Trigeminal Neuralgia

Current Concepts and Management

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South Sound Gamma Knife at St. Joseph

Outline of Presentation

Introduction
Epidemiology
Etiology and Pathophysiology
Clinical Presentation
Diagnosis
Clinical Course
Medical Treatment
Surgical Treatment Options/ Anatomy
Stereotactic Radiosurgery (Gamma Knife)

Introduction and General Comments

Trigeminal Neuralgia (TN) is defined as paroxysmal, stereotyped attacks of intense and sharp pain in the distribution of one or more branches of the trigeminal nerve

History:

- Aretaeus of Cappadocia, 3000 years ago
- Nicholaus Andre, 1756
  - "Tic douloureux" = painful movements
- John Fothergill, 1773
  - "On a Painful Affliction of the Face," London Medical Society

Incidence: 4-5 per 100,000 persons annually

Epidemiology

Females > Males, 3:2 ratio

Primary risk factor is age

- Classic TN usually begins after age 50
- Secondary TN often in 20-40 year-olds

Demyelinating disease (multiple sclerosis)

- 1% of MS patients have TN
- 2% of TN patients have MS

Hypertension appears to be an independent risk factor

Etiology

Entire mechanism not known

- Central, peripheral or both

Classification

- Classic (idiopathic)
- Secondary (symptomatic)

Classic TN

- Compression of trigeminal nerve root by aberrant loop of artery or vein (80-90%)
- No structural lesions identified (10-20%)

Etiology (continued)

Classic TN (cont'd.)

- Focal demyelination at root entry zone of pons
- Ectopic impulse generation
  - Ephaptic transmission
  - Ephaptic cross-talk

Secondary TN

- Similar mechanism as with compression by vascular loop and resultant focal demyelination
- Demyelinating diseases
  - Multiple sclerosis (MS)
  - Acute Disseminated Encephalomyelitis (ADEM)
  - Demyelination of root entry zone or sensory nucleus

Etiology (continued)

Secondary TN (cont'd.)

- Tumors of cerebello-pontine angle
  - Acoustic neuroma
  - Meningioma
  - Epidermoid cysts
- Inflammation of meninges (chronic meningitis)
  - TB, syphilis, Lyme, sarcoidosis
  - Carcinomatous meningitis
- Rarely due to aneurysm or arteriovenous malformation

Clinical Presentation

Usually involves V2 and V3 distributions

- 60%, pain goes from corner of mouth to angle of jaw
- 30%, pain goes from upper lip to eye

Rarely involves V1 (less than 5%)

- V1 more often affected by postherpetic neuralgia

Attacks generally last weeks or months

Remissions with recurrence is the norm

Clinical Presentation (continued)

Paroxysmal – maximum intensity at onset
Pain is sharp, stabbing, lancinating, shock-like
Pain is brief but may occur repetitively

- Paroxysms up to several seconds
- Burning-ache or dull pain may persist after paroxysm ends

Usually unilateral, occasionally bilateral

- “never” simultaneous

Rarely awakens patient from sleep

Clinical Presentation (continued)

Pain often provokes facial grimacing or wince

- Tic douloureux

Triggers are common precipitants of pain

- Chewing, talking, smiling
  - May hold face to limit movement
- Drinking hot or cold liquids
- Touching face; makeup, shaving, washing
- Cold air hitting face
  - Often wear scarves

Diagnosis

International Headache Society Criteria – Classic TN

- Paroxysmal attacks of pain lasting seconds to minutes and affecting one or more divisions of trigeminal nerve
- Must include at least one of the following:
  - Pain is intense, sharp, superficial, or stabbing
  - Pain is precipitated by triggers
- Attacks are stereotypic for the patient
- No clinically evident neurologic deficit
- Not attributed to another disorder

Diagnosis (continued)

Secondary TN

- Attacks often don’t abate
- No refractory period
- Young age, 20-40 years
- Sensory deficit on exam
- Bilateral symptoms
- Lack of therapeutic response
- V1 involvement

Diagnosis (continued)

Neuroimaging

- Brain MRI
  - May show secondary cause in up to 15% of patients
- Head MRA may show vascular loop
- Questionable utility
  - Sensitivity 52-100%
  - Specificity 29-93%

Electrophysiologic trigeminal reflex testing

Trigeminal evoked potential testing

Clinical Course

TN may remit for months or years after initial attack.
Attacks tend to cluster and wax and wane over time.

- May become more frequent, severe, disabling
- May become more easily triggered
- Long-term medications more likely necessary

Exacerbations more frequent in Fall and Spring

Medical Treatment

Medical management is the initial treatment of choice

- Adequate treatment for about 75% of patients
- May periodically reduce or discontinue treatment
- Remissions common

Secondary TN less responsive to medications

- Initial treatment same as for classic TN
- Gabapentin may be more effective

Medical Treatment (cont.)

- Effective

  Carbamazepine

  Oxcarbazepine

- Probably Effective

  Baclofen

  Lamotrigine

  Pimozide

Possibly Effective

Clonazepam
Gabapentin
Pregabalin
Dilantin
Topiramate
Tizanidine
Valproate

Medical Treatment (continued)

Carbamazepine

- First-line agent
  - Diagnostic and therapeutic value
- Literature review AAN, 2008
  - 58-100% effective (placebo 0-40%)
- Start 100-200mg BID
  - Gradually increase by 200mg/day
  - Max dose 2400mg, divided 2-5 times daily
- Side effects; drowsiness, cognitive dysfunction, diplopia, GI upset, dizziness

Medical Treatment (continued)

Oxcarbazepine

- Second-line agent
- Analogous to carbamazepine, less side effects
- Start 300mg BID
  - Gradually increase by 300mg/day
  - Max dose 1800mg/day, dosed BID
- Side effects; drowsiness, cognitive dysfunction, GI upset, dizziness

Carbamazepine v. oxcarbazepine

- randomized, controlled studies (178 patients)
- Equal efficacy (>50% reduction in attacks in 88% of patients)

Medical Treatment (continued)

Baclofen

- 70% of patients report improvement (placebo 10%)
- Start 10mg BID
  - Increase by 10-20mg increments
  - Max dose 80mg/day, divided 2-4 times daily
- Side effects: sedation, fatigue, dizziness

Narcotics

- May be useful for acute attacks
- Provide short-term pain management while traditional medications are started

Medical Treatment (continued)

First-Line Medications

- Carbamazepine
- Oxcarbazepine

Second-Line Medications

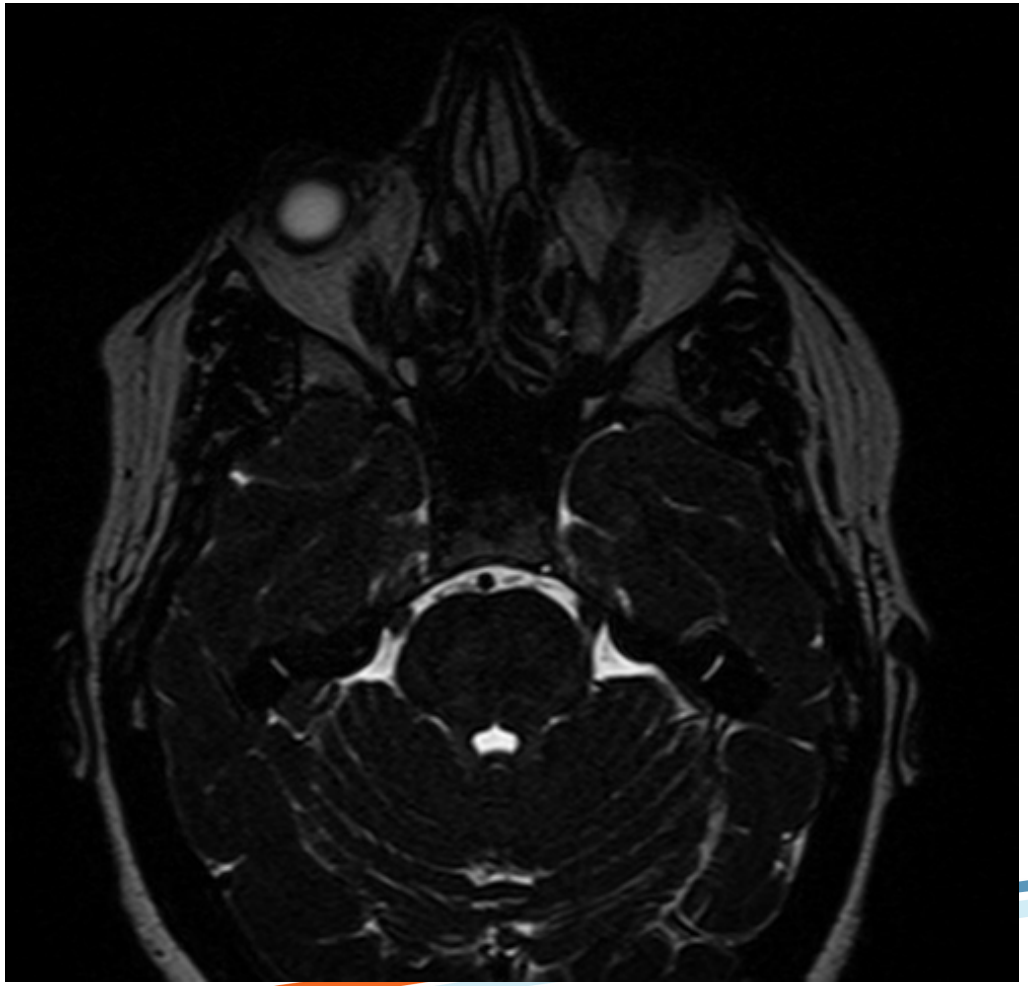
- Baclofen

Additional Medications (add to 1st/2nd line)

- Lamotrigine
- Gabapentin
- Narcotics

Anatomy of trigeminal nerve

Enters/exits ventrolateral pons at root entry zone
Short course though CPA cistern
Enters Meckel's Cave (dural reflection posterolateral to cavernous sinus/carotid artery, medial to temporal lobe)
Then divisions exit skull (V1 – SOF, V2 rotundum, V3 ovale)



