Pharmacotherapy for spine-related pain in older adults

...and a few shots too

No disclosures

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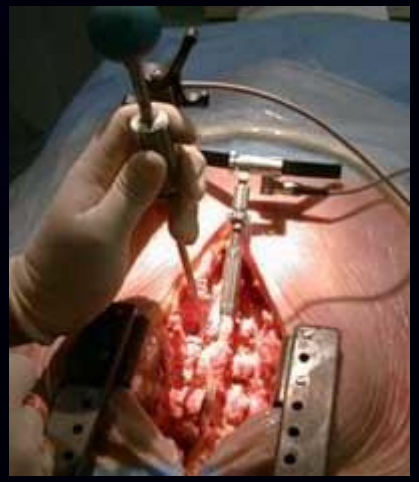
Low back/neck pain: common

- Mainstay therapy: Multimodal approach
  - Physical therapy
  - Patient education/time
  - Short term analgesics
  - Injections, epidurals, facet blocks, etc

- Surgery: persistence or anatomy
  - Failed radicular (symptoms/time)
  - Spinal stenosis
  - Spondylolisthesis
  - "Something must be done"



Low back and neck pain

lifetime prevalence)

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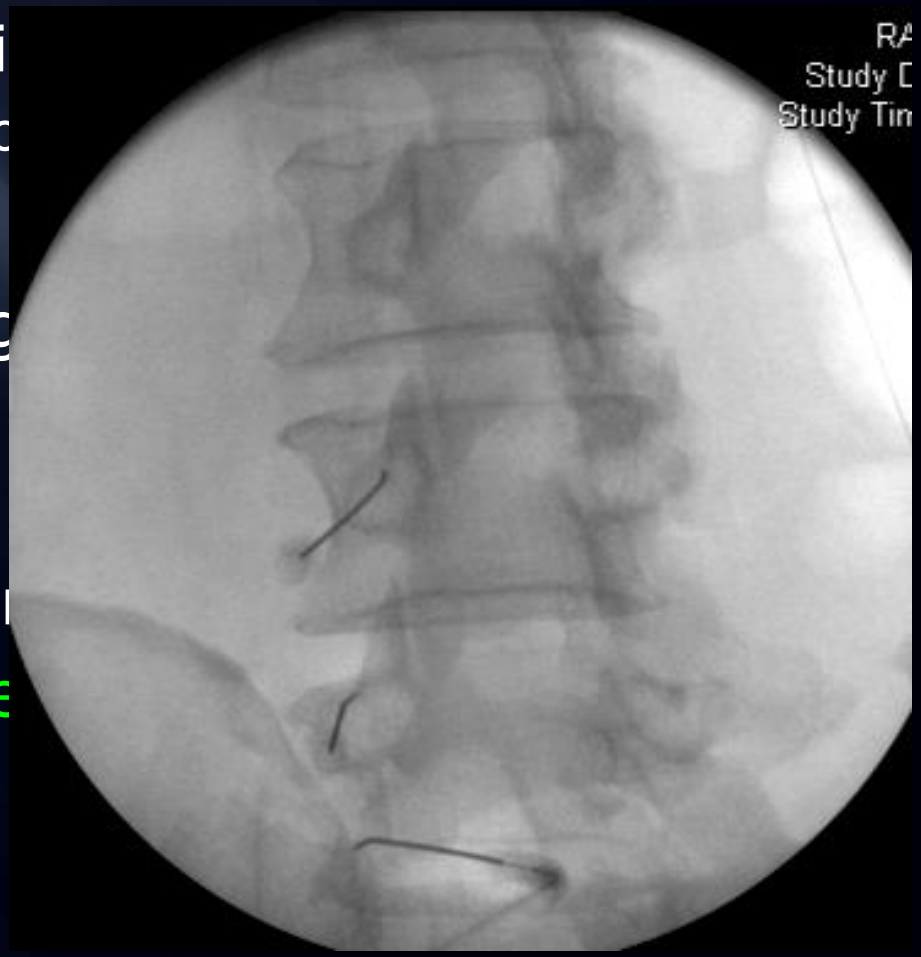


Spine pain medication In older adults:

Muscular and arthritic complaints

Radicular/spinal stenosis/neuropathic

…Decreased renal and liver function, MMP, polypharmacy, fall/sedation risk

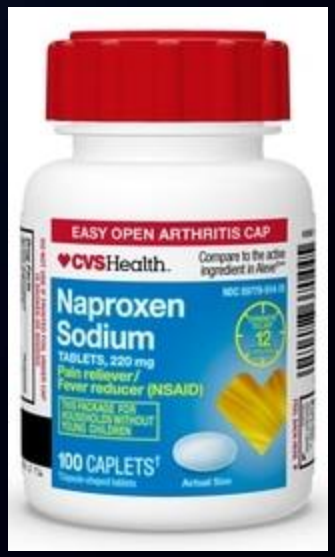
Spine pain medication In older adults:

