PAIN

Ask for visual analogue scale (VAS) ± Neck Disability Index (NDI) for neck or Oswestry for lumbar

HYPERALGESIA - stimuli that would *normally cause only minor pain* produce exaggerated response.

ALLODYNIA - *normally innocuous stimuli* (such as touch) cause pain.

PARESTHESIA - SPONTANEOUS abnormal sensation
DYSESTHESIA - abnormal sensations WHEN AREA IS TOUCHED

Three pain categories:

Nociceptive pain – caused by ongoing inflammation and damage of **tissues**

Neuropathic pain – caused by **nerve** damage

Nociplastic pain – caused by altered nociception (**central** sensitization): augmented CNS pain processing and altered pain modulation: intense multifocal chronic pain + CNS-derived symptoms, such as fatigue, sleep, memory, mood problems.

- examples: fibromyalgia, tension-type headache, chronic LBP
- decreased responsiveness to peripherally directed therapies (NSAIDs and opioids, surgery, or injections)
- best treatment – exercises, psychotherapies.

Pain - *complex subjective sensation reflecting real / potential tissue damage + affective response to it.*

pain and **suffering** should be distinguished
N.B. pain receptors are specific (i.e. *pain is not produced by overstimulation of other receptors*!).

Pain impulses are **TRANSMITTED TO CNS** by two fiber systems:

1. Small myelinated **Aδ fibers**;

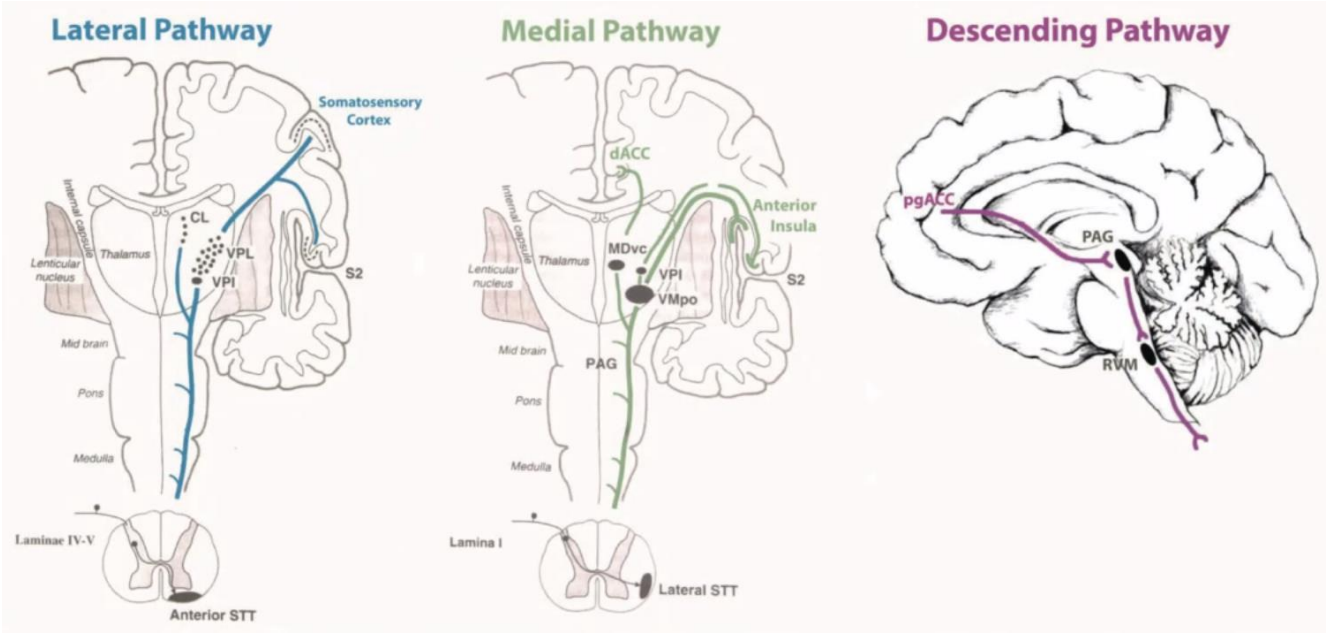
- transmit fast mild pain - "bright", sharp, localized;
- use **GLUTAMATE** as transmitter;
- evoke ***withdrawal reflex*** and ***sympathetic discharge*** (BP↑, etc).

2. Unmyelinated **C fibers** - found in **lateral division of dorsal roots**;
   - transmit slow severe pain - dull, intense, diffuse, burning, unpleasant;
   - use **SUBSTANCE P** as transmitter;
   - evoke ***autonomic responses*** (nausea, sweating, BP↓, generalized muscle tone↓)

Gate control - synapses on dorsal horn neurons are sites of considerable plasticity - pain impulses can be "gated" i.e. augmented or inhibited (dorsal horn has been called "**gate**"):

a) descending serotonergic pathways from ***brainstem RF*** (raphe nuclei) can inhibit pain transmission.
b) stimulation of ***large-diameter afferent TOUCH fibers*** (from area from which pain is being initiated) presynaptically inhibits pain transmission.

Pain CNS pathways:
Lateral – intensity, location
Medial – emotional reaction
Descending – inhibitory



Acute pain (< 1 month) - associated with *sympathetic nervous system hyperactivity* (e.g. tachycardia, ↑respiratory rate and BP, diaphoresis, dilated pupils) and ***anxiety***.

Chronic pain - associated with *vegetative signs* (e.g. lassitude, sleep disturbance, ↓appetite, weight loss, ↓libido, constipation) and ***depression***.

NCS & EMG evaluate motor and large-caliber afferent fibers, *leaving unexplored small-caliber afferents*; conventional electrophysiological studies are *unable to explore pathophysiological substrate of positive sensory phenomena*.

N.B. *normal nerve conduction study* does not necessarily rule out peripheral nerve lesion as cause of pain; *abnormal study* does not necessarily imply that peripheral nerve lesion is cause of symptoms.

NONINVASIVE PAIN TREATMENT

Neuropathic pain responds poorly to *narcotics* and to *ablative procedures* (exceptions - trigeminal rhizotomy, DREZ lesioning).

Always use multimodal treatment + PT + psychological support

SYSTEMIC TREATMENT

Treatment of depression, anxiety!

Pain acknowledgment is even more important than cure!

Physical therapy

LOCAL

- ice (acute pain) / heat (chronic pain) applications, CAPSAICIN ointment, LIDOCAINE patches / **EMLA cream**, US, diathermy, massage, acupuncture, TENS

DRUGS

N.B. for analgesic orders, it is better instead of PRN to use "ATC unless refused" order

1. **NSAIDs** (ASPIRIN, INDOMETHACIN, DICLOFENAC, KETOROLAC) + **acetaminophen**
   - used in *trauma & inflammation*.

2. **Tricyclic antidepressants** (AMITRIPTYLINE, NORTRIPTYLINE, DESIPRAMINE)
   - most effective drugs in *ONGOING BURNING pain* (e.g. in *diabetic, post-herpetic*).
   - analgesic effect is related to ***blockade of serotonin and norepinephrine reuptake*** (in periaqueductal gray).

3. **Selective Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)** – activate descending pathway
   DULOXETINE (CYMBALTA) - FDA approved for ***chronic musculoskeletal pain***, ***diabetic neuropathy***, ***fibromyalgia***.

4. **Anticonvulsants** (GABAPENTIN, PREGABALIN, OXCARBAZEPINE, PHENYTOIN, LAMOTRIGINE)
   - particularly useful for *LANCINATING (neuralgic) pain*.

5. **Corticosteroids** (DEXAMETHASONE) - for pain due to malignant infiltration of neural structures.

6. **Muscle relaxants** (BACLOFEN), BOTOX - for pain with muscle spasms

7. **Opioids**

Receptors in analgesia:

brain stem RF – mainly **μ receptors** (site of morphine action): *activation of periaqueductal gray* (midbrain) → *raphe magnus nucleus* (rostral medulla) → descending SEROTONERGIC fibers → inhibition at dorsal horn "gate"

spinal cord - dorsal horn "gate" – mainly **κ receptors**

PNS, at injury site – mainly **δ receptors**

σ receptor activation - *dysphoria*

Add NALOXONE Rx (esp. if > 50 MME/d, co-Rx benzos, hx of opioid abuse/overdose)

TRAMADOL, TAPENTADOL – double action:

1) agonist at **μ receptors**.
2) **catecholamine reuptake** inhibition.

physical (pharmacological) dependence occurs in virtually all patients treated for chronic pain with opioids for long time

- most appropriate for ***moderate ÷ moderately severe chronic noncancerous pain*** is **long-acting opioid**; **immediate-release opioid** - for breakthrough pain.

N.B. patient develops tolerance to all side effects except constipation and pinpoint pupils (present in drug addicts)

- if any dose will seriously depress respiratory function, it is usually much more than twice stable tolerated dose

Opioid	Approximate Equianalgesic Dose (Oral & transdermal)	MED Factor
Morphine (reference)	30 mg	1
Codeine	200 mg	0.15
Fentanyl transdermal	12.5 mcg/hr X 24 hr	2.4
Hydrocodone	30 mg	1
Hydromorphone	7.5 mg	4
Oxycodone	20 mg	1.5
Oxymorphone	10 mg	3

Source: Work Loss Data Institute ODG Opioid MED Calculator

10 mg parenteral morphine = 60 mg* oral morphine

*20-30 mg for repetitive dosing

Opioid Tapering

- goal is to taper ≤ 10% dose per week.
- ***rapid taper*** (over 2-3 weeks) is reserved if patient had episode of overdose.
- if there are signs of inappropriate opioid use (such as diversion), may stop ***immediately*** (confirm safety with negative urine drug test).
- **withdrawal** produces incapacitating, unbearable autonomic-motor-psychologic symptoms (but very rarely severe enough to cause death).

NALOXONE

- clinical use – rapid (within 30 sec. ÷ 2 min) reversal of opioid overdose.

- administered i/v 0.1 mg (with total up to 1 mg)
  Do not to administer too rapidly if there is no crisis - drug causes profound agitation, hyperventilation in patient rapidly and completely reversed from morphine sedation and analgesia!
- in morphine-dependent patient, naloxone is used *only when absolutely necessary* and *only 1/10-1/5 usual dose* (normal doses produce profound withdrawal reactions!).

8. **NMDA-receptor antagonists** (e.g. KETAMINE in subanesthetic doses)
9. Medical **marijuana**

Neuropathic pain treatment: anticonvulsants (gabapentin, carbamazepine) → antidepressants → baclofen → medical marijuana → nerve repair

INVASIVE PAIN TREATMENT

1. **Neuromodulation** procedures (activate intrinsic modulating systems):
   a) chronic intrathecal infusions
   b) electrical stimulation (mainly for *neuropathic* pain)
2. **Neuroablative** procedures (mainly for *nociceptive* pain)

Rarely jump to operate pain only – do full conservative first!

Patients undergo **psychological evaluation!**

SYMPATHETIC BLOCKS

a) blocks of **stellate ganglion** - for *upper* extremity.
b) blocks of **lumbar chain (L1-2)** - for *lower* extremity.

- main indication - complex regional pain syndromes (*reflex sympathetic dystrophy, causalgia*).
- if blocks improve pain → **sympathectomy**.

