Bone Grafting Options for Spine Fusion

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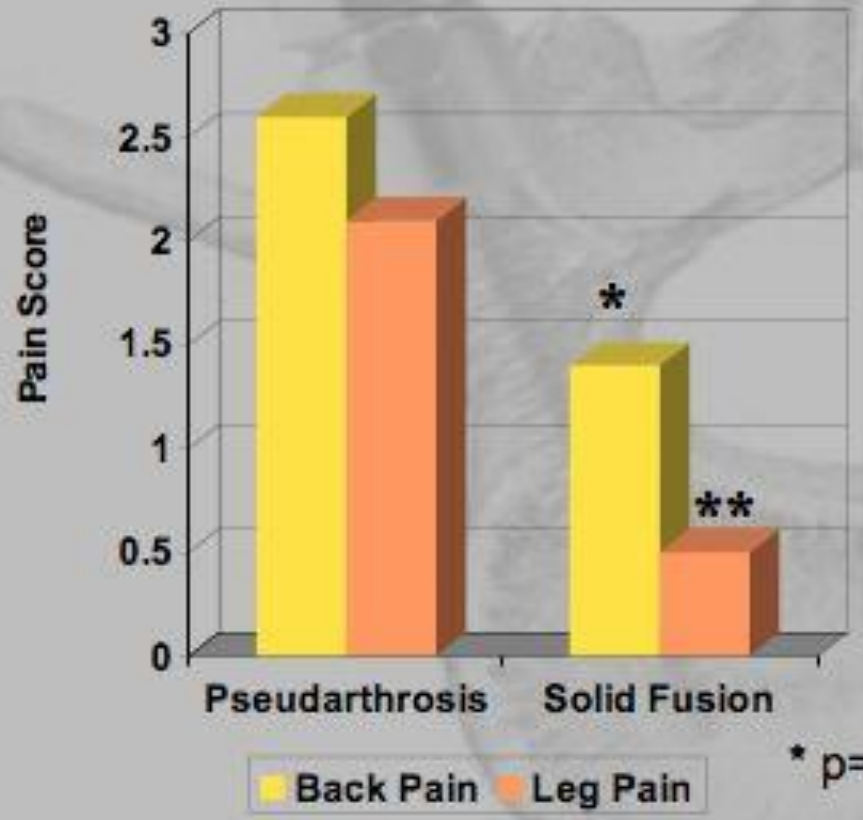
Spinal Fusion

- Provides motion segment stability
- Prevents abnormal motion
- Initially described in 1911 for the treatment of Pott's dz

Solid Fusion Positively Influences Long-Term Clinical Outcomes



- Short-term follow-up[1]
  - Successful fusion did not influence patient outcome
- Long-term follow-up[2]
  - Significant improvement shown in clinical outcomes with successful fusion
    - Overall success (p=0.01)
    - Back pain (p=0.02)
    - Leg pain (p=0.001)

* p=0.02, ** p=0.001

1 Fischgrund et al, SPINE ,1997
2 Kornblum, Fischgrund et al., SPINE 2004

Ideal Graft Environment

- Osteoconductive
  - scaffolding
- Osteoinductive
  - Induces osteoprogenitor cells to differentiate into osteoblasts that eventually form bone
- Osteogenic
  - Cells capable of forming new bone
    - Bone Marrow

Stages of Bone Healing and Remodeling

- Induction: formation of hematoma
  - Release of growth factors & cytokines
- Inflammation: Recruitment
  - Macrophage/fibroblasts
- Cartilage Formation
- Woven Bone: Differentiation of osteoblasts
- Lamellar Bone: Resorption/remodelling

Growth Factors and Cytokines

- BMP's
- TGF-B (Transforming growth factors)
- Insulin-like growth factors
- Platelet derived growth factor
- Epidermal growth factor
- Fibroblast growth factor
- Vascular endothelial growth factor
- Tumor necrosis factor

Available Bone Grafting Options

- Autograft
  - Iliac crest
  - Local bone
- Extenders
  - Allograft
    - DBM
  - Ceramics
- Replacements
  - rhBMP

Bone Graft Extenders

Reduces amount of patient bone harvested

- Less OR time
- Lower morbidity

- Usually osteoconductive
  - Must be combined with bioactive components (?BMA, autogenous bone, etc.)
  - Allows ingrowth

Autograft Extender Options

Osteoconductive Materials

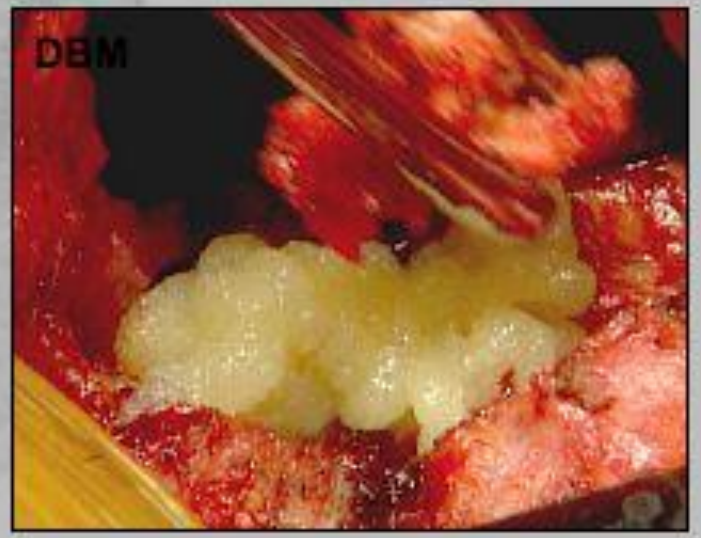
- Calcium phosphate (CaP) ceramics
- Collagen/CaP composites
- Calcium sulfate ceramics

Osteopromotive

- Platelet concentrates (PRP)

Osteoinductive Materials

- Demineralized Bone Matrix (DBM)
  - Contains BMP but concentration variable.



Autograft Replacement Options

Osteoinductive Materials

- Recombinant human BMP
  - rhBMP-2
    - Medtronic Sofamor Danek
      - INFUSE® Bone Graft
  - rhBMP-7
    - OP-1™ Implant

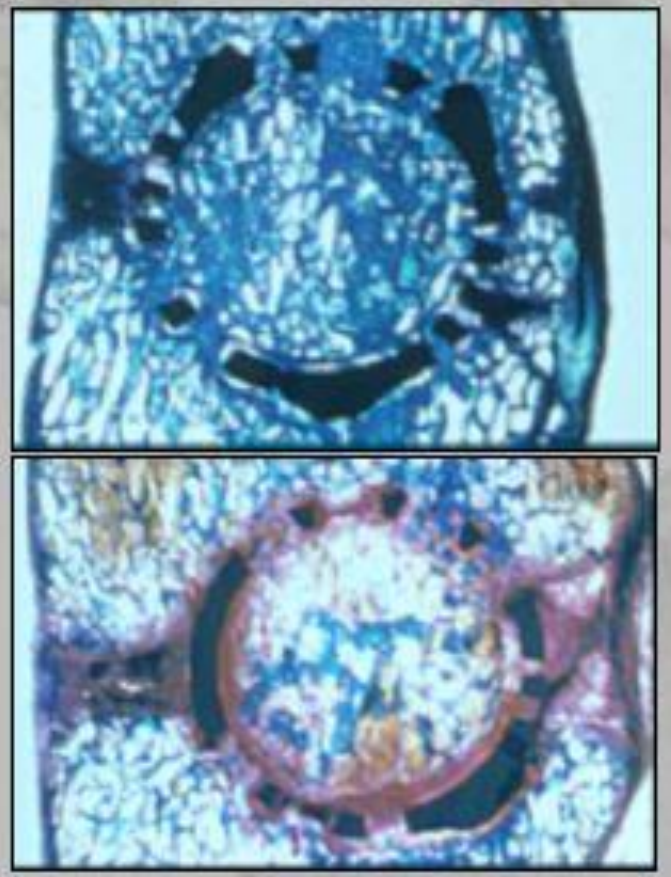
MICHELSON TECHNOLOGY AT WORK

Preclinical Study Results

rhBMP-2/ACS vs Autograft

rhBMP-2/ACS

Autograft



- rhBMP-2
  - 100% fusion
  - Significantly higher bone continuity
- Autograft
  - 16 times more fibrous tissue

Sandhu *et al.*, SPINE, 2002

BRIEF SUMMARY OF INDICATIONS, CONTRAINDICATIONS, AND WARNINGS FOR: INFUSE™ BONE GRAFT

The INFUSE™ Bone Graft is indicated for treating acute, open tibial shaft fractures that have been stabilized with IM nail fixation after appropriate wound management. INFUSE™ Bone Graft must be applied within 14 days after the initial fracture. Prospective patients should be skeletally mature.

The INFUSE® Bone Graft is contraindicated for patients with a known hypersensitivity to recombinant human Bone Morphogenetic Protein-2, bovine Type I collagen or to other components of the formulation and should not be used in the vicinity of a resected or extant tumor, in patients with an active malignancy or patients undergoing treatment for a malignancy. The INFUSE™ Bone Graft should also not be used in patients who are skeletally immature, in patients with an inadequate neurovascular status, in patients with compartment syndrome of the affected limb, in pregnant women, or in patients with an active infection at the operative site. Antibody formation to rhBMP-2 or its influence on fetal development has not been assessed. The safety and effectiveness of this device has not been established in nursing mothers. Women of child-bearing potential should be advised to not become pregnant for one year following treatment with this device.

Please see the package insert for the complete list of indications, warnings, precautions, adverse events, clinical results, and other important medical information.

CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician with appropriate training or experience.