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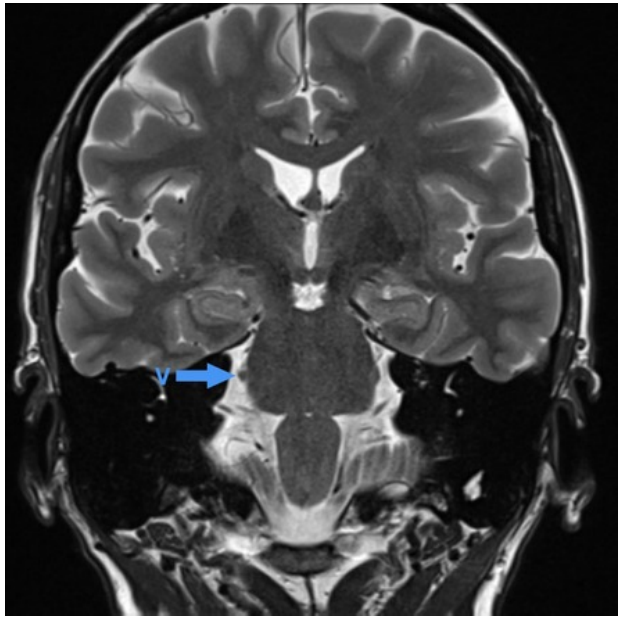
NORMAL TRIGEMINAL NERVE



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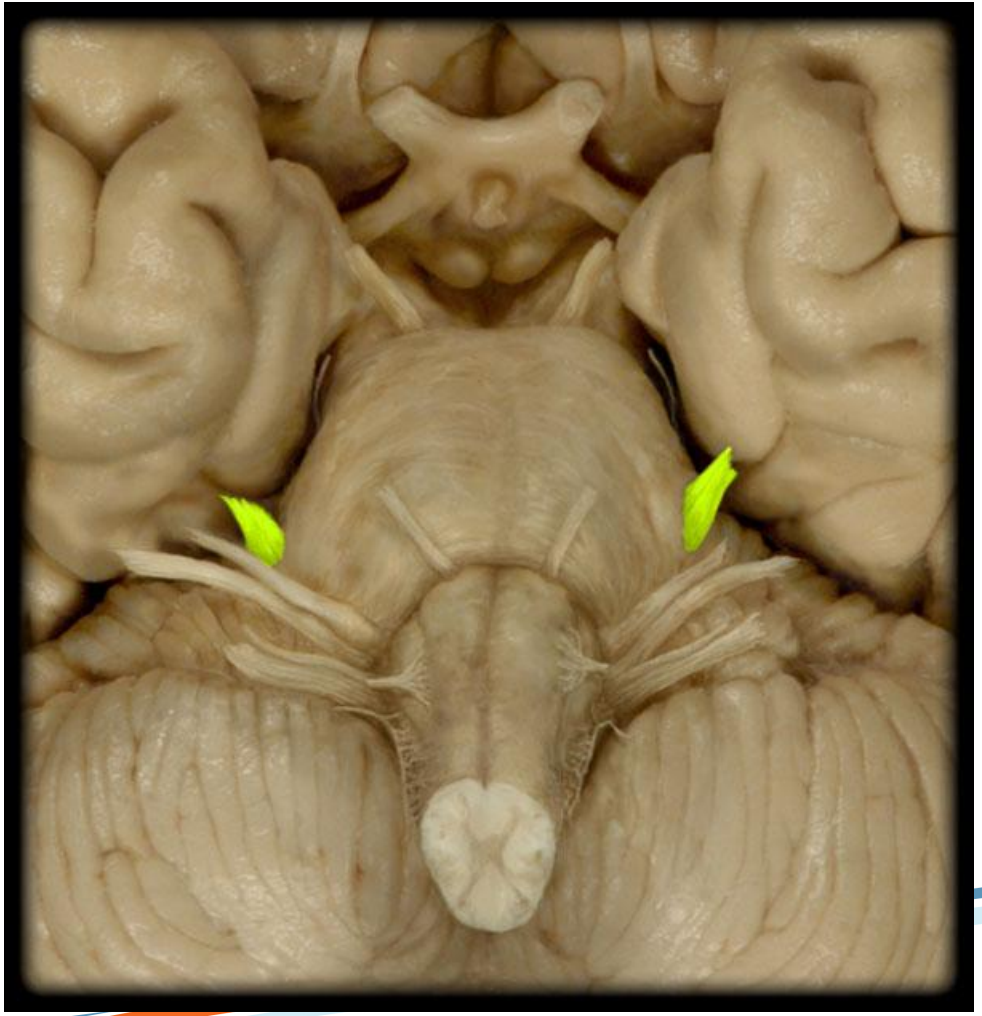

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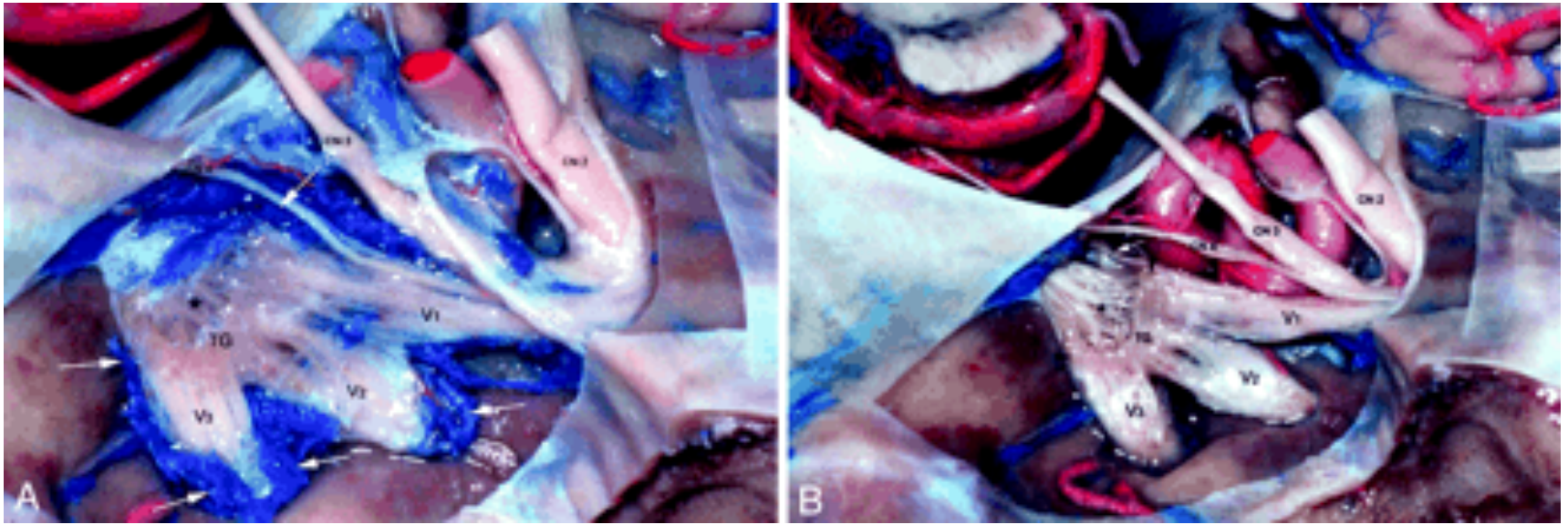

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SURGICAL MANAGEMENT OF TRIGEMINAL NEURALGIA

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Indications for surgery

Reserved for cases refractory to medical management, or when side effects of medication exceed risks and drawbacks of surgery

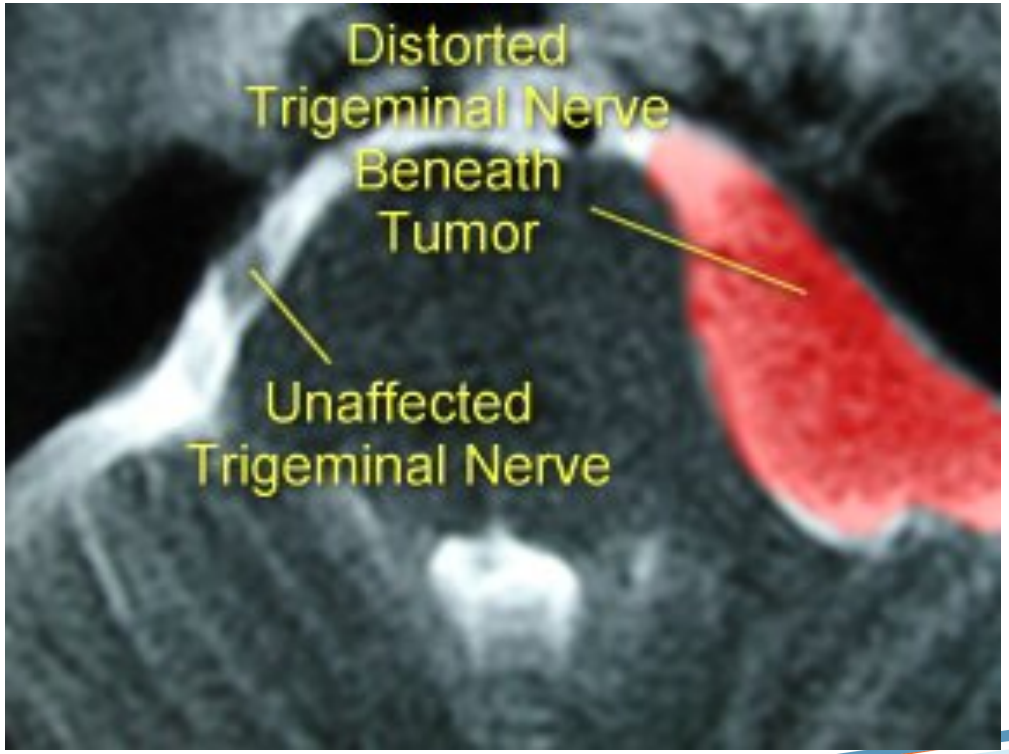
Surgical options

- Peripheral branch treatments
- Percutaneous trigeminal rhizotomy
- Microvascular decompression

Multiple other lesser used options: nerve sectioning, spinal trigeminal tract lesioning, motor cortex stimulation, branch stimulation symp

If tumor is present on imaging – treat the tumor

Meningioma



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Large Trigeminal Schwannoma

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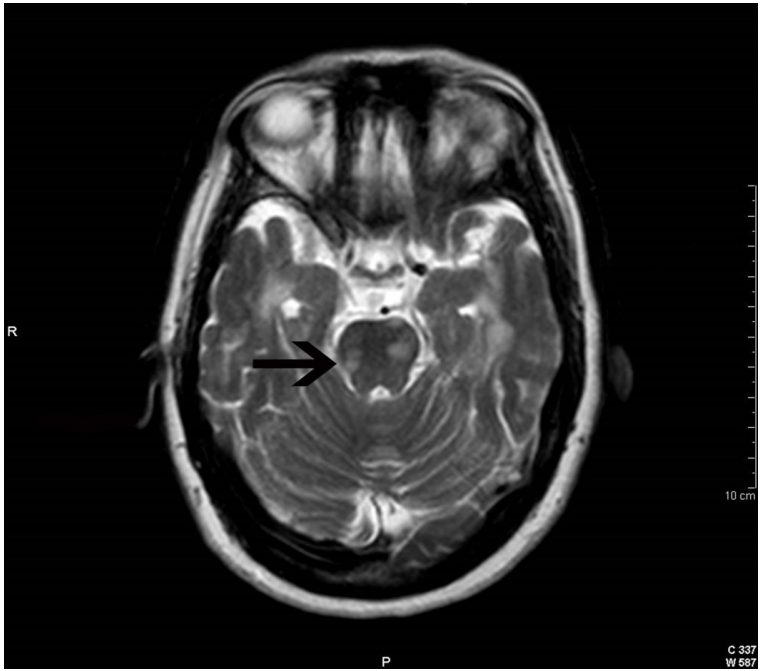
MS Plaques in Pons