Contraindications (specific)

1) glaucoma
2) cardiac conduction block
3) severe emphysema

Anatomy

- SG (present in 80% of the general population) = inferior cervical ganglion + first thoracic ganglion fusion.
- SG lies anterior to the neck of the first rib and extends to the inferior aspect of the transverse process of C7.
- if inferior cervical ganglion and first thoracic ganglion are not fused, SG refers to the inferior cervical ganglion located adjacent to anterior C7 tubercle (but procedure is done at C6 level to avoid risk of complications)

PROCEDURE

- 22-gauge spinal needle (9 cm length)
- 5 mL lidocaine 2%
- guidance:

a) C-arm
b) ultrasound (use echo-enhanced needle)

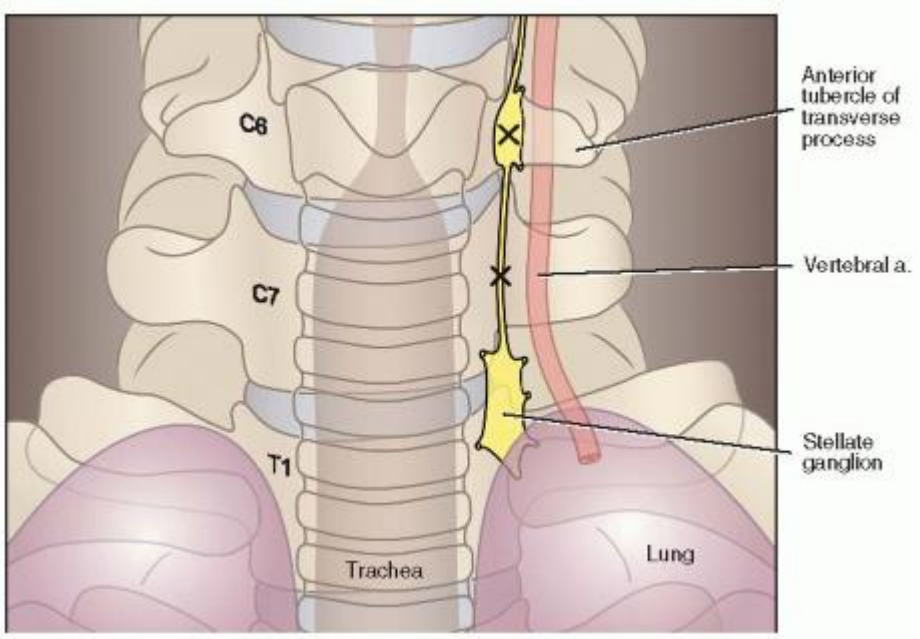
- anesthetic is injected at the C6 or C7 vertebral level with the Chassignac's tubercle, the cricoid cartilage, and the carotid artery serving as the anatomic landmarks to the procedure.
- high risk of complication (pneumothorax and vascular puncture) – use **image-guided approach** even with "safer" C6 approach.
- procedure can be performed at C7 level if needed, but be aware of the higher risks of vascular puncture
- transient Horner syndrome (T1)

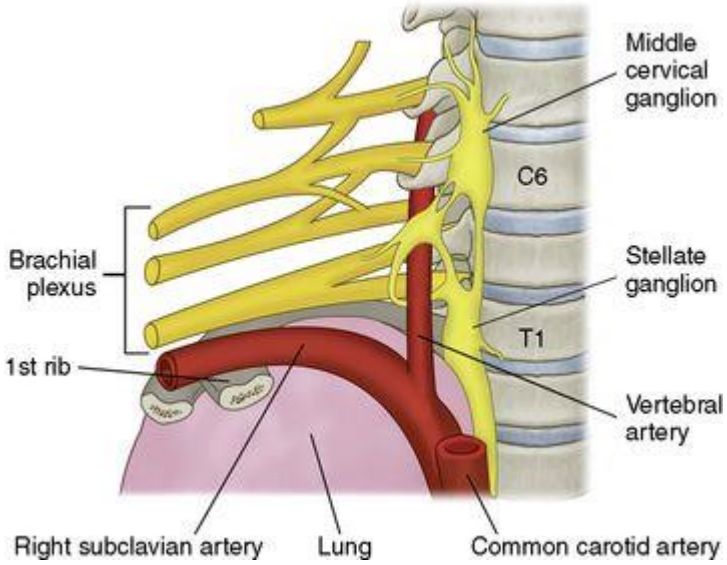
Ultrasound-Guided Technique

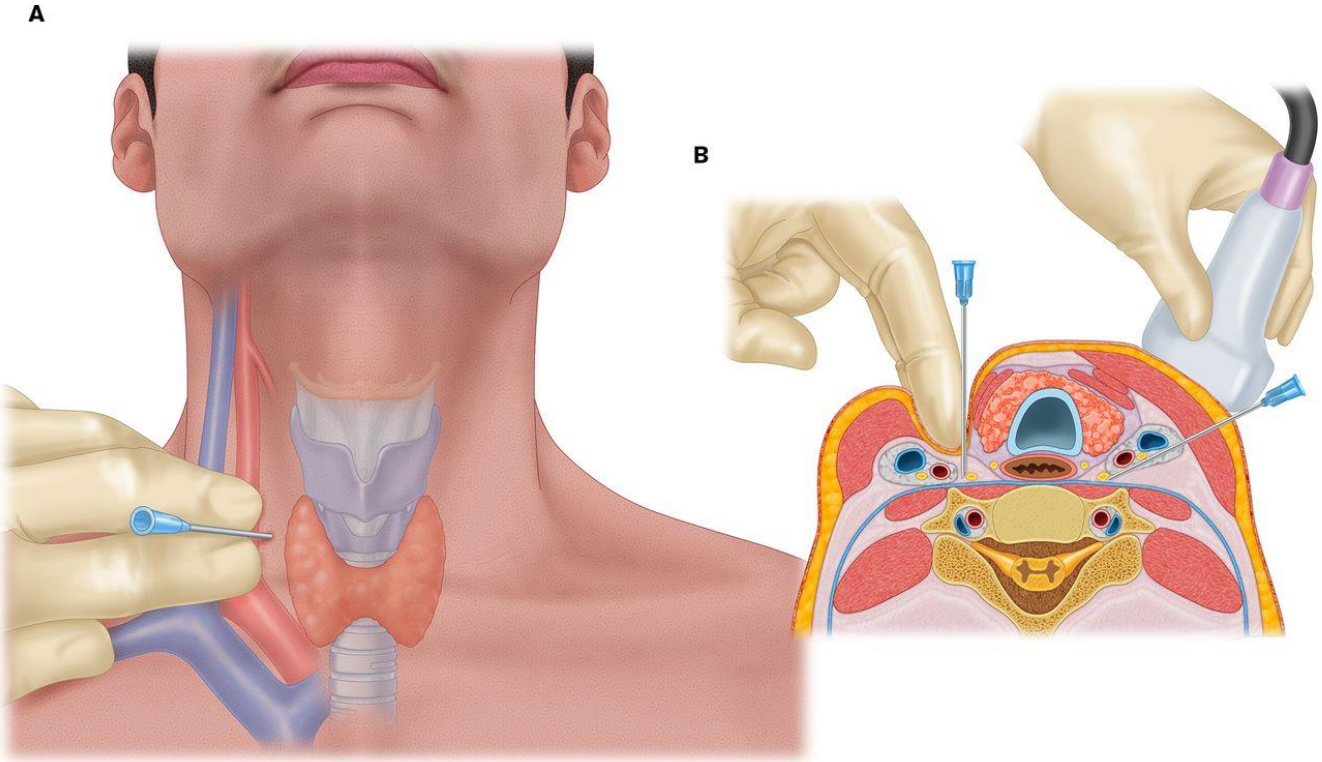
- supine with neck slightly extended and head slightly rotated contralaterally
- US transducer is placed perpendicular to tracheal axis at cricoid cartilage and is moved inferiorly until the superior aspect of the thyroid gland is visualized → transducer is relocated laterally to visualize anterior aspect of the Chassaignac's tubercle on C6 transverse process.
- color Doppler should be used to detect position of vessels.
- in-plane approach: needle is placed beside the trachea with a lateral to medial direction. The tip must reach the prevertebral fascia of the Longus colli muscle located between the posterior aspect of the carotid artery and the tip of the C6 anterior tubercle.
- aspiration test (blood or CSF) → local anesthetic is injected, and the diffusion of the injectate is seen in real-time.
- injection is suggested not inferior to C6 level because vertebral artery is unprotected at C7 level due to its absent or rudimentary anterior tubercle.
- injected until fluid spread along paravertebral fascia to stellate ganglion.

Fluoroscopic-Guided Technique

- supine position
- AP view to identify C6 → C-arm is tilted to line up the superior aspect of the C6 vertebral body and is rotated obliquely at 25-30 degrees ipsilaterally to obtain a foraminal view.
- target is junction of vertebral body and uncinate process (of C6).
- position needs to be checked through AP and lateral views.
- small amount of contrast (0.5 to 1 ml) injected to localize needle.
- tiny test dose of local anesthetic


C6
C7
T1
Trachea
Lung
Anterior tubercle of transverse process
Vertebral a.
Stellate ganglion


Middle cervical ganglion
C6
Brachial plexus
Stellate ganglion
T1
1st rib
Vertebral artery
Right subclavian artery
Lung
Common carotid artery


A
B

INTRATHECAL INFUSIONS (PUMPS)

- bypassing BBB

- lowest catheter complication rate - **paramedian oblique approach**
- ***catheter is advanced under fluoroscopy***;
    - receptors for back pain are at Th9-10
    - receptors for spasticity are at T10-11 for spastic diplegia and C7-T4 for spastic quadriparesis
- any excess catheter is looped beneath the pump, so that it is not punctured or lacerated during pump refills.
- expected battery life is a function of flow rate (expect maximum 7 years):
- when ERI is reached it starts beeping (pump also beeps if motor stalls) - pump continues to operate within specifications for 90 days.

N.B. pump does not detect catheter occlusion; so if patient has signs of drug withdrawal (with otherwise normally working pump) / increasing requirement for drug lately - do catheter dye study

- preop - ***aspirate***:
    a) if cannot aspirate from catheter → post for catheter replacement
    b) if can aspirate, then aspirate full catheter volume (recommendation is to aspirate 1-2 mL) → proceed with dye injection to verify catheter integrity and intrathecal delivery.

  N.B. never inject before aspirating catheter volume or else will bolus medication!!! (i.e. if cannot aspirate, then cannot do dye study).

Overinfusion

Drug Overinfusion – Emergency Procedure: no antidote to baclofen!

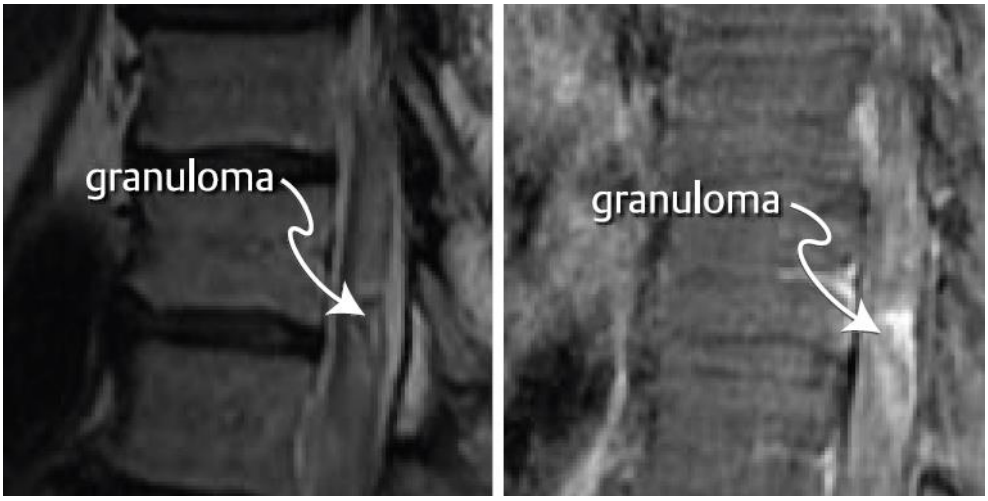
1) empty pump reservoir with noncoring 22G needle to stop drug flow.
2) withdraw 30-40 mL* of CSF through the catheter access port (or by LP) to reduce CSF drug concentration
3) for opioids: 0.4-2.0 mg NALOXONE IV; repeat PRN q2-3mins (or start IVI); if no response is observed after 10 mg of naloxone, the diagnosis of narcotic-induced toxicity should be questioned.