BRIEF SUMMARY OF INDICATIONS, CONTRAINDICATIONS, AND WARNINGS FOR: INFUSE™ BONE GRAFT/LT-CAGE™ LUMBAR TAPERED FUSION DEVICE, INFUSE™ BONE GRAFT/INTER FIX™ THREADED FUSION DEVICE, INFUSE™ BONE GRAFT/INTER FIX™ RP THREADED FUSION DEVICE

The INFUSE® Bone Graft/Interbody Fusion Device is indicated for spinal fusion procedures in skeletally mature patients with degenerative disc disease (DDD) at one level from L2-S1, who may also have up to Grade I spondylolisthesis or Grade 1 retrolisthesis at the involved level. The INFUSE™ Bone Graft/LT-CAGE® Lumbar Tapered Fusion Device (Flat Nose) is to be implanted via an anterior open or an anterior laparoscopic approach. The INFUSE™ Bone Graft/LT-CAGE™ Lumbar Tapered Fusion Device (Round Nose) is to be implanted via an anterior open approach. INFUSE® Bone Graft with either the INTER FIX™ or INTER FIX™ RP Threaded Fusion Device is to be implanted via an anterior open approach. The INFUSE® Bone Graft component must not be used without the Interbody Fusion Device component. These components must be used as a system.

NOTE: The INTER FIX™ Threaded Fusion Device and the INTER FIX™ RP Threaded Fusion Device may be used together to treat a spinal level. LT-CAGE™ Lumbar Tapered Fusion Device implants are not to be used in conjunction with either the INTER FIX™ OR INTER FIX™ RP implants to treat a spinal level.

The INFUSE® Bone Graft/Interbody Fusion Device is contraindicated for patients with a known hypersensitivity to recombinant human Bone Morphogenetic Protein-2, bovine Type I collagen or to other components of the formulation and should not be used in the vicinity of a resected or extant tumor, in patients with any active malignancy or patients undergoing treatment for a malignancy, in patients who are skeletally immature, in pregnant women, or in patients with an active infection at the operative site or with an allergy to titanium or titanium alloy. Antibody formation to rhBMP-2 or its influence on fetal development has not been assessed. The safety and effectiveness of this device has not been established in nursing mothers. Women of child-bearing potential should be advised to not become pregnant for one year following treatment with this device.

Please see the package insert for the complete list of indications, warnings, precautions, adverse events, clinical results, definition of DDD, and other important medical information. The package insert also matches the sizes of those sized devices that are indicated for use with the appropriate INFUSE Bone Graft kit.

CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician with appropriate training or experience.

MICHELSON TECHNOLOGY AT WORK

BMP

- Coined by Urist in 1965
  - Crude bone extracts induced new bone formation in rat model.
- Bioassay by Sampath & Reddi in 1981
- Purified by Wozney et al 1988 and Johnson 1992.
- Gene sequencing 1990's
- FDA approval for recombinant BMP 2002 (BMP-2 and BMP-7)

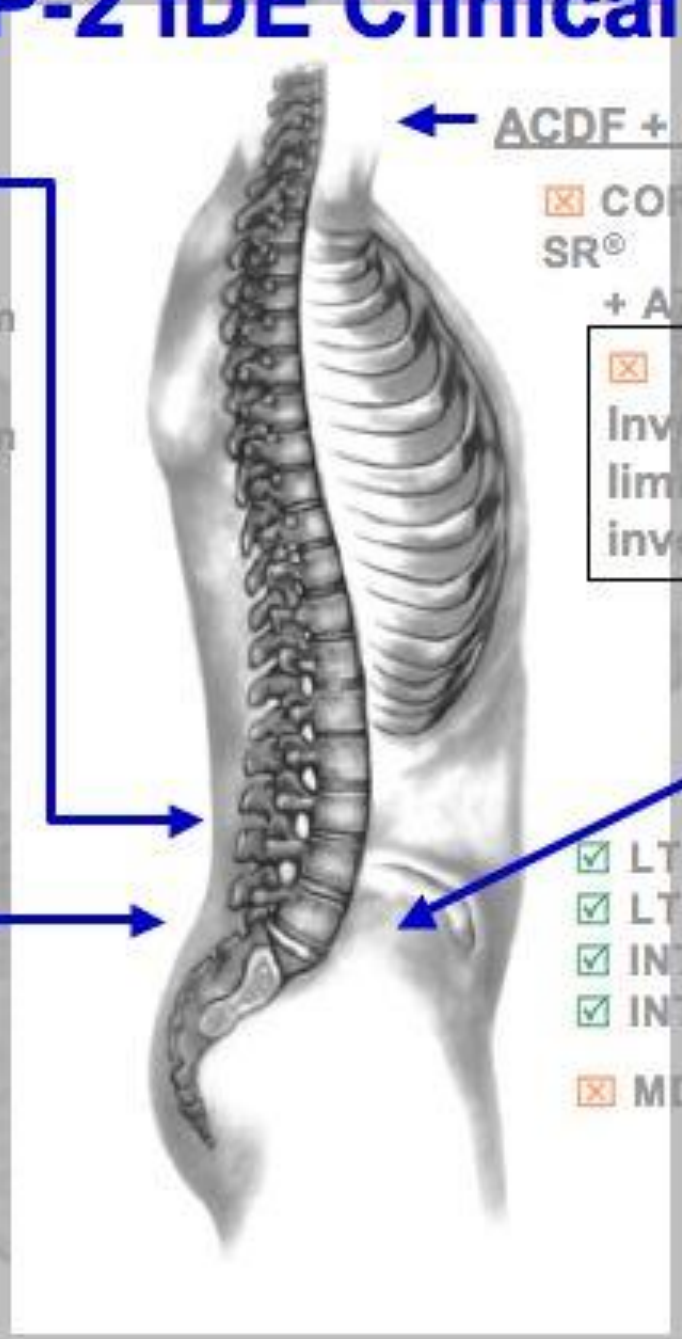
BMP

- Only growth factor that has the ability to transform connective tissue cell into osteoprogenitor cells.
- All other growth factors induce multiplication of cells but do not transform.
- Fusion rates interbody of greater than 92 -95%.
- Fusion rates intertransverse similar or greater than autograft.
- Avoid donor site morbidity (6% - 40%)
  - Morbidity increases as graft amount increases

BMP

- Infuse does not resist compression so if to be used posteriolaterally, make a taco/sushi/egg roll.
- Countersink the graft at least 4 mm.
- Be careful if used in the cervical spine.

MSD rhBMP-2 IDE Clinical Studies



POSTEROLATERAL FUSION + rhBMP-2

- rhBMP2/BCP + TSRH® System *(USA)*
- rhBMP2/BCP + TSRH® System *(Canada)*
- rhBMP2/CRM + CD HORIZON® System
- INFUSE® Bone Graft/ MASTERGRAFT® + CD HORIZON® System

PLIF + INFUSE® Bone Graft

- INTER FIX™ Cage
- PEEK TELAMON®P + CD HORIZON® System

ACDF + INFUSE® Bone Graft

- CORNERSTONE SR®
  + ATLANTIS® Plate

CAUTION: Investigational device limited by US law to investigational use only.

ALIF + INFUSE

- LT-CAGE® Device *(Open)*
- LT-CAGE® Device *(Lap)*
- INTER FIX™ Cage *(Open)*
- INTER FIX™ RP Cage *(Open)*
- MD II™ Bone Dowel

MICHELSON TECHNOLOGY AT WORK

Level 1 Clinical Data

Peer-Reviewed Publications

- **ALIF**
  - **"The use of rhBMP-2 in interbody fusion cages. Definitive evidence of osteoinduction in humans: A preliminary report"**
    Boden et al *Spine*, 25 (3): 376 – 381, 2000
  - **"Anterior interbody fusion using rhBMP-2 with tapered interbody cages"**
    Burkus et al *J Spinal Disorders*, 15 (5): 337 – 349, 2002
  - **"Clinical and radiographic outcomes of anterior lumbar interbody fusion using recombinant human bone morphogenetic protein-2"**
    Burkus et al. *Spine*, 27 (21): 2396 – 2408, 2002
  - **"Radiographic assessment of interbody fusion using rhBMP-2"**
    Burkus et al. *Spine*, 28 (4): 372 – 377, 2003
  - **"Is INFUSE® Bone Graft superior to autograft bone? An integrated analysis of clinical trials using the LT-CAGE® Lumber Tapered Fusion Device"**
    Burkus et al. *J Spinal Disorders* 16 (2): 113 – 122, 2003

MICHELSON TECHNOLOGY AT WORK

Level 1 Clinical Data

Peer-Reviewed Publications

- **Posterolateral**
  - **"Use of rhBMP-2 to achieve posterolateral lumbar spine fusion in humans: A prospective and randomized clinical pilot trial"**
    Boden et al *Spine*, 27 (23): 2662 – 2673, 2002
- **PLIF**
  - **"Posterior lumbar interbody fusion using recombinant human bone morphogenetic protein type 2 with cylindrical interbody cages"**
    Haid et al. *Spine J*, 4: 527 – 539, 2004
- **ACDF**
  - **"A prospective, randomized, controlled cervical fusion study using recombinant human bone morphogenetic protein-2 with the CORNERSTONE-SR® Allograft Ring and the ATLANTIS® Anterior Cervical Plate"**
    Baskin et al. *Spine* 28 (12): 1219 – 1225, 2003
- **Economics**
  - **"A cost analysis of bone morphogenetic protein versus autogenous iliac crest bone graft in single-level anterior lumbar fusion"**
    Polly et al. *Orthopedics* 26(10): 1027 – 1037, 2003