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Peripheral branch treatments

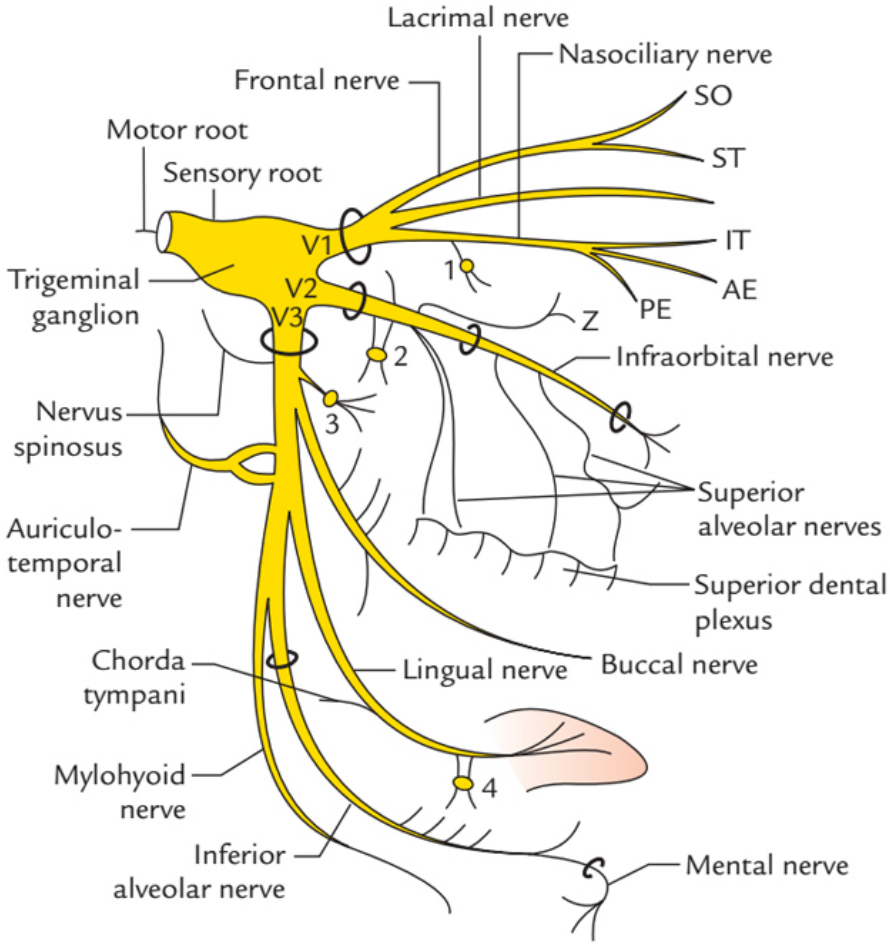
Blocks/neurectomy

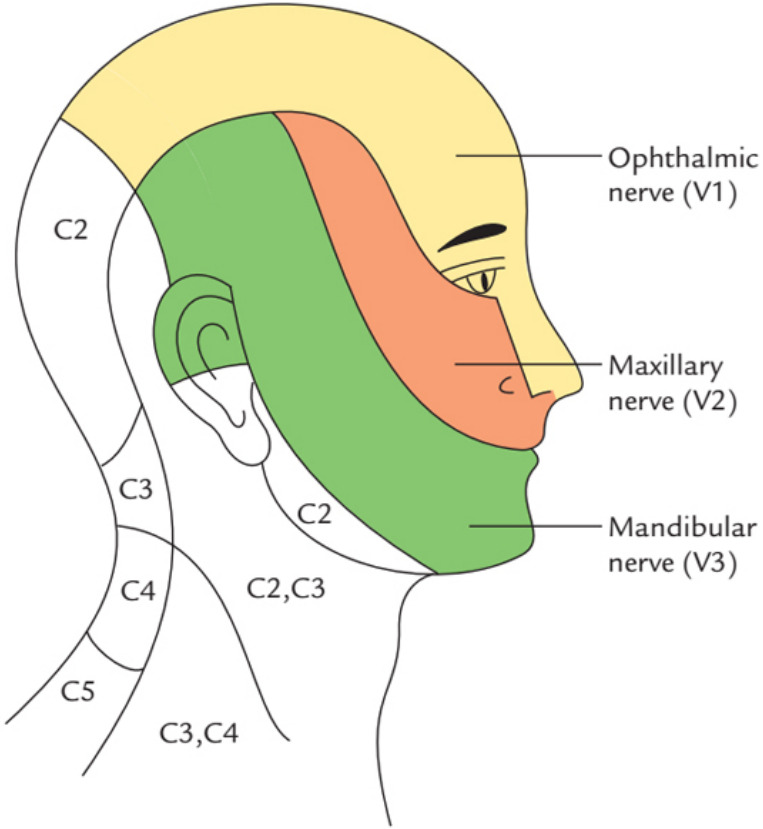
- Local anesthetic (diagnostic), Phenol, alcohol
- Neurectomy

Stimulation (rare)

Anatomy

- V1
  - Supraorbital, supratrochlear
- V2
  - Blocked at rotundum or infraorbital branch
- V3
  - Blocked at ovale/inferior alveolar nerve


Lacrimal nerve
Nasociliary nerve
Frontal nerve
SO
ST
Motor root
Sensory root
IT
V1
AE
Trigeminal ganglion
V2
PE
V3
Z
Infraorbital nerve
Nervus spinosus
Superior alveolar nerves
Auriculo-temporal nerve
Superior dental plexus
Chorda tympani
Lingual nerve
Buccal nerve
Mylohyoid nerve
Inferior alveolar nerve
Mental nerve


Ophthalmic nerve (V1)
C2
Maxillary nerve (V2)
C3
C2
Mandibular nerve (V3)
C4
C2,C3
C5
C3,C4

Percutaneous Trigeminal Rhizotomy

Recommended for patients with:

- Poor risk of GA
- Elderly
- Unresectable tumors
- MS
- Limited life expectancy (< 5 yrs…. < 2 yrs)
- Those who need immediate relief

Recurrence rates, dysethesia rate similar among various techniques

Numbness can be as high as 98%

PTR

3 types

- Balloon
- Glycerol
- Radiofrequency

Balloon

Might be best for V1/V2 –
Preserves corneal reflex

RFR

V3 neuralgia
Can selectively treat without other lesions
Can curve electrode to treat V1/2

Glycerol

Shortest acting
Non selective

Complication rate

Dysethesia

- Minor 9%
- Major 2%
- Anesthesia dolorosa 0.2-4%

Meningitis 0.3%

Alterations in salivation 20%

- Decreased in 3%
- Increased in 17%

Oculomotor paresis < 2%

Neuroparalytic keratitis 2-4%

Overall complication rate

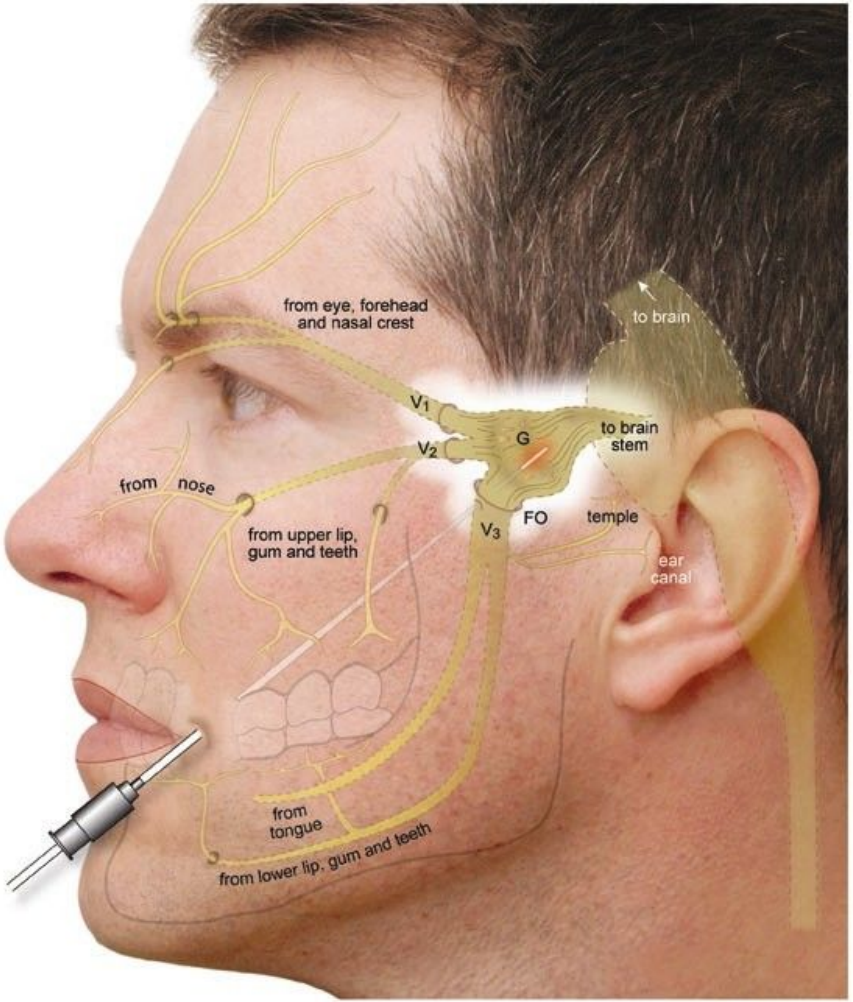
Balloon Compression - 16% complication rate

RFR - 15% complication rate

Glycerol - 25% complication rate

Technique for needle insertion

Supine
Fluoroscopy
Insert electrode-needle 3cm lateral to oral commissure
Plapate buccal mucosa inside mouth to guide needle staying outside oral cavity passing medial to coronoid process of mandible toward plane intersecting 3cm anterior to EAC and medial aspect of pupil
On fluoro aim at intersection between top of petrous ridge and clivus (5-10mm below floor of sella)
Upon entering ovale masseter should contract and should see CSF



