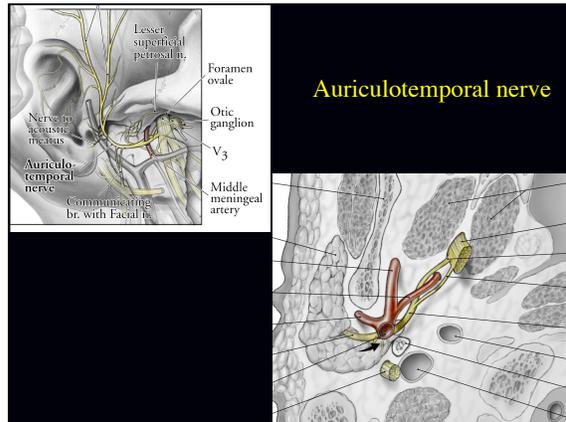
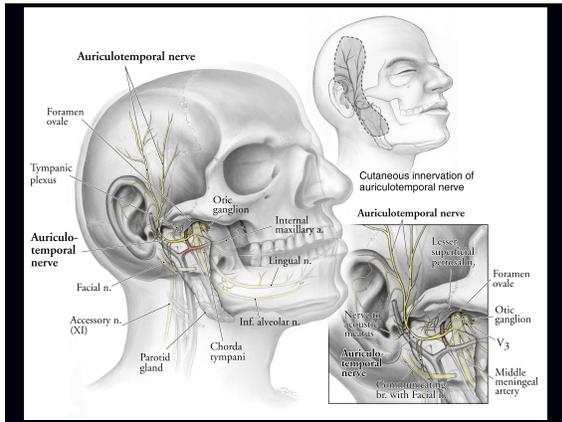


Recurrent left lower lip SCCa with proven PNS along the mental/inferior alveolar nerve to level of main trunk V₃

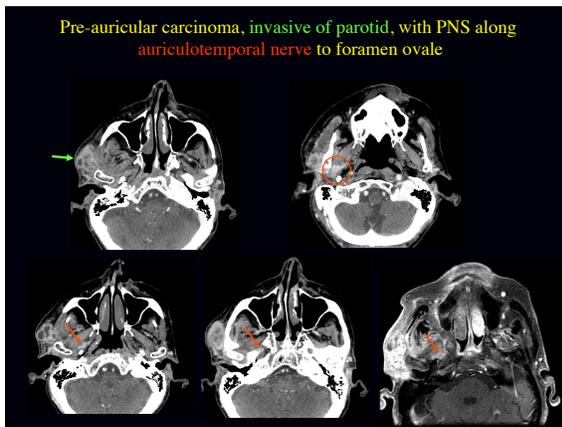


Auriculotemporal Nerve

- Branch of mandibular nerve (V₃)
- Arises just below foramen ovale
- Provides cutaneous innervation to lateral face, preauricular, external ear, and TMJ
- Also acts as conduit for post-ganglionic parasympathetic fibers (originating as LSPN), that provide secretomotor innervation to the parotid gland
- ATN and therefore V₃ at risk for PNS in 1° or 2° malignancies of parotid gland and skin cancers in its cutaneous distribution
- Evaluation of all parotid malignancies should include foramen ovale and proximal course of V₃



Auriculotemporal nerve



PNS-Anatomic Considerations-Facial Nerve

- Generally related to parotid pathology, either primary parotid malignancy, or lesions, generally skin cancers, that secondarily invade the parotid, at diagnosis or at recurrence
- Less commonly, skin cancers that have not yet invaded the parotid
- Beware the subdermal skin cancer, that is difficult to detect clinically
- When is “Bell’s Palsy” a Bell’s Palsy?

How Can Cancer Access the Facial Nerve Perineurally?

