EPIDURAL ADHESIOLYSIS A.K.A. THE RACZ PROCEDURE

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DISCLAIMER

- President of the World Institute of Pain

OBJECTIVES

- Review necessary equipment to perform the lysis procedure
- Overview of the procedure:
  - Caudal approach
- Identify complications

“CLASSIC” LYSIS PROTOCOL

- Needle placed with paramedian approach
- Epidurogram with 10 ml non-ionic, water-soluble contrast
- Catheter inserted ventral-lateral epidural space to target level
- Contrast 1-3 ml
- 150-300 units Hylenex in 10 ml PFNS
- Contrast 1-3 ml
- 10 ml local anesthetic/steroid
- 10 ml hypertonic saline (10%) infusion

} May repeat times 2

MEDICATION

- Contrast
  - Non-ionic, water-soluble (Iohexol-240)
  - DO NOT USE ionic, non-water soluble contrast including: Hypaque®, Renagrafin/Urografin®, or Conray®
- Steroids
  - Particulate (Non-soluble) vs. non-particulate (Soluble)
- Local Anesthetic
  - 0.25% bupivacaine, 0.2% ropivacaine
- Hyaluronidase
  - Human recombinant: 150-300 units
- Hypertonic saline (10%)

MEDICATION

- Volume
  - Depends on the targeted level
  - 5-10 ml’s total volume of each medication
    - Contrast
    - Local anesthetic/steroid
    - Hypertonic saline
  - Usually:
    - 5-6 ml cervical
    - 8 ml thoracic
    - 10 ml caudal

HYALURONIDASE

- Mechanism of action
  - More correctly termed hyaluronoglucosaminidase
  - Liquifies the interstitial barrier between cells by cleaving β-1,4 glycosidic bonds
    - Improves the diffusion of injected substances within most connective tissue planes except for collagenous barriers.

      Watson D. Hyaluronidase. *Br J Anaesth* 1993;71:422-425

HYALURONIDASE

- Mechanism of action
  - In the lysis procedure, it presumably breaks down the ground substance in the epidural scar tissue to “free up” the nerve root and to better allow deposition of local anesthetic/steroid/hypertonic saline to the target level

Hyaluronidase decreases neutrophils infiltration to the inflammatory site

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Abstract

Objective To evaluate the in vivo anti-inflammatory potential of bovine hyaluronidase (HYAL) using two different models of acute inflammation.

Methods Air pouches were produced in the dorsal subcutaneous of mice and injected with phosphate saline solution or HYAL. The antiinflammatory action of HYAL was evaluated in carrageenan (Cg)-inflamed air pouches. After 4 and 24 h the cellular influx, protein exudation, cytokines and lipid mediators were evaluated. The action of HYAL on the rolling and adhesion of leukocytes was investigated in the LPS-stimulated mesenteric microcirculation by intravital microscopic.

Results Treatment with HYAL reduced the cellular influx and protein exudation in non-inflamed and inflamed air pouches. HYAL treatment of Cg-inflamed air pouch reduced the production of tumor necrosis factor-alpha (TNF-α), interleukin-8 (IL-8), leukotriene B4 (LTB_4) and LTC_4, whereas prostaglandins E_2 (PGE_2) and D_2 (PGD_2) concentrations were unchanged. Histological analyses showed that HYAL administration diminished cell infiltration in the air-pouch lining. In LPS-stimulated mesenteric microcirculation, HYAL usage decreased rolling and adhesion of leukocytes, but did not affect the blood vessels diameters.

Conclusion The results demonstrate that HYAL inhibited cellular recruitment, edema formation and pro-inflammatory mediators production, resulting in decreased adherence of leukocytes to blood vessels and tissue infiltration. Our data suggest that HYAL may be considered an effective candidate to ameliorate acute inflammation.

Keywords Air pouch · Cytokines · Lipid mediators · Intravital microscopy · Leukocyte–endothelial interactions · Neutrophil influx · Carrageenan · LPS

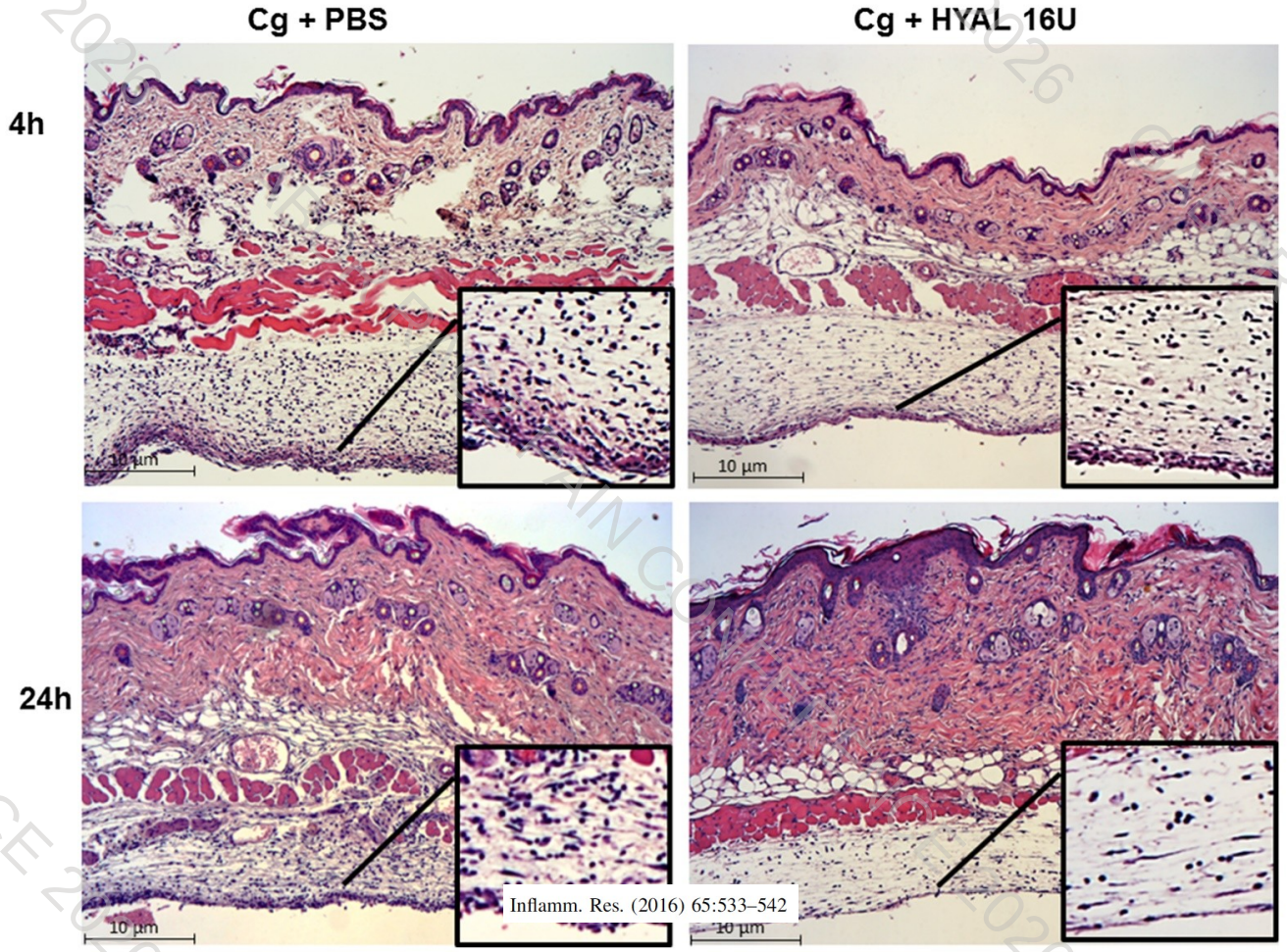
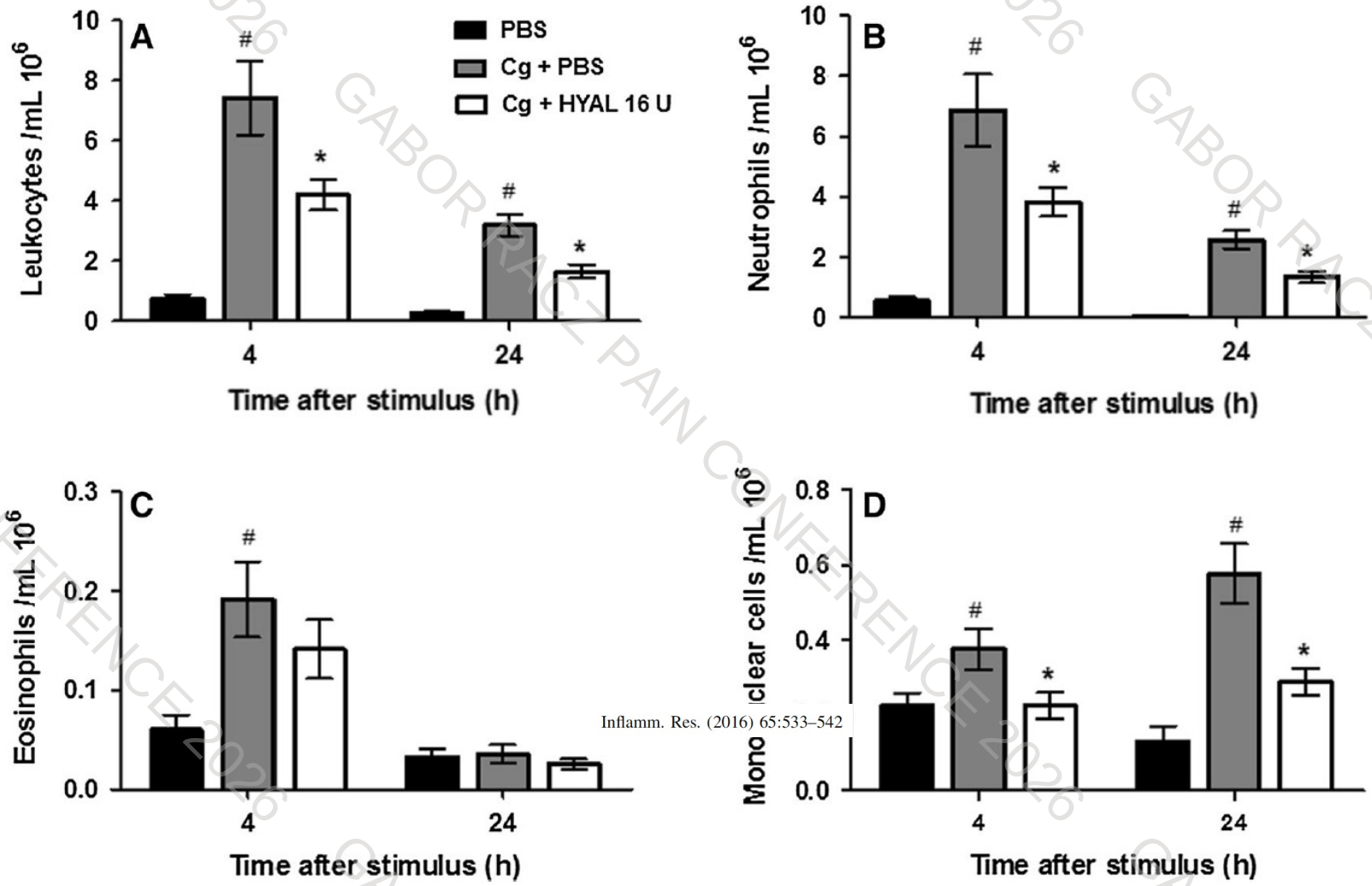


Fig. 5 Hyaluronidase (HYAL) affects cellular recruitment in the inflamed air-pouch lining tissue. Pouches were inoculated with Cg (1 % concentration) and 1 h later treated with HYAL (Cg + HYAL 16 U/0.5 mL/pouch) or phosphate buffered saline (PBS) (Cg + PBS/0.5 mL/pouch). Paraffin-air pouch membrane sections were stained with hematoxylin and eosin to evaluate the inflammatory infiltrate response by image analysis. The inserts depicted from the skin-tissue linings surrounding the pouch cavity (×400 original magnification) shows the infiltrating cells. The sections were photographed at ×100

Cg = carrageenan



Inflamm. Res. (2016) 65:533–542

HYALURONIDASE

- Currently available hyaluronidase preparations
  - Hylenex®
    - Human recombinant hyaluronidase
    - Produced by genetically engineered Chinese hamster ovary cells
  - Vitrase®
    - Ovine hyaluronidase
  - Amphidase®
    - Purified bovine testicular hyaluronidase
  - Compounded hyaluronidase formulations

CORTICOSTEROIDS

- Mechanism of action
  - Reduce inflammation either by inhibiting the synthesis or release of a number of pro-inflammatory substances or by causing a reversible local anesthetic effect
  - Others
    - Membrane stabilization
      - Inhibition of neural peptide synthesis or action
      - Blockade of phospholipase A2 activity
      - Prolonged suppression of ongoing neuronal discharge
      - Suppression of sensitization of dorsal horn neurons

CORTICOSTEROIDS

Table 1. *Profile of commonly used epidural steroids*

Drug	Equivalent Dose	Epidural Dose	Anti-inflammatory Potency	Sodium Retention Capacity	Duration of Adrenal Suppression		
					IM	Single Epidural	Three Epidurals
Hydrocortisone	20 mg	N/A	1	1	N/A	N/A	N/A
Depo-Methyl Prednisolone (Depo-Medrol)	4 mg	40-80 mg	5	0.5	1-6 weeks	1-3 weeks	N/A
Triamcinolone diacetate (Aristocort)	4 mg	25-50 mg	5	0	1-2 weeks	1-5 weeks	N/A
Triamcinolone acetonide (Kenalog)	4 mg	40-80 mg	5	0	2-6 weeks	N/A	2-3 months
Betamethasone (Celestone Soluspan)	0.6 mg	6-12 mg	25	0	1-2 weeks	N/A	N/A

N/A = Not applicable Data adapted and modified from McEvoy et al (71), Jacobs et al (73), Kay et al (72), Hsu et al (74), Mikhail et al (75, 76), and Schimmer and Parker (77).