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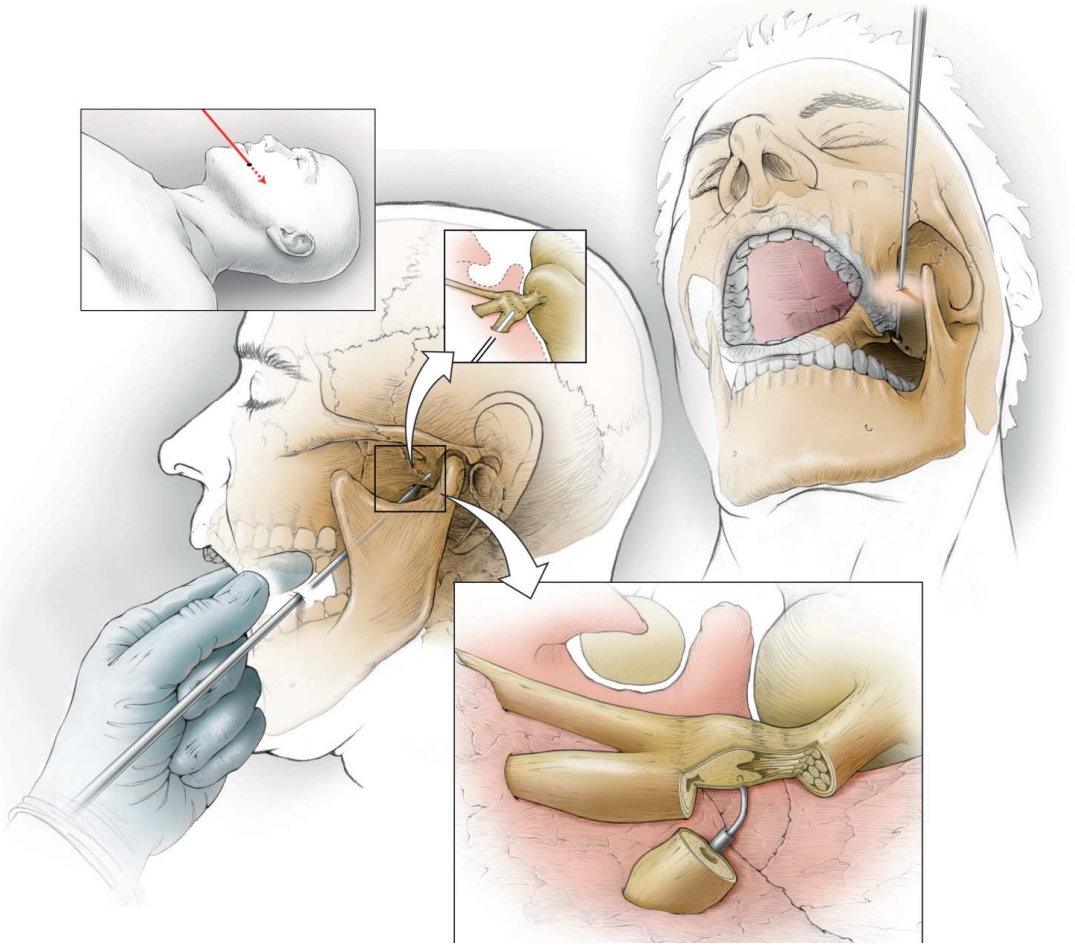
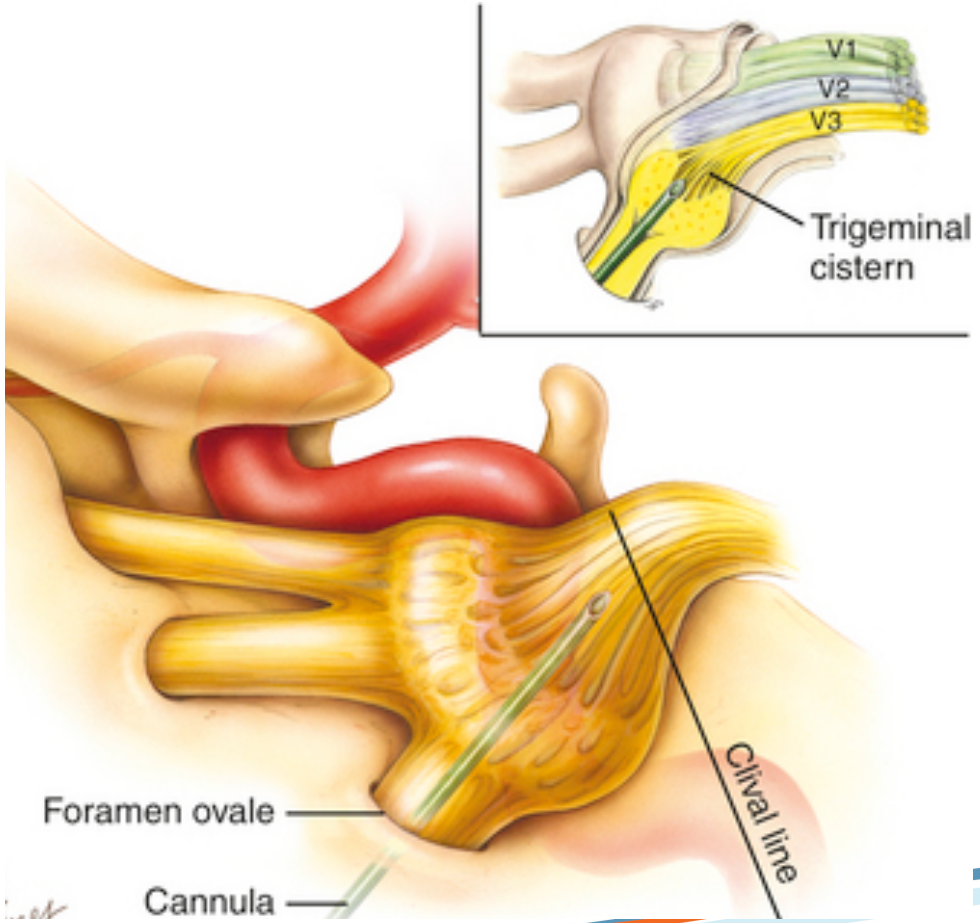
Radiofrequency Rhizotomy





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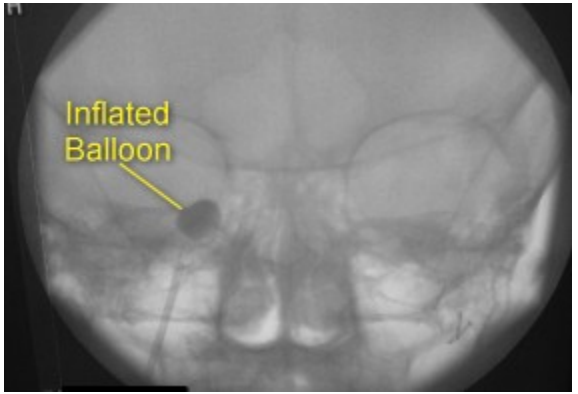
Balloon Rhizotomy



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Microvascular Decompression

Indications

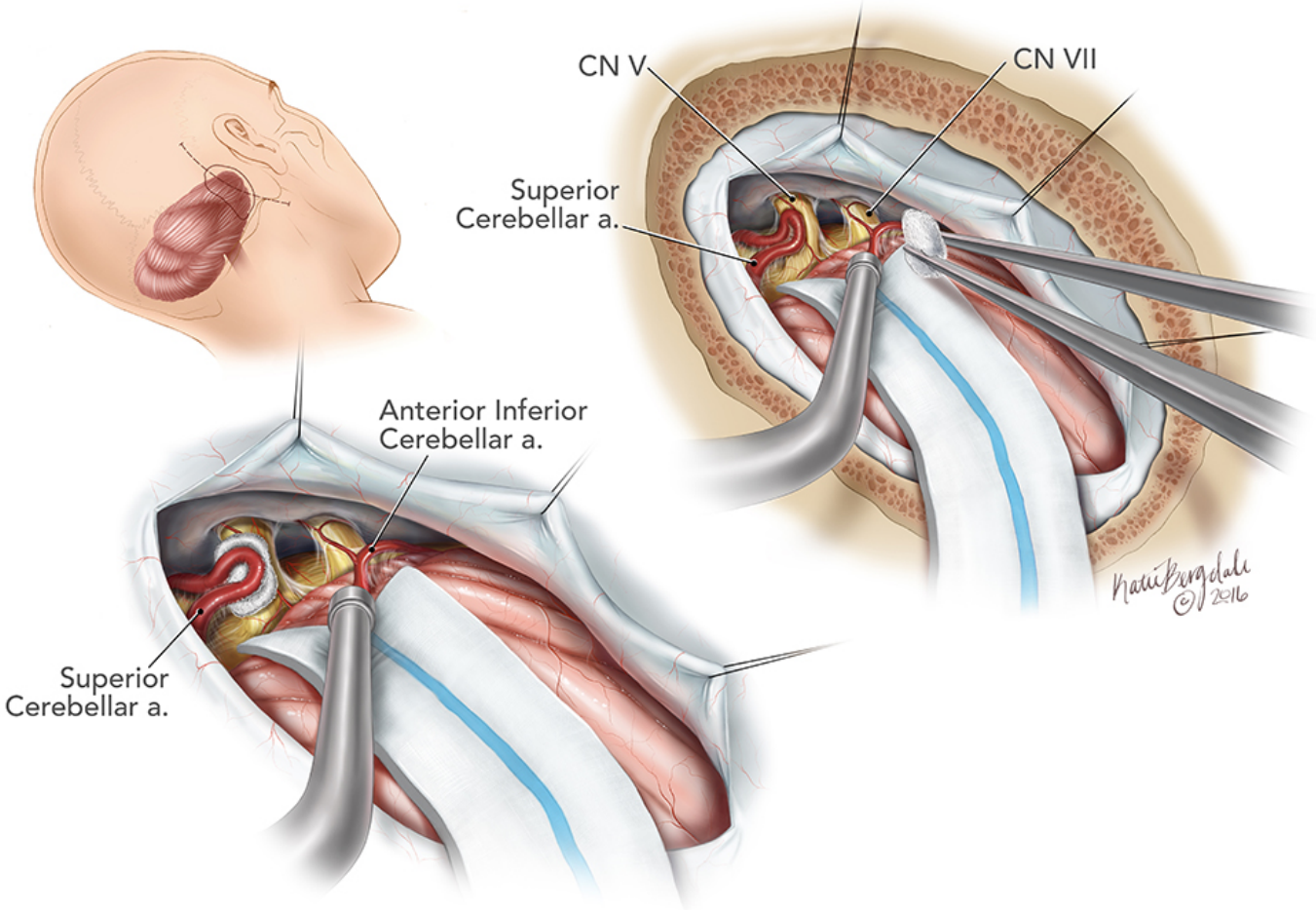
- Unable to achieve adequate medical control of TN without significant medical risk factors, > 5yrs survival
- Failed other surgical/SRS treatments
- Need immediate relief (not able to eat, losing weight, incapacitated)
- More efficacious if defined vascular loop on MRI