- Via peripheral branches and back into main trunk
- Directly into the stylomastoid foramen
- Back along GSPN (to follow)

Peripheral facial PNS. 65-y/o man previously treated for multiple right facial skin cancers, including a right anterior facial SCCa. Recent onset right buccal branch facial nerve paralysis and numbness

9/17 6/17 1/17

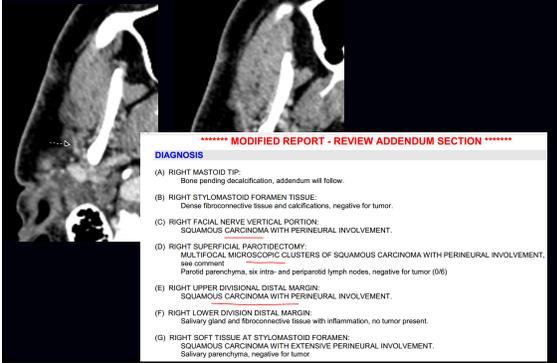
Stable. No findings to suggest local or nodal recurrence

ATN

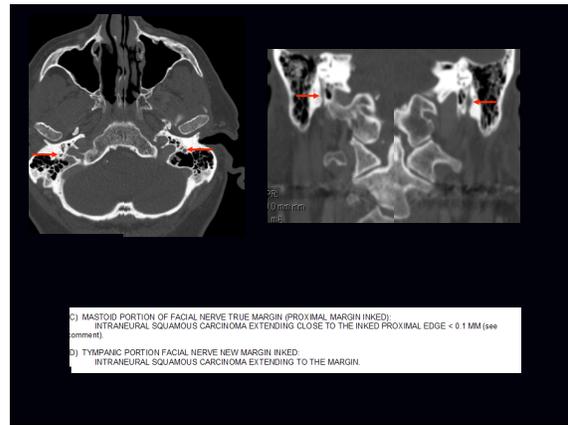
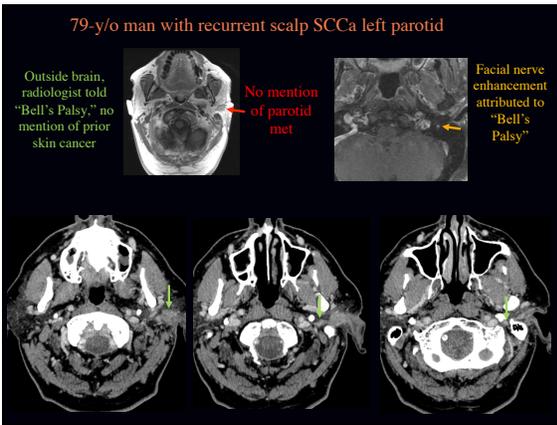
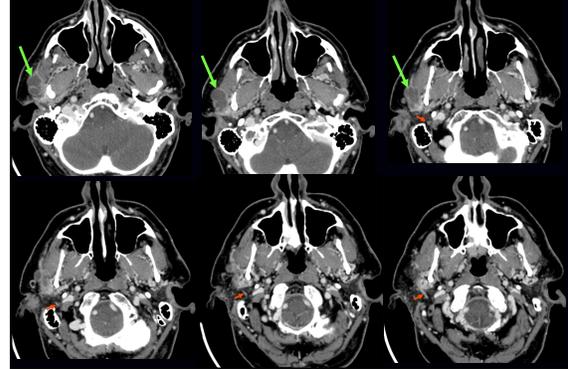
CN7 - Facial Nerve
 Paths of the 5 Motor Branches

1. Temporal Branch
2. Zygomatic Branch
3. Buccal Branch
4. Mental Branch
5. Cervical Branch

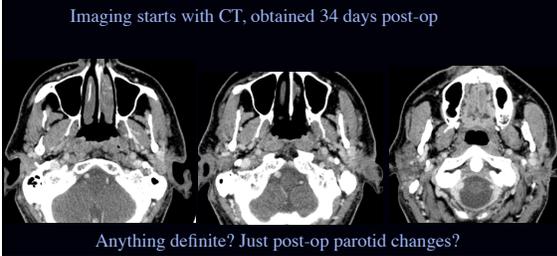
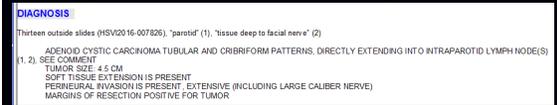
Peripheral facial PNS, but more subtle, 73-y/o man previously treated for right cheek SCCa, told facial palsy