From Manchikanti L: Role of Neuraxial Steroids in Interventional Pain Management. *Pain Physician* 5(2); 182-199.

HYPERTONIC SALINE

- Possible mechanisms of action when injected in the epidural space for analgesia
  - Evidence from studies on cats and monkeys that hypertonic saline has a local anesthetic-like effect on intact dorsal rootlets
    - The chloride ion seems to play a major role in the persistent C-fiber blockade
    - Choline chloride just as effective as sodium chloride

Jewett D, King JS. Conduction blockade of monkey dorsal rootlets by water and hypertonic saline solutions. *Exp Neurol* 1971;33:225-237.

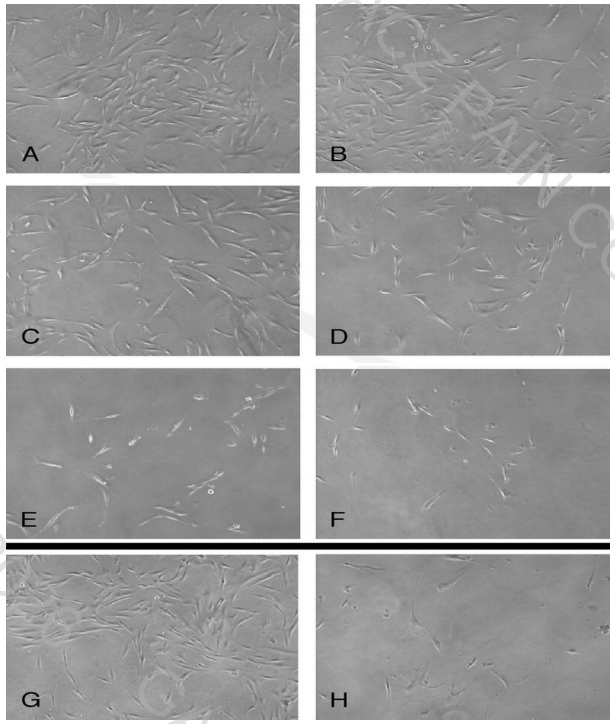
King JS, Jewett D, Sundberg H. Differential blockade of cat dorsal root C-fibers by various chloride solutions. *J Neurosurg* 1972;36:569-583.

HYPERTONIC SALINE

- Possible mechanisms of action when injected in the epidural space for analgesia
  - Reduction of cell swelling (edema) by causing water to migrate out of cells
    - Osmotically induced water shift
      - Decreased swelling → less pressure on nerve

Racz G, Heavner J, Singleton W, Carline M. Hypertonic saline and corticosteroid injected epidurally for pain control. In Raj P (ed):*Techniques of Neurolysis*. Boston, Kulwer Academic Publishers, 1989, pp 73-86.

MONOLAYER OF CULTURED HUMAN FIBROBLAST IN NACL AND DMEM 3 DAYS OF INCUBATION AND 1 HOUR EXPOSURE TO VARIOUS PERCENTAGES LISTED BELOW



A. Control-DMEM
B. 0.9% NaCl-DMEM
C. 2% NaCl-DMEM
D. 4% NaCl-DMEM
E. 6% NaCl-DMEM
F. 10% NaCl-DMEM

Below black line represents 3 days incubation and 24 hour exposure:

G. Control-DMEM
H. 0.9% NaCl-DMEM

DMEM-Dulbecco's Modified Eagle Medium (cell culture medium)

Birkenmaier *et al*., 2011

COMPLICATIONS RELATED TO LYSIS OF EPIDURAL ADHESIONS

- Allergic Reactions
- Headache
- Iatrogenic Cushingoid Syndrome
- Macular Hemorrhage
- Somatosensory and Somatomotor Dysfunction
- Bowel, Bladder, Sexual dysfunction
- Infection
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- Local anesthetic toxicity – CNS, cardiovascular
- Catheter shearing
- Subdural or intrathecal spread of medication

INTERVENTIONAL PROCEDURES LEVEL 1 EVIDENCE

I	Caudal ESI	Caudal epidural with local only	480 (140)	2 yrs	Manchikanti *et al.* Pain Physician 2013
	Percutaneous adhesiolysis	ESI	92 (92)	6 mo	Chun-jing *et al.*[35]
	Caudal ESI with hyaluronidase	Caudal ESI	38 (38)	1 yr	Yousef *et al.*[36]

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INTERVENTIONAL PROCEDURES LEVEL 2 EVIDENCE

II	6-step treatment algorithm	None	133 (133)	1 yr	Avellanal *et al.*[37]
	Percutaneous adhesiolysis	None	130 (60)	2 yrs	Manchikanti *et al.* Pain Pract 2015
	Caudal ESI	Caudal epidural with local only	140 (140)	2 yrs	Manchikanti *et al.* Int J Med Sci 2012 Manchikanti *et al.* Pain Physician 2010 Manchikanti *et al.* Pain Physician 2008
	Percutaneous adhesiolysis	Caudal ESI	120 (120)	2 yrs	Manchikanti *et al.* Journal of Pain Research 2012 Manchikanti *et al.* Pain Physician 2009
	Endoscopic adhesiolysis with local and steroid injection	Endoscopy with local and steroid injection	83 (66)	1 yr	Manchikanti *et al.* BMC Anesthesiol 2005
	Percutaneous adhesiolysis with ESI	ESI	75 (52)	1 yr	Manchikanti *et al.* Pain Physician 2004
	Selective nerve root injection and ESI	Selective nerve root injection or ESI	60 (60)	6 mo	Abdel-Raouf *et al.*[47]
	ESI with 2 needles	ESI with 1 needle	40 (40)	6 mo	Abdel-Raouf *et al.*[46]
	Nerve root sleeve injection with bupivacaine and hyaluronidase or bupivacaine and methylprednisone	Nerve root sleeve injection with bupivacaine, hyaluronidase, and methylprednisone	60 (60)	6 mo	Devulder *et al.*[49]
	Forceful caudal ESI	Caudal ESI	60 (60)	18 mo	Revel *et al.*[48]
	Epidurography with epidural adhesiolysis	None	34 (28)	1 yr	Devulder *et al.*[49]

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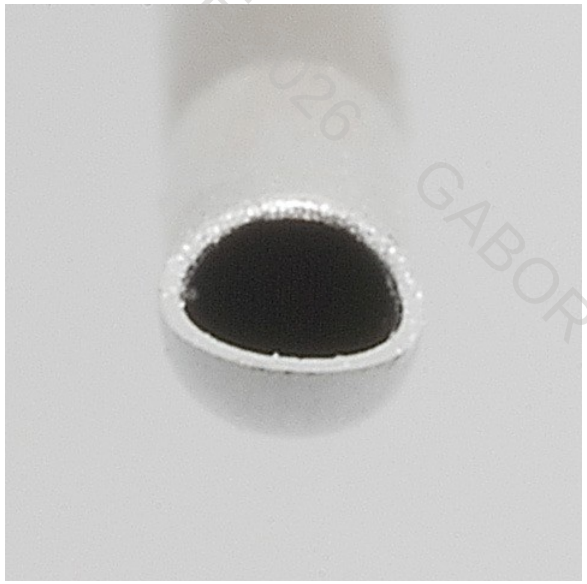
CAUDAL APPROACH

Tuohy needle tip.
Note curved sharp tip.

R-X Coude needle tip.
Note open tip - curve moved more proximally.