*alternative: 20 mL of CSF is withdrawn and replaced with 20 mL of a 5% dextrose–0.25% normal saline 2 or 3 times.

N.B. seizures have been reported both - during overdose and with withdrawal from baclofen!

Catheter-associated inflammatory mass (catheter tip granuloma)

- usually **intradural extramedullary**.
- typically sterile (although infectious cases have been described).
- associated with all known intrathecal medicines (esp. MORPHINE)
- risk factors - *high doses and concentrations* (+ low flow, CSF flow disruptions) of opioids, use of pharmacy compounded analgesic *admixtures*.
    - no relation to catheter material or location have been identified.
    - previous recommendations to place catheter tip below conus have not proven to be clinically significant.
- preventative measures: dorsal placement of catheters: larger CSF space, granuloma formation would be easier to treat surgically
- incidence: 0.1–5% of intrathecal drug systems.
- clinically: need for rapid dose escalation (due to decreasing opioid delivery, not due to opioid tolerance) + mass effect (new radicular pain, esp. at catheter tip level, myelopathy).
    - average time for development after initiation of infusion therapy is 40 months.
- diagnosis – MRI w/wo (rim enhancing mass) or CT myelogram



- treatment:
  a) **asymptomatic** (incidentally discovered granuloma):
     1) reduce drug concentration
     2) use bolus dosing (instead of continuous infusion)
     3) switch to another opioid (e.g. lipophilic) or to ZICONOTIDE
     4) pull catheter down 2-3 cm.
  b) **symptomatic mass effect** → catheter removal (granuloma will auto-absorb) in awake patient: if paresthesias appear, stop → surgical removal.
     Board answer: if cord compression, do not pull catheter down but do open resection (be careful if stuck to cord – do not aim for gross total resection)

BACLOFEN
- for spasticity Ashworth scores of ≥ 4

- trial bolus 50 µg of baclofen infused via LP - PT evaluates before and after trial - Ashworth score improvement by 1 point is positive trial!
- usual start – 500 µg/mL 50 µg/d (during refills may increase concentration to 2000 µg/mL).
- tolerance for baclofen is uncommon!
- dosage equivalents: *oral* : *intrathecal* = 1000 : 1 or **100 : 1**
  N.B. there is no direct conversion from intrathecal to oral or intravenous dosing of baclofen - dose must be titrated to achieve relief of withdrawal symptoms

PAIN DRUGS without preservatives!
1. **MORPHINE**
2. **BUPIVACAINE** (off-label use)
3. **Hydromorphone** (off label use)
4. **CLONIDINE** (off-label use)
5. **ZICONOTIDE** - severe psychiatric and neurological symptoms may occur – can be stopped abruptly but NO KNOWN ANTIDOTE!

Requirements
1) favorable response (> 50% pain relief) to IT trial
2) life expectancy > 3-6 months (if < 3 mos → contralateral cordotomy)
3) for cancer patients: visual analog scale (VAS) of ≥ 5, despite 200 mg/day of oral morphine equivalent

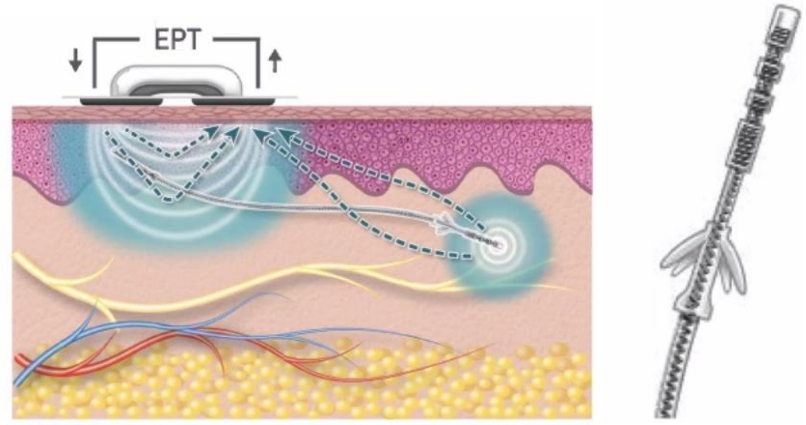
See N3 case >>
See Case F4 >>

NEUROMODULATION / ELECTRICAL STIMULATION

N.B. pain relief diminishes with time (stimulation tolerance)!

PNS

external battery up to 2 months



DBS

Stimulation of ***descending endorphin system*** – most effective for nociceptive pain.

- target in **periventricular gray (PVG), periaqueductal gray (PAG)**

Stimulation of ***ascending lemniscal system*** – most effective for neuropathic pain.

- target in **somatosensory ventrocaudal (Vc) THALAMIC nucleus (VPM-VPL)** or in **sensory portion (posterior third of posterior limb) of INTERNAL CAPSULE**.

For affective component of chronic pain – target in **anterior cingulate cortex**.

Motor cortex stimulation

SCS

Classical Tonic Stimulation - low-frequency (40-60 Hz, 300-600 msec, 4-9 mA) pulses; patient feels paresthesias (allows anatomical coverage mapping) – 50% responder rate

Proprietary HF10 - Nevro: high frequency (10 kHz), low-amplitude (1-5 mA), short-duration (30 msec) pulses - relieves ***back and leg*** *pain without causing constant paresthesias* (so no awake intraop testing is needed or available – always T9-10) – 80% responder rate for leg / back pain (incl. diabetic neuropathy).

- high drain on battery - only rechargeable battery that lasts 10 years under typical settings.

Burst stimulation – Abbott / St. Jude: De Ridder D - does not generate paresthesias (possible to do placebo-controlled studies)

DTM (Differential Target Multiplexed) – Medtronic: Dr. Vallejo invention – algorithm with variation of waveform, frequency, amplitude, pulse width - targets ***glial cells***; may feel some paresthesias. – 80% responder rate

Surround Inhibition – Boston Scientific

Closed-loop – Saluda (Evoke system)

Patient inclusion criteria

1. Intractable pain for > 3 months
2. Objective evidence of pathology
3. No untreated substance abuse
4. Mandatory psychological clearance - to examine factors such as patient expectations, psychosomatic components of the pain, and secondary gain motivation.

20-30% patients later request SCS removal ("Does not work for me")!

5. Satisfactory results from neurostimulation trial; most agree that trial with 50% pain relief warrants permanent implantation
   N.B. trial always has placebo effect, so permanent implant always does slightly worse – aim for 70% pain relief with trial plus definitive functional improvement (not just "reduced amount of pain pills")

Indications

1) failed back pain (i.e. recurrent back pain after multiple low back operations); Class I evidence demonstrating success of SCS over repeat spinal surgery
2) radicular pain
3) painful peripheral neuropathy (e.g. inguinal pain after herniorrhaphy, diabetic polyneuropathy)
4) spinal arachnoiditis
5) complex regional pain syndrome I, II
6) traumatic nerve injury
7) postherpetic neuralgia
8) stump pain

Absolutely necessary to review a thoracic spine MRI - to avoid cord injury by implanting in congenitally narrow thoracic canal! - avoid inserting the paddle:

- thickness of the CSF layer is < 3 mm
- thickness of the paddle allows < 1 mm of CSF clearance

- if stenosis at level of insertion, may insert retrogradely (hemilaminotomy 1-2 levels above target).

Neurostimulation Appropriateness Consensus Committee (NACC) guidelines:
"***Confirmation of correct lead placement*** has been advocated with either **awake** intraoperative verbal confirmation of paresthesia coverage or use of **neuromonitoring in asleep** placement, such as EMG responses or SSEP collision testing."

- current gradually increasing from 1 to 5 mA - **SSEP** is monitored to find ***physiological midline of dorsal column*** – watch for SSEP response attenuation until complete flattening (current where clinical effect will be observed) – must be symmetric
- further increasing current, watch for **EMG** changes (side effect; current should be higher than for SSEP flattening).

N.B. spinal cord dysfunction may manifest hours after procedure – due to cord ischemia, epidural hematoma – rationale for postop observation (6 hours, up to overnight)

Failed stimulation - check if paresthesias are covering the pain area:

a) **yes** - the patient is nonresponder.
b) **no** - the error of selecting incorrect implantation level → revision surgery.

No abandoned leads (no battery) are compatible with MRI – risk of spinal cord damage with induced electrical currents!

SCS-CERVICAL

- may want burst (St. Jude) or HF10 (Nevro) so patient won't have paresthesias in hands.
- paddle needs additional clearance to allow for flexion and extension of the neck

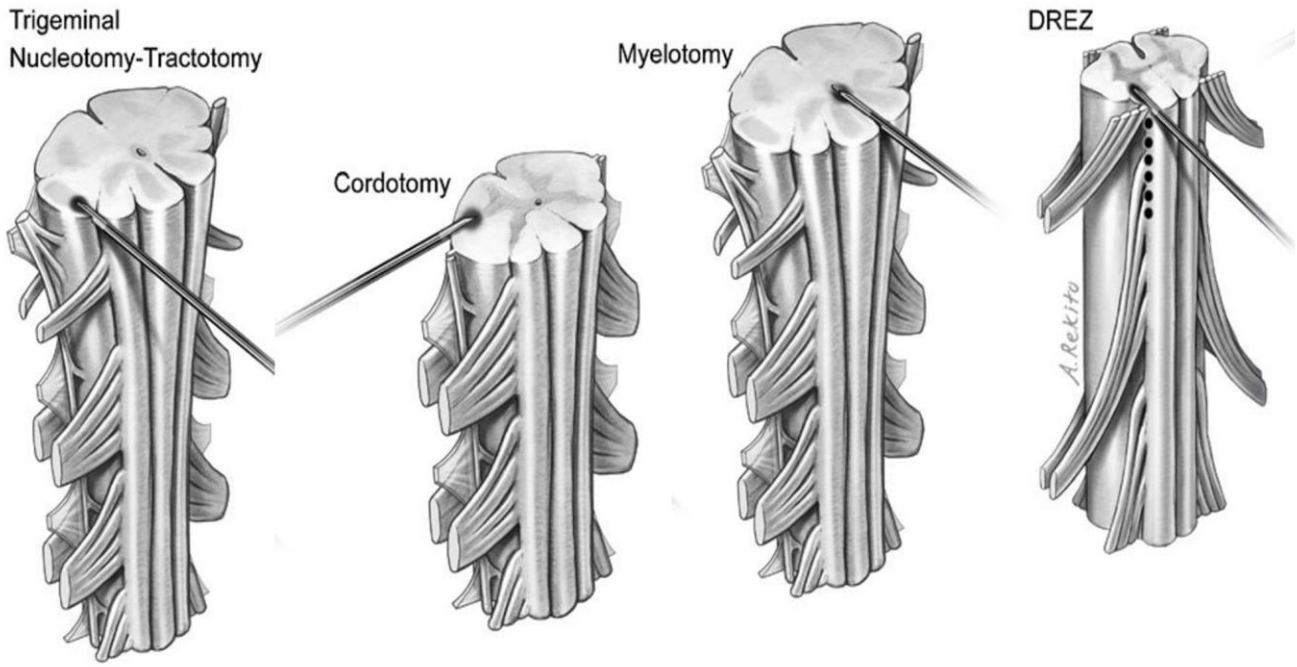
See Case F5 >>

NEUROABLATIVE PROCEDURES

I. **Peripheral**: preop do test block injections!
   1. **Neuroma resection** → burying nerve in muscle, burying nerve in bone, covering nerve with Silastic
   2. **Neurectomy** (e.g. denervation of facet joints in spine; ablation of infraorbital, supraorbital, or mental nerves - for trigeminal neuralgia)
   3. Sympathectomy
   4. **Ganglionectomy** – for C2 (for intractable occipital neuralgia); other levels need facetectomies
   5. **Rhizotomy** - ablation of sensory root (e.g. CN5); in spine majority of large series are disappointing
   6. **Intrathecal absolute alcohol** - instantaneously neurolytic: patient cooperation is imperative – inject in 0.1-mm increments - if stinging, burning pain anywhere other than at pain site, patient is instructed to cough (to break up small alcohol volume) and is then repositioned immediately