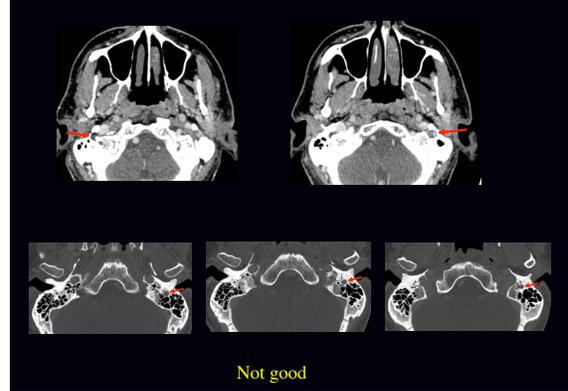
59-y/o man with multiple recurrences right facial SCCa, now with parotid region recurrence and facial palsy

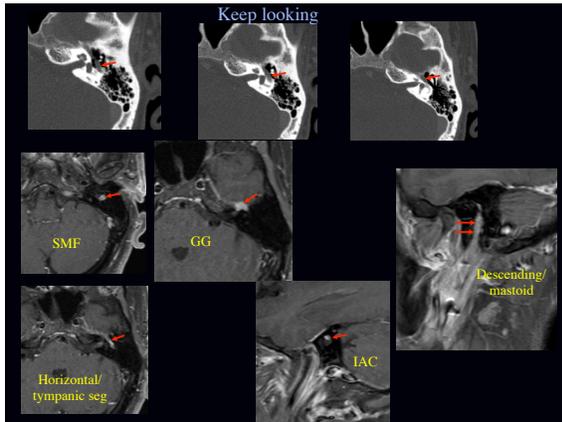


44-y/o man with facial neuropathy dismissed as "Bell's," ultimately develops parotid mass, ACCa, resected elsewhere, presents to MDACC



How about the stylomastoid foramen? Hard to see both on single slice.



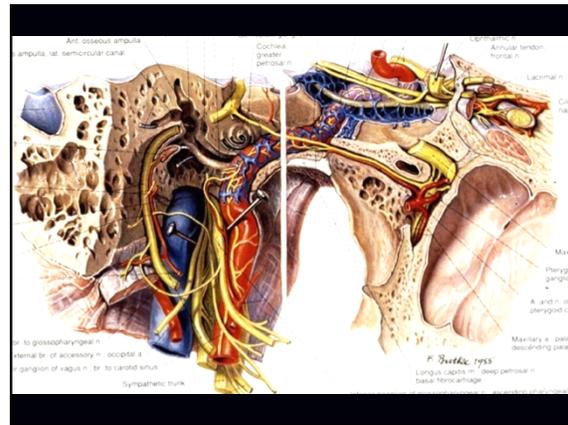


Relationship Between CN 5 and 7

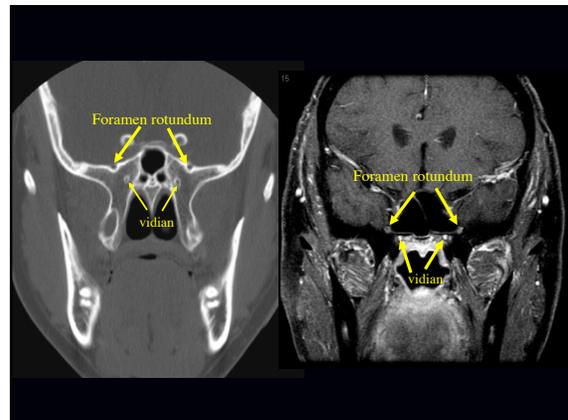
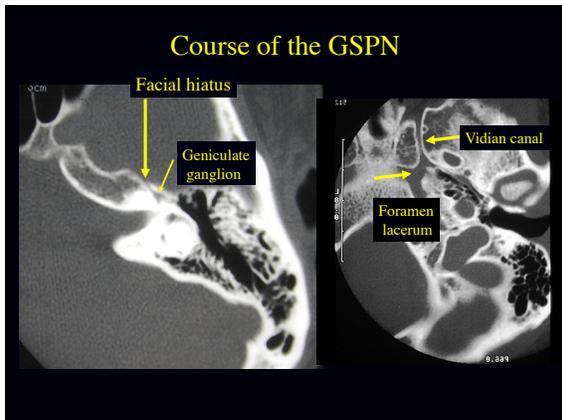
■ Distal branches of V serve as conduits for small branches of VII and IX. These represent real or potential routes of PNS