Decreased metabolism vs toxicity

Common comorbidities & comedications

…fall secondary to sedation, more risk than sedation

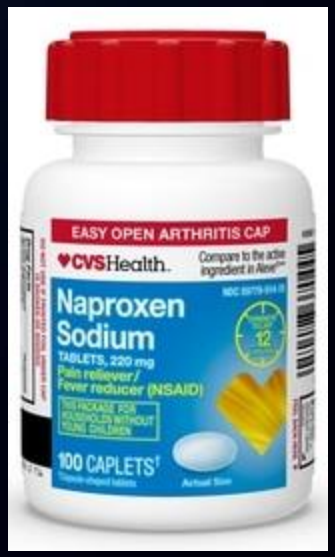
NSAIDs: LBP



- Understandable GI/renal/CAD caution
- More commonly used in younger patients

- Double-blind, controlled trials
  - Naproxen: CLBP benefit in 2 week, 16 week trials
    - Patients into their 80s, large cohort > 65 years
  - Many NSAIDs demonstrate efficacy in ALBP
    - Ibuprofen, diclofenac, piroxicam, etc
    - Younger patient cohorts, mean age ~ 40 years

Celecobix: CLBP



- Other Cox-2s off market, CAD
- Limit use with CAD
- Double-blind, controlled trials
  - Celecobix: CLBP >benefit over 6 weeks vs tramadol
    - Patients into their 80s, 13% of cohort > 65 years
    - Less AEs in celecobix group
  - Similar efficacy to non-selective NSAIDs for CLBP
    - Multiple studies
    - Patients into their 80s, significant cohort > 65 years

*Topical NSAIDs: LBP/arthritic

- Topical creams and patches demonstrate efficacy
  - Double-blind, placebo controlled trials
  - Younger patients, < 65 years
  - Piroxicam patch and cream with benefit, LBP/arthritic
    - 8 day trial for arthritic LBP
    - Patch and cream with 42% efficacy, compared to 26% placebo
    - Included up to age 75 years, mean age 51

NSAIDs: radicular LBP

- Typically used as a short course
- Double-blind, placebo controlled trials
  - Meloxicam and diclofenac with efficacy
  - Indomethacin and piroxicam with negative studies
  - Studies mean age was ~48 years
    - Smaller cohorts > 65 years

NSAID Dosing/AEs

- Red flags: renal, C
- "caution": mild CK
- Rule: short course NSAID "burst therapy"
- Linear relation of GI ulcer and age with NSAID use
  - GI protection (PPI* or H2 blocker)
  - Celecobix
  - Both

Direct CAD effects, also interrupts ASA mechanism

Proper PPI use?

Topical NSAIDs first?- depends

? Sulindac

*Acetaminophen, Corticosteroids?

- Acetaminophen less AEs, but less efficacy
  - Considered 80% as effective as celecoxib for arthritic neck and LBP
    - mean age 65 years, up to 80 years
  - Typical lower efficacy for spine pain than NSAIDS
  - Higher doses, ER formulations suggested

- Corticosteroids more AED, and less efficacy
  - Mixed evidence in older a
  - Can have benefit radicula
  - More for true Rheumatologic d/o or bone mets

Worth the AEs?-
Call someone

Gabapentin (GBP)/pregabalin (PGB): Radicular

- Blinded clinical trials
  - Better evidence: Peripheral neuropathy, PHN
  - Mixed evidence for radicular/neuropathic LBP
    - Helpful for radicular sx, perhaps more so in younger patients
      - Great benefit when combined with a TCA (AEs though)
      - Evidence basis GBP> PGB
    - Helpful as adjuncts in spinal stenosis (with other routine care)
    - Study age means ~55-60 years, up through age 70

Poor evidence in blinded-PLACEBO CONTROLLED trials

WHY?: AEs, intention to treat analysis, dose titration

Key pa balin:

Neurol. 2019

- GBP 40 ID
  - Doubl crossover
    - Mea
  - VAS p 0.002)
  - ODI d <0.001)

GBP l

Dose,

Table 3. Adverse Events Experienced by Population[a,b,c]

Description	Prevalence, No. (%)	Population With Adverse Event, %
Pregabalin (n = 31)		
Nausea, vomiting, headache	7 (22.6)	39
Bowel disturbance	5 (16.1)	28
Diplopia, dysarthria	5 (16.1)	28
Dizziness, vertigo	4 (12.9)	23
Drowsy, sedation	3 (9.7)	17
Lethargy, numbness	2 (6.5)	11
Dry mouth	1 (3.2)	6
Alertness	1 (3.2)	6
Weight gain	1 (3.2)	6
Erectile dysfunction	1 (3.2)	6
Psychiatric disturbance	1 (3.2)	6
Gabapentin (n = 7)		
Drowsy, sedation	3 (42.9)	17
Dizziness, vertigo	2 (28.6)	11
Nausea, vomiting, headache	1 (14.3)	6
Alertness	1 (14.3)	6

[a] Frequency and severity measured on a scale of 1 to 10 with 10 being the worst possible score.