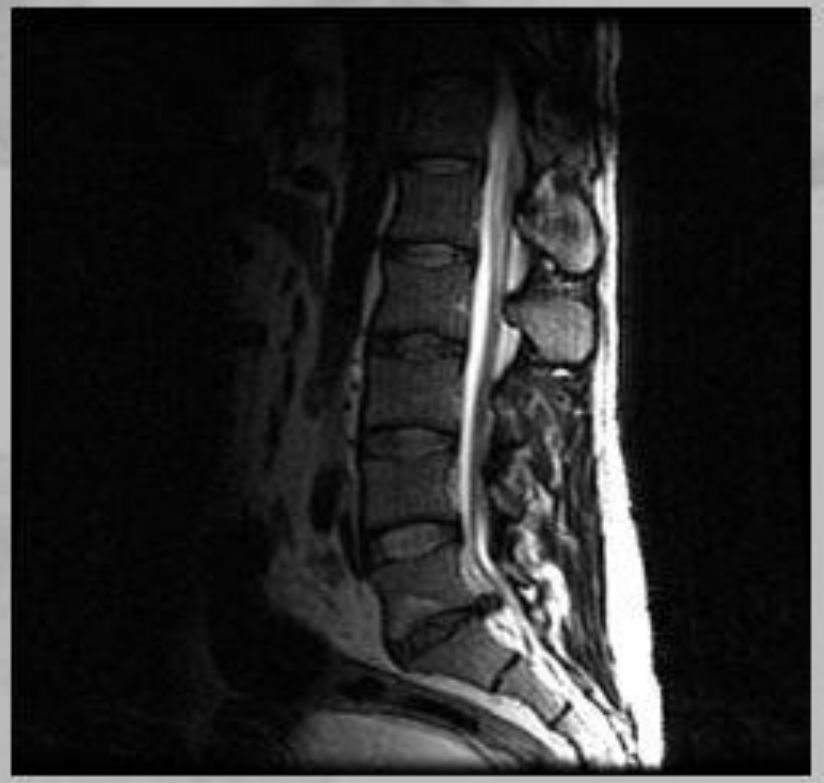
MICHELSON TECHNOLOGY AT WORK

Conclusion

- BMP is a major adjunct in the goal of fusion.
- It is ideal in MAST procedures.
  - Decrease morbidity
  - Decrease hospitalization
  - Optimizes successful fusion even with limited quality graft sources
- I routinely perform MAST TLIF's using BMP anteriorly with local autograft and Capstone cage filled with BMP
  - One pseudoarthrosis in 250 MAST TLIF cases over 4 years

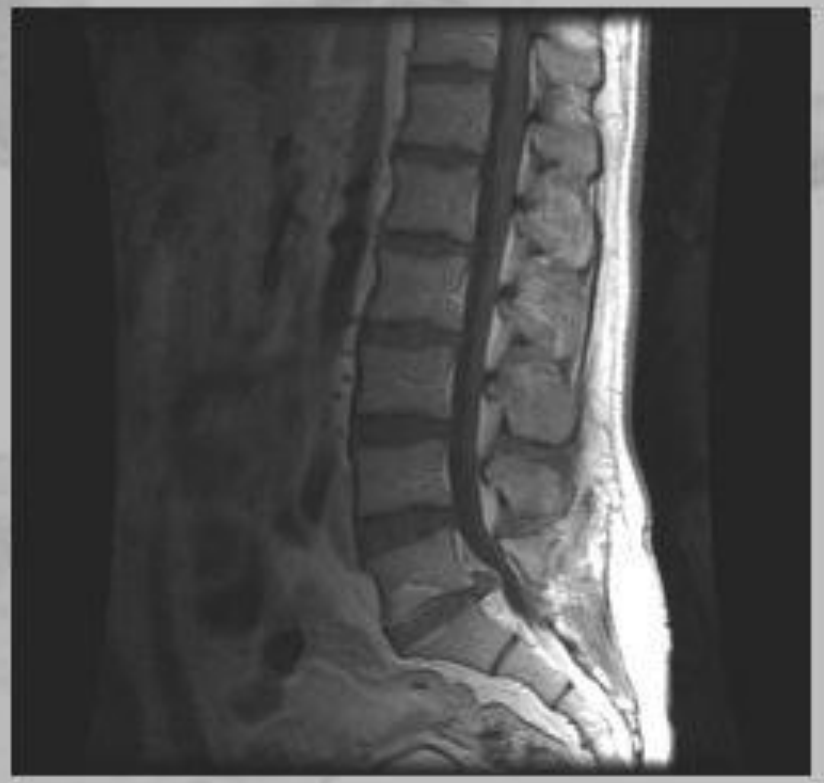
CASE 1

- 36 year old man s/p resection of large left L5/S1 HNP
- Did well for 6 months



CASE 1

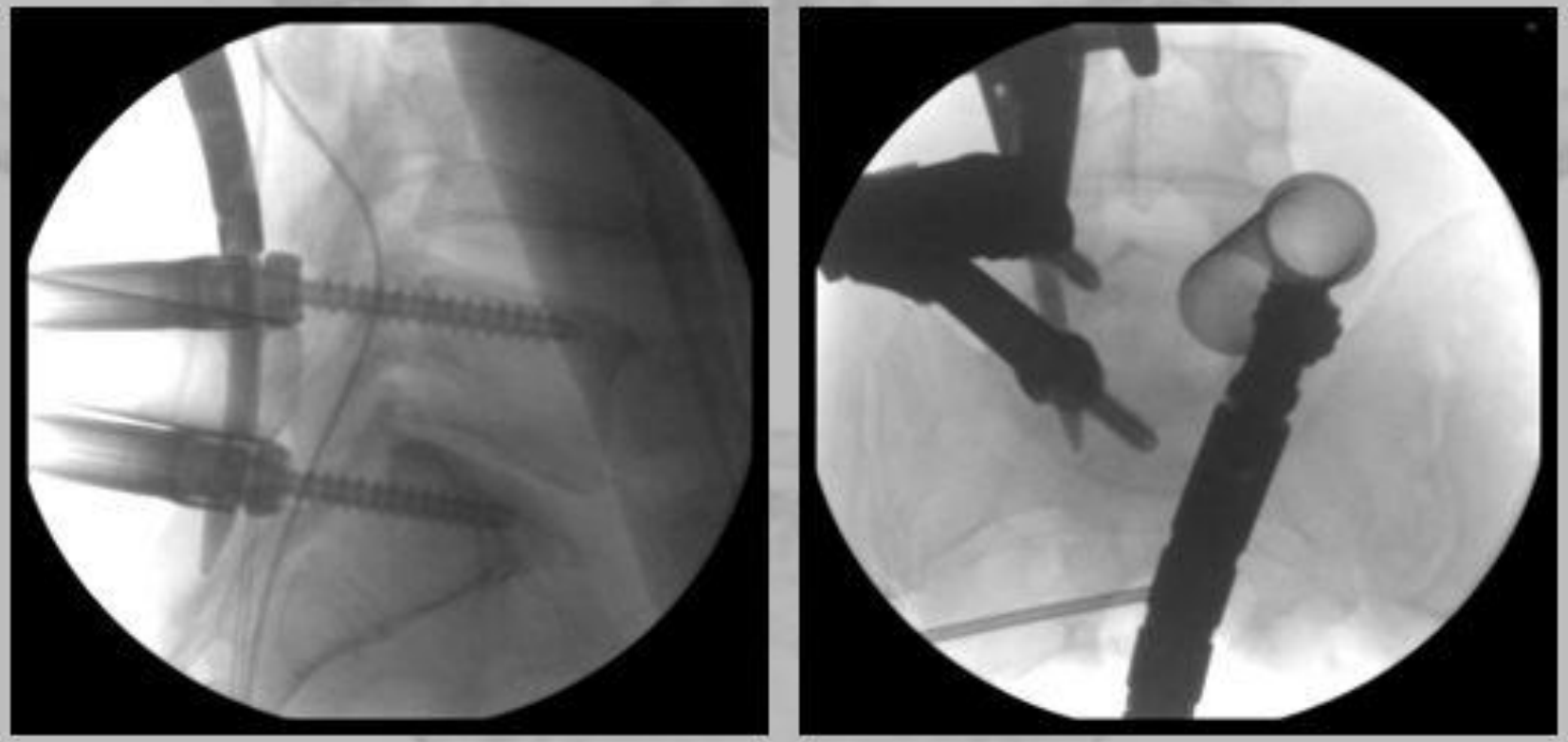
- Developed recurrent LLE pain and significant back pain (50/50)