II. **Spinal**:
   1. Cordotomy
   2. Midline myelotomy
   3. DREZ myelotomy
   4. Trigeminal tractotomy

Monitoring
A. Awake patient
B. SSEP, MEP – to avoid complications (not to guide effect)



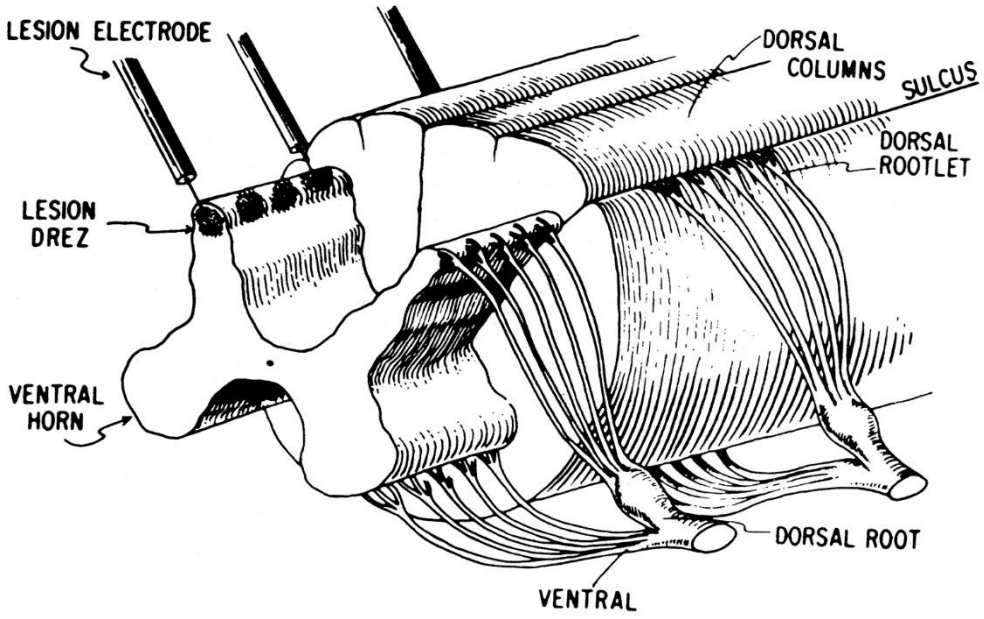
III. **Cranial**:
   1. **Mesencephalic tractotomy** - when pain involves *dermatomes above C5*; complications - gaze palsy
   2. **Thalamotomy (mediodorsal and basal, e.g.** centromedian nucleus**)** (RF or SRS) esp. for *pain involving face and upper body*;
   3. **Hypophysectomy** - 160 Gy delivered to pituitary gland: pain relief in > 70-80% of cases for *opioid refractory nociceptive or mixed cancer pain*

4. **Cingulotomy** (bilateral) – for *severe anxiety (suffering)* that accompany chronic pain - patients report that they feel pain but that it "doesn't bother" them; risks - cognitive and behavioral problems (avoid in sociopaths!)
   vs. prefrontal lobotomy - causes *extensive personality changes*! - rarely performed today!

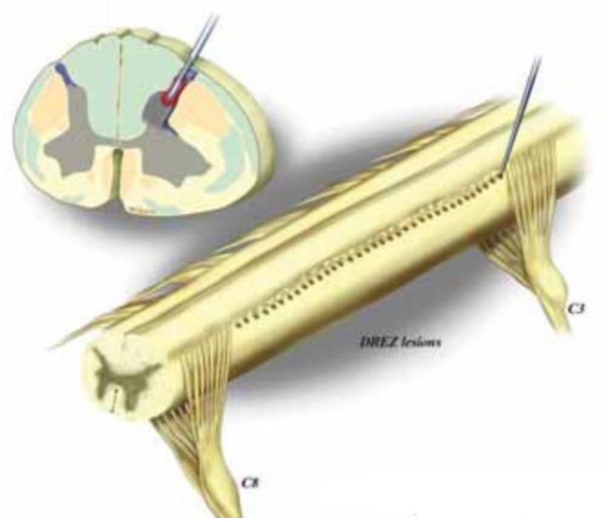
DREZ (DORSAL ROOT ENTRY ZONE) MYELOTOMY

- indications (effective in deafferentation pain!; initially was developed to treat **spasticity**):
  brachial plexus avulsion pain – 60-80% improvement
  phantom limb pain
  postherpetic neuralgia – only 25% efficacy

- DREZ anatomy:
  - DREZ = dorsal rootlets + Lissauer's tract + dorsal horn.
  - afferent nociceptive fibers, before entering the dorsal horn, bifurcate *rostrocaudally* or trifurcate *rostrocaudal laterally* to run for a few segments in a thin Lissauer's tract.
  - lateral part of Lissauer's tract contains the propriospinal fibers; therefore, destruction of the medial part of Lissauer's tract should result in decreased excitability of nociceptive fibers.
- mechanism of action:
  - originally designed to destroy superficial layers of posterior horn; recent evidence suggests - should destroy **Lissauer tract** and **layers I to V**.
- mechanism of destruction (RF current, laser, incision and microbipolar coagulation) is not as important as accuracy & completeness of destruction.



- technique:
  - **expose one level above and one level below** the avulsed roots (look for nerve root pits)
  - **midline durotomy.**
  - **RF lesions** - Nashold electrode at 30 degrees oblique of coronal plane; lesions are made 1 mm apart with 75ºC for 15 seconds per lesion.



(ANTEROLATERAL) CORDOTOMY

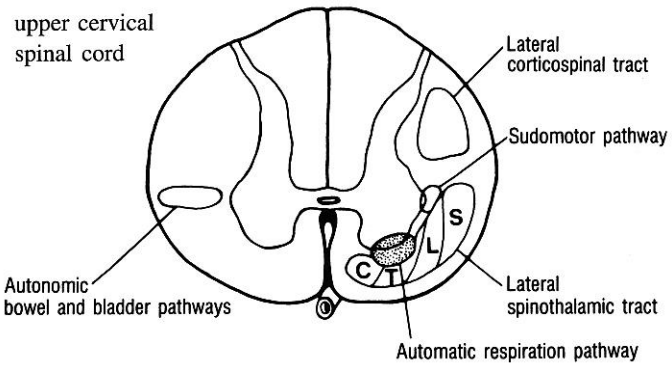
- for **contralateral multisegmental** pain.

Preoperative rule out:

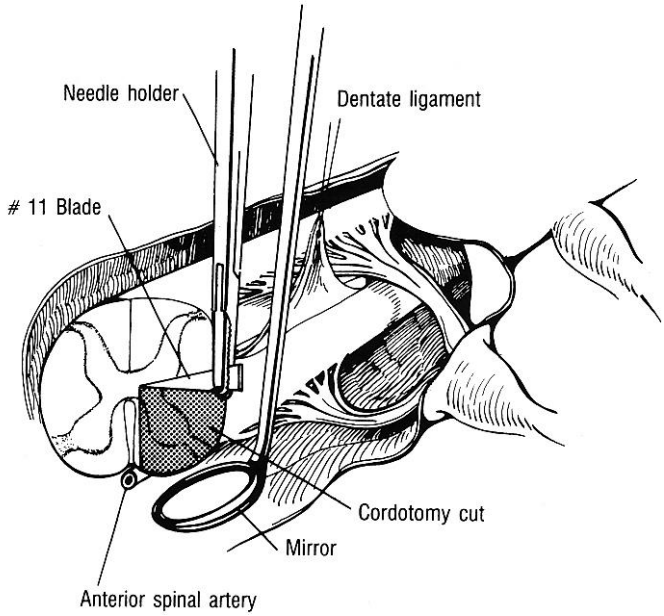
1) ***deafferentation*** pain (→ worsening of already intractable pain).
2) any pain on ***opposite side*** (H: bilateral high thoracic cordotomy or commissural myelotomy).

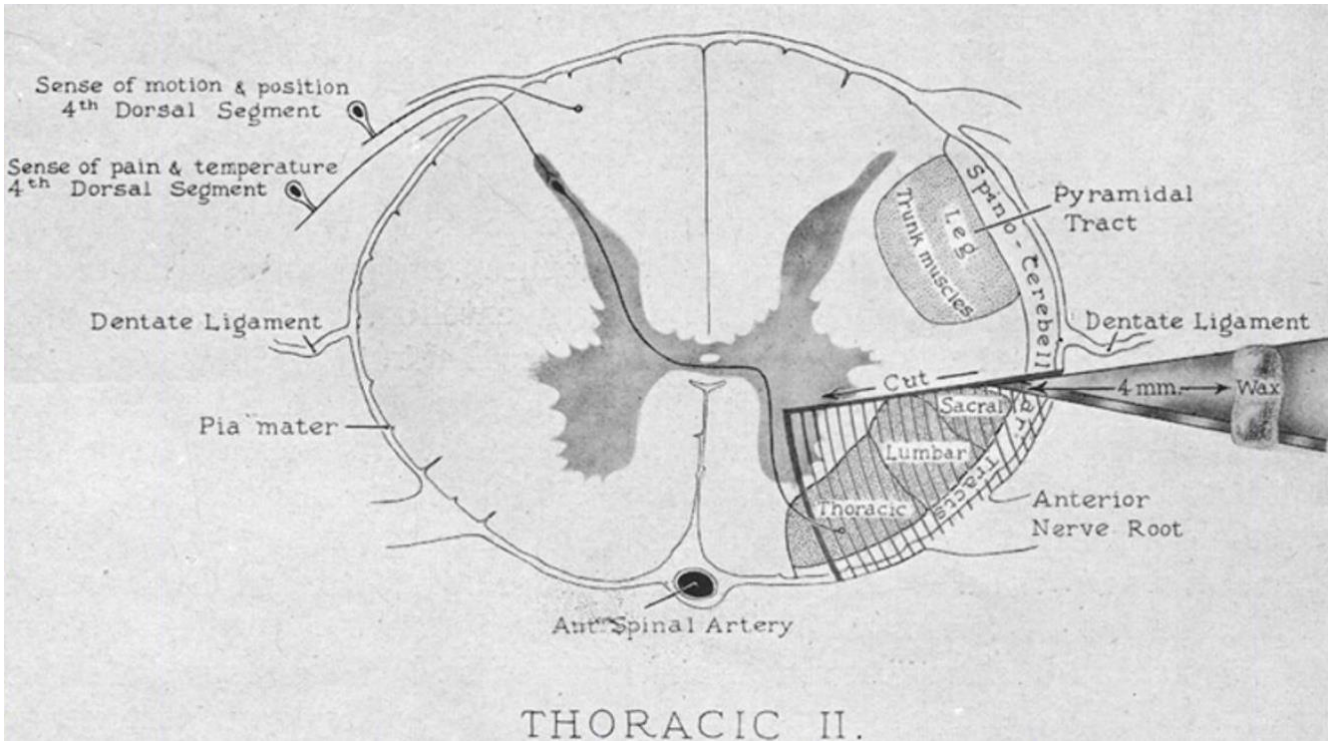
involuntary respiration control – in anterolateral quadrant immediately medial to cervical spinothalamic fibers – if severed in bilateral high* cervical cordotomy (→ *fatal sleep apnea* [Ondine's curse]); failure to respond to CO_2 challenge with hyperventilation may predict this complication preoperatively.