[b] The same participant may have experienced multiple adverse events of different descriptions.

[c] Gabapentin count was 7, and pregabalin count was 31 (P = .002).

GBP, PGB Dosing/AEs

- Lowest possible dose, that "could" be effective
- Adjust for creatine clearance, then titrate
- Dizziness/somnolence -> gait?

- Substance abuse, respiratory suppression:
  - Takes effort, fairly dramatic polypharmacy/substance

- Sexual problems, often not discussed

Muscle relaxants

- In short: Avoid antispasmodics
  - carisoprodol, chlorzoxazone, cyclobenzaprine*, metaxalone, methocarbamol*, and orphenadrine

    Antichol, sedation, fall….
- Use more often, but with caution: Antispastics
  - Baclofen and tizanidine >> *dantrolene*
  - Tizanidine with benefit in blinded clinical trials, ALBP
    - Multiple studies demonstrate tizanidine benefit
    - Younger patients, mean age ~42 years, up through age 70
  - Baclofen, one blinded, placebo-controlled trial, ALBP
    - Younger patients, mean age ~42 years, up through age 74

Muscle relaxants: AEs

- Anticholinergic AEs limit antispasmodics use
  - Associated with fall, retrospective case-control study
  - Cyclobenzaprine with some TCA activity (5HT caution)
- Antispastic AEs sedation/cognitive impairment
  - Associated with fall, opinion papers only
  - Tizanidine (use 1-2mg) associated with urinary retention and hepatoxicity, check LFTs
  - Higher dose baclofen: withdraw/seizure if stop abruptly
    - Renal adjust (5mg, not 10mg)
  - Dantrolene potentially fatal hepatotoxicity (black box)

*Radicular Pain: A clinical approach

Table 1 Attributes and demographics

	Classic presentation	Common level	Common age	Gender	Risk fa		Mimicker
Cervical radicular pain	Typically no inciting event, "woke up with pain"[1,13]	C7 > C6[13,19]	40–60[13]	Variable with	ity, axial load[19]	Spurling's[14,19]	Shoulder pathology, carpal tunnel syndrome, ulnar neuropathy[14,19]
Lumbar radicular pain	May be associated with physical exertion, or not[2,7]	L4–L5 L5			Smoking, heavy labor, obesity[5,6]	+ Straight leg raise[2,7]	Piriformis syndrome, peripheral neuropathy, spinal stenosis[2,7]
Lumbar spinal stenosis	( ) and relieving factors (sitting)[10,12]	L4–5[40]	>50, peak 60s[46]	M > F[46]	Aging, heavy labor, smoking[46,47]	+ Shopping cart sign (relief with lumbar flexion)[11,12]	Vascular claudication, arthropathies, peripheral neuropathy[10]

IMAGING? NO, YES, IT DEPENDS

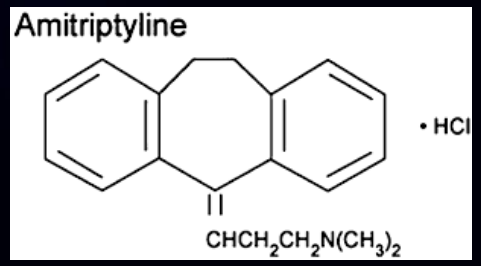
- Cervical: Hyperreflexia, ↑ Tuenels

Tricyclic antidepressants, TCAs & 5HT-norepi reuptake inhibitors, SNRIs

- Standard of care in neuropathic and chronic pain
  - Often coupled to GBP/PGB (neuropathy, neuralgia)
  - Indicated for radicular or neuropathic spine pain

.....It depends, complex.