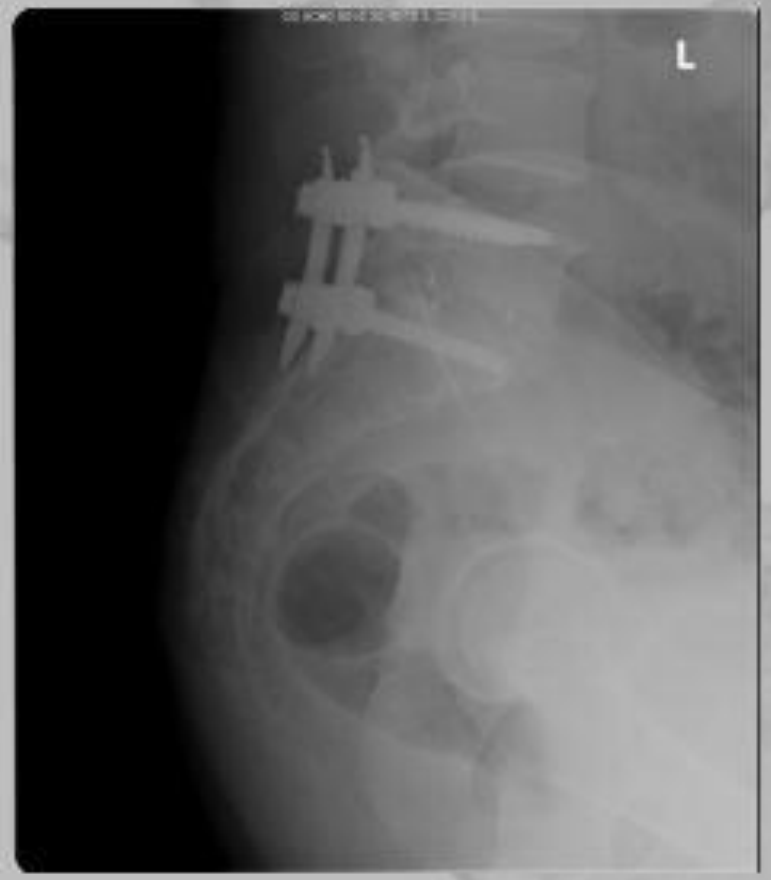
CASE 1

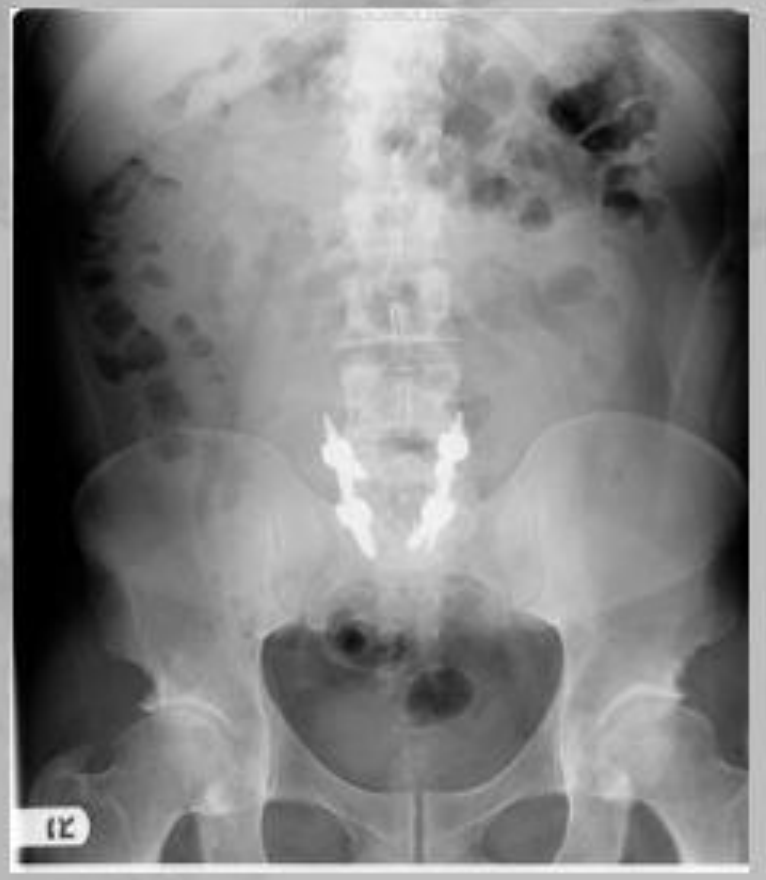
- Failed conservative treatment
- What next?
  - Artificial disc
  - Posterolateral fusion
  - ALIF
  - TLIF/PLIF
  - MAST
- Performed MAST TLIF with resection of HNP and fusion

CASE 1



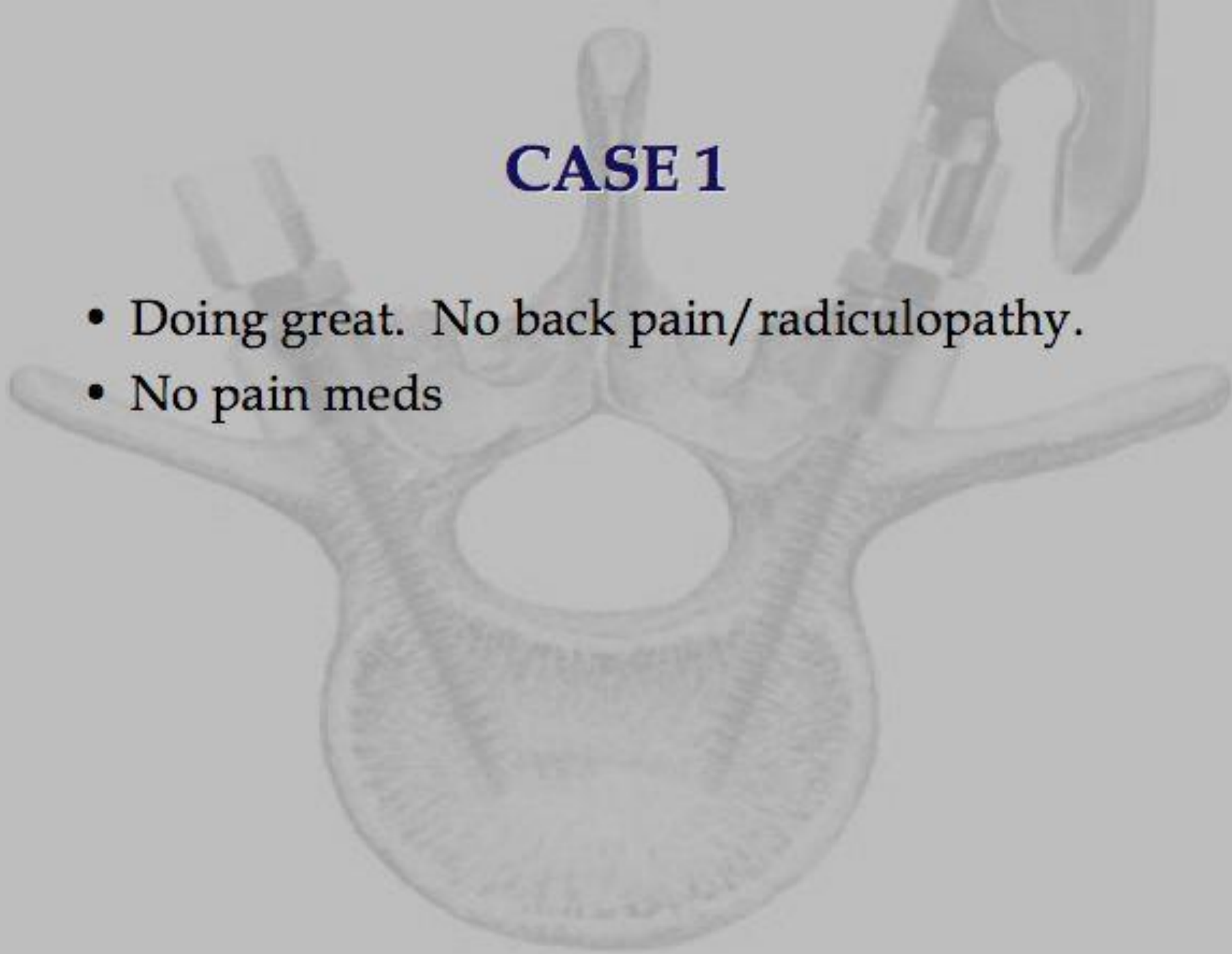
CASE 1





CASE 1

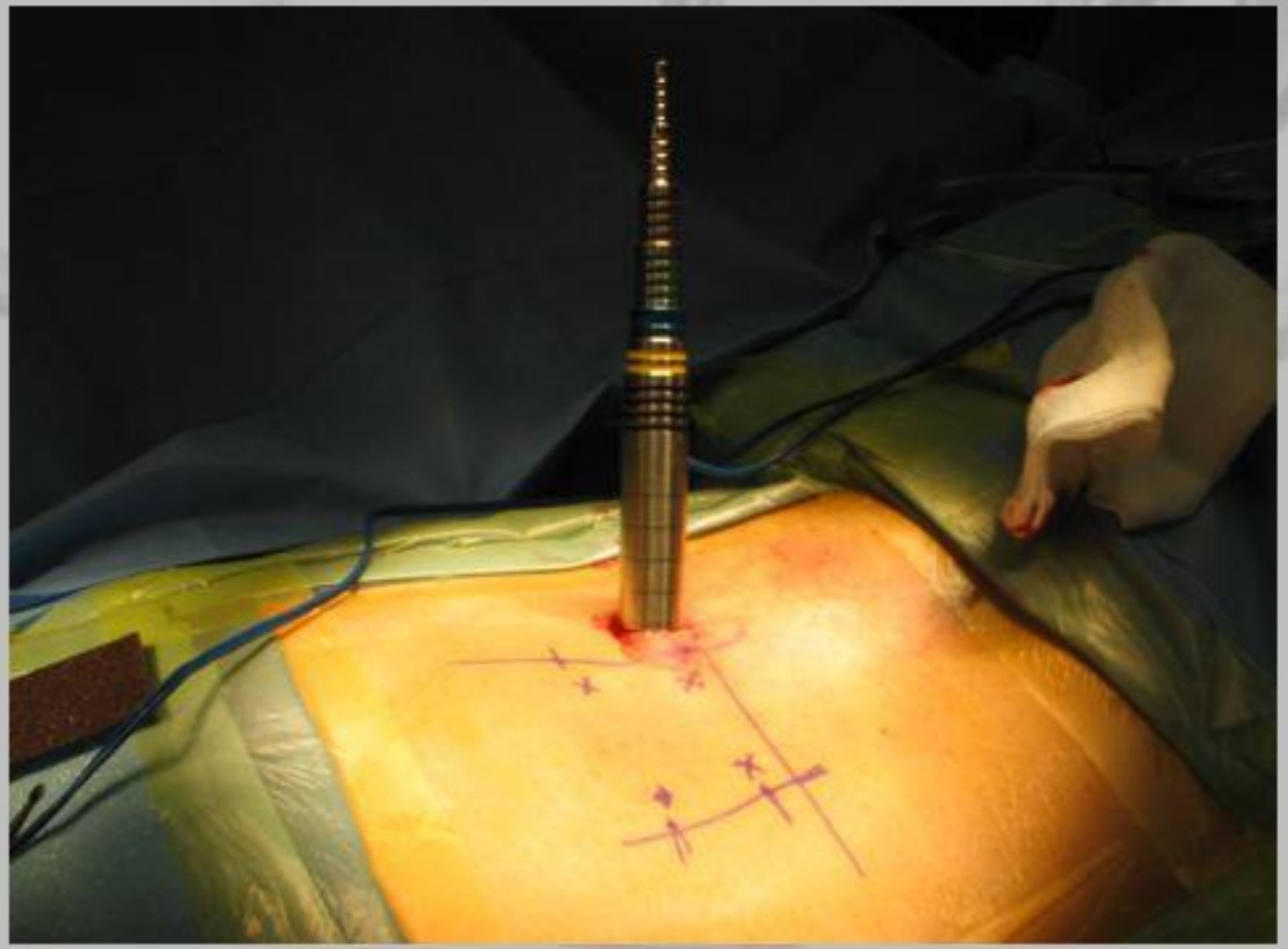
- Doing great. No back pain/radiculopathy.
- No pain meds