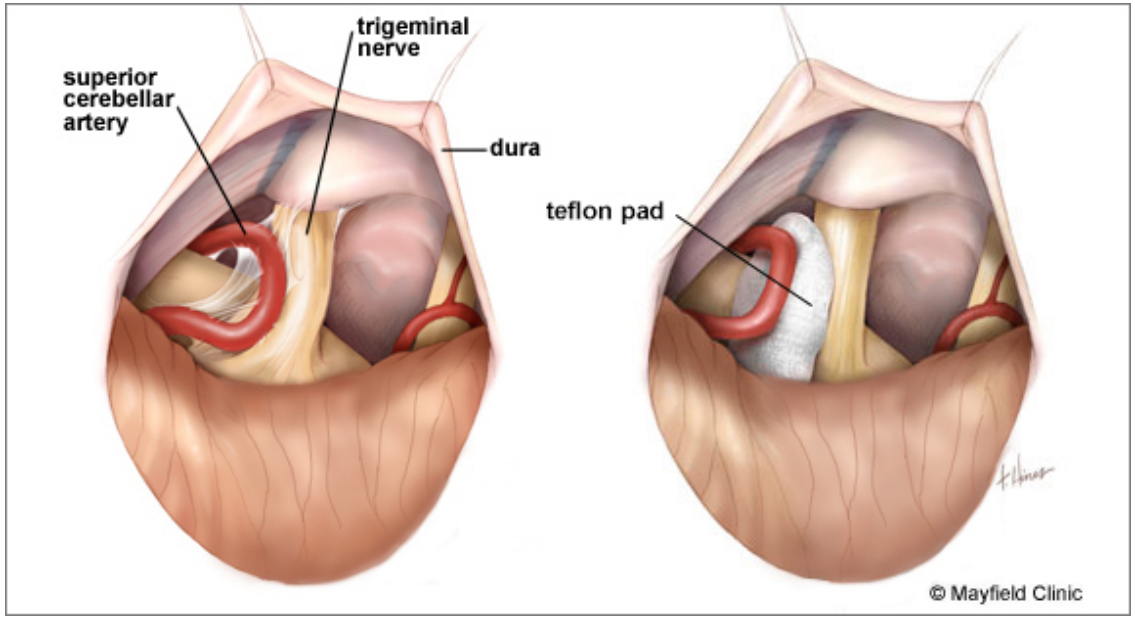
MS is usually a contraindication

Microvascular Decompression, continued

Risks/Complications

- CSF leak (up to 10%)
- Facial numbness – 25% temporary, 2% permanent
- Permanent hearing loss < 2%
- < 1% diplopia, facial paralysis, brainstem stroke
- Bleeding, infection


CN V
CN VII
Superior
Cerebellar a.
Anterior Inferior
Cerebellar a.
Superior
Cerebellar a.



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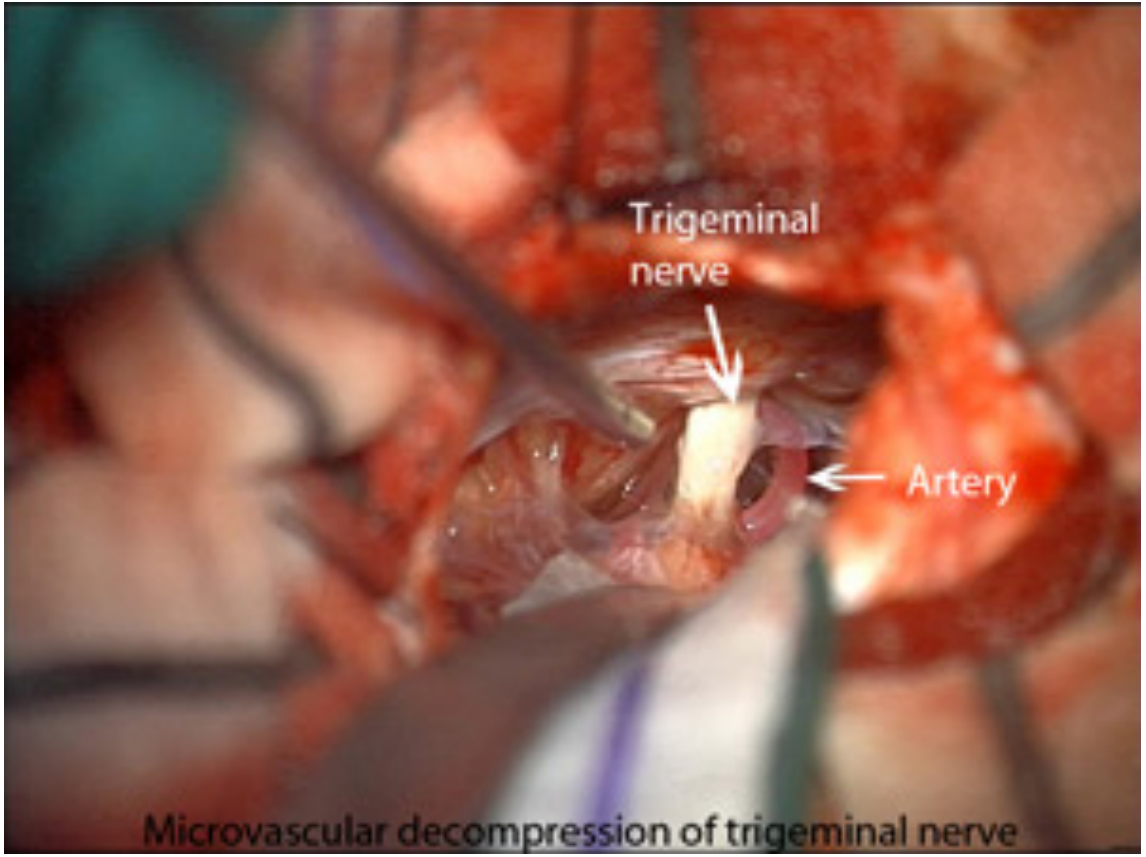
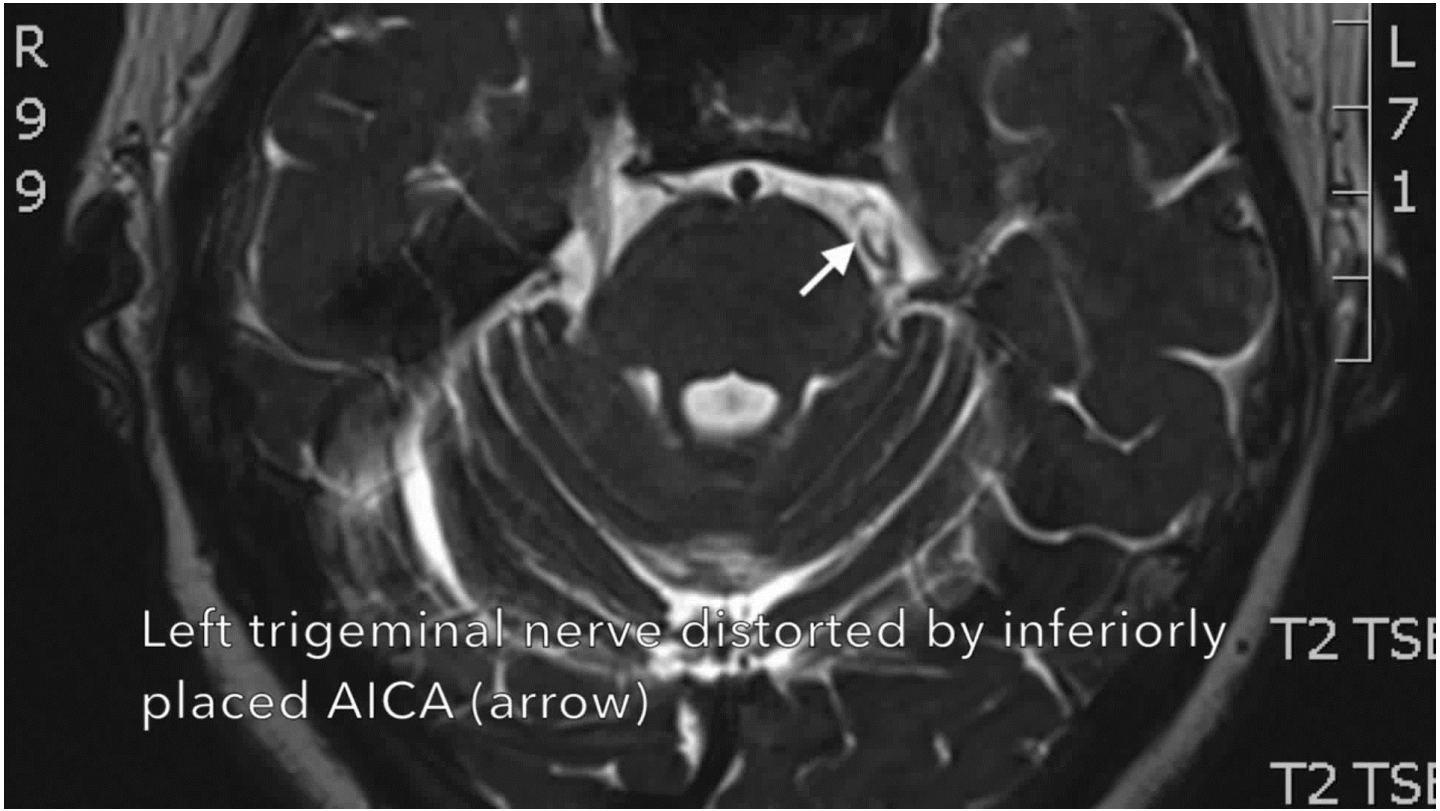

Trigeminal
nerve
Artery
Microvascular decompression of trigeminal nerve



Left trigeminal nerve distorted by inferiorly placed AICA (arrow)

Parameter	Percutaneous Technique			MVD
	RFR	Glycerol	Balloon	
Initial success rate	91%	91%	93%	85-98%
Medium-term Recurrence	19% at 6 yrs	54% at 4 yrs	21% at 2 yrs	15% at 5 yrs
Long-term Recurrence	80% at 12 yrs			30% at 10 yrs
Facial numbness	98%	60%	72%	2%

South Sound Gamma Knife at St. Joseph

Facial Pain: Is it Trigeminal Neuralgia?

Herbert Wang, MD
Radiation oncologist
Marc Goldman, MD
Neurosurgeon

South Sound Gamma Knife at St. Joseph

Herbert Wang, MD

Radiation Oncologist

South Sound Gamma Knife at St. Joseph

Gamma Knife (SRS)

Stereotactic Radiosurgery:
The precise delivery of a single fraction of high-dose ionizing radiation to an image-defined target.