- Older drugs (amitriptyline) often have:
  - More evidence (for efficacy)
  - More AEs



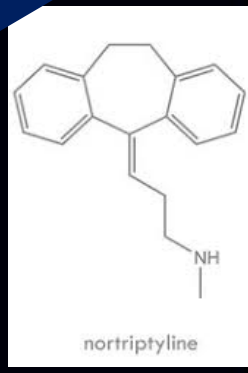
Tricyclic antidepressants, TCAs

- Amitriptyline
  - Multiple blinded trials: efficacy for CLBP and neck pain
    - Improvements in pain and disability, some mixed results
    - Study age means ~50 years, up through age 75

Efficacy in neuropathic pain: Nortrip = Amitrip, but less AEs

- Nortriptyline
  - Few blinded trials: mixed efficacy LBP
    - Younger patients only, no over 65 y

clinical OVER evidence basis?- at times



- Desipramine: similar

5HT-norepi reuptake inhibitors, SNRIs

- Duloxetine: LBP +/- Depression
  - Good efficacy: Multiple Blinded, placebo [illegible] trials
    - Many studies including older patients [illegible]
  - Older adult focused trial: LBP [illegible] (*Am J Psych 2007*)
    - Mean age 72.6 years [illegible] patients
    - Very good LBP [illegible] (~ 5 points)
    - Very g[illegible] [illegible]iple depression scales
    - [illegible] to see benefit
    - [illegible] lack of efficacy; dulox 2.9% versus placebo 9.6%
    - [illegible] study: due to AEs; dulox 9.7% versus placebo 8.7%
  - Other Older adult CLBP studies
    - Benefit when longer(14 weeks) or neuropathic aspect
    - Mean age 60, with patients up to 80s

Is depression a prerequisite? No, yes

Some similar efficacy for venlafaxine, much less evidence

TCAs & SNRIs AEs

- Duloxetine/Venlafaxine are safe/good, but slow
- TCAs: It's Ok, start low, warn patient
- Rule of 3: CNS agents
- SNRIs
  - Nausea, insomnia, sexual side effects (TCAs too)
  - 5HT syndrome

Tramadol IR, ER

- AGS: caution with tramadol, but OK
  - Tapentadol/Nucynta, strong potency- reserved use
  - When other therapies fail, tramadol is a reasonable trial
    - GI/CNS AEs possible (classic opioid), but usually mild
    - Very little abuse or diversion potential
  - Trial Tramadol 25-50mg, prior to XR formulation
  - Do not use with seizure PMH, *5HT problems very rare*

- Tramadol-Acetaminophen
  CLBP Efficacy: 4, 14 weeks studies, 37.5mg/325mg
  ALBP Efficacy: 2.5 days, ER 75/650
  Mean age ~60 chronic, 42 acute, patients up to 80 years

*On Opioids…

- OutPt: All else fails, moderate-severe pain
  - Respiratory/overdose/death risk, also diversion
- InPt/ED: Go ahead
  - CNS effects, constipation
- Blinded trials, chronic neck and LBP/acute flairs

Opioid related death/abuse, young patients highest risk- but older patients are fastest group on the rise

    - Dosing in the hands of MD, close watch
  - Combos with naltrexone did not catch on

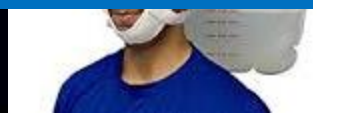
*Radicular Pain: RX/TX

Table 2 Common radicular pain treatments

Therapeutic treatment	Cervical radicular pain	Lumbar radicular pain	Lumbar spinal stenosis
Rest	Cervical collar and rest may benefit[24,44]	Only if activity intolerant[23]	Tem ,12
Physical therapy	After acute flare[15,24,44]	After acute flare[7,8]	nction, pain[41,42]
NSAIDs	Clinically used based on lumbar radicular evidence[19]	Mild-mod	commonly used
Oral corticosteroids	Clinically used based on lumbar radicular evidence[19]	efit[22]	Not commonly used
Nortriptyline	Mild-m	ild-moderate benefit[26]	Clinically used, but no blinded trials
Gabapentin		Mild-moderate benefit[25]	Clinically used, but no blinded trials[31]
Pregabalin			
Tramadol	ally use blinded trials		
Opioids	Acute use on		

Therapy based on Pt profile and ADRs

Then, if 6-12 weeks of continued moderate- severe pain....



Summary: Diagnostically driven Older adult spine pain

- Axial v radic, acute v chronic, severe v moderate
- Acute/exacerbation
  - NSAIDs burst/cox2>1/celecoxib/Tylenol ES/ER (1g/1.3g)
- Acute axial/myofascial/facet
  - Same NSAIDs, + smart antispastic (baclofen, tizanidine)
  - Severe-> tramadol
- Acute radicular
  - Same NSAIDs, GBP/PBG, tramadol
  - Severe-> telephone-> ESI
  - Surgery?-> red flags only

Summary: Diagnostically driven Older adult spine pain

- Axial v radic, acute v chronic, severe v moderate
- Chronic axial/myofascial/facet
  - Same NSAIDs, bursts only, chronic smart antispastic
  - Severe-> tramadol (limit #)
  - PT, LMBB/facet block -> RFA
- Chronic radicular
  - Same NSAIDs, bursts, duloxetine > TCAs (but can use)
  - GBP/PBG, tramadol (limit #), PT course
  - Pain clinic follow, ESI, etc
  - Surgery?-> Elective works well (not for axial)