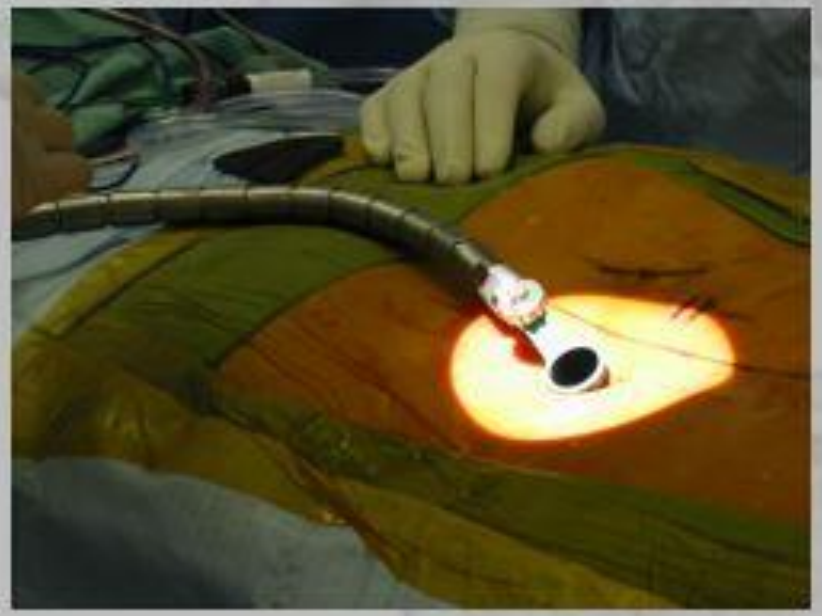
CASE 2

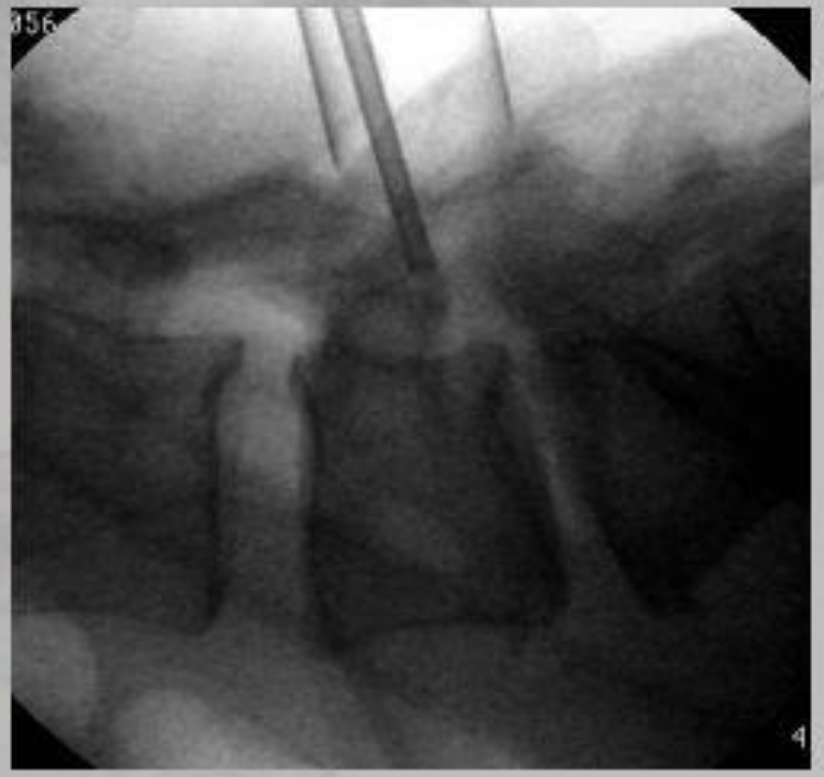
- 55 year old man with Axial LBP only
- Black disc at L5-S1. Other levels pristine
- Concordant pain on discogram
- Failed all conservative tx

CASE 2

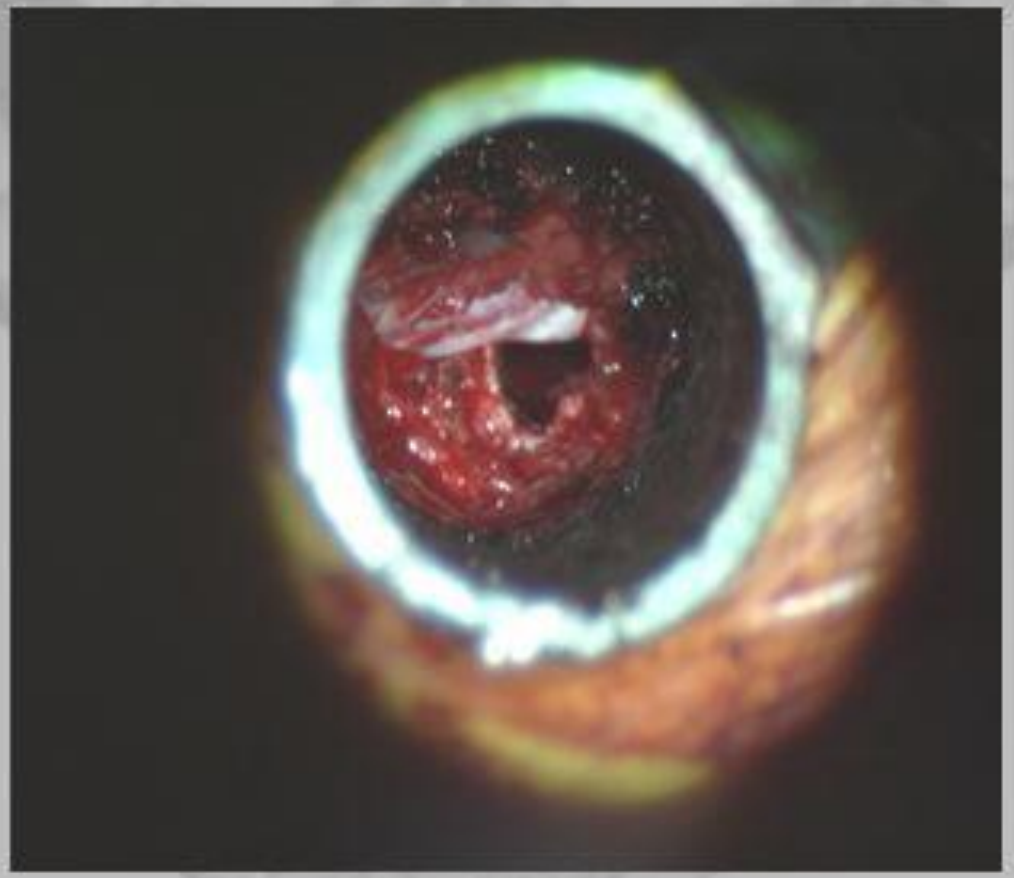


CASE 2





CASE 2



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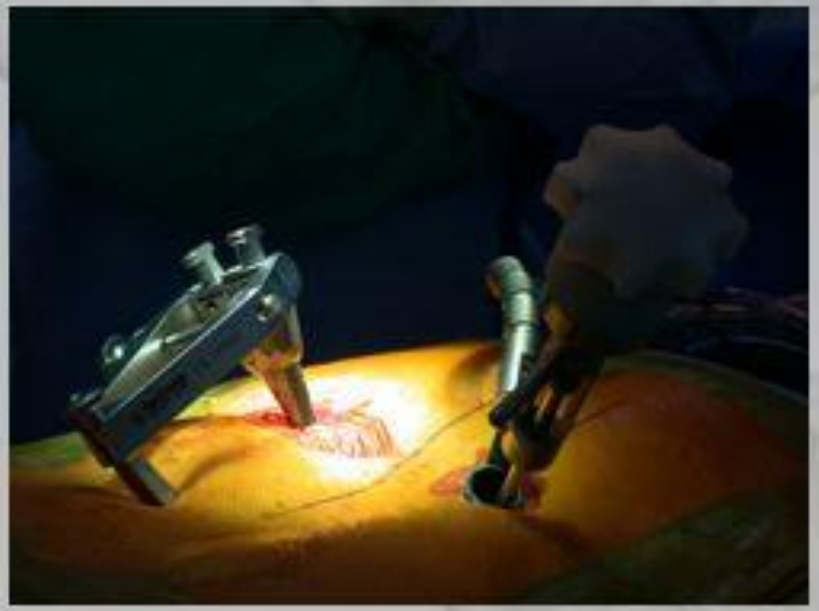