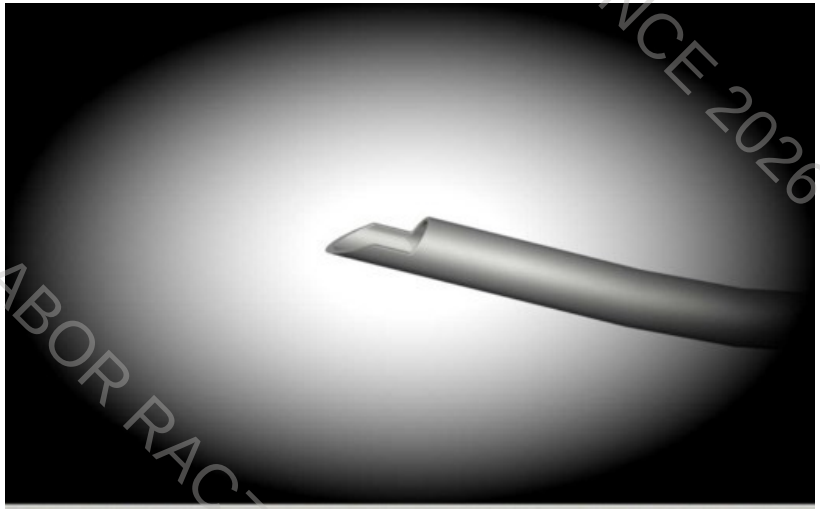


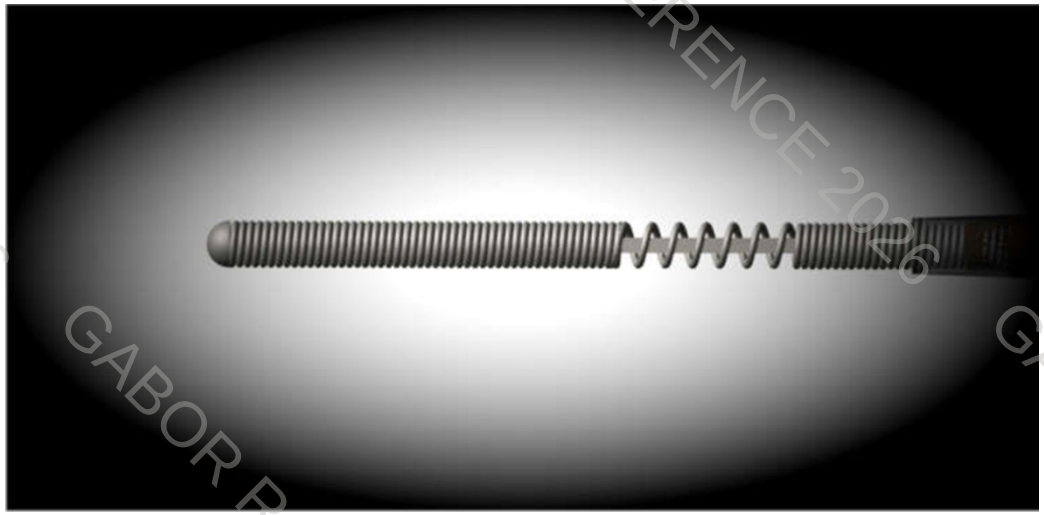
C

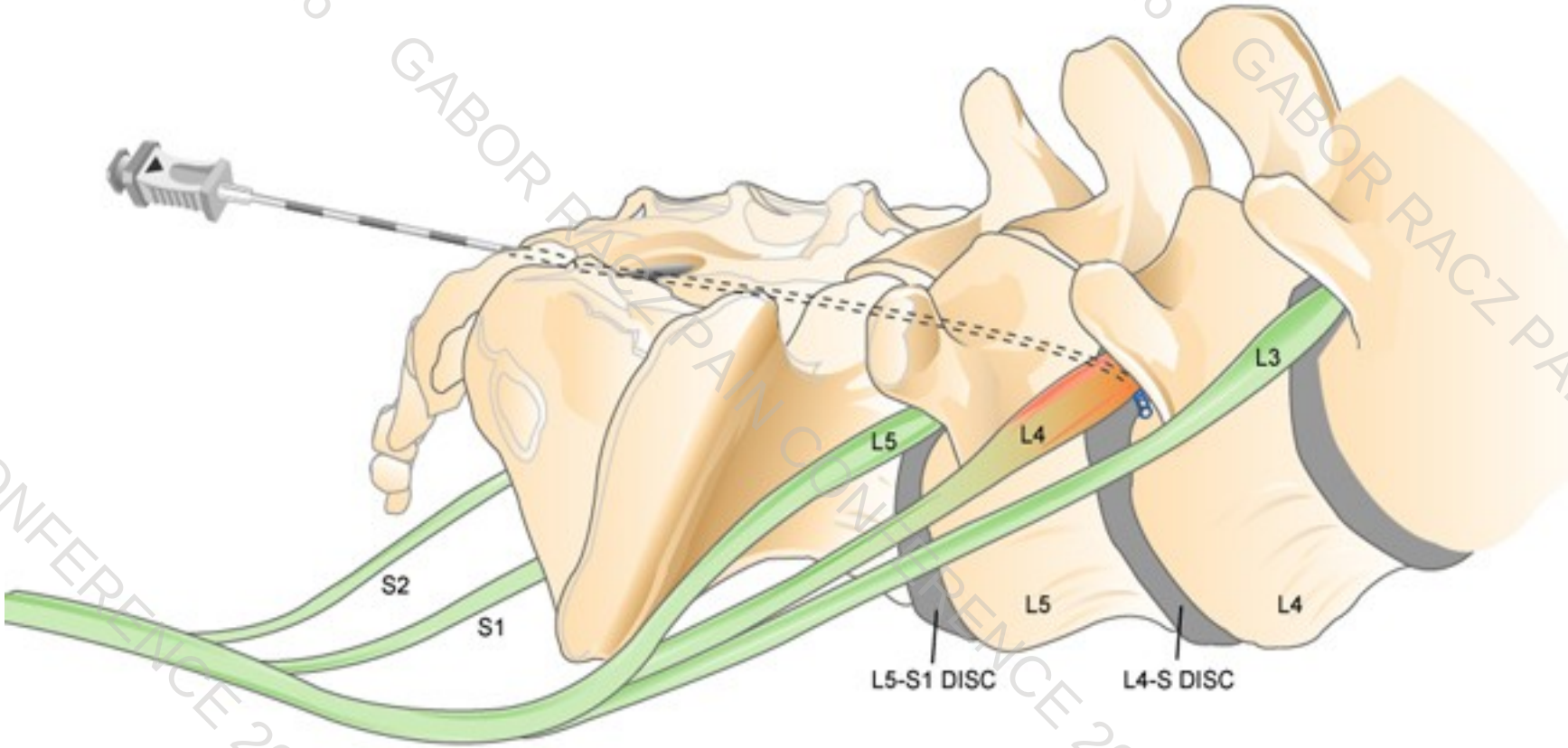
Tuohy needle tip end on view. Note oval shape opening.

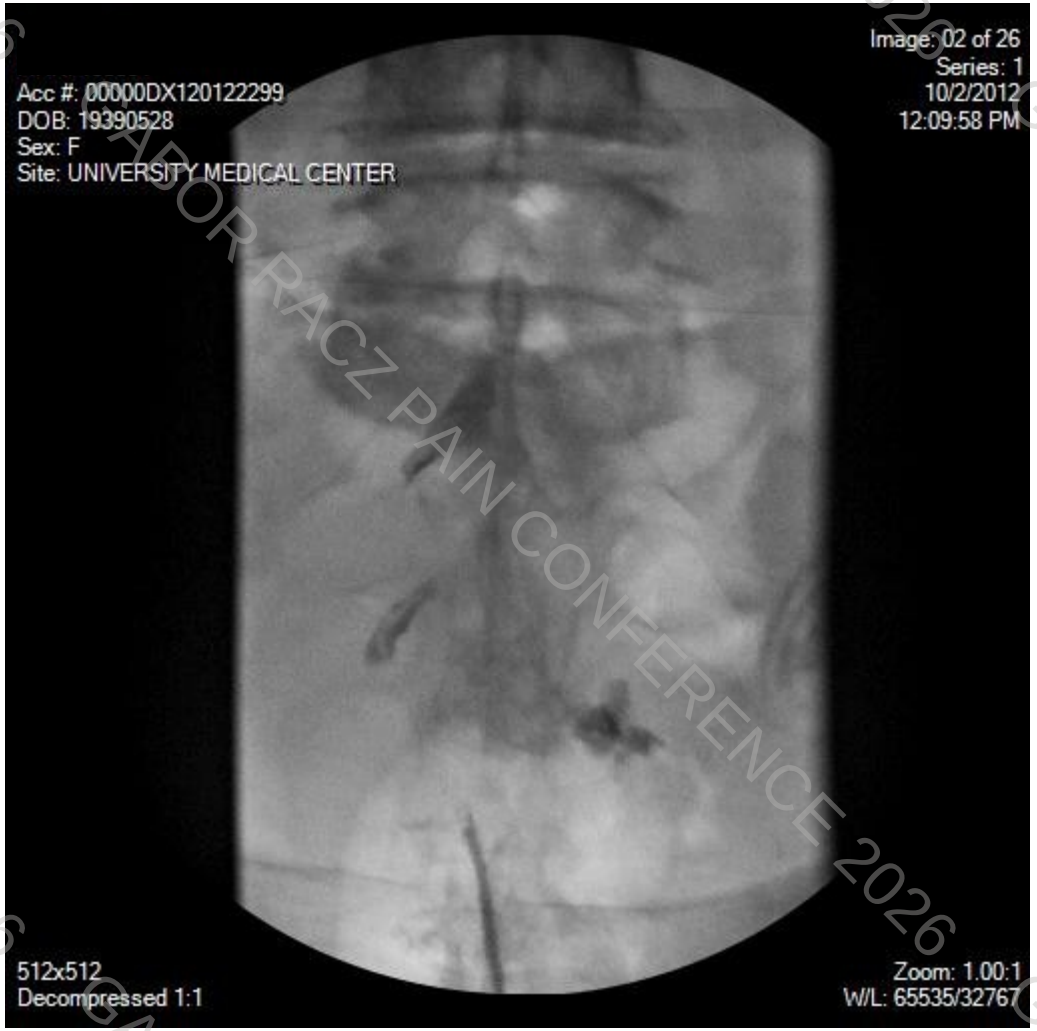
D

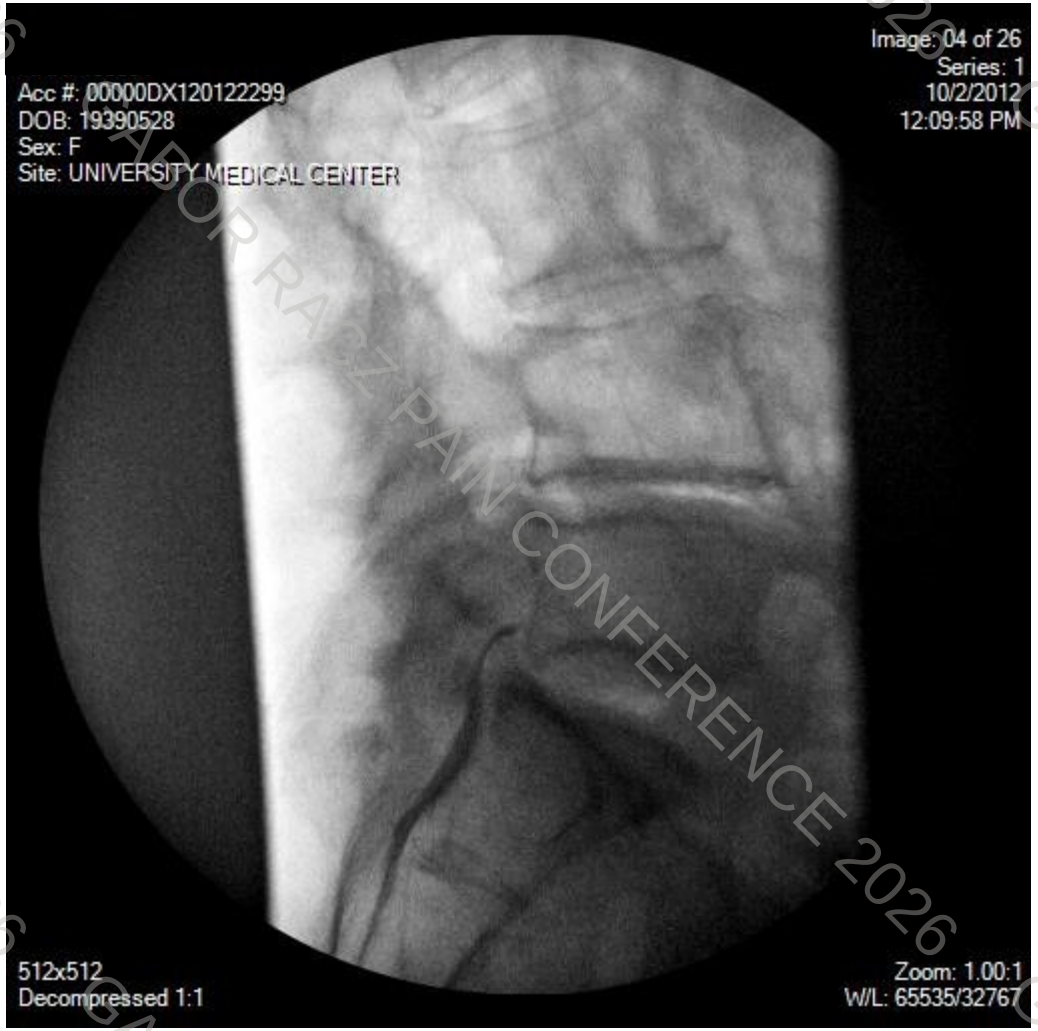
R-X Coude needle tip end on view. Note round shape opening.