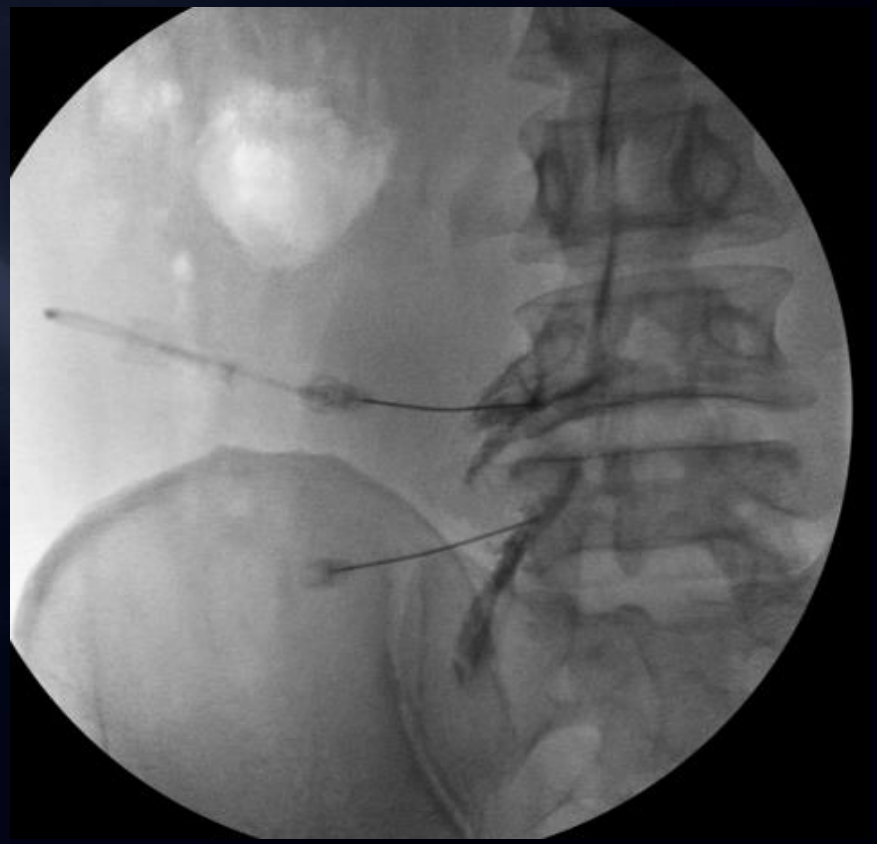
Thank you

- Presented material: Fu JL, Perloff MD. Pharmacotherapy for spine-related pain in older adults. Drugs Aging. 2022 Jul;39(7):523-550

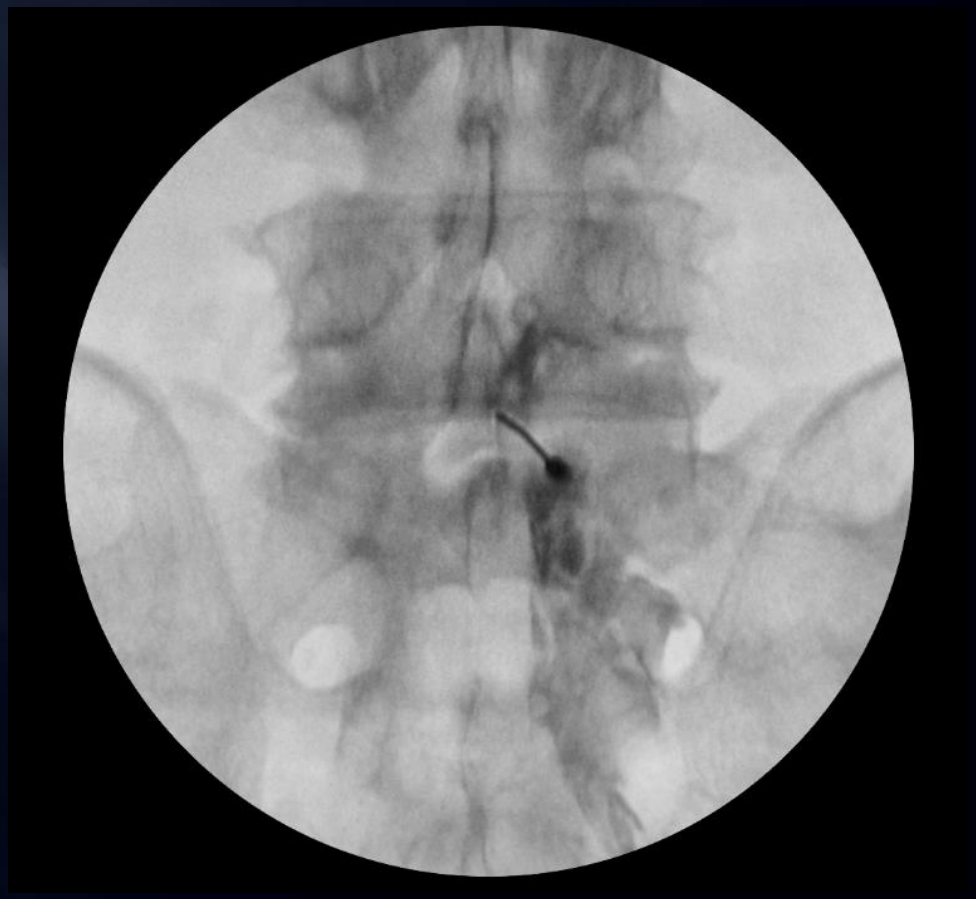
  - QUESTIONS?