*bilateral cordotomy – only for below C5



- T2-4 dentate ligament is cut and retracted posteriorly and medially.
- after measuring half cord width (usually no more than 5 mm), equal length of No. 11 blade is grasped by needle holder.
- blade is inserted at *dentate ligament level* and then drawn anteriorly.
- dental mirror is held anterior to assure that blade tip avoids anterior spinal artery as cut is completed anteriorly.





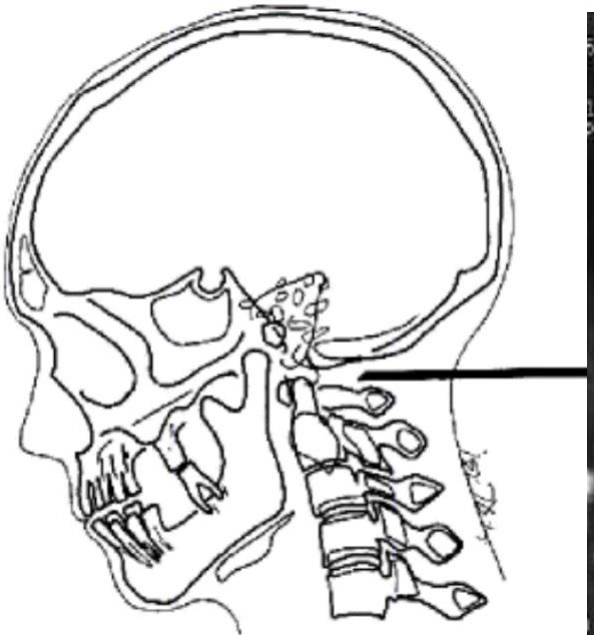
- pain relief is immediate but pain recurs in 6-12 months (cordotomy is reserved for patients with limited life expectancy).
- target pain is always relieved but new mirror pain* occurs in 6-73% of patients after unilateral cordotomy (referred pain mechanism). *may be as severe as the original dominant pain

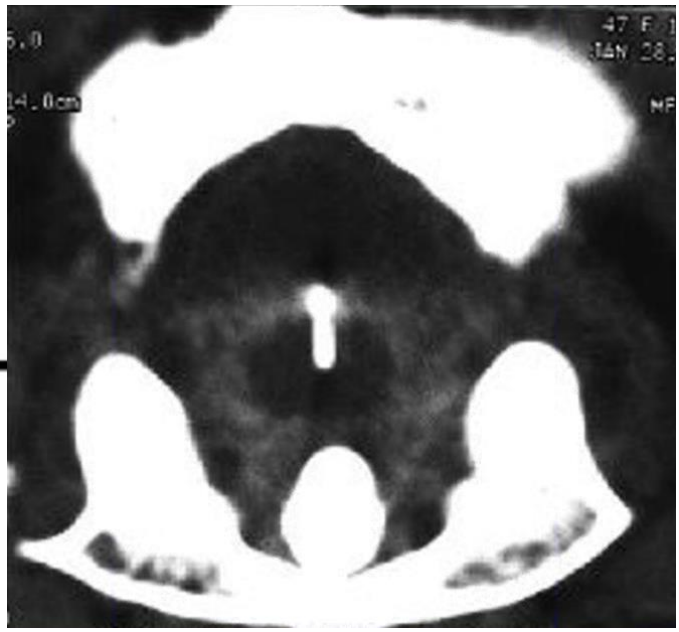
COMMISSURAL (S. MIDLINE) MYELOTOMY

- main indication – visceral **cancer** pain - bilateral pain below neck (alternative to bilateral cordotomy).
- (open or percutaneous) splitting spinal cord in midline sagittal plane (at and above level of pain).
- mechanism - destruction of central ascending nonspecific multisynaptic pathway (extralemniscal system) in central grey commissure / decussating fibers.
- not enough evidence to suggest a size of the myelotomy lesion

CT-guided:

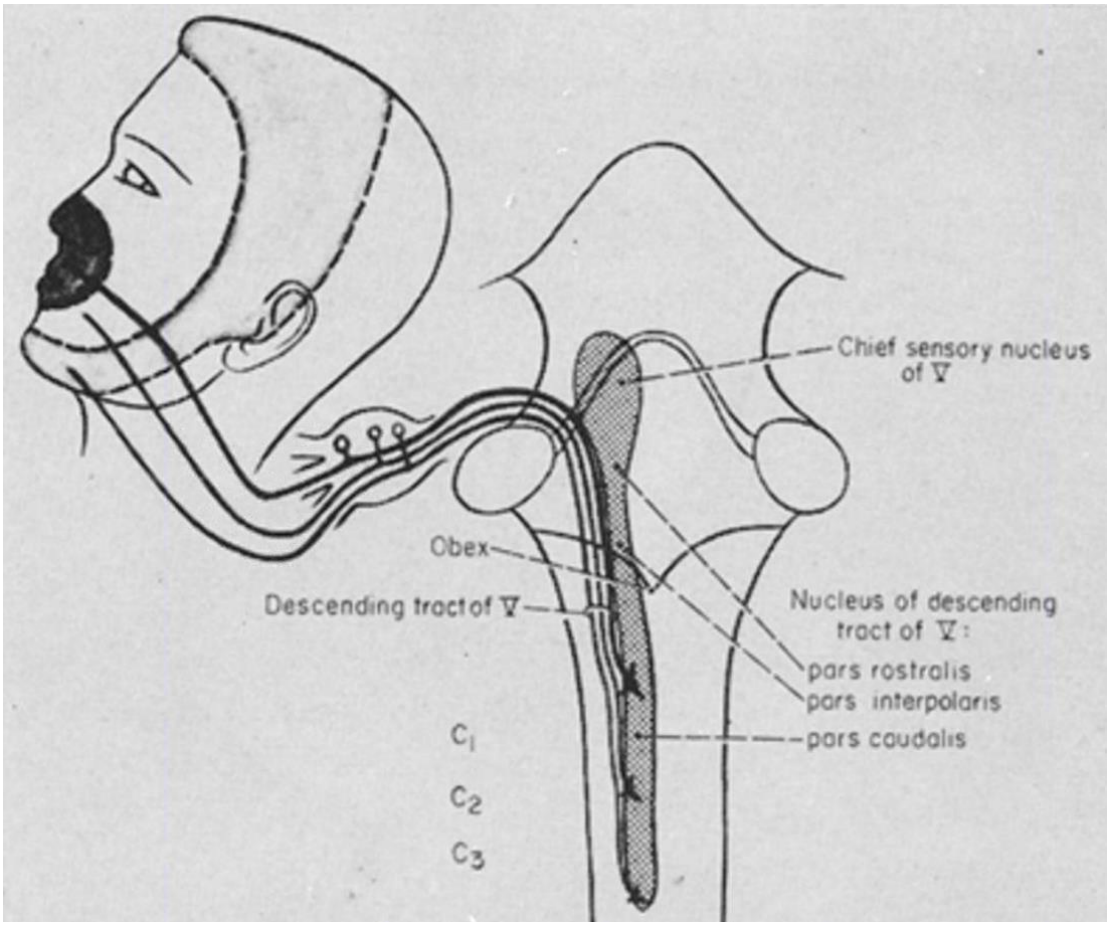
- local anesthesia.
- head well flexed in stereotactic apparatus.
- guide needle is introduced posteriorly in midline through **occiput-C_1 interspace** (under fluoroscopic guidance).
- 50 Hz 1.0 volt stimulation is carried out as electrode is advanced - symmetrical paresthesias should be obtained in legs & perineum → both arms.
- after arm responses are no longer obtained, electrode is advanced another 2 mm.
- **RF coagulation** until significant hypalgesia / analgesia occurs (or unwanted neurologic deficit).
- 80% initial pain relief, < 50% long-term pain relief (usually, pain relief for months – years).