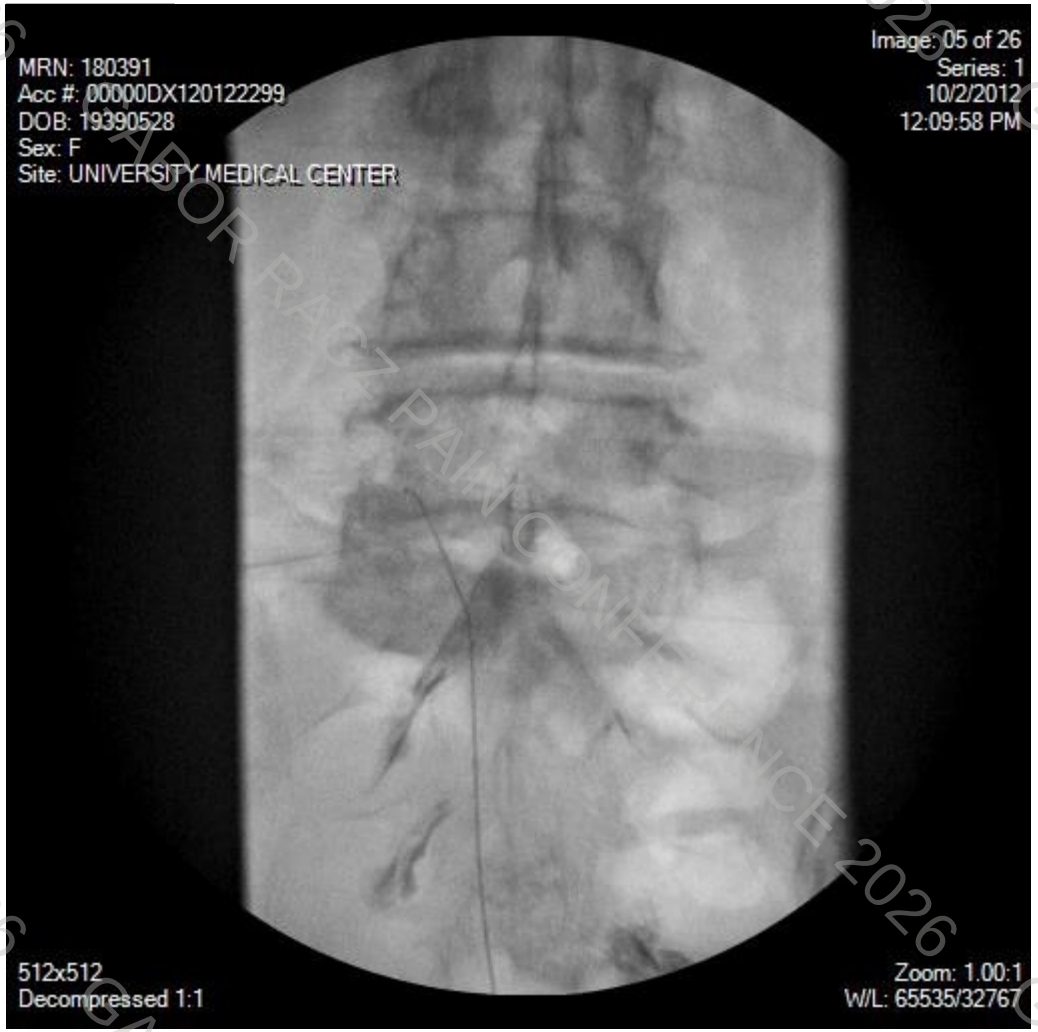


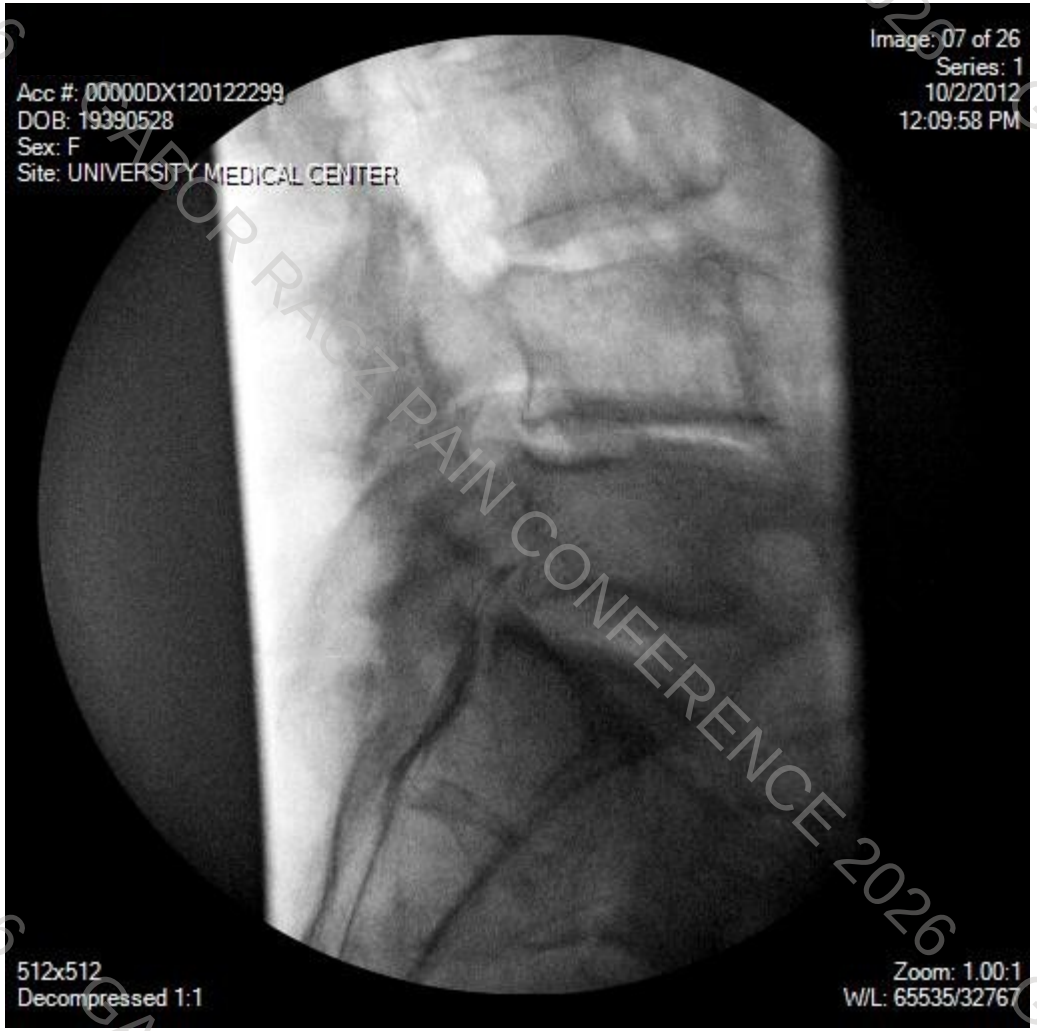


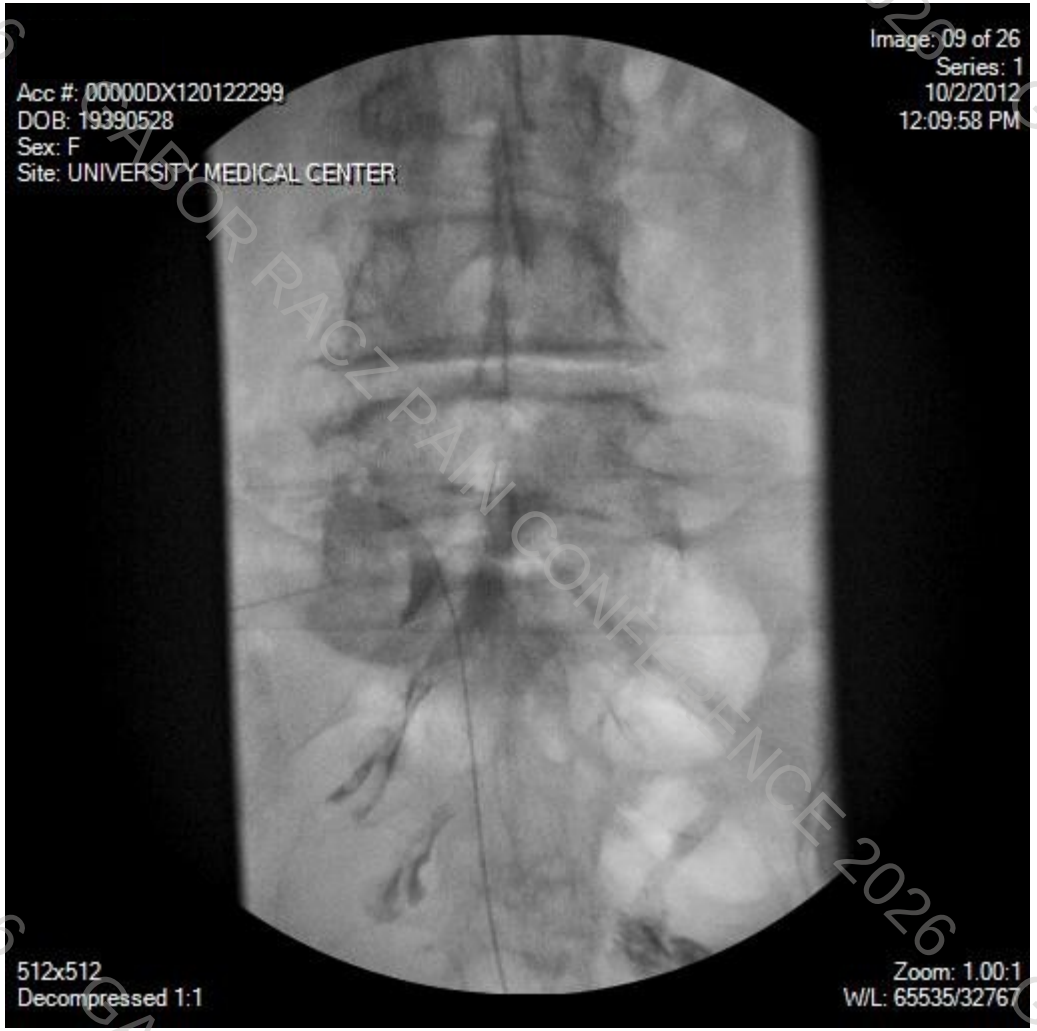


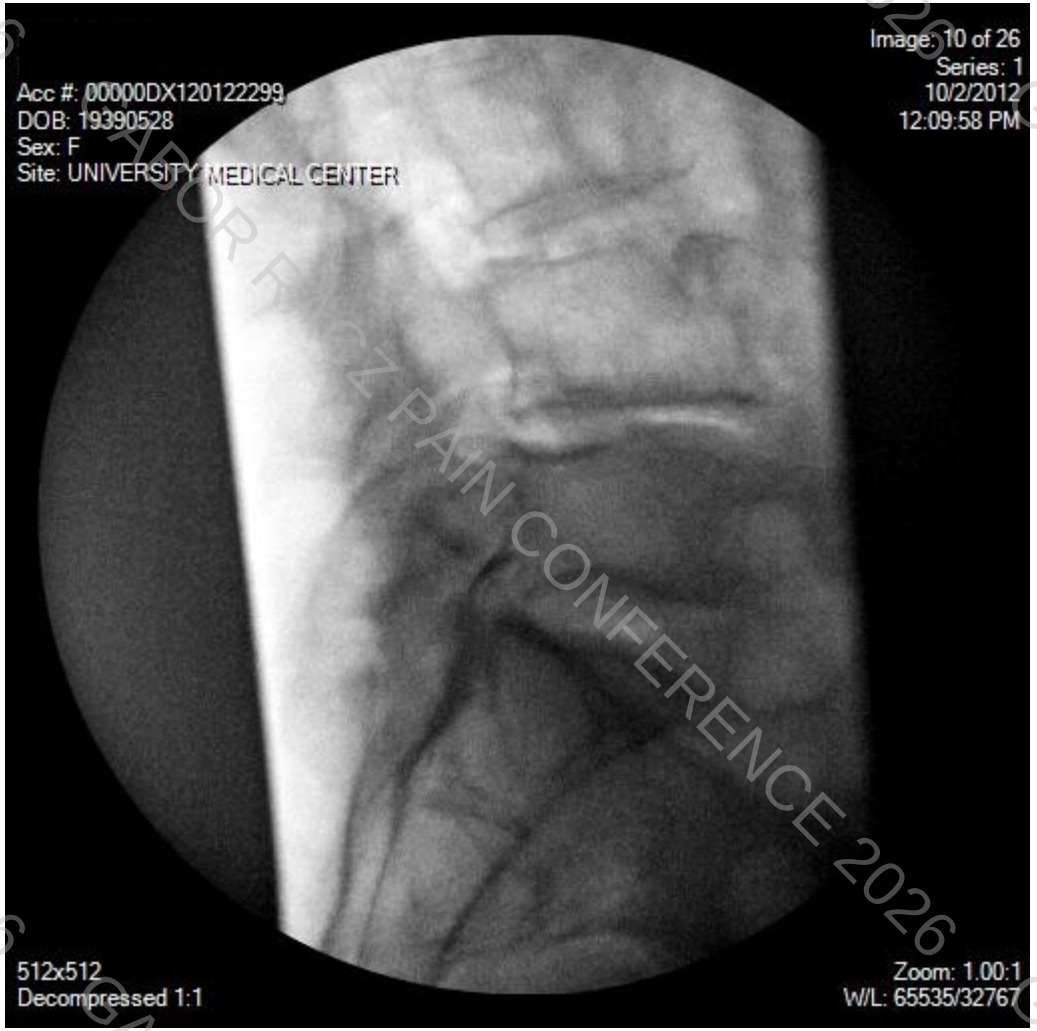


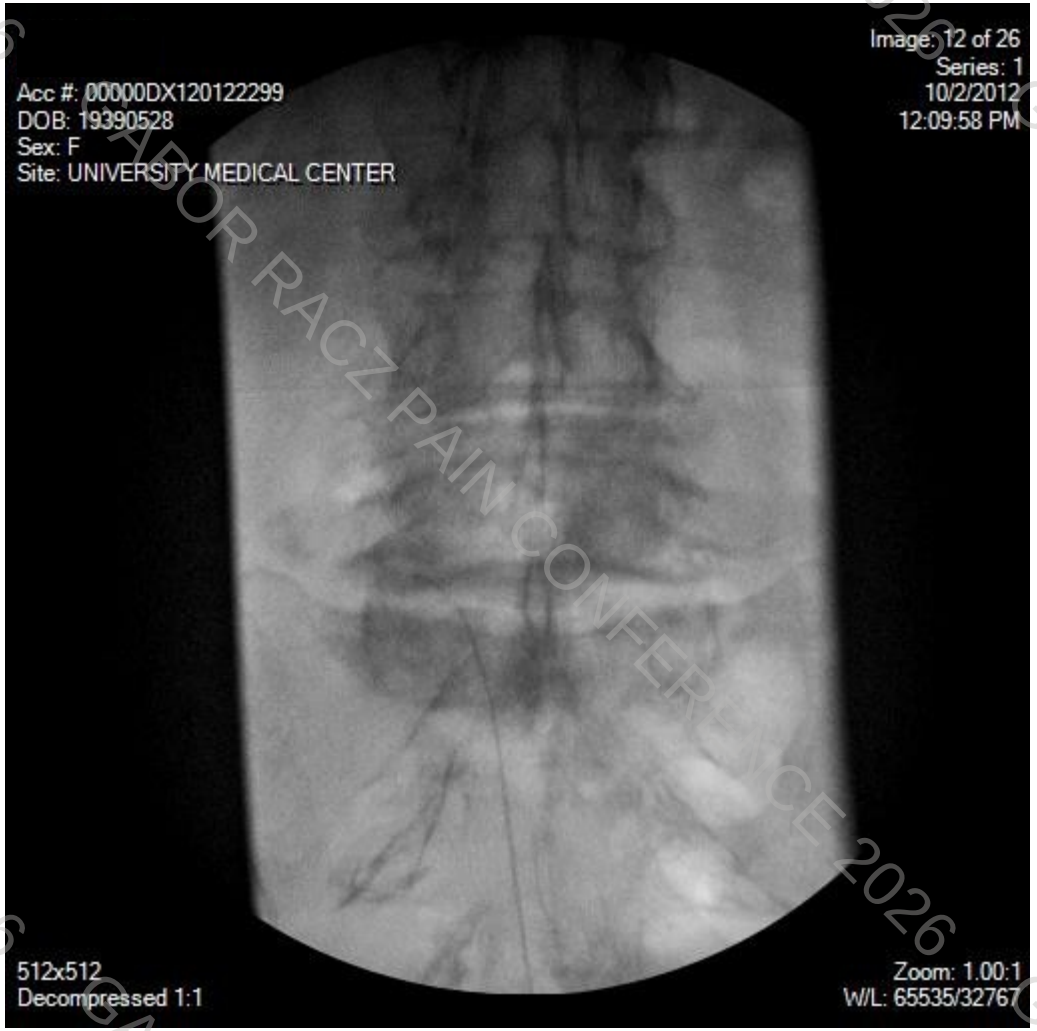


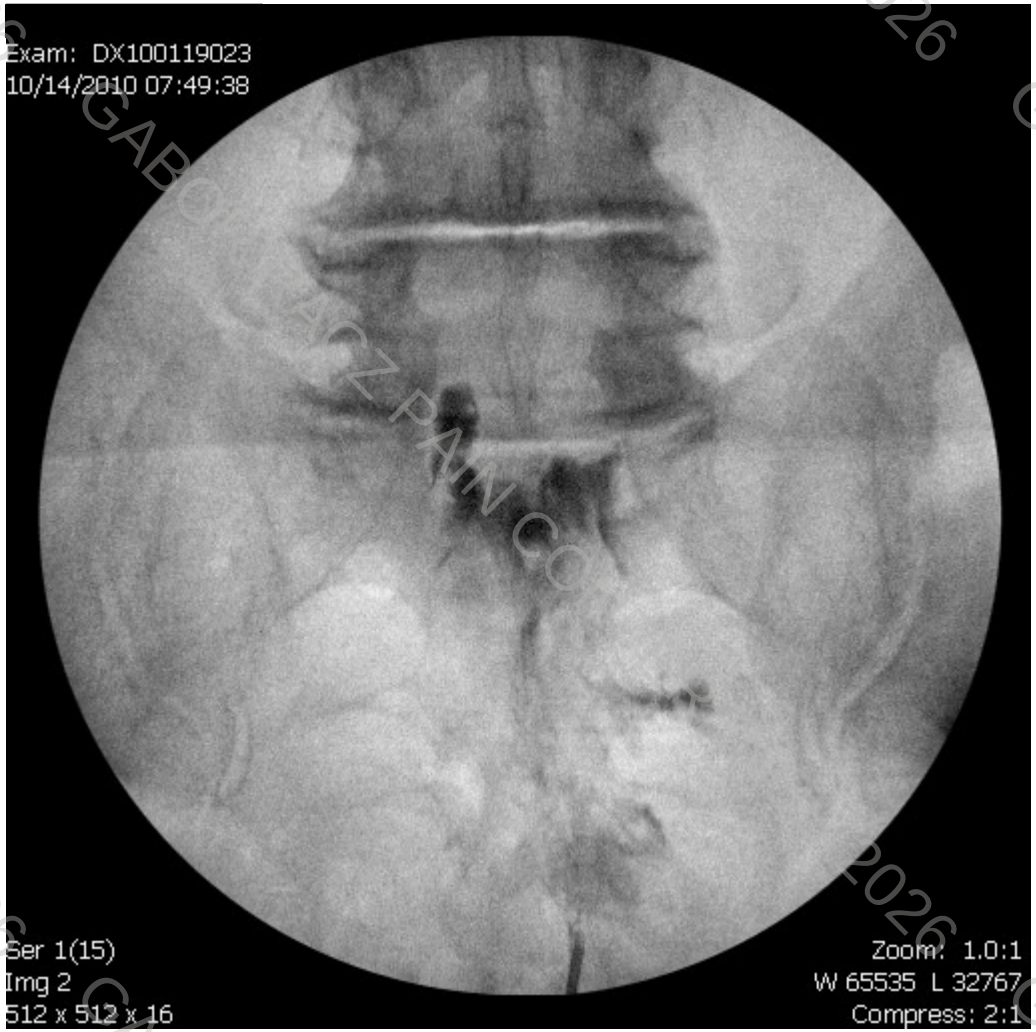


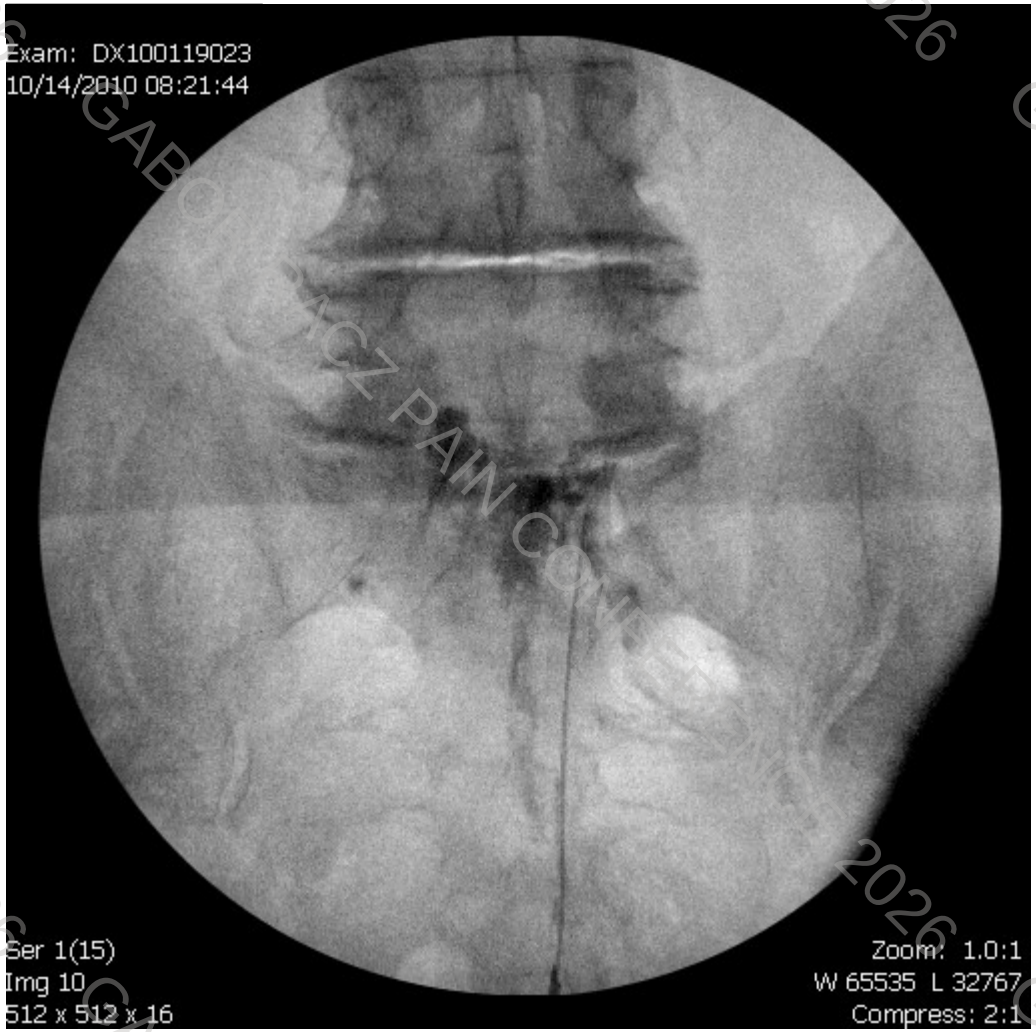