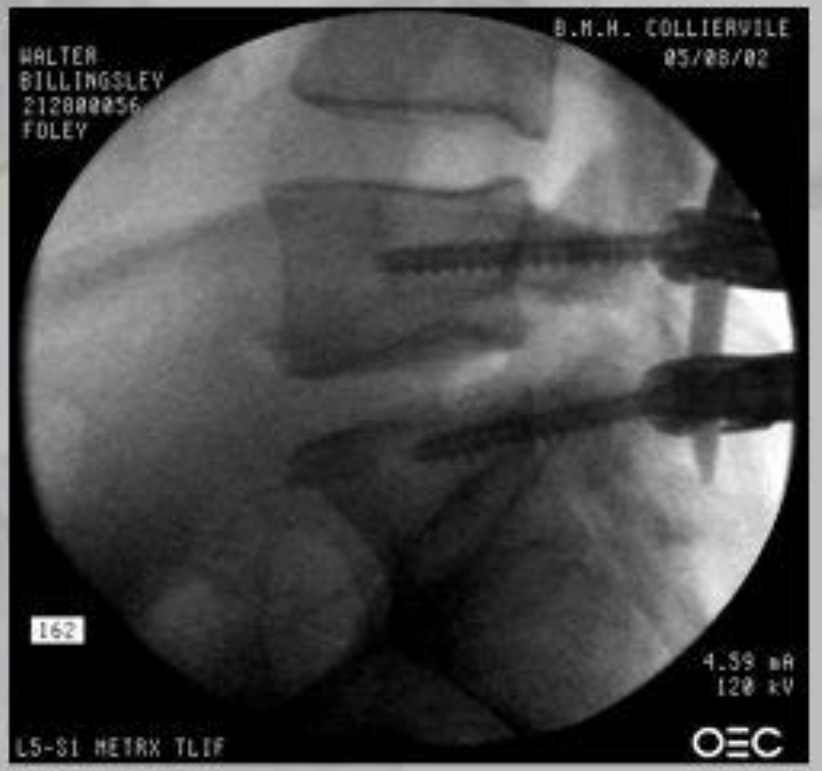
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05/08/02
WALTER
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162
4.59 mA
120 kV
L5-S1 METRX TLIF
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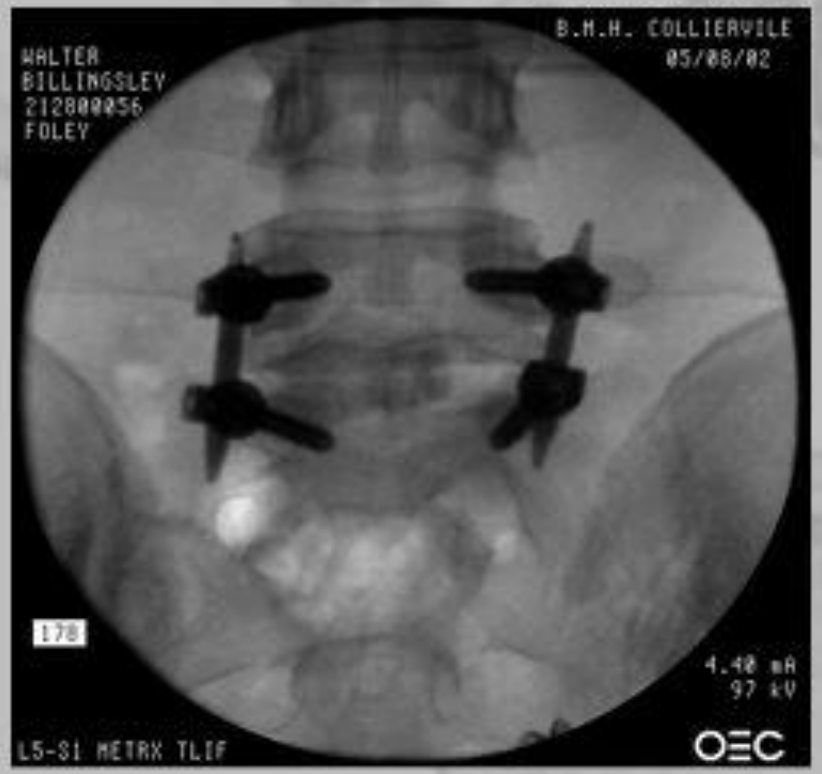
CASE 2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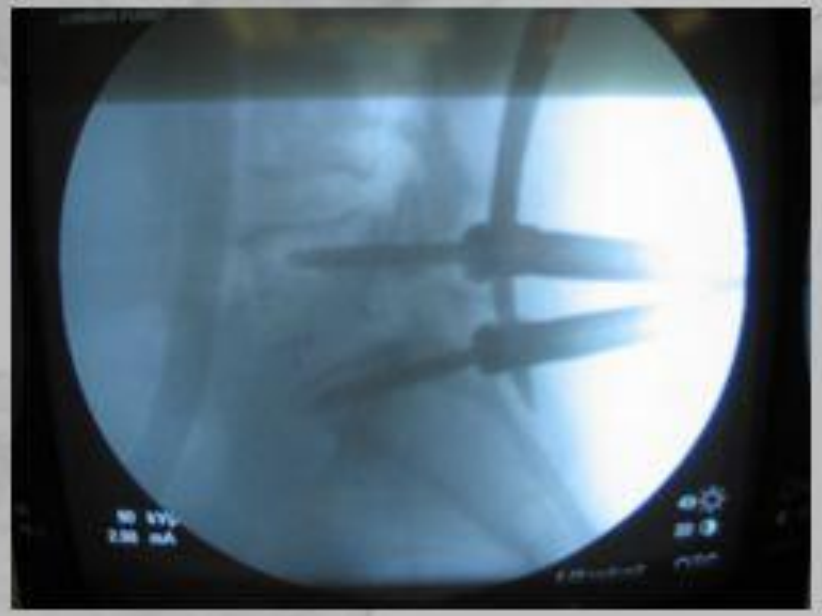

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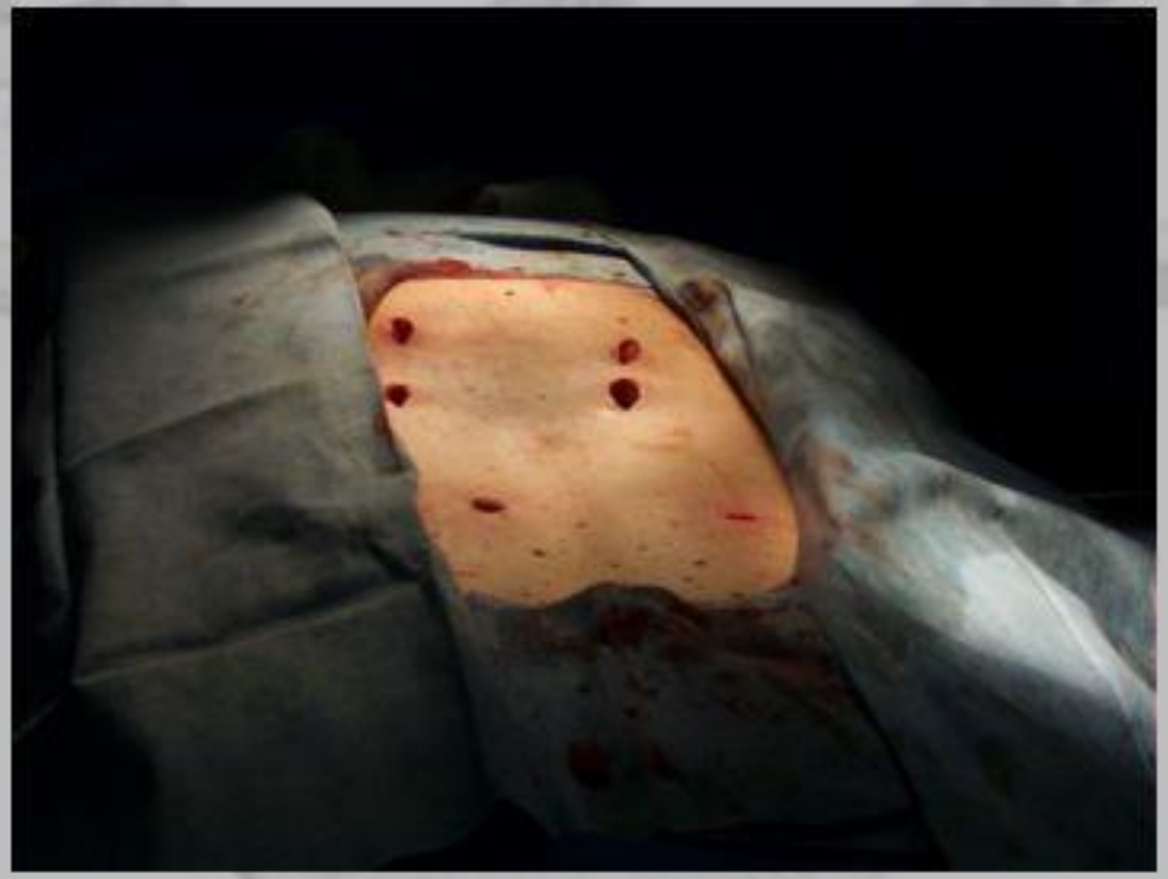


BMP and MAST

- Now some more controversial cases
- We know that BMP allows for faster fusion and better quality boney fusion
- Perhaps the combined use of BMP along with MAST will allow for more successful outcome in high risk or fringe patients