● Potential sources of PNS:

- chorda tympani-tongue, SM/SL glands
 - LSPN (runs with auriculotemporal nerve)-parotid gland
- Greater superficial petrosal nerve (GSPN)
- branch of CN7 originating in nervus intermedius
 - preganglionic fibers, motor root of SP ganglion
 - post ganglionic supply to palate, nasal, lacrimal
 - potential for perineural tumor spread quite real



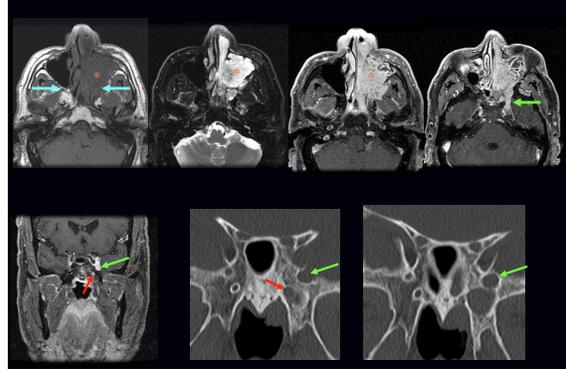
Course of the GSPN



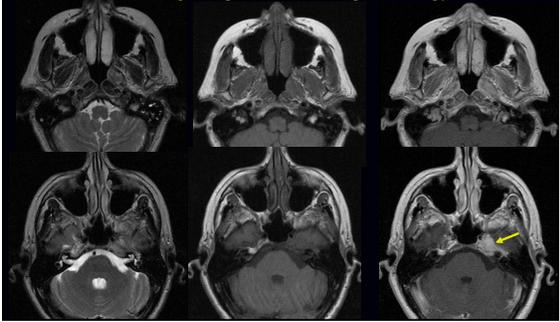
43-y/o woman with right facial pain and numbness. Dx: ACCa of the hard palate with PNS to the PPF and vidian nerve



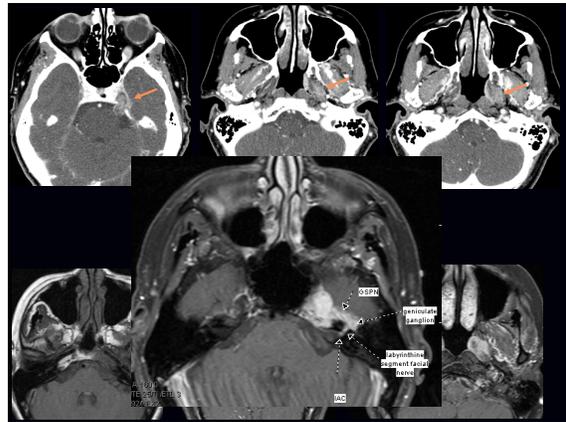
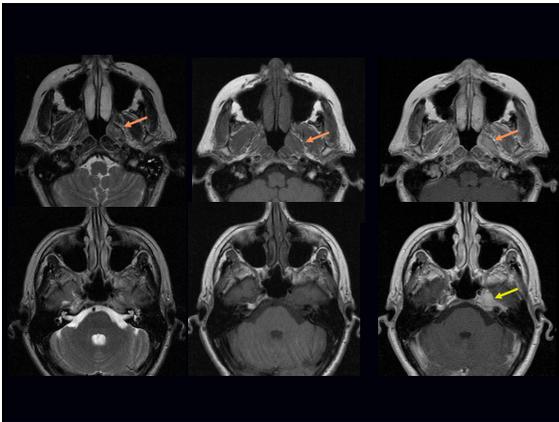
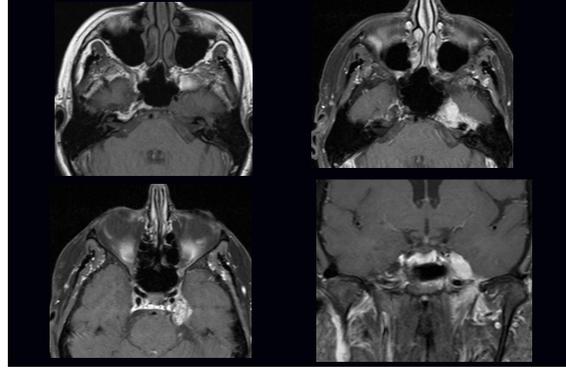
69-y/o man with ACCa left nasomaxillary. Spread to PPF facilitates PNS to vidian and rotundum