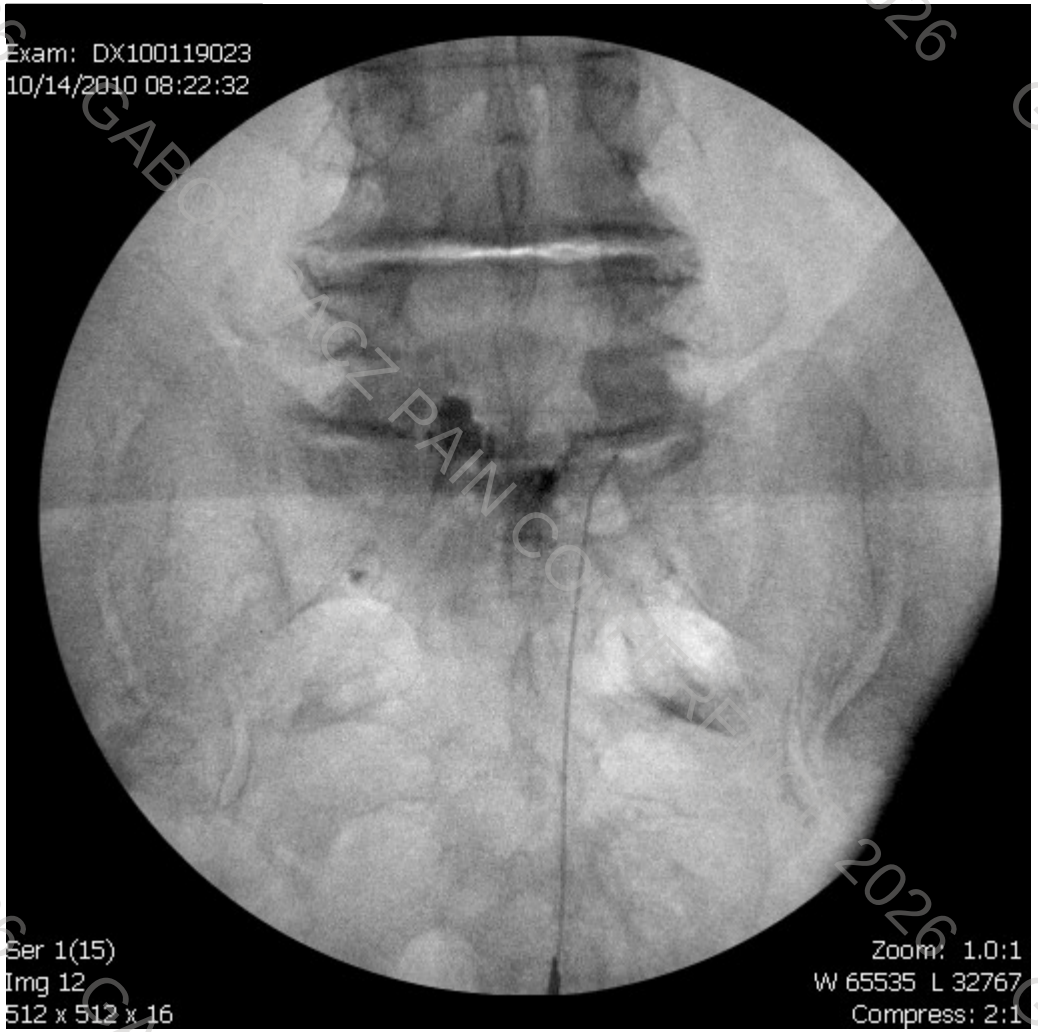


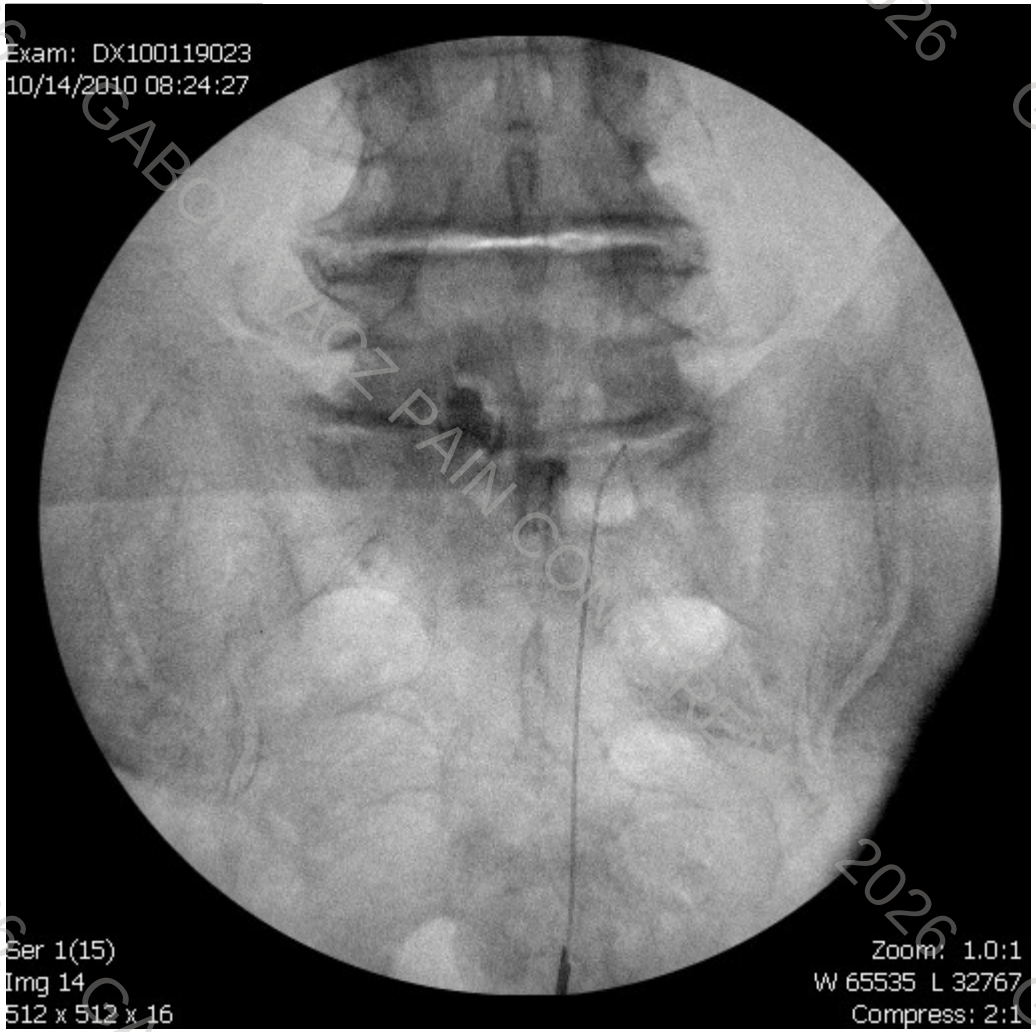


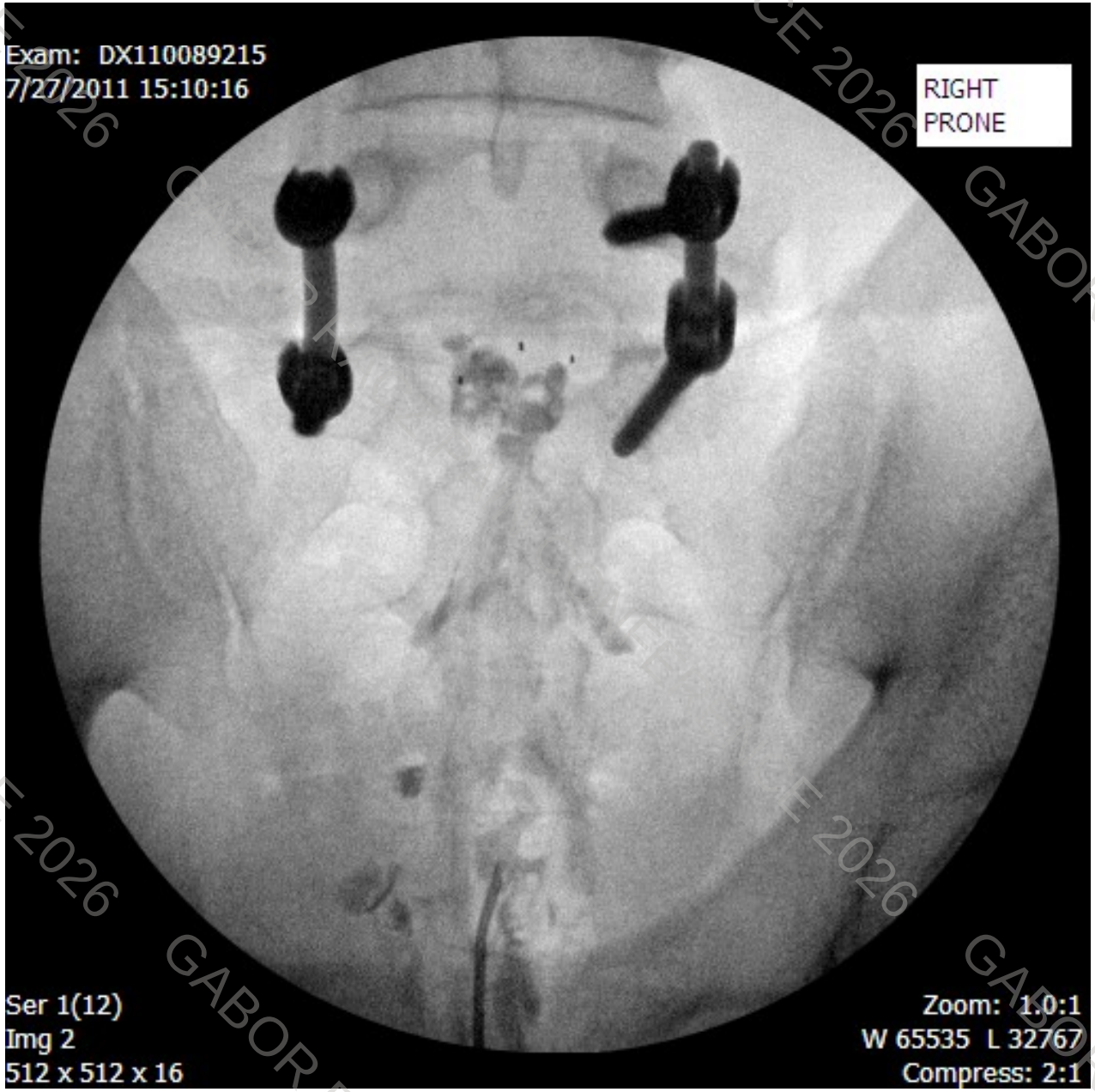


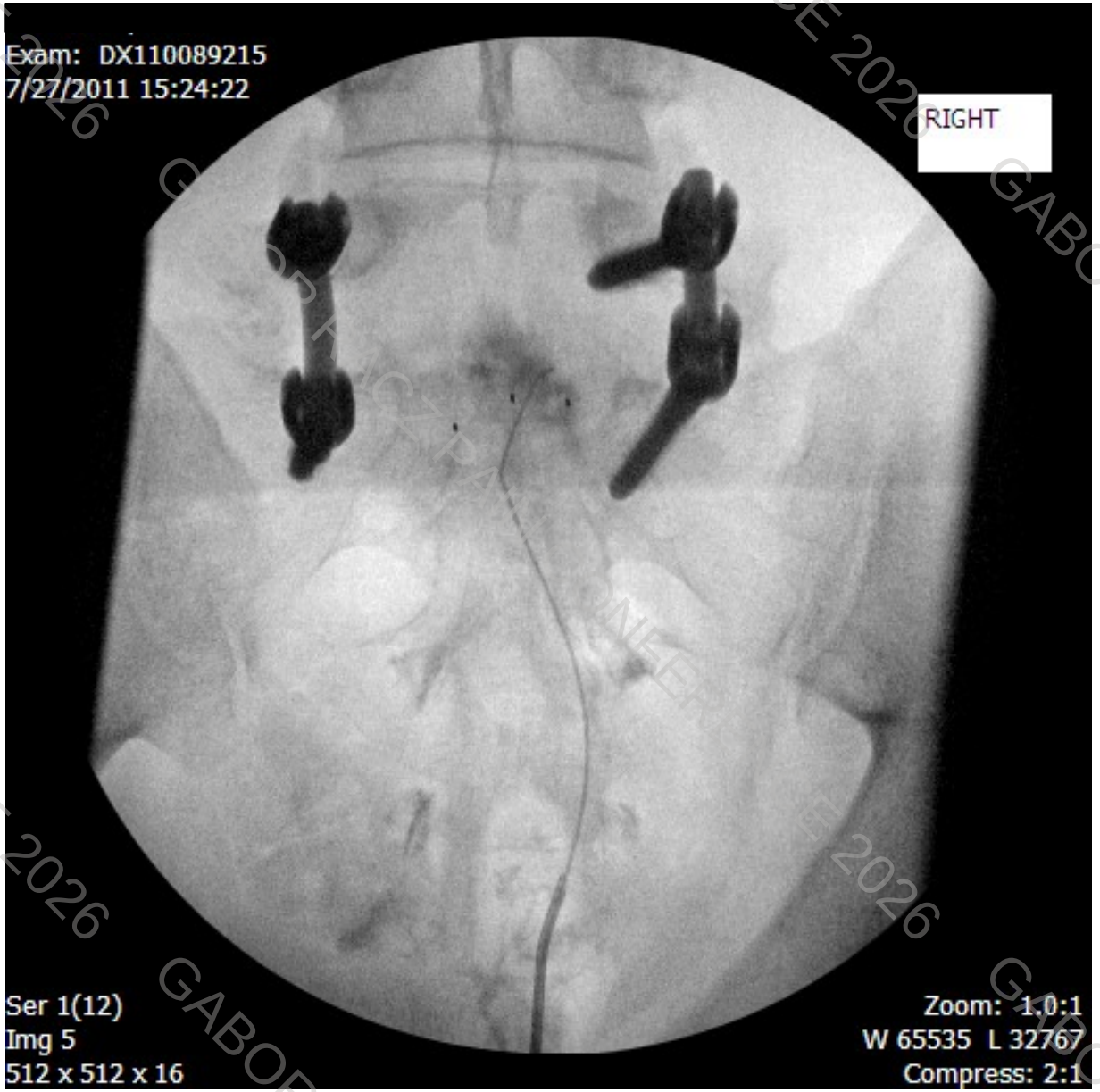


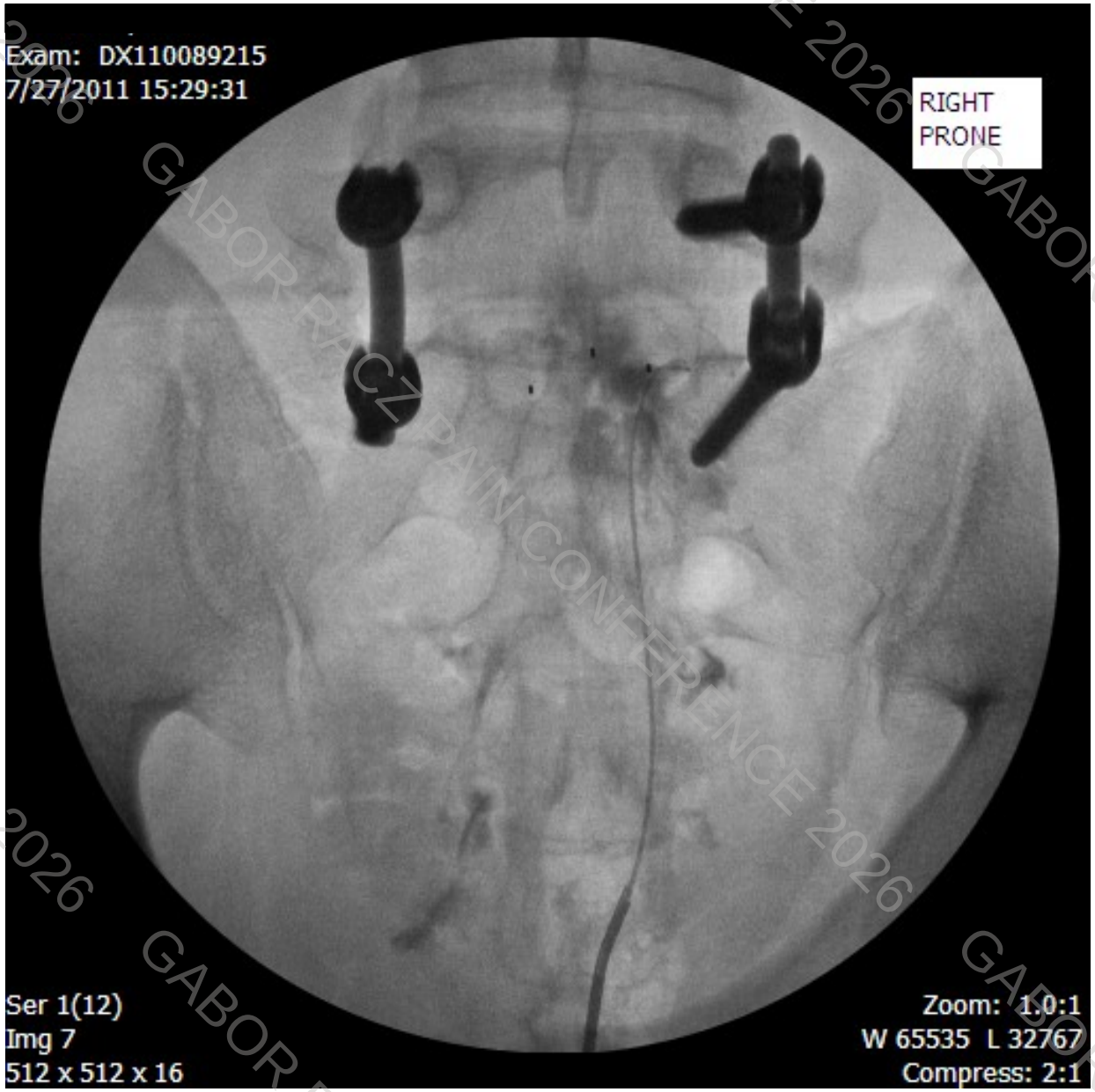


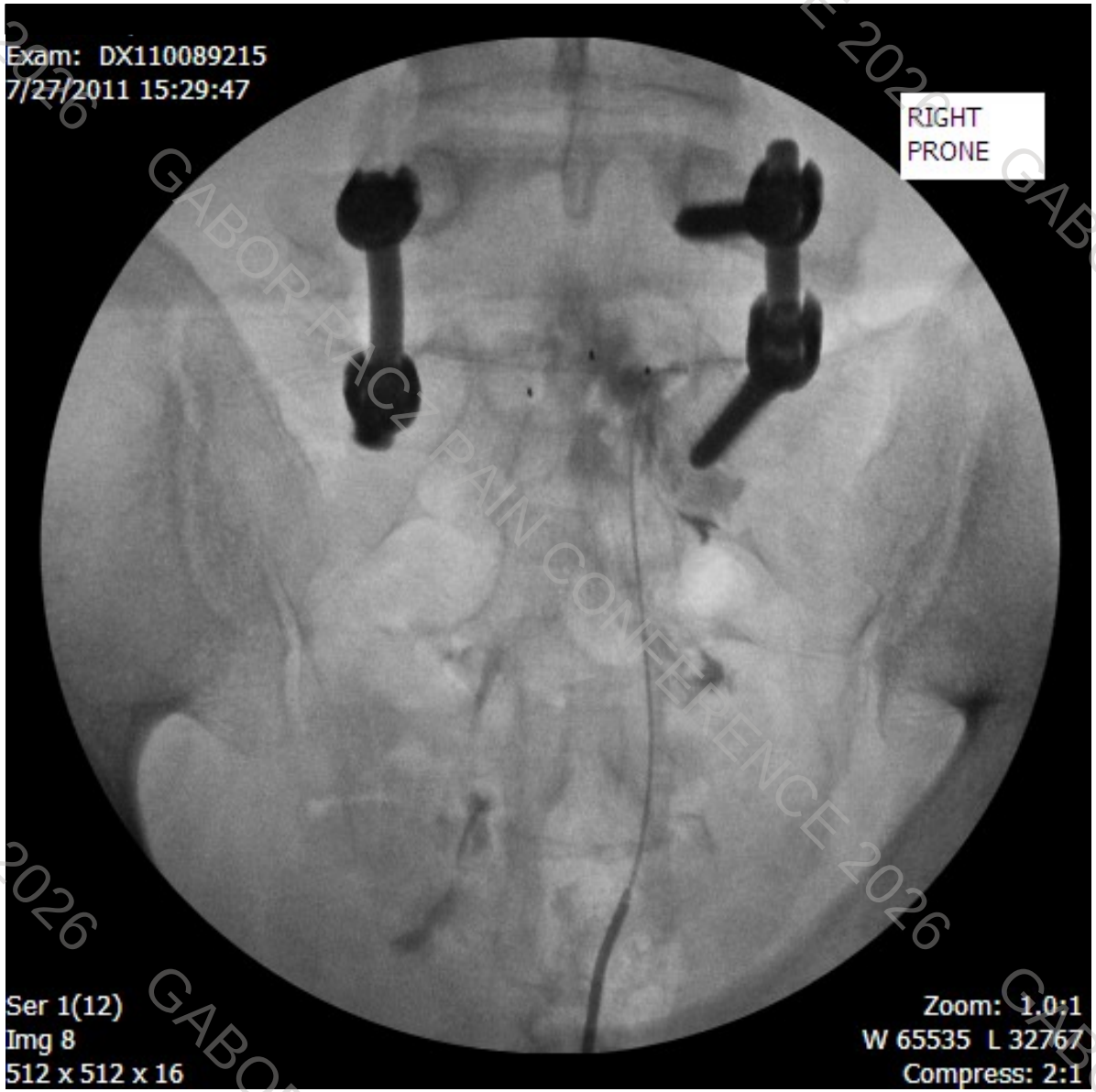


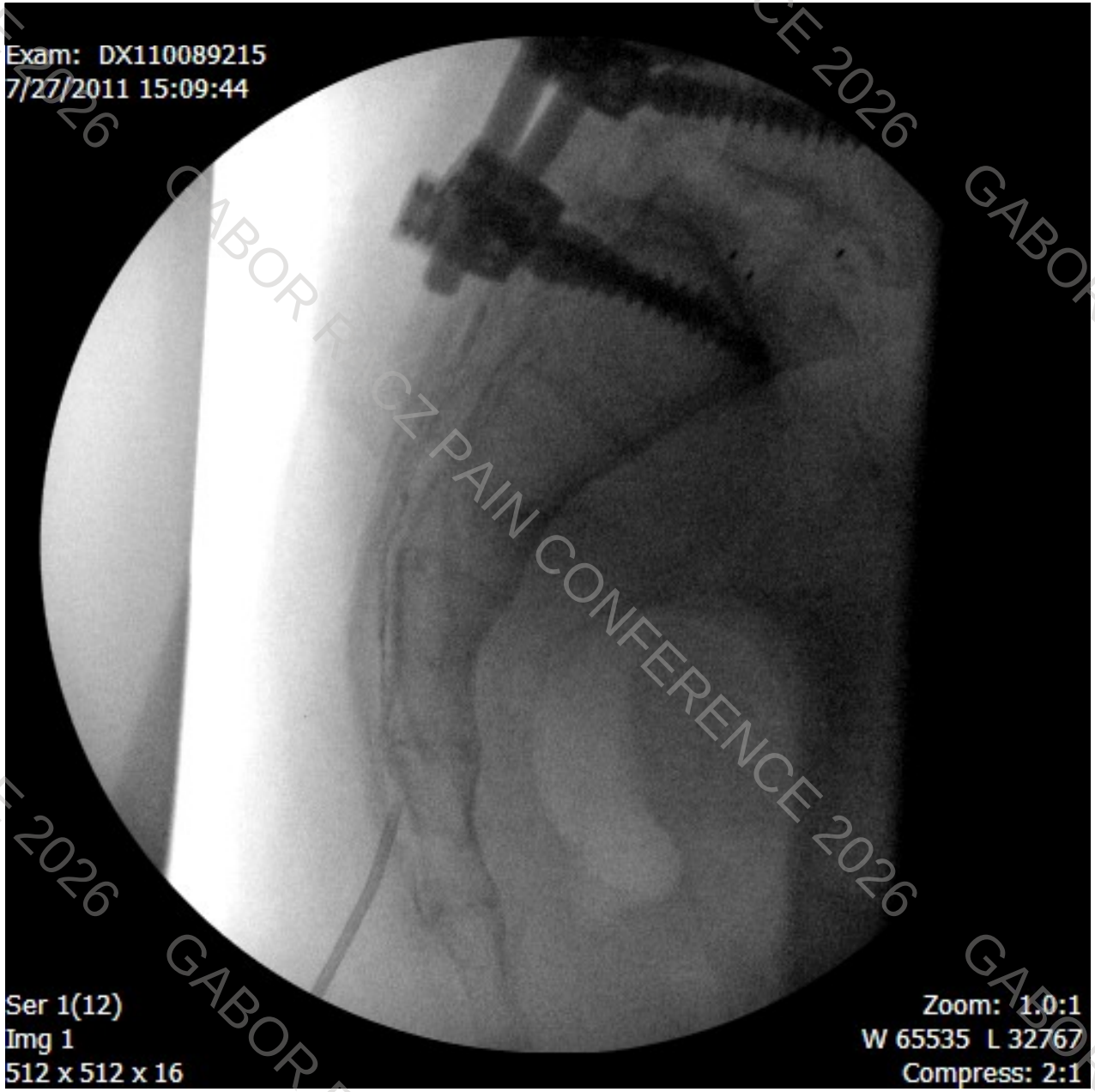


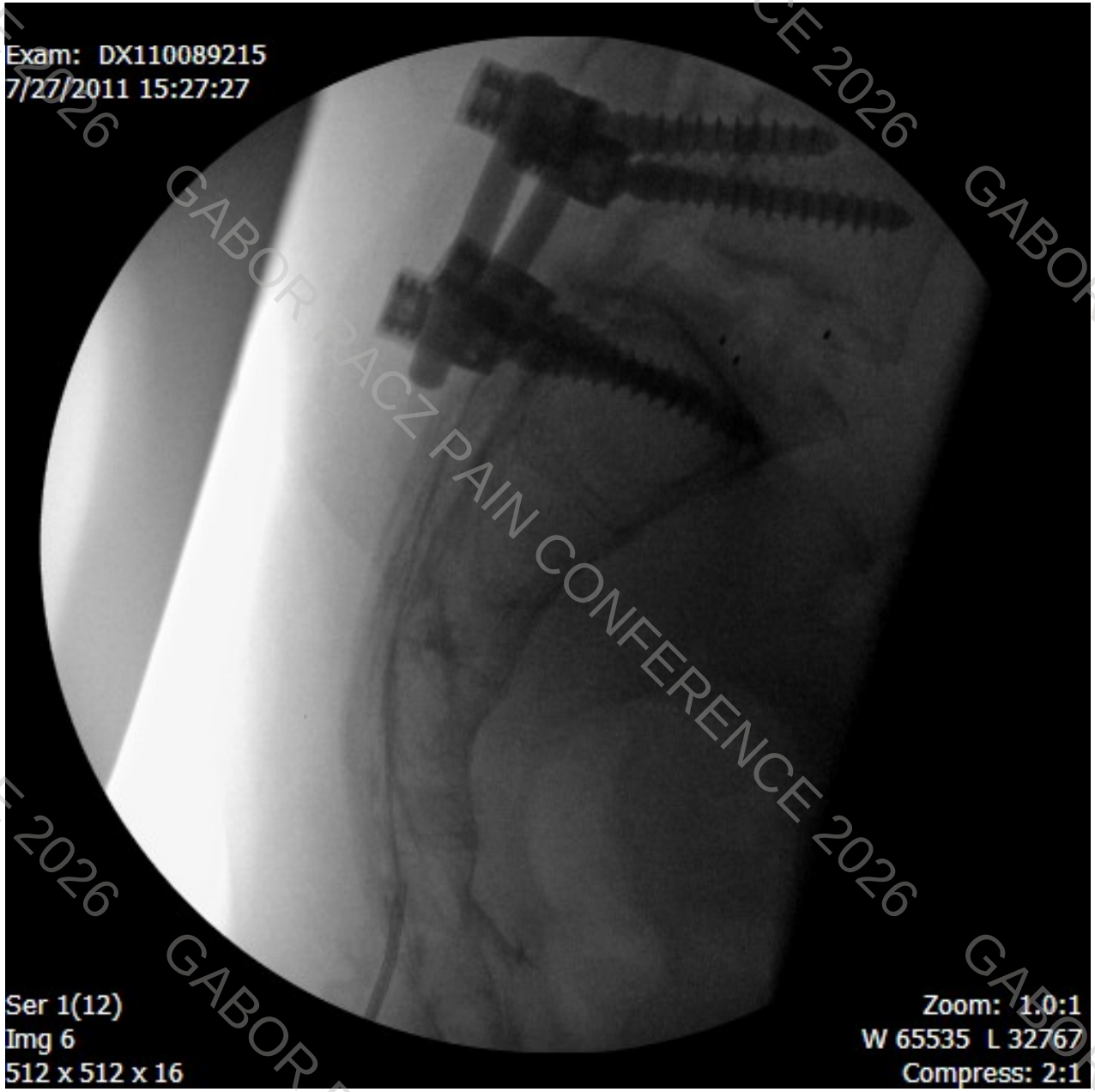