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Indications for Treatment

Brain Metastases*
Meningiomas
Acoustic Neuroma
Pituitary Tumors
Arteriovenous Malformation (AVM)
Trigeminal Neuralgia*
Movement Disorders*
Epilepsy
Obsessive Compulsive Disorder (OCD)

South Sound Gamma Knife at St. Joseph

History Gamma Knife

Invented by Lars Leksell

- Swedish Neurosurgeon

1951 Treatment Trigeminal Neuralgia

- Modified Dental X-ray Tube coupled with a Stereotactic device

1968 Model S Treatment Craniopharyngioma plaster headpiece

1986 U model computer planning

1999 C unit APS (automatic positioning system)

2006 Perfexion larger cavity, rapid treatment, improved conformity, very low body dose

Professor Lars Leksell with the first Gamma Knife - 1968

Model S

South Sound Gamma Knife at St. Joseph

Gamma Knife ICON

Multiple Co sources - 192 in ICON unit
Sources focus at a fixed isocenter
Patient is moved into desired position
In order to treat a volume multiple treatments(shots) given
Stereotactic frame
MRI imaging with frame creating reference system

Advancement in SRS

Imaging MRI
Dose Planning Software
Improved Delivery Systems

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Leksell Frame

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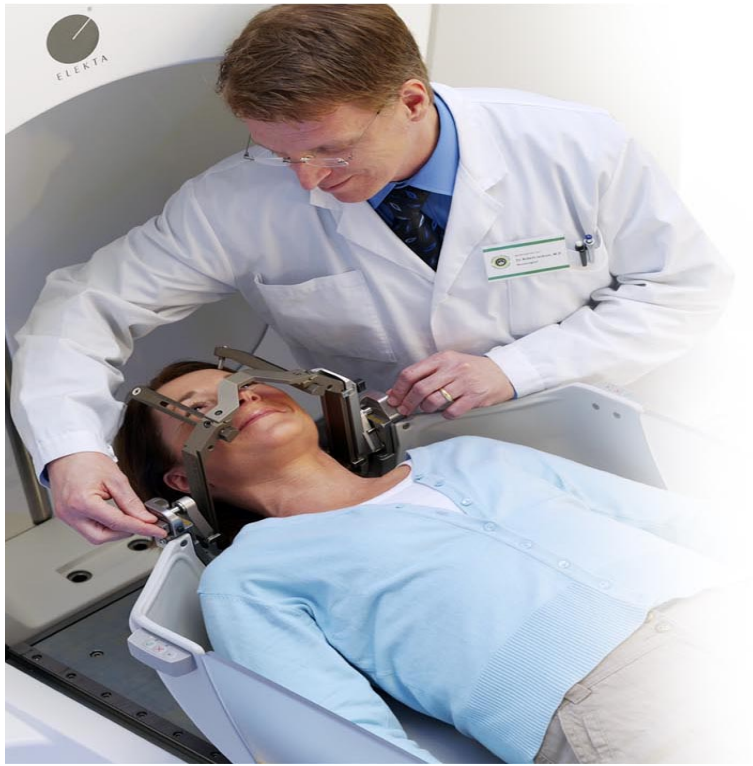
Leksell Gamma Knife Frame Attachment



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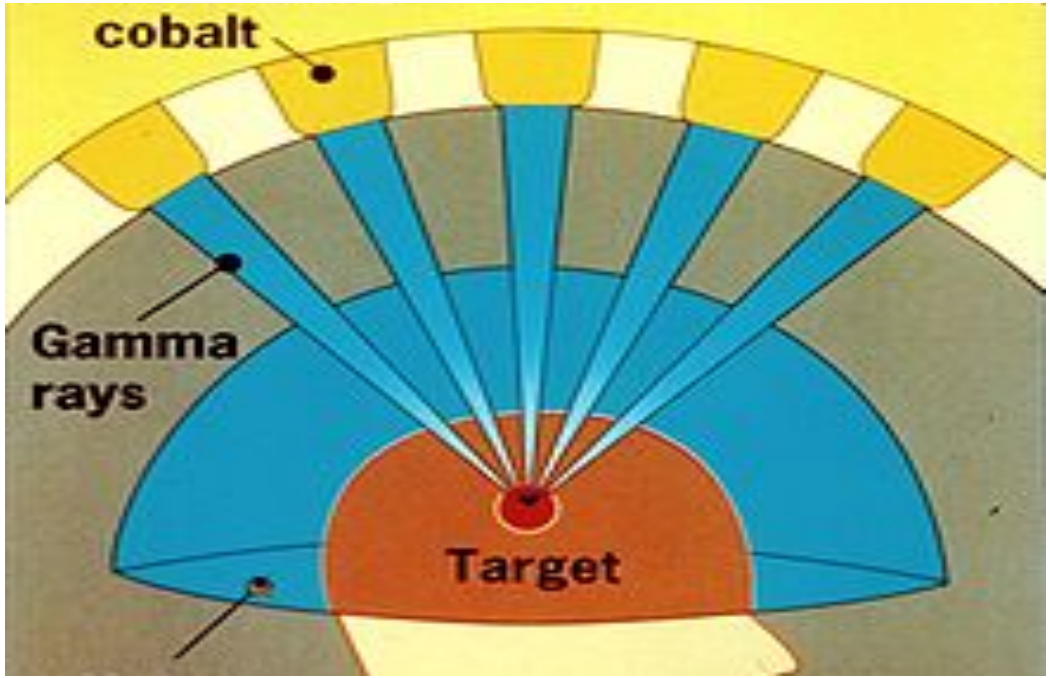
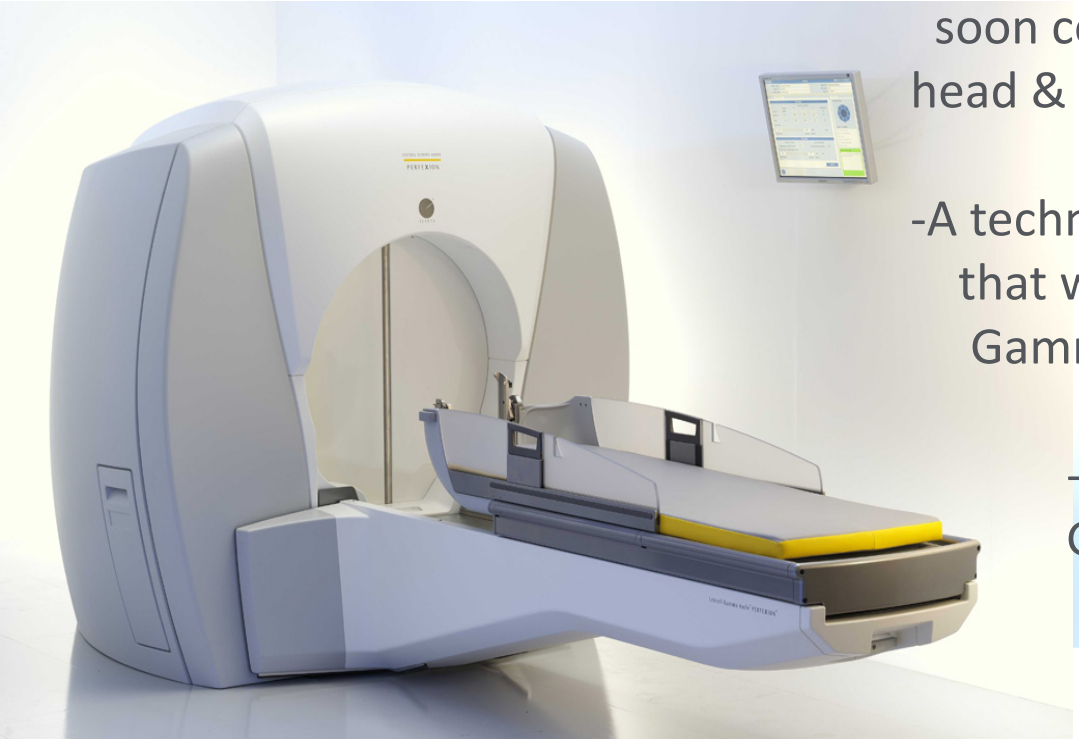


Basic Schematic

South Sound Gamma Knife at St. Joseph

And after five years of research and development …this is the result

Leksell Gamma Knife® ICON

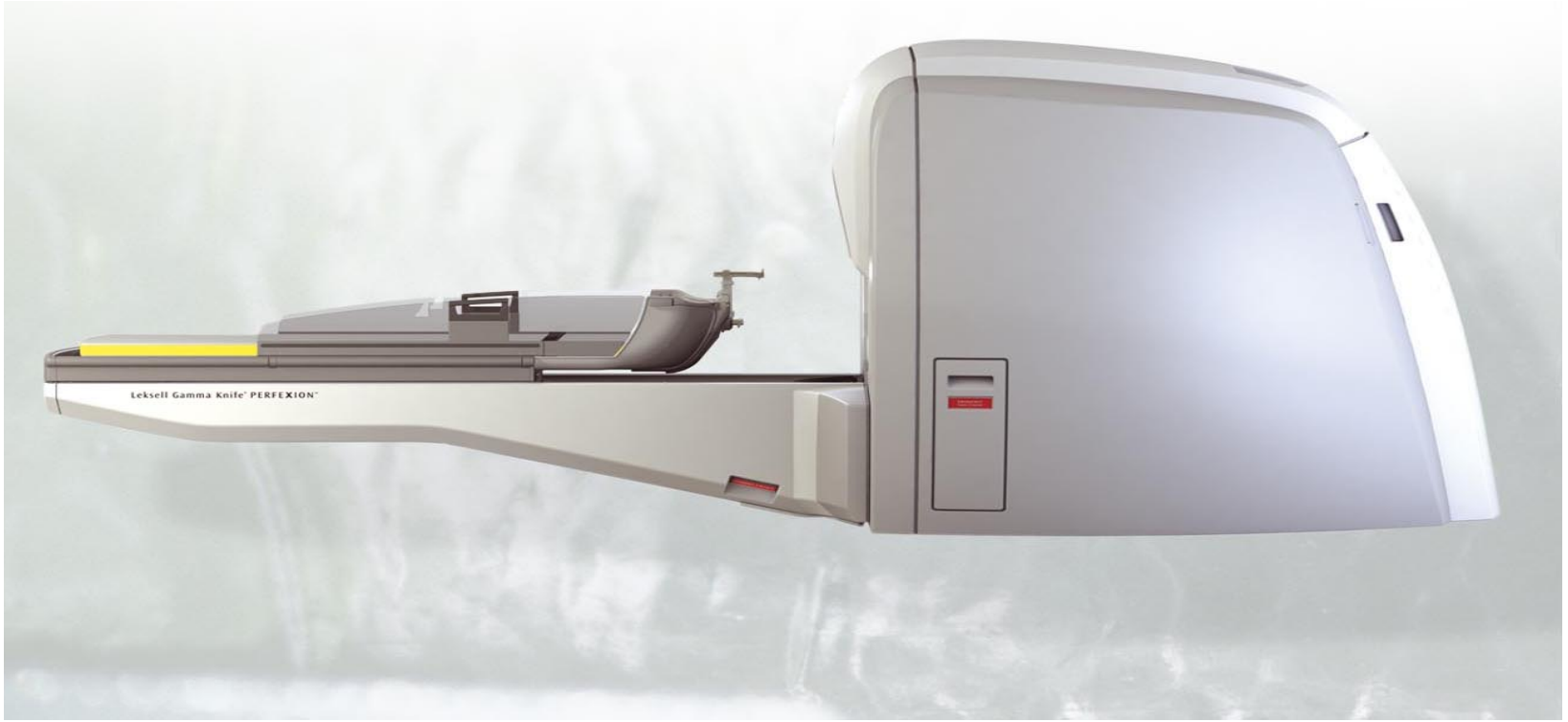


-A new and revolutionary platform for radiosurgery in the brain, and soon cervical spine and head & neck regions