62-y/o woman with several year history of left ear discomfort and placement of tympanostomy tube for treatment of eustachian tube dysfunction. More recently developed left trigeminal sensory neuropathy, and oh yeah, just noticed she's NOT TEARING FROM THE LEFT EYE. Outside brain MR read as cavernous sinus meningioma, patient referred for proton therapy.



Repeat imaging obtained primarily for XRT planning. How to make a very long story short...?

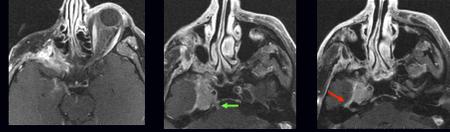


Other Unusual Pathways of PNS

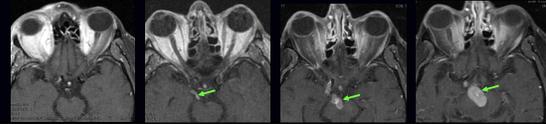
- Other, small cranial nerves
- Cervical Plexus-spinal nerves
 - greater and lesser occipital n.
 - great auricular n.
 - transverse cutaneous n.
 - supraclavicular n.

Rare Nerves-advanced, slow growing malignancies can spread to 3rd, 6th cranial nerves, maybe others, if cavernous sinus involved

Advanced recurrent lacrimal ACCa, 6th nerve involvement (and GSPN)

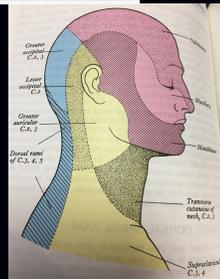


Advanced recurrent facial melanoma, already had cavernous sinus disease. Progressive 3rd nerve involvement



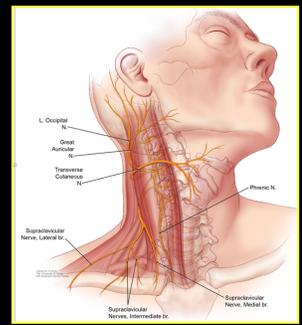
CN-08: Advanced Cutaneous Malignancy of the Head and Neck with Perineural Tumor Spread Along Cervical Nerves: A Plexus of Cancer
Melissa M. Chen MD, Ashley May MD, and Lawrence E. Ginsberg MD

MDAnderson
Cancer Center



Cervical plexus

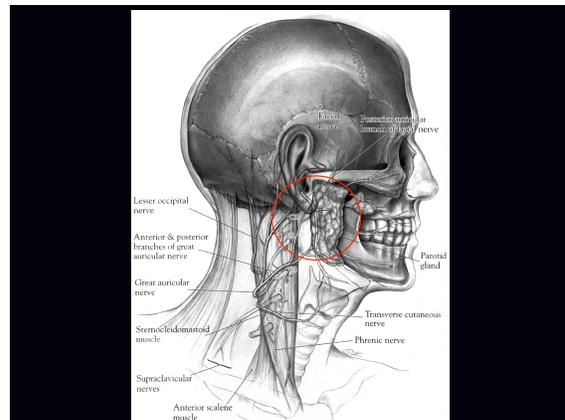
1. Great auricular nerve
 - ventral ramus of C2 and C3
 - overlies auricle and parotid regions with a mastoid branch communicating with lesser occipital nerve
2. Lesser occipital nerve
 - ventral ramus of C2 and C3
 - skin of scalp, posterior third of temporal fossa and neck posterior and superior to the auricle
3. Transverse cutaneous nerve
 - ventral ramus of C2 and C3
4. Supraclavicular nerve
 - ventral ramus of C3 and C4
 - common trunk divides into 3 branches