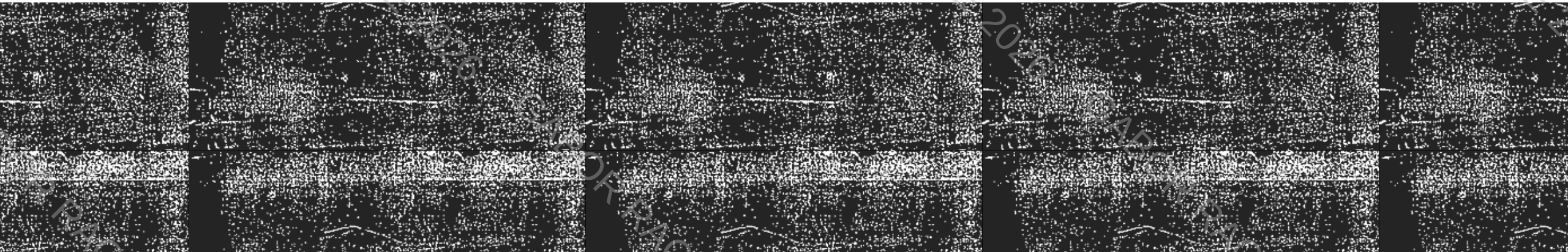








COMPLICATIONS AND PITFALLS IN LOA



COMPLICATIONS RELATED TO LYSIS OF EPIDURAL ADHESIONS

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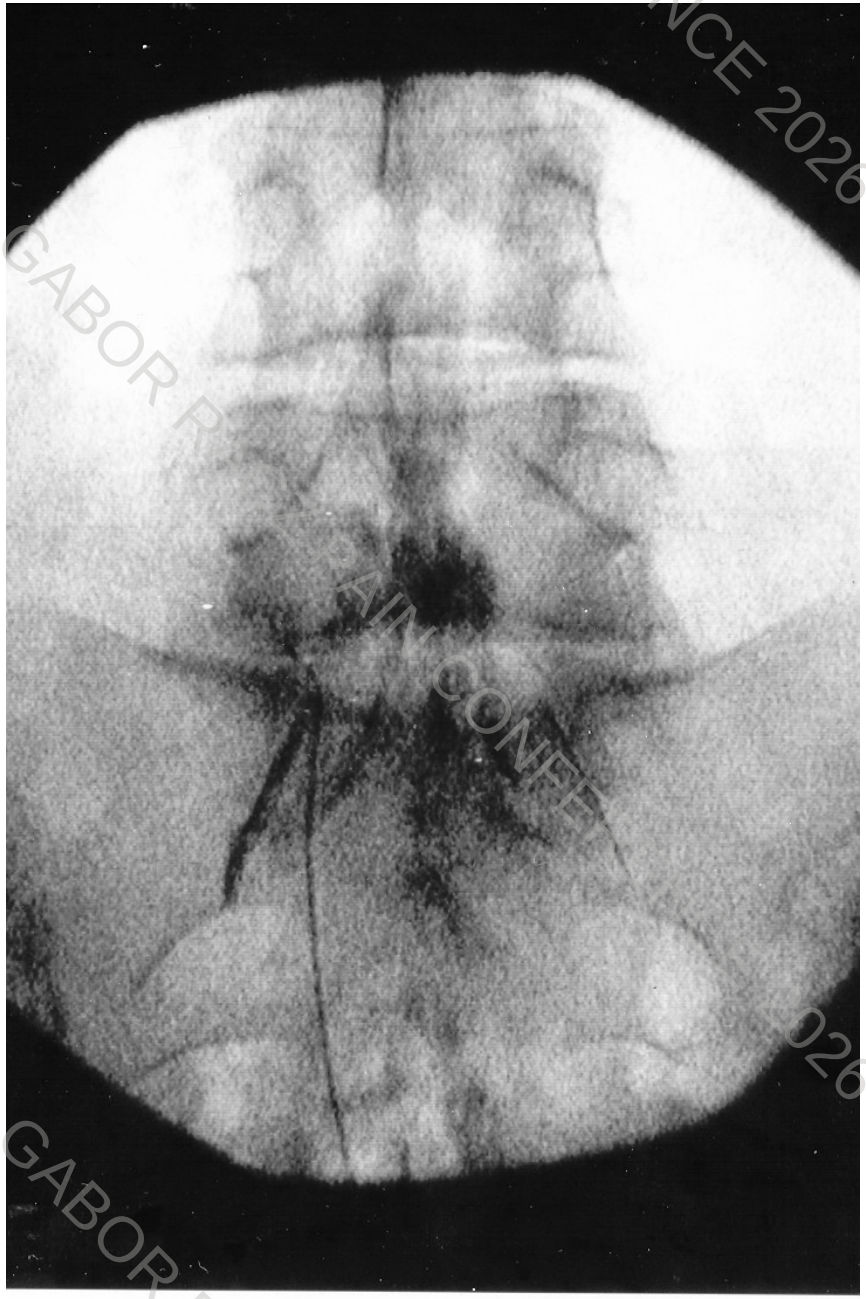
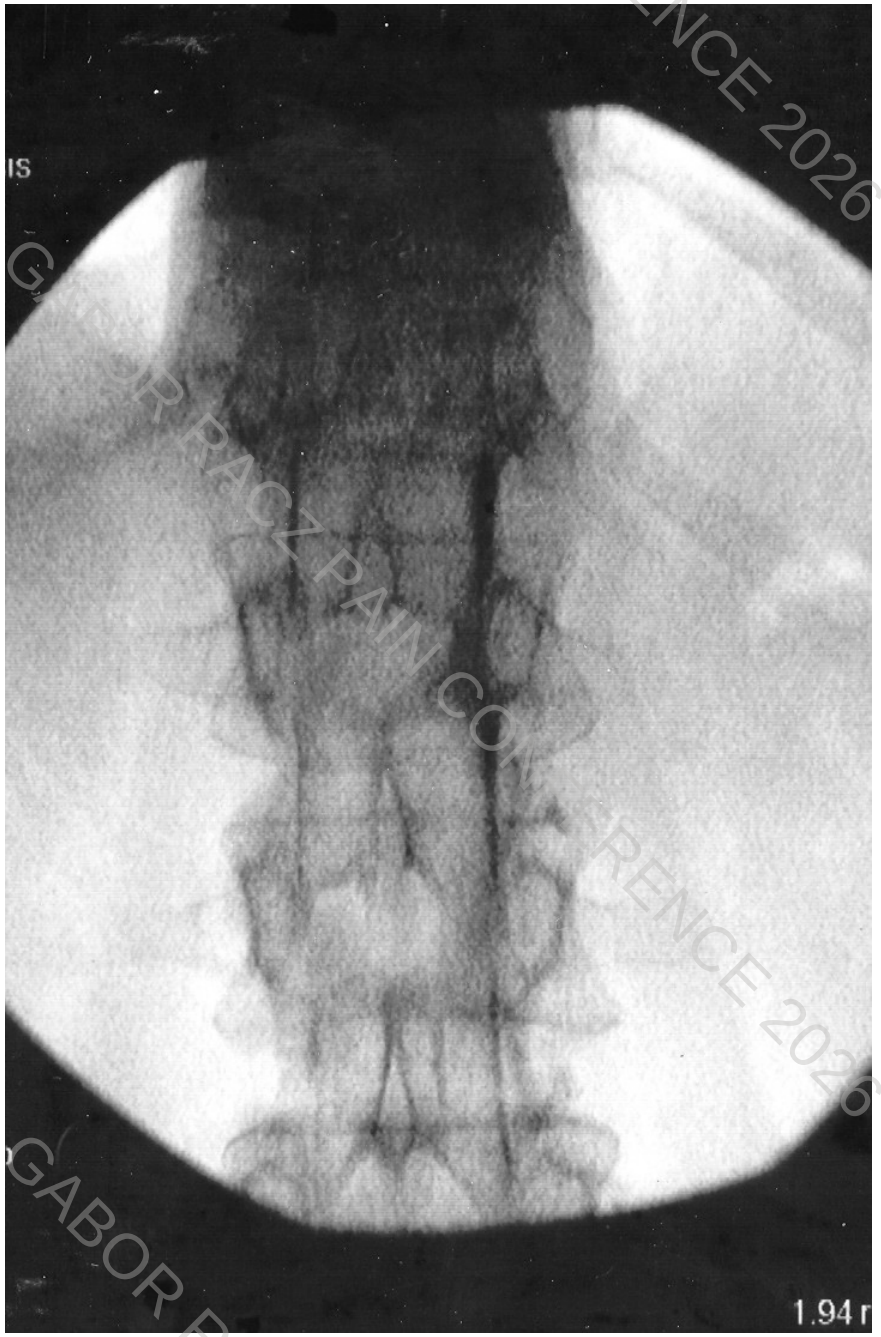
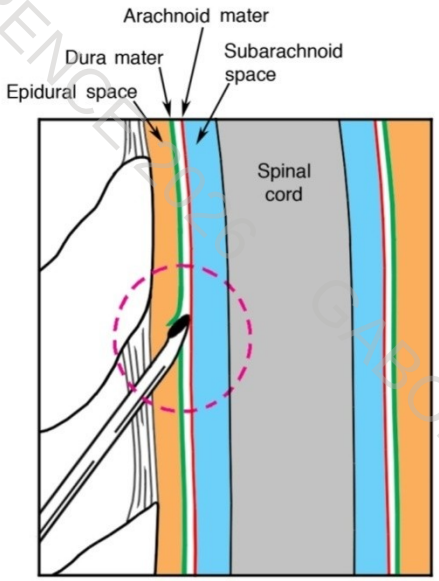