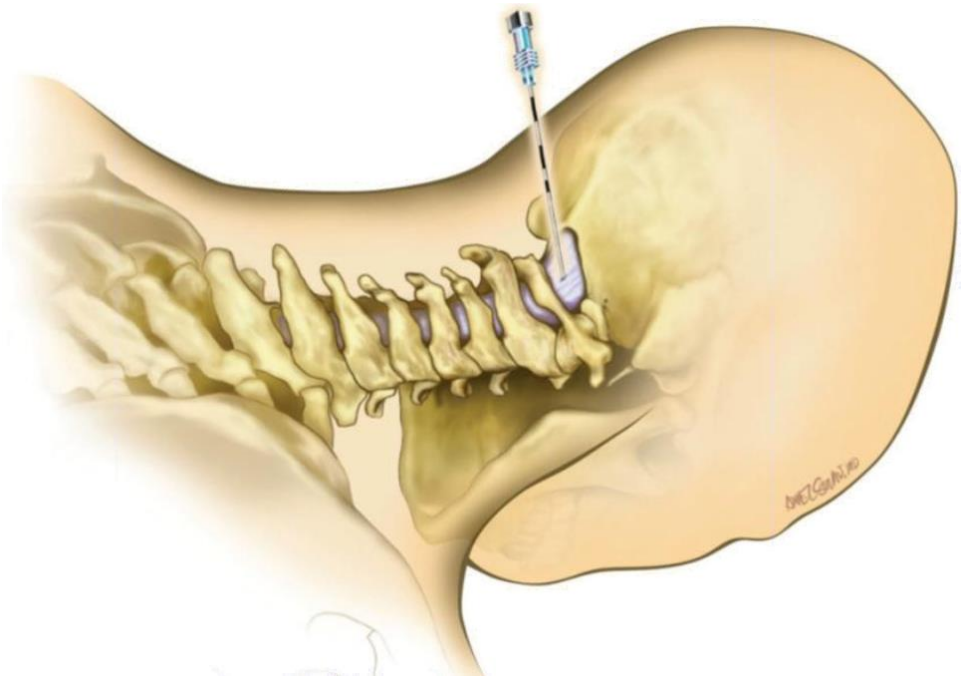


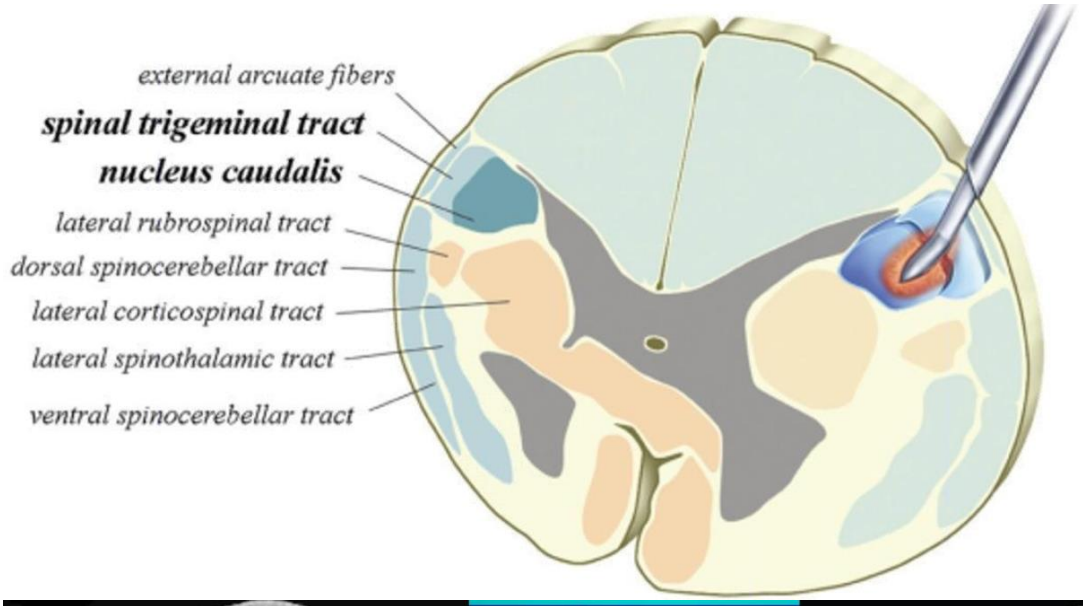
TRIGEMINAL TRACTOTOMY / NUCLEOTOMY

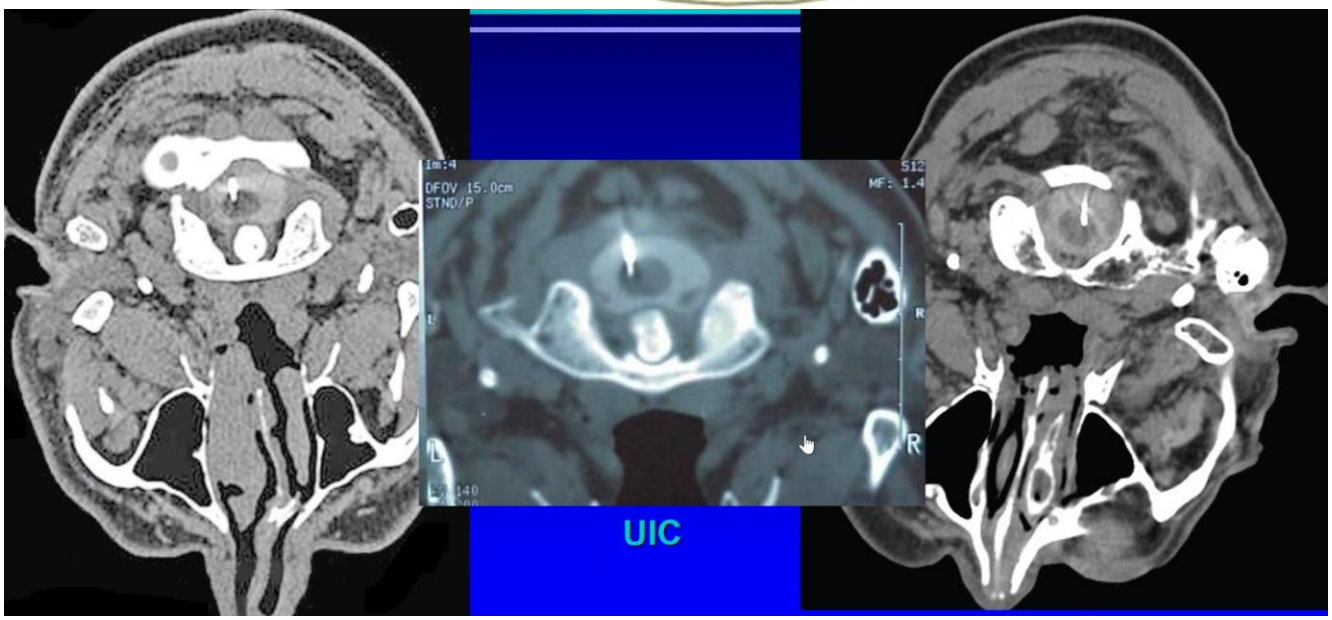
Only for CN5 oncological pain!
Second indication – CN5 deafferentation pain.



- occiput-C1 approach, CT-guided
  N.B. procedure is painful!







CANCER PAIN

N.B. use drugs on non-prn (noncontingent) schedule (avoid pain reoccurrence!)
Pharmacologic dependence may result but causes no problems in dying patients except need to *avoid inadvertent withdrawal*!

N.B. most **cancer pain syndromes** have prominent ***nociceptive*** component but may also include ***neuropathic*** pain (nerve damage by tumor or its treatment) and ***psychogenic*** pain (related to loss of function and fear of disease progression).

- when stable opioid dose becomes inadequate → increase dose 1.5-2.0 times (respiratory depression does not occur unless dose is >> twice previously tolerated dose).
- adjunctive measures (help decrease opioid doses):
  corticosteroids – decrease pain of inflammation and swelling.
  tricyclic antidepressants, ***anticonvulsants*** – in neuropathic pain.
  benzodiazepines – if pain is worsened by anxiety.
  regional nerve blocks, ***indwelling epidural / intrathecal catheters*** – for regional pain.

CNS Guideline on Neuroablative Procedures for Cancer Pain (2021)
A. Unilateral somatic nociceptive/neuropathic body cancer pain
   A) **Rhizotomy**
   B) DREZ - insufficient data.

C) **Cordotomy**
D) **Mesencephalotomy** - alternative to cordotomy *when pain involves dermatomes above C5*
E) Mediodorsal and basal **thalamotomy**, esp. for *pain involving face and upper body*

B. Craniofacial cancer pain - insufficient evidence to recommend one procedure over the other:
A) Cranial nerve **rhizotomy**
B) Nucleus caudalis **DREZ**
C) Trigeminal **tractotomy-nucleotomy**

C. Midline subdiaphragmatic visceral cancer pain - **myelotomy**
- not enough evidence to suggest a size of the myelotomy lesion or to favor open vs percutaneous method.

D. Disseminated cancer pain - **cingulotomy**
- additional options - SRS hypophysectomy, opioid pump

CHRONIC NEUROPATHIC PAIN SYNDROMES

- two broad categories:
  a) **deafferentation pain** (due to partial or complete interruption of peripheral or central afferent neural activity); e.g. *postherpetic neuralgia, central pain (after CNS injury), phantom limb pain*.
  b) **sympathetically maintained pain** (dependent on efferent sympathetic activity).

CENTRAL POST-STROKE SYNDROME (S. THALAMIC PAIN, DÉJÉRINE-ROUSSY SYNDROME)

- damage to **posterior thalamic nuclei** (usually infarct of thalamogeniculate branch of posterior cerebral artery).
- contralateral severe loss of all sensory modalities → after few weeks ÷ months → attacks of **prolonged, severe, lancinating, extremely unpleasant pain***.

*"flesh is being torn from my limbs" or "bathed in acid"

- no autonomic or trophic changes!
- resistant to all kinds of treatment: AMITRIPTYLINE.

PHANTOM LIMB PAIN

- pain (in addition to other sensations) felt in amputated limb (not in stump!)
- treatment – ultrasound, drugs (e.g. GABAPENTIN), ***DREZ***.
  vs. stump pain does not respond to DREZ lesioning! (H: SCS)

OCCIPITAL NEURALGIA

Options:
A. Injections
B. Stimulation
C. C2 ganglionectomy

POST-HERPETIC NEURALGIA

- pain persistence after skin healing is complete (i.e. pain for ≥ 1 month after skin healing).
- ***elderly*** are more susceptible.

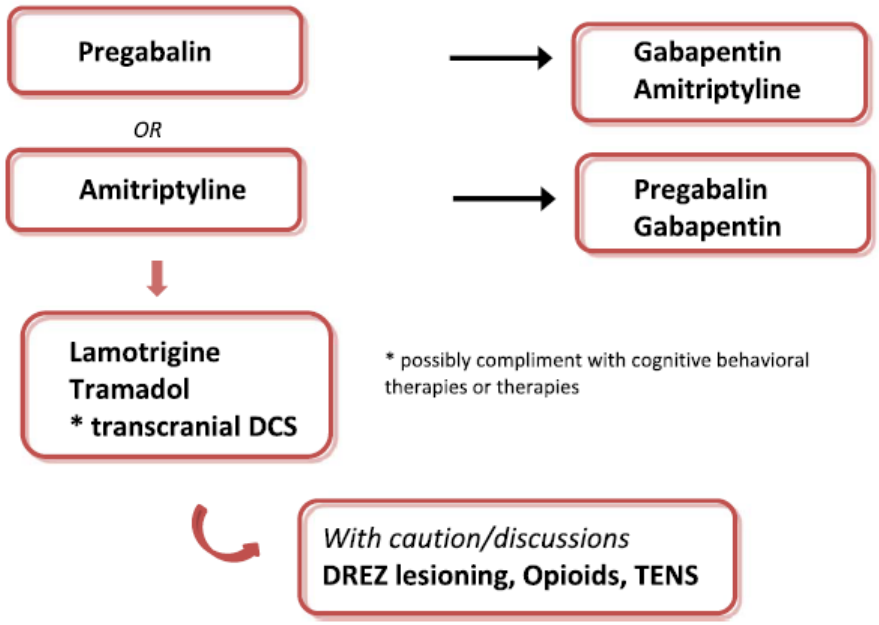
Prophylaxis – PREDNISONE at onset of herpes zoster in immunocompetent patients or patients > 60 yrs.
N.B. not recommended for HIV-positive patients.

Lidoderm® (transdermal lidocaine patch) – FDA approved
All spectrum of pain meds trial
Minority are refractory to all currently available medications; surgical options:

a) SCS
   N.B. try neuromodulation options first!
b) IT pumps
c) neurolytic nerve blocks
d) ablative procedures (DREZ is not very effective).

PAIN OF SPINAL CORD INJURY

- often complex and multifactorial; **central neuropathic** type:
  a) spontaneous
  b) evocable



Antiepileptics:
PREGABALIN – first line treatment, FDA approved (2012) for SCI pain.

- older generations – LAMOTRIGINE (historic first line treatment)

Tricyclics: AMITRIPTYLINE – best medication!

Opioids last resort.

Intrathecal pumps – insufficient evidence.

- clonidine, opioids, ziconotide.

A. **End-zone pain** (evocable pain) - triggered by local nonpainful stimuli.
   - located at level of SCI, i.e. *dermatomes* immediately caudal to level of sensory loss.
   - treatment - ***DREZ***, ***nerve blocks*** – only for patients with **complete SCI**

B. Nonevokable pain.
   - diffuse *nondermatomal*.
   - constant, burning.
   - treatment: (responds poorly to DREZ)
     shooting pain - ***cordotomy*** or ***cordectomy*** (excision of damaged cord area).
     burning pain - ***thalamic*** or ***SCS***

Aware of posttraumatic syrinx. H: ***syrinx shunting***.

N.B. any procedure involving the spine always carries a small risk of further iatrogenic neurologic injury from the procedure itself.