-A technological breakthrough that will improve and expand Gamma Knife surgery

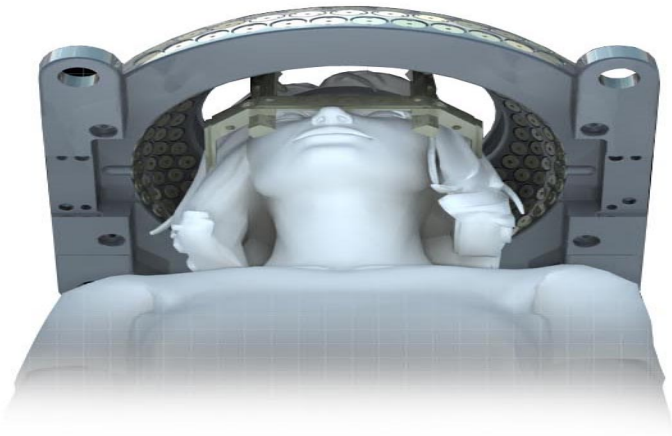
- Full clinical compatibility with Gamma Knife procedures & protocols based on 400,000 treated patients

Leksell Gamma Knife® ICON™

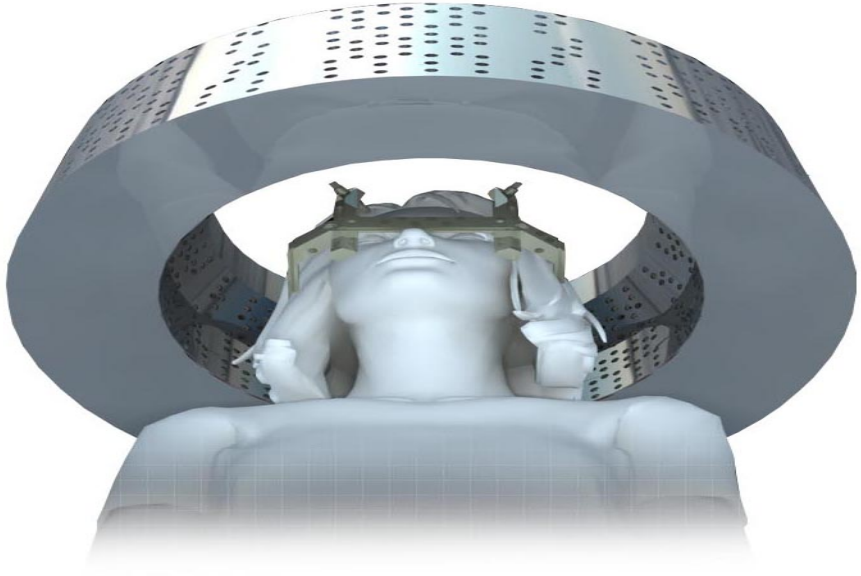


Treatable volume

Leksell Gamma Knife C



Leksell Gamma Knife ICON



Gamma Knife Team

- Neurosurgeon
- Radiation oncologist
- Physicist
- Support staff
  - Radiation therapist
  - Gamma Knife nurse
  - Gamma Knife coordinator

South Sound Gamma Knife at St. Joseph

Gamma Knife Results
University of Pittsburgh

- 220 Patients
- 93% Typical TN (Paroxysmal, sharp, electric shock, triggers)
- 7% Atypical TN (dull, aching or burning)
- 100% prior medical therapy
- 61% prior surgical therapy

University of Pittsburgh Results

- 70-90Gy max dose 2-4mm from pons, max surface dose 30%
- Mechanism of Action unclear
  - Baboon studies focal axonal degeneration at 80Gy partial necrosis at 100Gy
  - Mechanism of action not completely understood

University of Pittsburgh Results - Pain Relief

- Complete pain relief
  - 88% with Typical TN
  - 56% with Atypical TN
  - More likely if fewer branches
  - More likely if no prior surgery
- Onset of relief, median 2mo
  - Few responders after 6mo

University of Pittsburgh Results - Relapse

- 14% of patients relapsed at 2-58mo (mean 15mo)

University of Pittsburgh Results - Numbness

- 8% of patients
- Median onset 8mo.(range 1-19mo)

Side Effects

- Numbness 0-37%
  - Correlates with control
- Brain stem
- Bleeding
- Infection

University of Kentucky 2013

250 patients – dose = 90Gy
Mean duration of follow up 68.9 months
Pain relief in 85.6% of patients

- 43.7% pain free without meds
- 27.7% pain free with meds
- 9.7% >90% reduction in pain
- 8.4% 50-90% decrease in pain
- 4.6% <50% reduction in pain
- 5.9% pain becoming worse

University of Kentucky 2013

32.9% developed numbness
74% with numbness had complete pain relief
87.7% of patients would recommend GK to another patient
Patients with prior surgical treatments had increased latency to pain relief and were more likely to continue meds.

Retreatment with Gamma Knife

- University of Pittsburgh
  - 31 Patients
  - 48% complete pain relief +/- pain meds
  - 13% numbness
- Mayo Clinic
  - 75% excellent or good response (n=19)
  - 58% developed numbness
  - Numbness correlated with response (82% with numbness had excellent response)
- University of Maryland
  - 93% excellent or good relief (n= 112)
  - 22% failure within one year (no failures after 9mo)
  - 11% Numbness

Local Case Study of GK Treatment for Trigeminal Neuralgia

- January 2005 – December 2016 case study of 139 patients, 18 were secondary treatments, five lost to follow up, leaving 116 cases available for retrospective analysis that included medical records, physical exams and patient phone interviews
- Single 4 mm shot of 75-85 Gy for primary treatment and 50-70 Gy for secondary treatment

Local Case Study Results and Conclusions

Median follow-up 12 months
83% of patients undergoing first GKSRS experienced pain relief at a median of 30 days post-treatment
Of these, 30% experienced recurrence of symptoms, at an average 10.5 months following treatment
No significant differences found between subgroups including patients with MS, atypical TN, or those who had undergone previous surgical treatment for TN

Local Case Study Results and Conclusions, continued

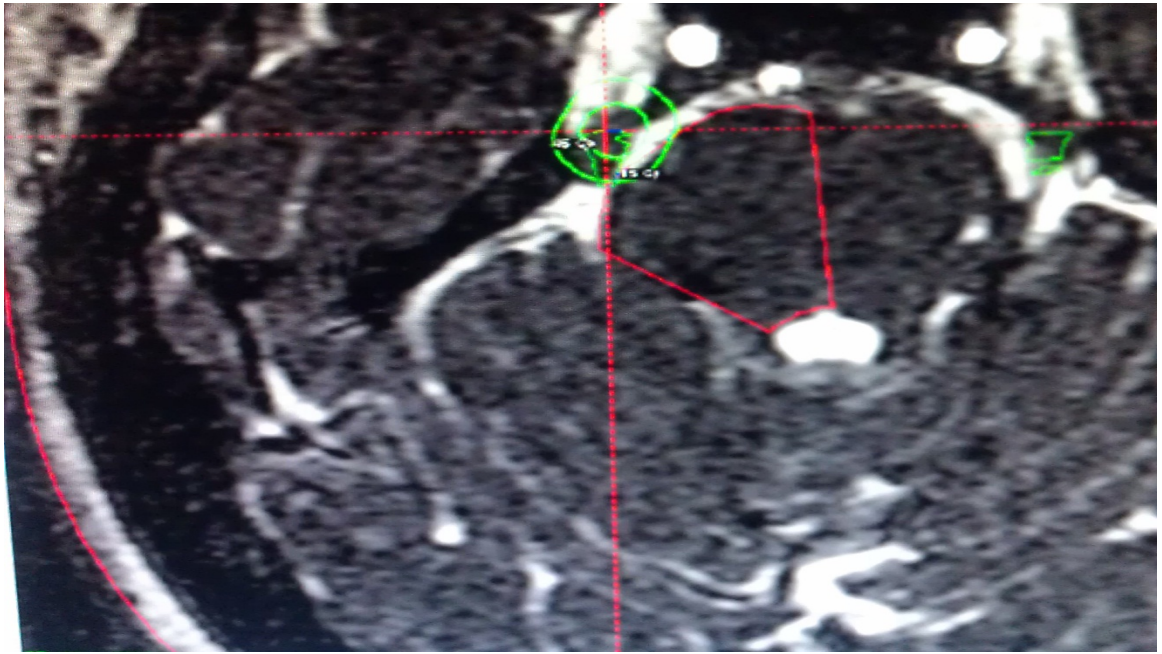
No difference in outcome between doses administered
For those receiving second GKSRS for TN, initial success rate was 90%, with 25% of those patients eventually having recurring symptoms
21% of cases developed some level of ipsilateral facial numbness
Study concludes Gamma Knife stereotactic radiosurgery is an effective treatment of trigeminal neuralgia

Presented at Leksell Gamma Knife Society Meeting, Dubai 2018

Surgical Salvage

- Allegheny General (MVD) – 54% excellent outcome: 11% fair to good outcome; 36% poor outcome
- Thickened arachnoid, adhesions between blood vessels and nerve, trigeminal nerve atrophy
- MVD completed in 97% of patients