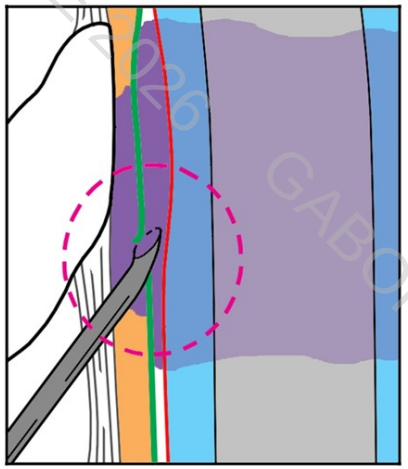


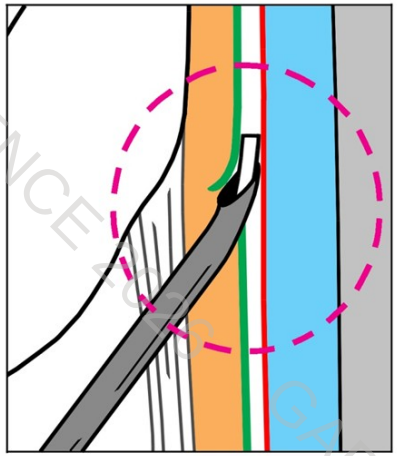




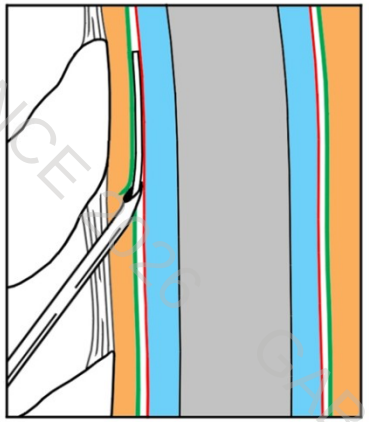
1. Needle tip can be in two spaces -



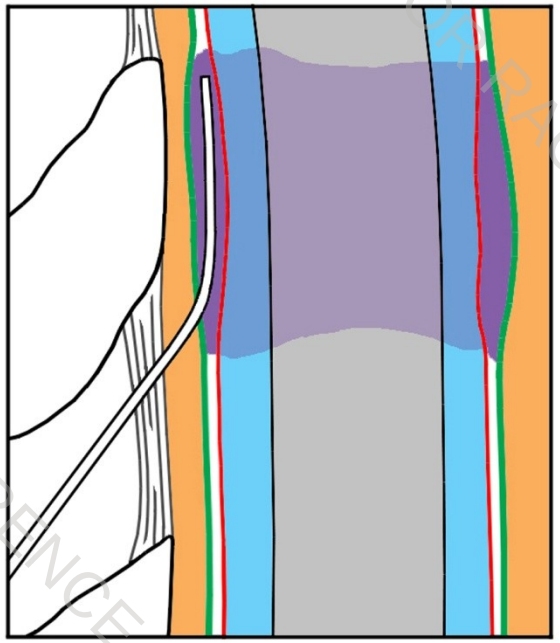
2. Injection through the Tuhoy needle can be epidural and subdural at the same time.