Neck/LBP myofascial: triggers

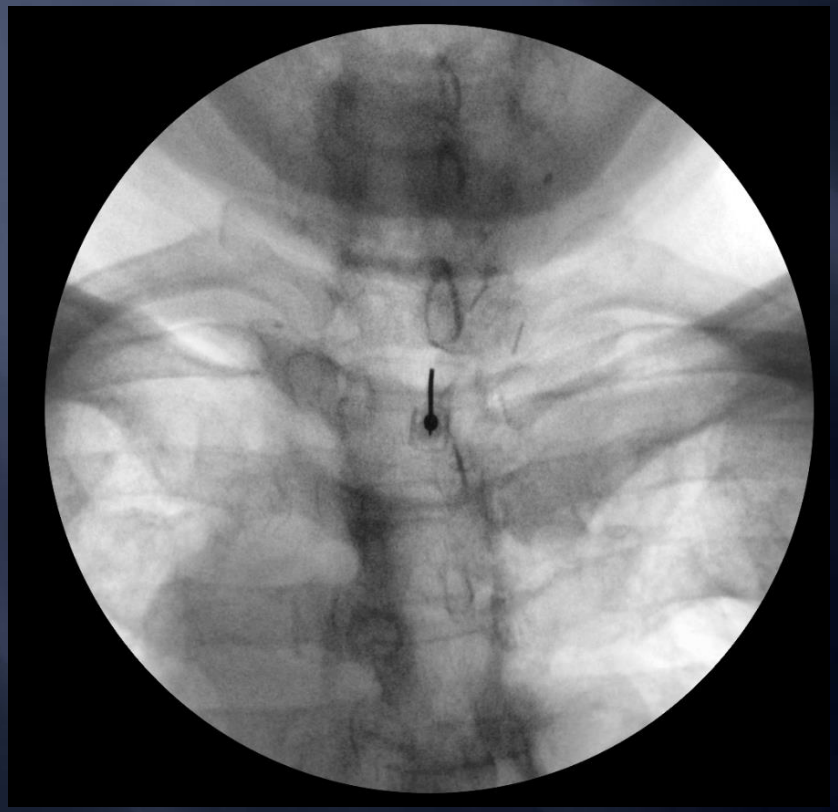
ESI for focal disc/foramen

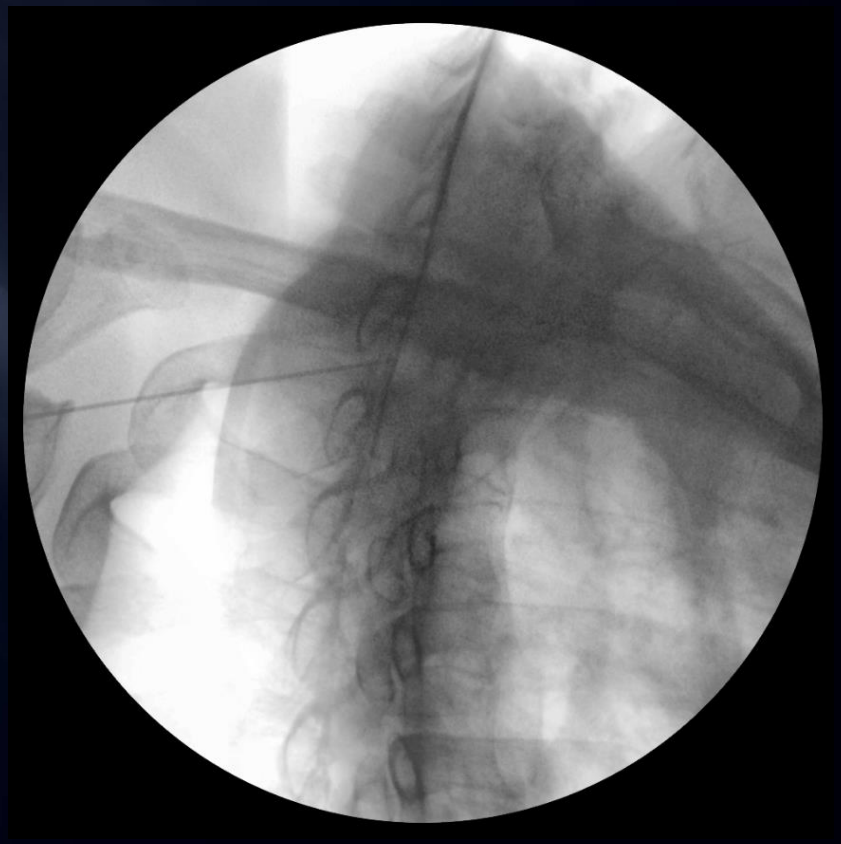


LESI for spinal stenosis

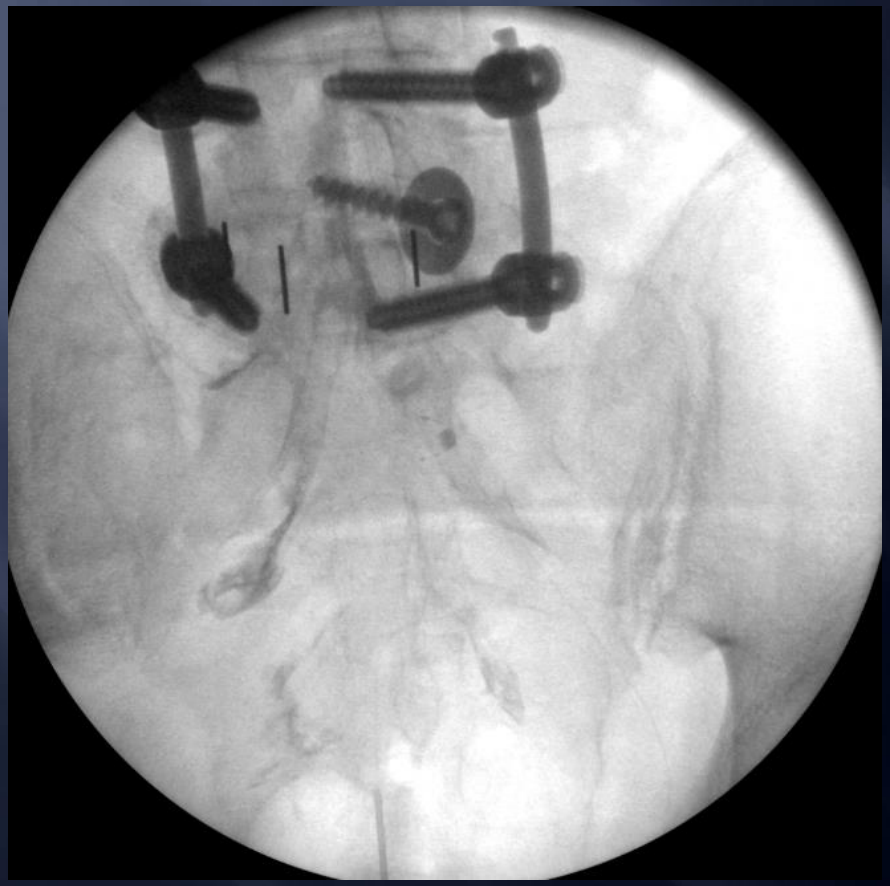