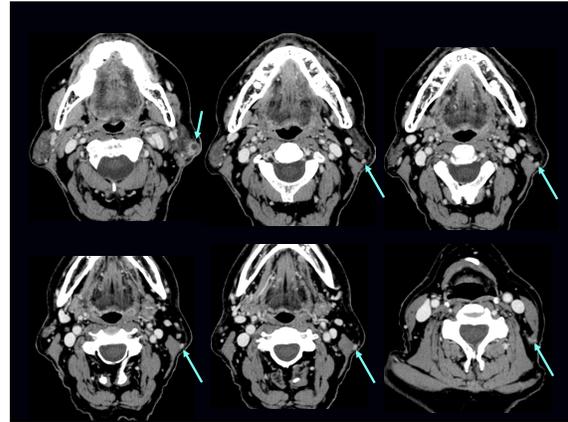
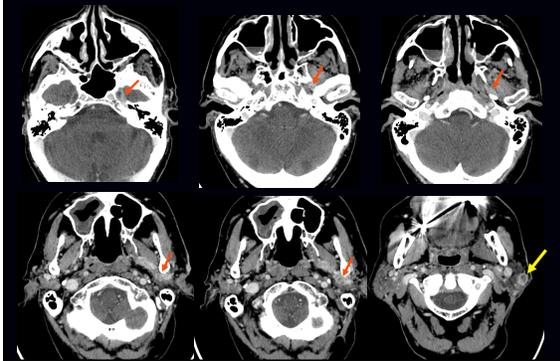
Great Auricular Nerve (GAN)

- Superficial branch of the superficial cervical plexus
- GAN provides sensory innervation to the skin over the parotid and lower pre-auricular region
- GAN leaves plexus, courses over and around the SCM (Erb's point) and then upward toward the ear
- Has communicating branches with the facial nerve within the parotid gland, and with the auricular branch of the vagus nerve
- GAN at risk for PNS in its cutaneous distribution

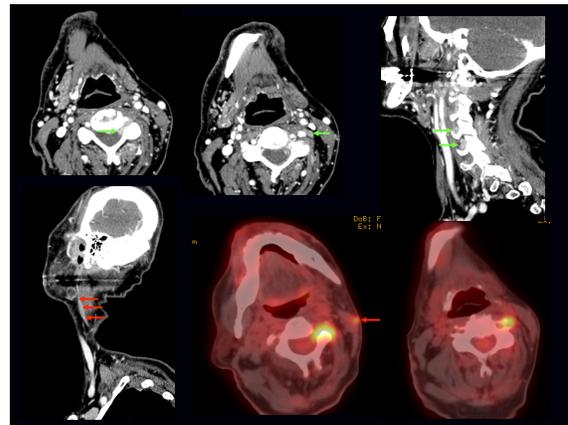
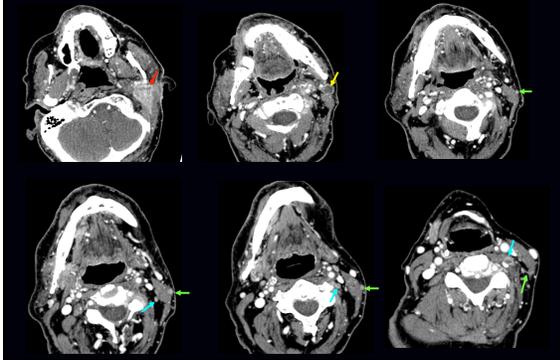
Ginsberg LE, Eicher SA. Great auricular nerve: anatomy and imaging of perineural tumor spread. AJNR 21: 568-571, 2000.