COMPLEX REGIONAL PAIN SYNDROMES

1) **type I** (**reflex sympathetic dystrophy**) – WITHOUT EVIDENCE of nerve injury; pain is not confined to distribution of single peripheral nerve.
2) **type II** (**causalgia**) – caused by apparent TRAUMATIC nerve lesion; pain in territory of affected nerve; if untreated, disorder sometimes is *progressive* (involves other body parts)

- partially damaged sympathetic fibers directly activate sensory fibers (that lost their coverings) - ***ephaptic conduction*** ("artificial synapses" - periphery has been short-circuited): ***sympathetic discharge brings on diffuse persistent pain*** - sympathectomy may cause relief

"vicious cycle" of sympathetic stimulation → pain → more sympathetic stimulation

N.B. causalgia does not occur when nerve is COMPLETELY severed!

- **reversible cause** (usually *orthopedic*) can occasionally be found!

Budapest Criteria

- for discrimination between CRPS and neuropathic painful conditions; four criteria must be met:

S. No	Criteria	Categories			
		Sensory	**Vasomotor**	**Sudomotor/Edema**	**Motor/Trophic**
1	Continuing **pain**, disproportionate to any inciting event	--	--	--	--
2	**Symptoms:** Must report at least one symptom in three of the four categories shown to the right	Hyperesthesia; Allodynia	Temperature asymmetry; Changes in skin color; Skin color asymmetry	Edema; Sweating changes; Sweating asymmetry	Decreased range of motion; Motor dysfunction; Trophic changes (hair, nails, skin)
3	**Signs:** At the time of evaluation, must have at least one sign in two or more of the categories shown to the right	Hyperalgesia (pinprick); Allodynia (light touch or temperature); Deep somatic pressure; Joint movement	Skin temperature asymmetry (>1°C); Changes in skin color; Skin color asymmetry	Edema; Sweating changes; Sweating asymmetry	Decreased range of motion; Motor dysfunction (weakness, tremor, dystonia); Trophic changes (Hair, nails, sin)
4	**No other diagnosis** can better explain the patient's signs and symptoms	--	--	--	--

Signs of **sympathetic overactivity!**

- always consider other treatment methods (physiotherapy, drugs, TENS, etc), because response cannot be predicted unless tried.
- **selective sympathetic blockade → sympathectomy** (response rates 12-97%).
- **dorsal root ganglion stimulation**, SCS
- ***for type II* → nerve repair**

HEADACHE

N.B. ***thunderclap headache*** - SAH or cerebral venous thrombosis

Only 1 in 250,000 patients with chief complaint of headache have ***secondary headache***. Almost all patients have one of three: **migraine**, **tension-type**, or **cluster** headache.

N.B. headache produced by *brain tumor* is not severe!

Diagnosis

- if benign diagnosis cannot be made (new-onset headache with nausea, vomiting, or abnormal signs) → **MRI**;
- **ESR** for those > 50 yrs.
- **ophthalmoscopy** – for papilledema.

TYPES

Migraine without aura (COMMON MIGRAINE)
Migraine with aura (CLASSIC MIGRAINE):
prodrome (various symptoms)
aura (caused by **CORTICAL SPREADING DEPRESSION**) - fully reversible focal signs: visual > paresthesias > motor; aura > 1 hour - ***complicated migraine***)
in < 60 mins **headache** starts (unilateral, side affected in each episode may be different; gradually builds up over 1-2 hours; throbbing-pulsating; ≥ 5 points; nausea-vomiting-sensory hyperexcitability; attack lasting > 72 hours – **STATUS MIGRAINOSUS**)
N.B. CBF↑ begins after headache onset!
Malignant migraine - patients who develop strokes

- **abortive** drugs (ERGOTAMINES, TRIPTANS) are 5-HT_1 agonists;
  - contraindicated in **complicated migraine**, **CAD**, **peripheral vascular disease**, severe **hypertension**, **pregnancy**!!!
  - all triptans ***constrict coronary arteries*** in vivo.
  - do not combine together and with SSRI → **vasospastic reactions**
- **prophylactic** drugs:
  5-HT_2 antagonists (METHYSERGIDE, CYPROHEPTADINE)
  β-blocker PROPRANOLOL, calcium blockers FLUNARIZINE, VERAPAMIL, antidepressants, anticonvulsants, NSAIDs

Tension-type headache - relatively ***featureless, mild headache***: bilateral, nonpulsating.

Cluster headache - occur at same time each day; pain rapidly increases (within 5-15 minutes) to ***excruciating*** levels; unilateral periorbital; untreated attacks last 30-90 minutes; ipsilateral autonomic dysfunction;

- treatment - 100% O2 (!!!),ERGOTAMINES, TRIPTANS; if dramatic response to INDOMETHACIN – **Chronic Paroxysmal Hemicrania**
- Topical (intranasal) 2-4% LIDOCAINE - to most caudal aspect of inferior nasal turbinate (patient supine) - *sphenopalatine ganglion block* - remarkably effective! → sphenopalatine ganglion stimulation! (level 1 evidence)
- prophylaxis – ERGOTAMINE, LITHIUM

Rebound headache - secondary to overuse of analgesics.

Postherpetic neuralgia H: trigeminal branch stimulation

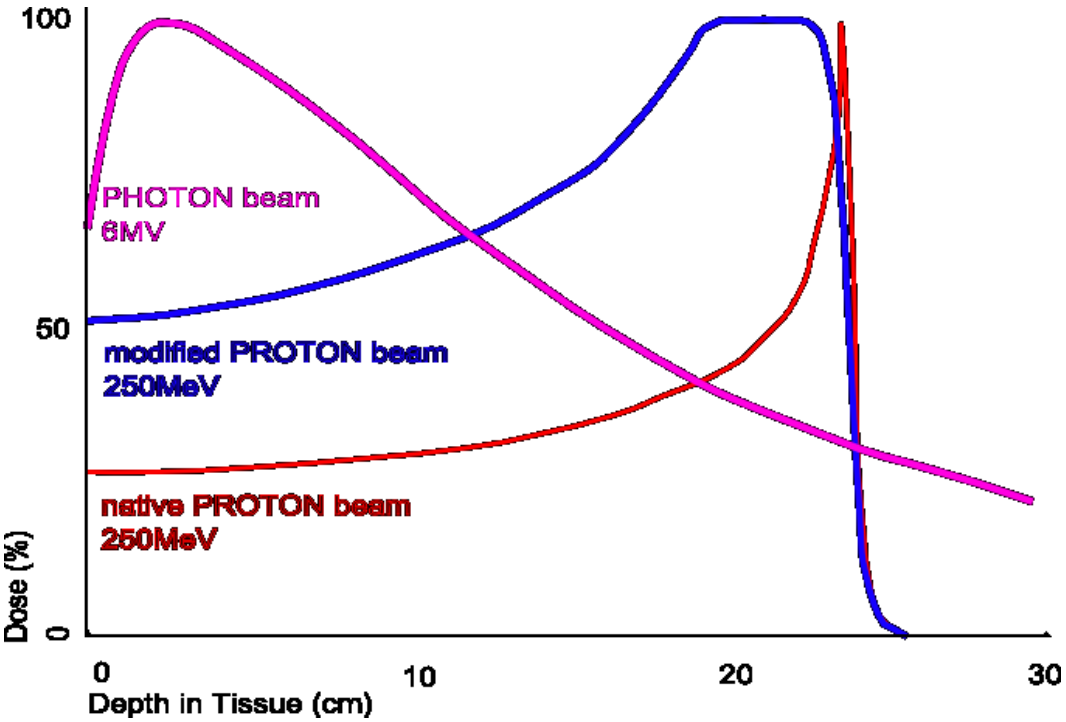
Intracranial Hypotension - orthostatic headache (in erect position and relieved with recumbency)

RADIOTHERAPY

ALARA (As Low As Reasonably Achievable): Time, Distance, and Shielding
Mitotically active cells are most prone to radiation injury!

- tumor cells are often deficient in *repair mechanisms* (vs. normal cells); ***fractionation*** (daily small doses of radiation) allows normal cells to repair while tumor cells are unable to do so.
- *poorly oxygenated cells* (make up significant proportion of many solid tumors) are 2-3 times less sensitive to radiation than well-oxygenated cells (*oxygen is most powerful radiation sensitizer*).
- no extent of surgery can change tumor biology – important for local control – radiation matters!

Bragg's Peak:



N.B. with proton beams higher doses can be achieved (vs. conventional photon irradiation) at the target because protons loose charge very quickly and there is no exiting beam that could damage nearby structures (like brainstem); skin sparing – energy is absorbed deeper.

Methotrexate with radiotherapy, whether synchronously or at separate times → *necrotizing leukoencephalopathy* (focal coagulative necrosis within white matter).

children < 3 years are more susceptible than adults (dose reductions of 20-25% vs chemotherapy in attempt to delay radiation)

SRS

- small daily fractions are safer and more effective than larger fractions over shorter periods.

RADIOSURGERY – term is used if number of sessions is ≤ 5
and only for cranial or spinal targets

- for lesions < 3-4 cm, probably up to 10 lesions

in > 4 cm, radiation dose to surrounding structures becomes too great – use fractionation!

- term formulated by Lars Leksell, MD in 1951
- treatments are called ***sessions*** (vs. ***fractions*** in fractionated conformal radiotherapy).
- even radioresistant tumors can be treated.

- gliomas, when malignant, are always poor indication for radiosurgery because of their diffuse mode of invasion (except pilocytic astrocytomas - excellent indication for radiosurgery if difficult to excise safely).

Cobalt specifics

- naturally occurring form (100%) is **Co59** (not radioactive)
- **Co59** can be transformed to **Co60** by the addition of a neutron (in a nuclear reactor)
- **Co60** undergoes beta decay* with T1/2 = 5.2714 years** – produces **Ni60** which immediately emits 1 or 2 gamma rays.

*i.e. emits beta particle

**treatment times get longer as Co60 sources decay (twice as long at the end of 5 years - cobalt needs replacement every 5 years (cost approx. 1 mln USD in 2017)

Gamma-ray photons vs. X-ray photons

- Gamma-ray photons and x-ray photons are physically alike, but differ in point of origin:
  A) Gamma-ray photons - originate from atom's nucleus
  B) X-ray photons - originate from atom's electron shell
- Gamma-rays are narrow spectrum (isotope dependent); X-rays are broad spectrum.

Conformality ratio (ability to conform dose to the target) =
= entire volume getting prescribed dose / target volume getting prescribed dose

Has to be ≤ 2 (except for very small targets); for perfect plan, ≤ 1.5

Inhomogeneity ratio IR = maximum dose MD / prescribed dose PD

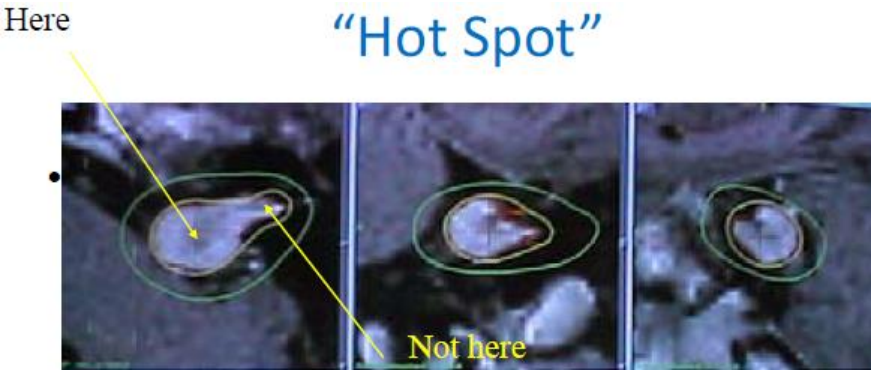
Dose Homogeneity –consistency of dose within treated volume

- IR has to be ≤ 2
- MD/PD = 100% IDL / 50% IDL = 2.0 ← don't prescribe to < 50% IDL (prescribe to 80%)

Hot Spot

- if treating to 50% IDL there will be a hot spot receiving twice that dose - where to put it? (risk of necrosis, risk of injury to vital structure)

Keep it in the target – not in normal brain!