- Mayo - 73% complete response



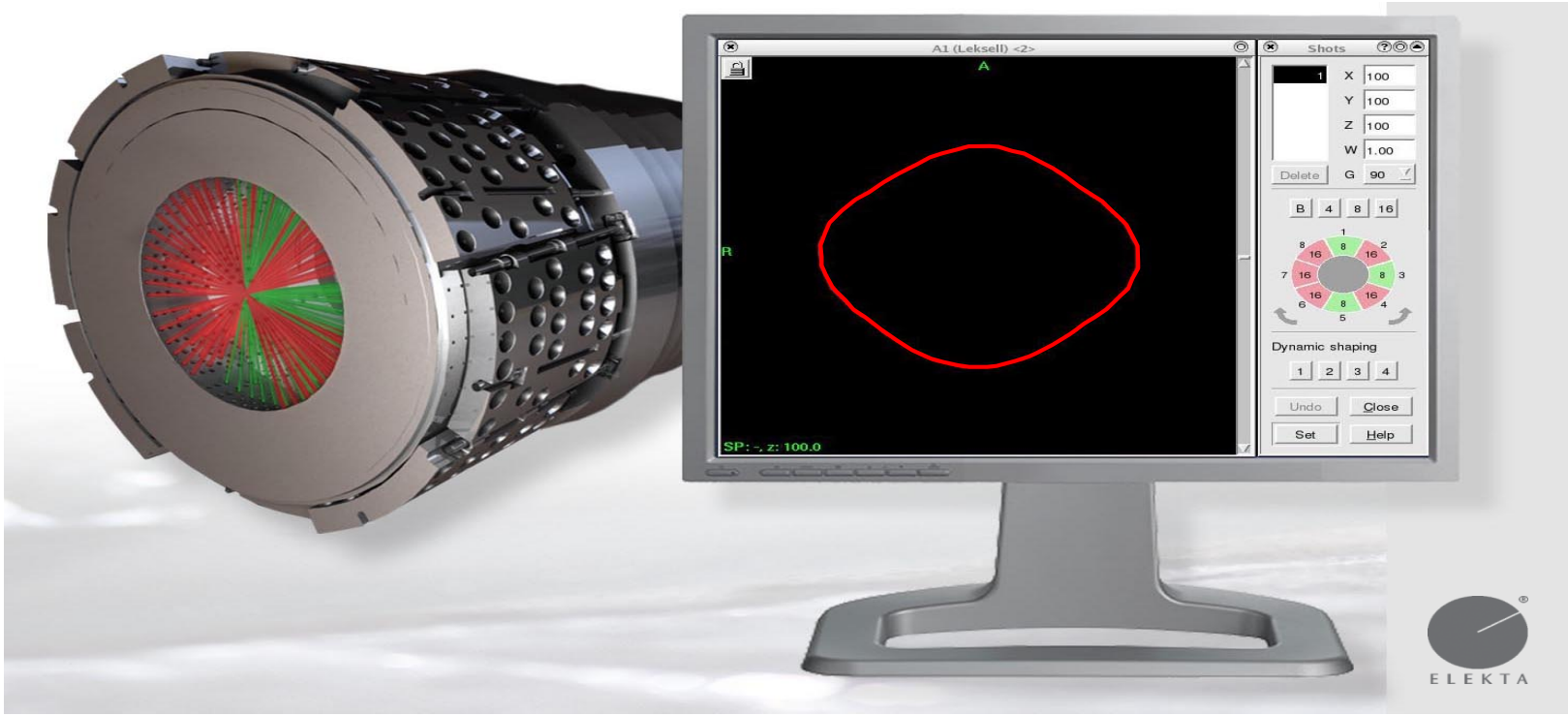
Gamma Knife Treatment Trigeminal Neuralgia

80Gy Typical Dose

Photo Regis

South Sound Gamma Knife at St. Joseph

Collimator system 8-16-8-16-8-16-16-16



Dynamic shaping

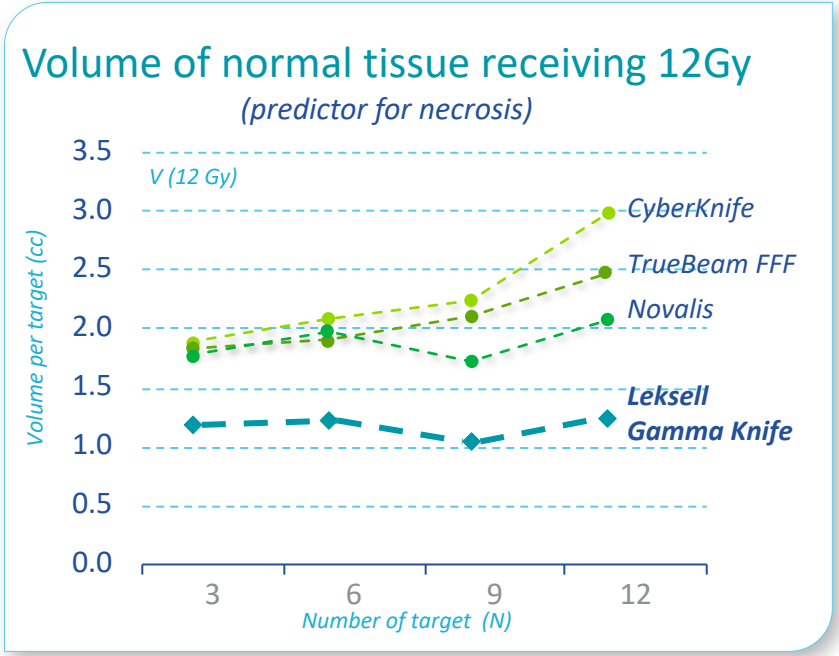
Safety

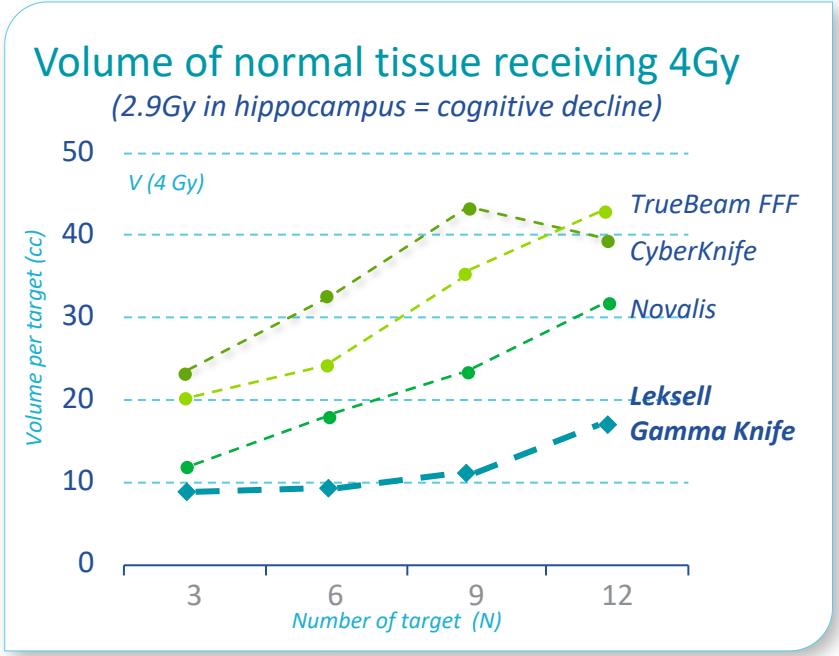
Peripheral Patient Dose Compared to Other Modalities

- At 30 cm from isocenter
  - PFX at least 10x less than CK
- At >60 cm from isocenter
  - PFX 30x less than C unit
  - PFX 100x less than CK

The results:

2-4 times better sparing of normal brain tissue

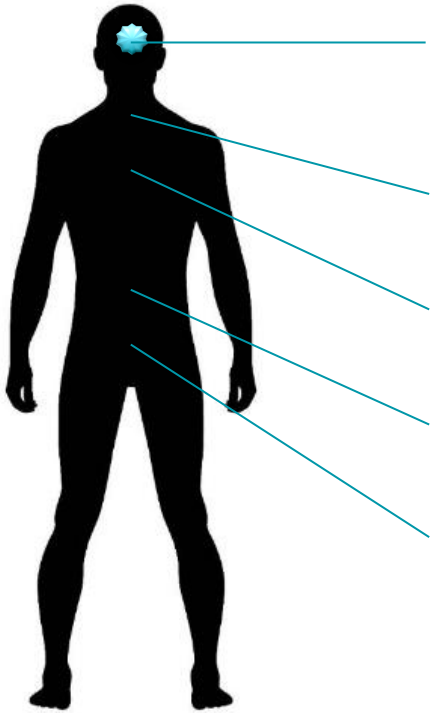




Source: Ma L, Nichol A, Hossain S, et al. (2014) Variable dose interplay effects across radiosurgical apparatus in treating multiple brain metastases. Int J CARS. Published online: 20 April 2014. doi:10.1007/s11548-014-1001-4

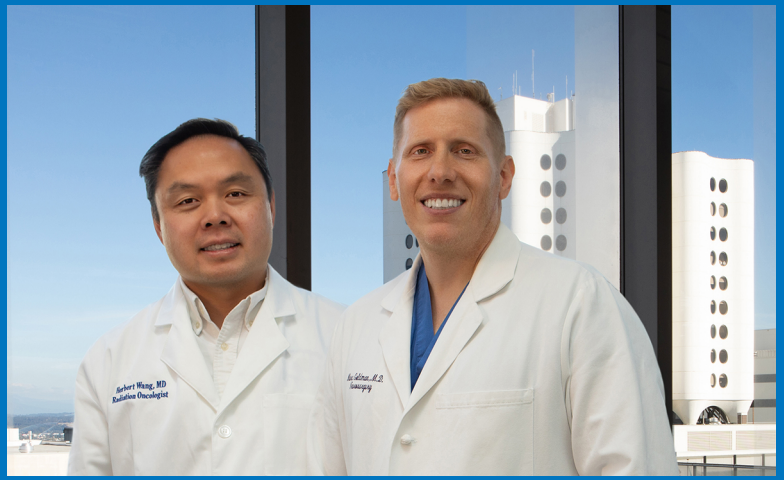
The results:

Extracranial dose in the order of 5-130x lower with Gamma Knife



	CyberKnife dose	*Linac dose*
Thyroid	**31x** Gamma Knife	**~4.5x** Gamma Knife
Chest	**28x** Gamma Knife	**6x** Gamma Knife
Abdomen	**129x** Gamma Knife	**~7x** Gamma Knife
Pelvis	**115x** Gamma Knife	**5x** Gamma Knife

Source: "The Leksell Gamma Knife Perfexion and comparisons with its predecessors", C. Lindquist and I. Paddick, Neurosurgery 61: ONS 130-141 2007; Vlachopoulou V, Antypas C, Delis H, et al. Peripheral doses in patients undergoing Cyberknife treatment for intracranial lesions. A single centre experience. Radiation oncology (London, England) 2011;6:157;



Marc Goldman, MD, neurosurgeon
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Thank you for attending

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