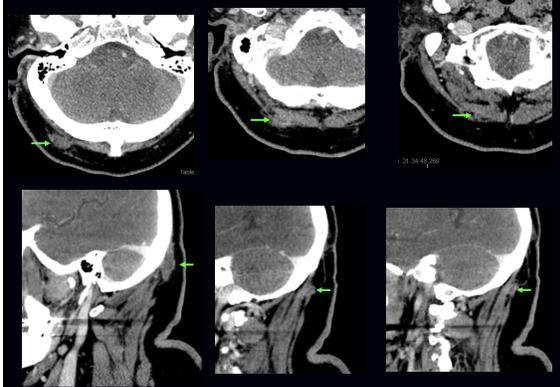
68-y/o man with prior skin resections, now with recurrent SCCa left parotid, and PNS along auriculotemporal and greater auricular nerve



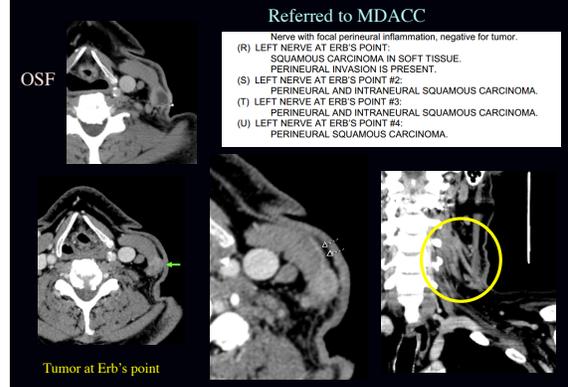
72-y/o man with multiply recurrent SCCa left face, now with recurrence over the left lower parotid region



56-y/o man with recurrent posterior scalp SCCa, occipital nerve PNS



66-y/o man with previously resected low neck SCCa, now recurrent subdermally



Referred to MDACC

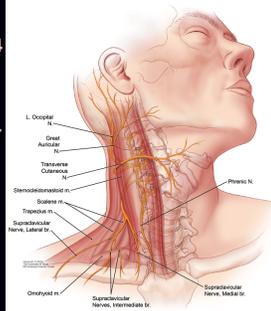
- Nerve with focal perineural inflammation, negative for tumor.
- (R) LEFT NERVE AT ERB'S POINT: SQUAMOUS CARCINOMA IN SOFT TISSUE. PERINEURAL INVASION IS PRESENT.
- (S) LEFT NERVE AT ERB'S POINT #2: PERINEURAL AND INTRANEURAL SQUAMOUS CARCINOMA.
- (T) LEFT NERVE AT ERB'S POINT #3: PERINEURAL AND INTRANEURAL SQUAMOUS CARCINOMA.
- (U) LEFT NERVE AT ERB'S POINT #4: PERINEURAL SQUAMOUS CARCINOMA.

OSF

Tumor at Erb's point

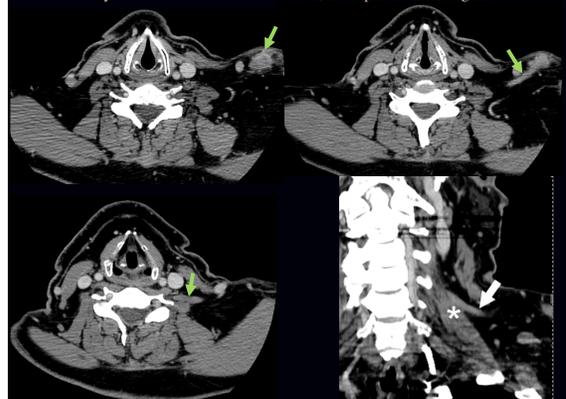
Supraclavicular Nerves

- Branches of cervical plexus
- Formed by twigs from C3, C4 spinal nerve ventral rami
- Provide sensory innervation to skin over the clavicle, anteromedial shoulder, upper chest
- Anterior, posterior, intermediate branches



Alsarraf L, Shah K, Hessel A, Williams M, Ginsberg LE. Perineural spread along the intermediate branch of the supraclavicular nerve- A case report. Neurographics. In Press.

61-year-old man with recurrent SCCa, left supraclavicular region



Conclusion

- Perineural tumor spread is a very serious and potentially life-threatening complication of head and neck cancer
- Because it may be asymptomatic at presentation or masked at recurrence due to prior therapy, it is critical that the radiologist make the diagnosis
- Diagnosing PNS requires careful attention to imaging technique and a solid understanding of the relevant neuro-anatomy

THE UNIVERSITY OF TEXAS

MD Anderson
Cancer Center

Making Cancer History®