- avoid cranial nerves: internal auditory canal, surface (esp. medial) of vestibular schwannoma, lateral wall of cavernous sinus.
- avoid arteries: carotid in cavernous sinus.

Cystic lesions (e.g. large cystic metastatic brain tumors) - use "donut's shape" dose planning with coverage of the contrast-enhancing tumor capsule by multiple small-sized isocenters.

Gamma Knife	LINAC

Radiation source is always on – needs replacement of Co-60 source every 5 years	Radiation is off when treatment is finished or paused
Can only be used to treat intracranial brain lesions and nothing else	Much more flexible and can treat "head to toe"
Securing head to treatment table, using fixed head frame – it is minimally invasive, because screws must be inserted into the patient's scalp. Because it is not practical to leave head frame in place, treatment with Gamma Knife is usually completed in one session	LINAC uses firm plastic mask – completely noninvasive, conforms to head, and is much more comfortable for the patient; mask can be easily removed and replaced for multisession treatment
Steepest gradient index is around the 50% isodose line*	Steepest gradient index is around the 80-90% isodose line*
Dose rate 3 Gy/min	Higher dose rate (up to 24 Gy/min) – faster treatment
Less moving parts - possible increased accuracy and precision.	
Local brain tumor control same or better (than with LINAC)	Local brain tumor control same or worse (than with GK)
Lower peripheral normal brain tissue dose	

*Gamma Knife dose plan has more heterogeneity within the target volume than a LINAC-based treatment

Preop
- NPO after midnight preop
- urine HCG on all menstruating females ≥ 12 y/o
- Cleveland Clinic gives 10 mg of DEXAMETHASONE before treatment.
- MIDAZOLAM for anxious patients.

Postop
- patients are observed for a few hours in the same day surgery unit.
- adult drive/accompany patient home.

SBRT (STEREOTACTIC BODY RADIOTHERAPY)

= SRS for extra-cranial sites in one to five sessions (fractions).

MAXIMUM RECOMMENDED SAFE SINGLE DOSE TO DIFFERENT STRUCTURES

Cochlea
≤ 4 Gy

CP angle
- cochlear nerve is much more sensitive than vestibular and facial nerves.

Lateral wall of cavernous sinus:
N.B. CN 2 and CN 8 are very sensitive – safe doses < 8 Gy.
N.B. CN 3, 4, 6 are rather resistant – safe doses < 16 Gy (studies found no relationship of dose to cavernous sinus and neuropathy in CN III-VI)

Lens (eyes)
- shield eyes (tissue at risk) when doing **functional/benign cases** to allow blocking beams transiting lenses.

Anterior visual pathway (optic nerve, optic chiasm)
≤ 10 Gy (to ≤ 1% of optic nerve) - 0-2% risk of optic neuropathy; risk rises quickly at doses > 10 Gy.
≤ 8 Gy – if had previous XRT.

- if the goal is close to zero percent risk of permanent optic neuropathy, consider 8 Gy to be a safe.
- optic apparatus may be more vulnerable because of previous compression / prior surgery / previous XRT.
- when is appropriate to deliver higher doses to optic apparatus? - *secretory pituitary macroadenomas* - discuss with the patient pre-operatively.
- with current technique a 1–5 mm distance between tumor and optic chiasm is enough.
- sparing techniques:
    - ***fractionated schedules*** for larger lesions or impinging on the optic apparatus.
    - initial first stage microsurgery to ***reduce the subsequent tumor volume*** and create space between the tumor and the optic apparatus.
- optic neuropathy develops 0.5-3 yrs post SRS - abrupt painless change in vision (monocular decreased VA or homonymous hemianopia).
    - **steroids** are ineffective.
    - 50% patients improve, some become blind.

Pituitary

- safe dose to gland and hypothalamus is < 15 Gy, to stalk < 17 Gy
- yearly endocrine evaluations for first 3 years, esp. *GROWTH HORMONE deficiency*

Brainstem
≤ 8-10 Gy

Pyramidal (corticospinal) tract
≤ 20 Gy

Major arteries (e.g. carotid)

- no need to segment as "organ at risk" but keep hotspot < 25 Gy

Spinal cord

- 10 Gy to 10% volume of spinal cord (or absolute volume of < 0.35 mL), defined as 5-6 mm above and below the target - 0% risk of myelopathy (14 Gy + less than 10% of cord with 10 Gy is safe in Cleveland Clinic).
- *cervical* and *thoracic* cords do not differ in radiosensitivity.
- *fractionated:*
    - 45 Gy in 22 fractions over 5 weeks – safe (0.2% risk of myelopathy).
    - tolerance increases with *decreasing fraction size*.
- Radiation Myelopathy – irreversible! - as in radiation necrosis of brain (i.e. cord infarction with necrosis, hemorrhage, and demyelination).
    - no known treatment (steroids may improve symptoms transiently).

COMPLICATIONS

mild skin **erythema** ***topical steroid creams***

permanent alopecia may occur

N.B. SRS decreases peritumoral edema with brain mts but increases with meningiomas (esp. single fraction SRS)

Incision healing problems - consider incisional VAC for irradiated wounds.

SECONDARY NEOPLASIA

– meningiomas (!!!), soft tissue sarcomas, nerve sheath tumors, thyroid cancer.

Definition of radioinduced tumors (**Cahan criteria**):

1) tumor must occur in previously **irradiated field**
2) **long interval** (usually several years) from time of irradiation
3) tumor must be **pathologically different** from the primary tumor
4) tumor must be **not present at the time of irradiation**.
5) patient must **not have genetic** predisposition for tumor.

Risk
Gamma Knife: 0.001 % (cytotoxicity, not mutagenicity)
fractionated radiotherapy: 1-3 %

WHITE MATTER INJURY

- most serious consequence of radiotherapy (single most dose-limiting factor) - idiosyncratic *white matter necrosis* caused by:

a) VASCULAR HYPOTHESIS: vascular ***endothelial*** injury → hyalinized thickening of blood vessels → thrombosis & occlusion → neovascularization
b) GLIAL HYPOTHESIS: direct effect on ***oligodendroglial*** cells.
c) IMMUNOLOGIC HYPOTHESIS: irradiated glial cells release antigens that induce ***autoimmune*** reaction.

- *asymptomatic ÷ potentially fatal*.

RADIATION NECROSIS

(major late complication of SRS) - focal lesion at/near original tumor site.

Manifests 6-24 months* after radiotherapy, lasts 18 months

*described cases starting > 10 yrs

- incidence with **SRS is 7-15%.**
- risk factors:

1) dose
2) treatment volume
3) fraction size and treatment duration (i.e. more common with SRS than with fractionated treatment)
4) dose homogeneity and conformality
5) chemotherapy
6) previous radiation

Clinical and **CT/MRI** changes indistinguishable from tumor progression – need for additional techniques

Clinically - acts as expanding mass lesion.

Diagnosis

MRI wo/w gadolinium - contrast-enhancing mass surrounded by vasogenic edema.

MRI signs suggesting necrosis (vs. tumor recurrence):

1) nonenhancing tumors prior to surgery.

2) lesion some distance from primary glioma but within radiation field.
3) lesion in periventricular white matter.
4) lesion has granular-reticular enhancement without much mass effect
5) contrast lingers long (vs. tumor – contrast gets washed out in 60 mins - TRAM)
6) diffusion restriction on DWI
7) no increase in FLAIR signal (vs. growing tumor – FLAIR↑)
8) stable in serial short-interval imaging (vs. tumor – rapidly growing)

Radiation necrosis is hypometabolic with stagnant flow and leaky capillaries;
tumor is hypermetabolic with brisk high flow and leaky capillaries

1) **perfusion-weighted MRI** (rCBV* cutoff value is 2.1** - sensitivity is 100%, specificity is 95.2%) – most practical test!

*letter "r" means "relative" (i.e. as compared to symmetrical contralateral area in the brain)
**< 2.1 – necrosis; > 2.1 – tumor recurrence

- works for primary tumors and metastases but particularly useful for **GBM**.

2) **TRAM (treatment response assessment map), s. delayed (60 min) postgadolinium MRI** – in tumors contrast gets washed out at 60 mins, in radiation necrosis contrast stays (gets "trapped" and even brighter at 60 mins) – very sensitive test (?even better than pMRI).
N.B. novel immunotherapies induce inflammatory reactions and results are more difficult to interpret

3) **MRS** (sensitivity and specificity similar to pMRI)**:**

Tumor – lots of MEMBRANES (choline↑), no normal neurons (NAA↓),
metabolism ANAEROBIC (lactate↑ and creatine↓)
Necrosis – only LIPIDS;
no normal neurons (NAA↓), no normal membranes (choline↓),
no metabolism (creatine↓, lactate↓)

4) **PET** – controversial and imperfect.

5) It is helpful to merge MRI T1 postgadolinium with **radiation treatment plan** – to see if enhancing area was in the area of high radiation dose.

6) **Biopsy**
N.B. because most patients have mixture of necrosis and tumor, biopsy may be required to confirm diagnosis!
- *histologic hallmark of radiation necrosis* - *demyelination and oligodendrocyte dropout*; necrotic tissue without predominance of malignant cells.

Treatment:
1) **observation** – for asymptomatic.
2) **steroids** – symptomatic improvement.
3) **antiplatelets** (ASPIRIN; Cleveland Clinic uses TRENTAL 1200 mg/d as a first choice drug for radiation necrosis; there are no guidelines how long to continue treatment - as long as needed).
4) VITAMIN E
5) hyperbaric oxygen therapy (efficacy is not well documented).
6) BEVACIZUMAB (AVASTIN®) – very effective!; no surgery for 1 month after last dose; anecdotal reports of increased risk of SDH; decreases enhancement of any remaining tumor.
— ***optimal dose and duration*** have not been established; > 50% of patients in available studies have responded durably to four-dose course of bevacizumab.

7) **LITT (offers biopsy & treatment)** – mechanism unknown: converts apoptotic (radiation) necrosis into coagulative (thermal) necrosis
8) **surgical debulking** – palliative measure for favorably situated symptomatic lesions.

Algorithm:

small, minimally symptomatic lesions → medical treatment
lesions grow on 2 scans → LITT
significant mass effect → debulking
Avastin – for inaccessible lesions

DIFFUSE WHITE MATTER INJURY

(after *whole-brain radiation*) - neuropsychological impairment (up to incapacitating dementia), gait apraxia.

- CT *diffuse white matter hypodensity* (atrophic dilatation of adjacent ventricle indicates demyelination rather than edema).
- MRI-T2 *diffuse nonenhancing periventricular white matter hyperintensity*.

periventricular white matter is highly susceptible to radiation injury!

DEMENTIA (COGNITIVE DECLINE)

(≥ 50% patients who survive whole-brain radiation for 5 years).

- special problem in children - IQ decrements and behavioral disturbances; even with radiation limited to posterior fossa.
- **MRI / CT** - cerebral atrophy.
- prophylaxis:
  1) hippocampus-sparing regimens (esp. for young patients)
  2) MEMANTINE.