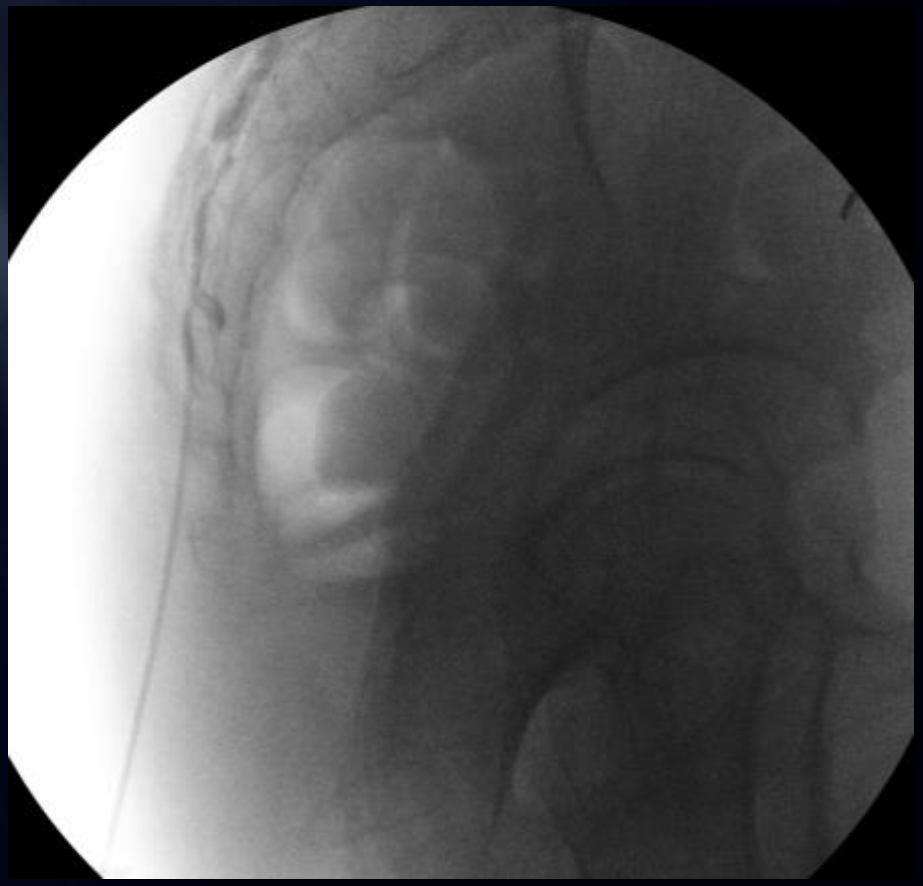
CESI for focal disc/foramen, and "+"





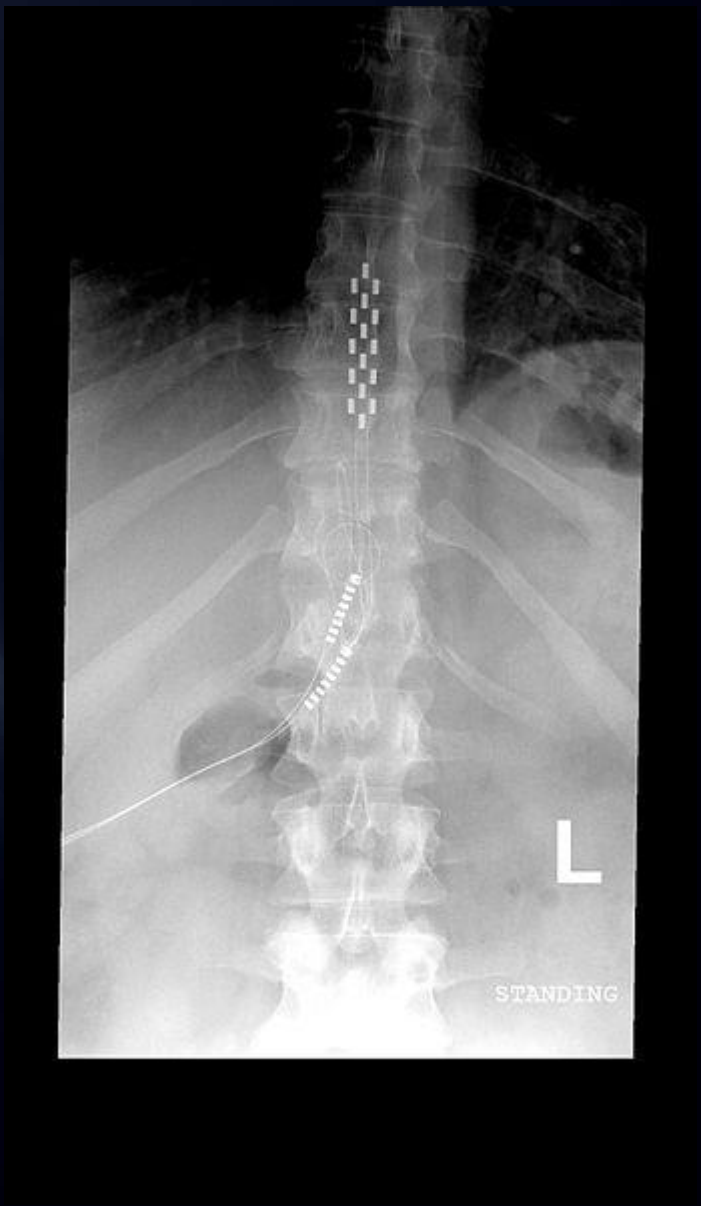
Epiduralysis: postsurgical radicular





Spinal cord stimulator: the big gun

- Big step, but….
- Excellent benefit for neuropathic pain that:
  - Has failed everything
  - Pt is mentally stable
- Proven benefit:
  - FBSS
  - CRPS (RSD)
  - Severe peripheral neuropathy
  - IC, Angina!
  - Anything-
- $30K, so…..



LBP: Joint arthropathy