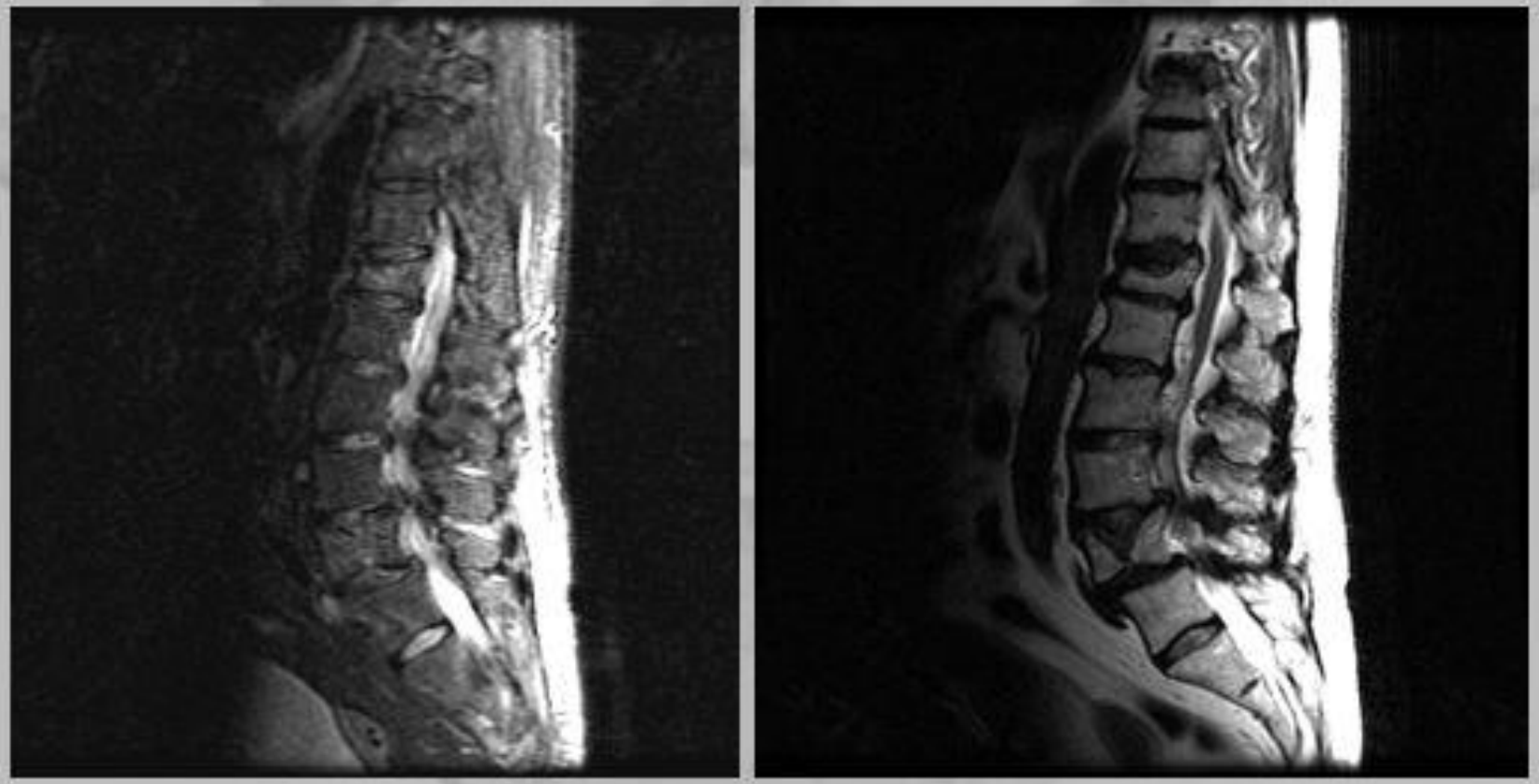
CASE 3

- 60 year old woman with history of prior L4/5 microdiscectomy presents with severe low back pain, neurogenic claudication down the right leg. MRI shows a degenerative spondylolisthesis at L4/5 that reduces on flex/ext. There is severe spinal stenosis at L3/4 and L4/5.
- She fails all conservative treatment.

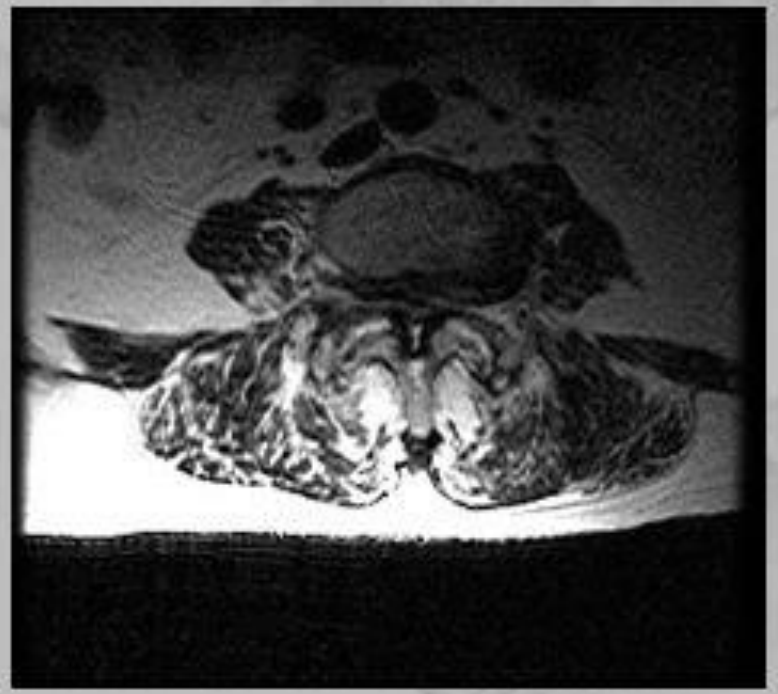
CASE 3

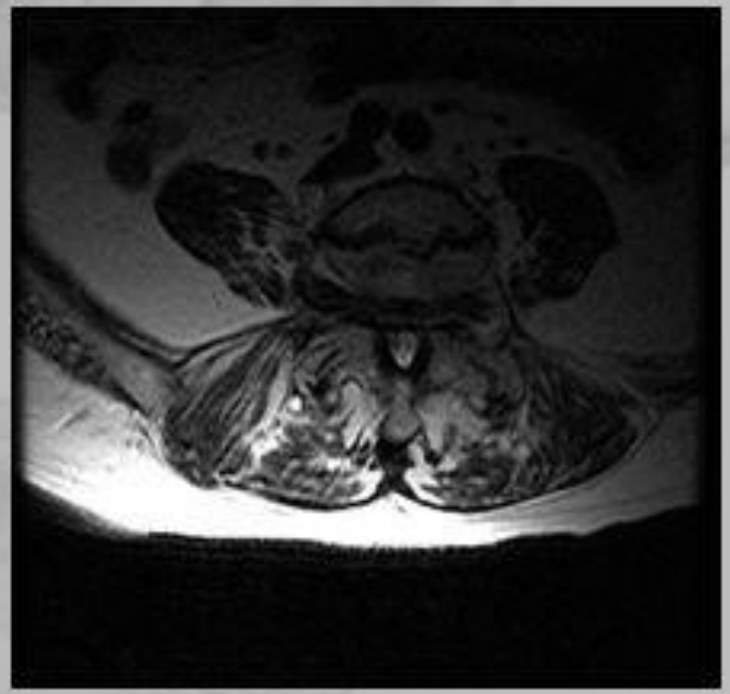
- Before surgery can be arranged, she falls.
- Low back pain is worse.