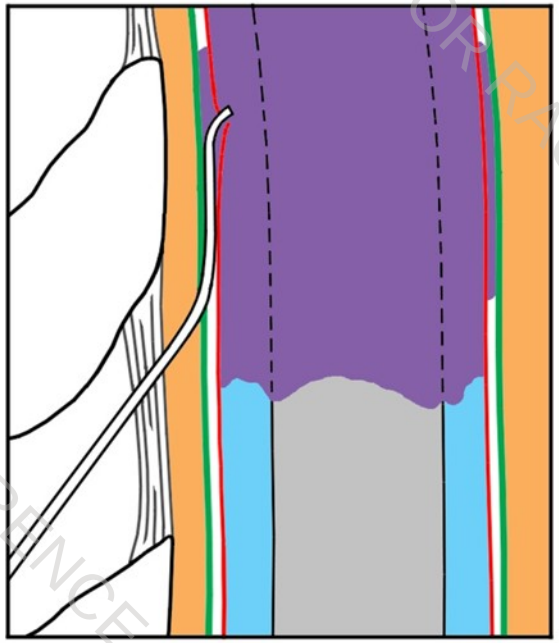
3. Catheter finds the dural tear and enters the subdural space.



4. Catheter advanced into subdural space.



6. Subdural curcumferential spread.



7. Catheter has perforated arachnoid, leading to subarachnoid spread.

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QUESTIONS