PRE-OP

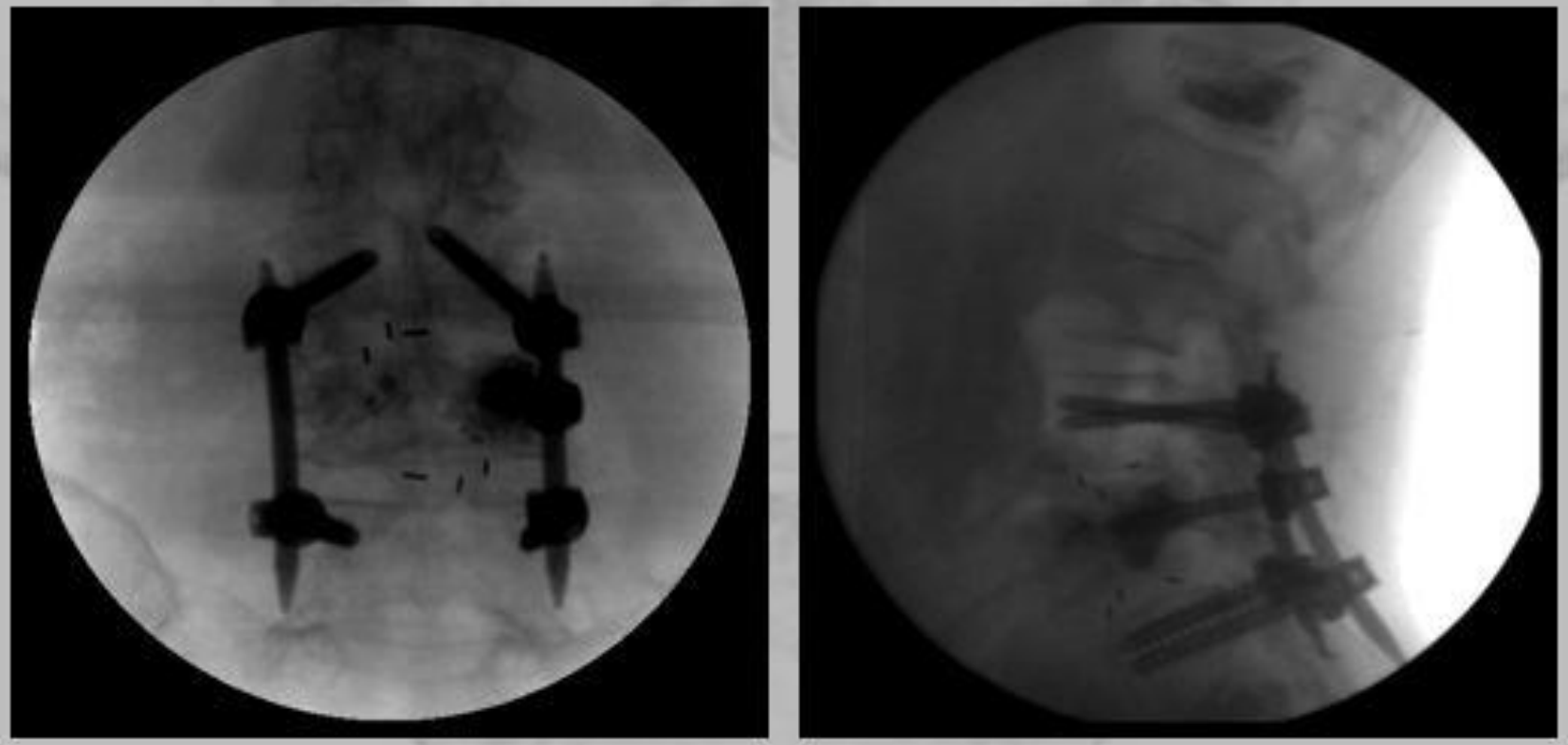


PRE-OP





POST-OP



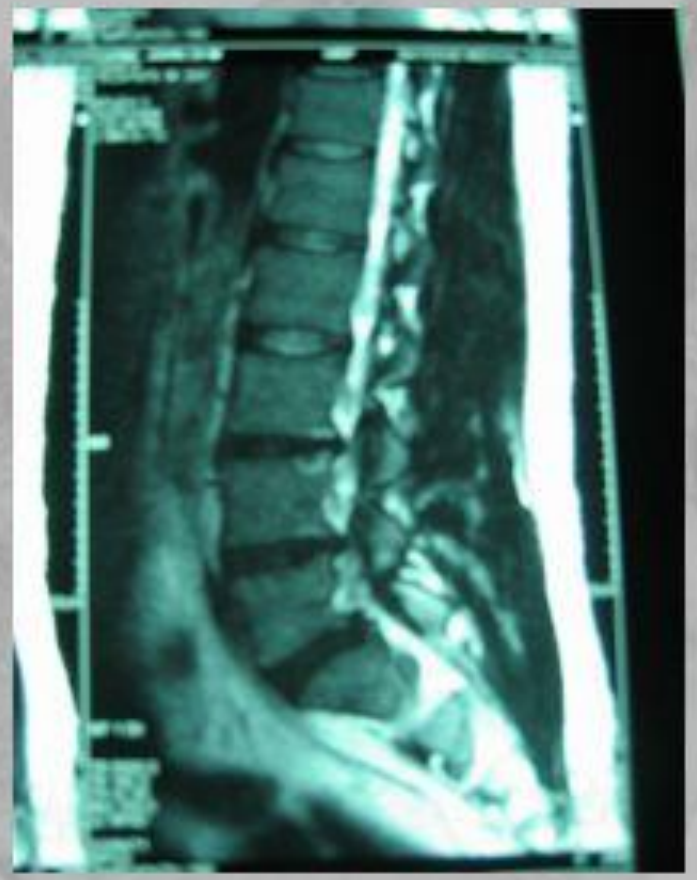
CASE 3

- Key points
  - All minimally invasive
    - Preserved posterior elements and musculature to enhance stability
    - BMP allowed fusion before severe subsidence
      - Postop studies did show subsidence but pt. did fuse and is clinically pain free

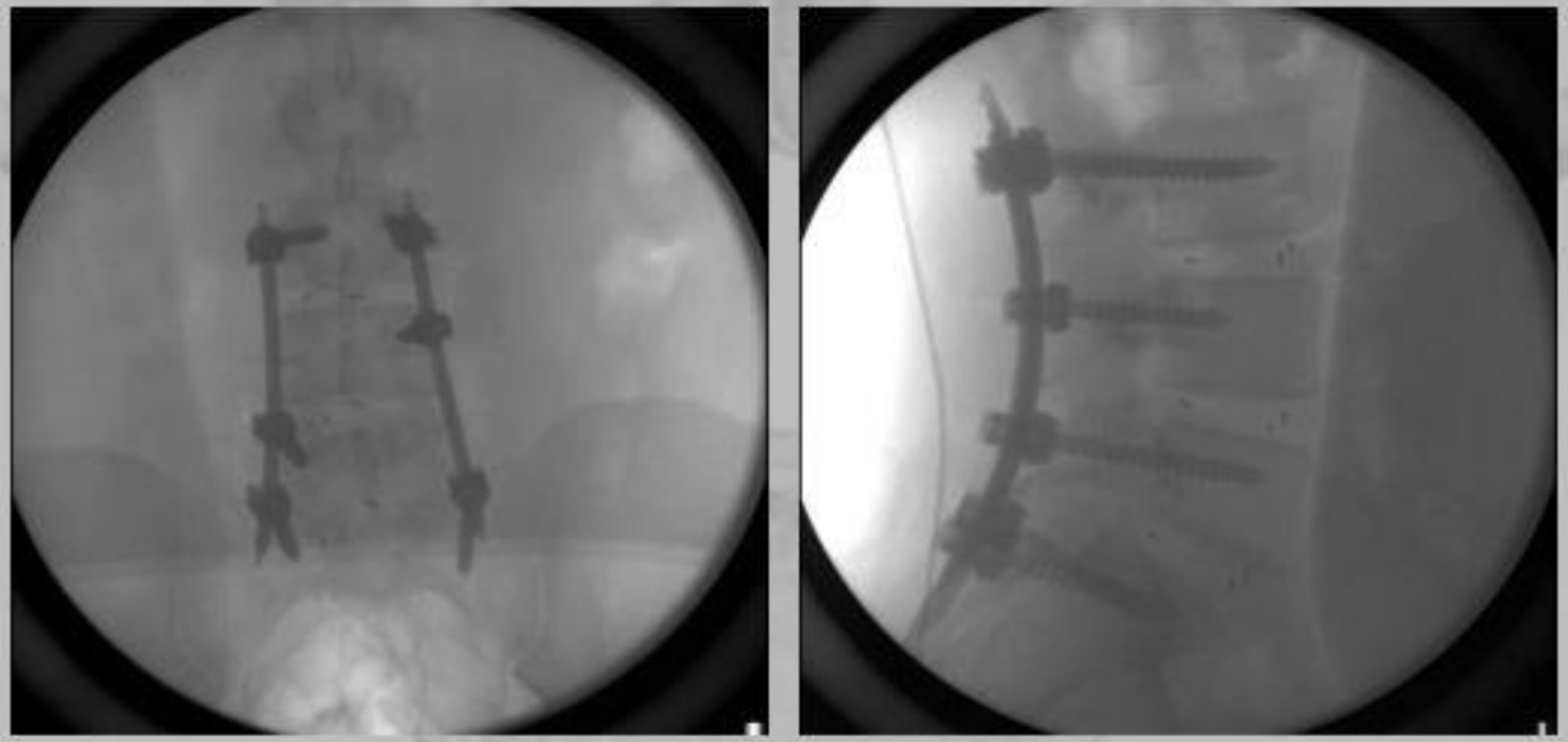
CASE 4

- 29 year old man with isolated low back pain. Can sit/stand for only 10 minutes without experiencing worsening pain. Has failed all conservative treatment.
- MRI with black discs at L3-4, L4-5, and L5-S1
- Concordant pain on all three levels by discogram. Negative control at L2/3

PRE-OP



POST-OP



CASE 4

- BMP and MAST together provides optimal chances of good clinical outcome in a difficult situation
  - No muscle stripping
  - Early ambulation
  - No graft issues

CASE 5

- 38 year old
- Severe LBP only for 4 years
  - Axial
  - Better with lying down
  - Worse with movement

CASE 5

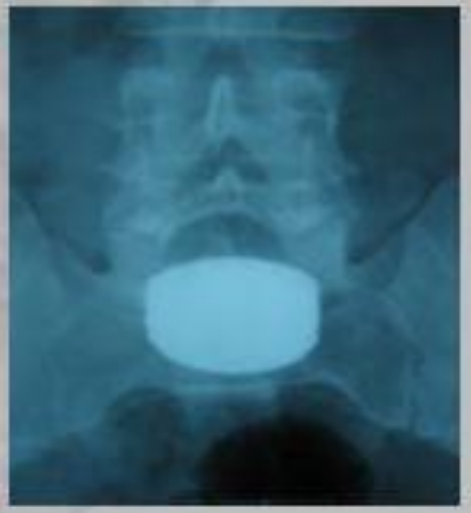
- Failed Physical Tx
- Failed Pain management including:
  - Facet Blocks
  - Epidurals
  - Narcotics
    - Duragesic
    - Percocet
    - Oxycontin/MS contin
    - Vicodin

CASE 5

- MRI DDD at L5-S1
- Normal Flexion/Extension
- Discogram
  - 10/10 Concordant pain at L5/S1
  - Negative controls at all other levels
  - Normal CT

CASE 5

- Charite Disc

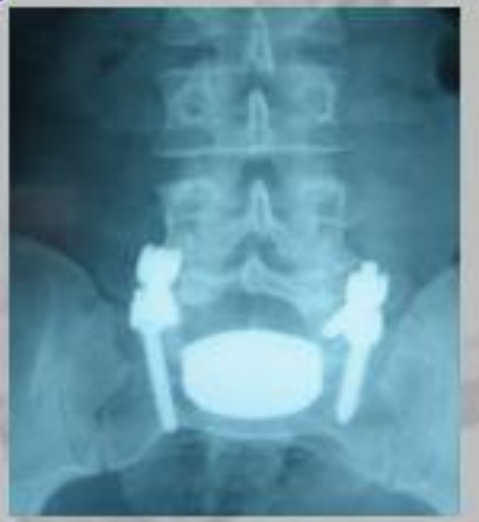


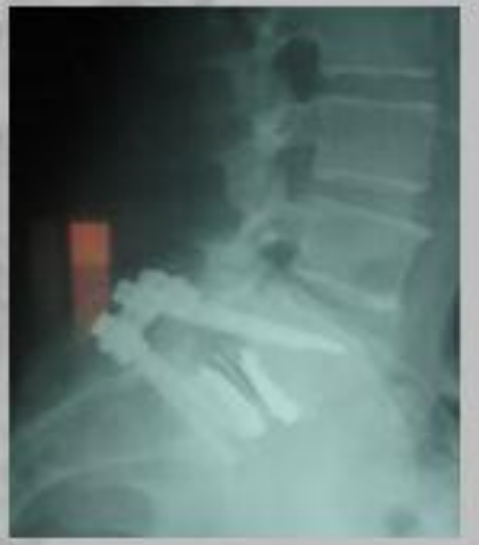
CASE 5

- Mild Improvement over first 3 months.
- Worsening LBP after
  - Better in extension
  - Worse in flexion
- No change in X-Rays?
  - Flex/Ext stable?
- What to do?

CASE 5

- Quadrant pedicle screw fixation and posterolateral fusion using BMP with TLSO brace for 3 months
- Doing well at 4 months with decreasing pain med requirements
- No follow up films yet





CASE 5

- Was this the right approach?
- Maybe not
  - Revisions of artificial discs probably best with removal and anterior fusion
    - Provides Anterior column support
    - But not without dangers of vascular, GU, GI injury
- Will BMP allow me to get a good result using only a posterior lateral fusion?

THANK YOU!