Growth Modulation of the Spine

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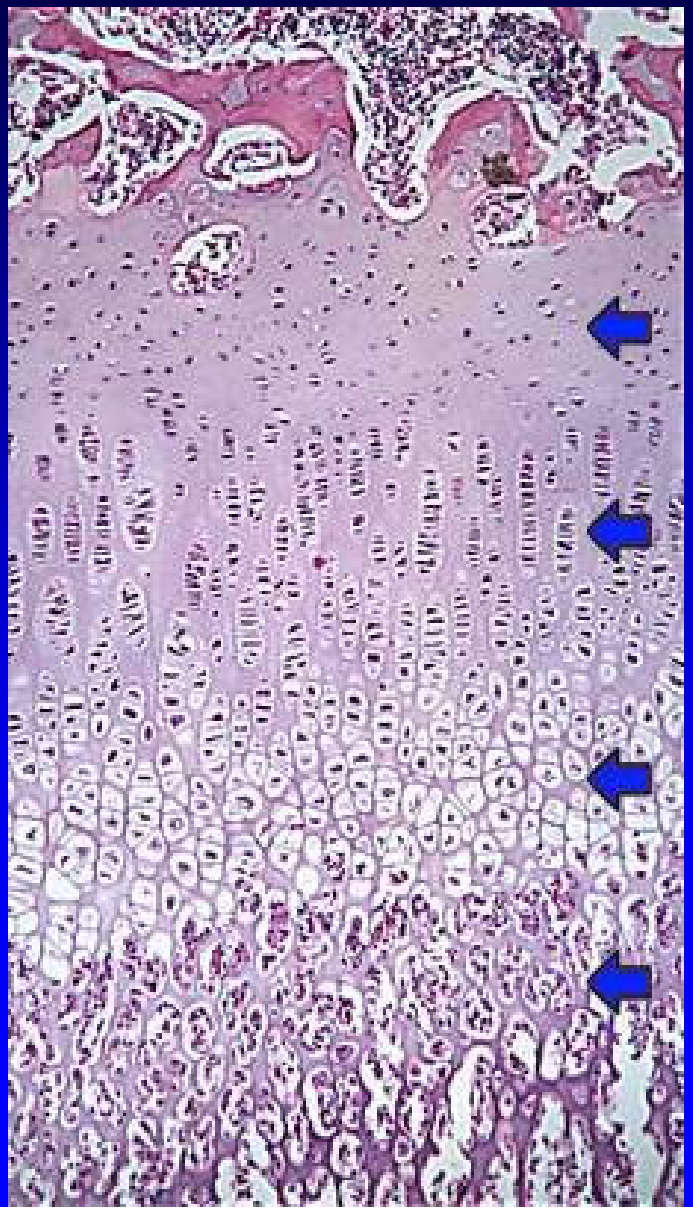
Disclosures & Acknowledgements

- **DePuy Spine: Royalties, Consultant, Research support**
- **EOS Biospace: Research**
- **OREF, POSNA, SRS, CSF: Research support**

UCSD

Rady Children's Hospital

Endochondral Ossification - Physis



Growth

Epiphysis

Resting Zone

Proliferative Zone

Hypertrophic Zone

Trabecular Bone

Metaphysis

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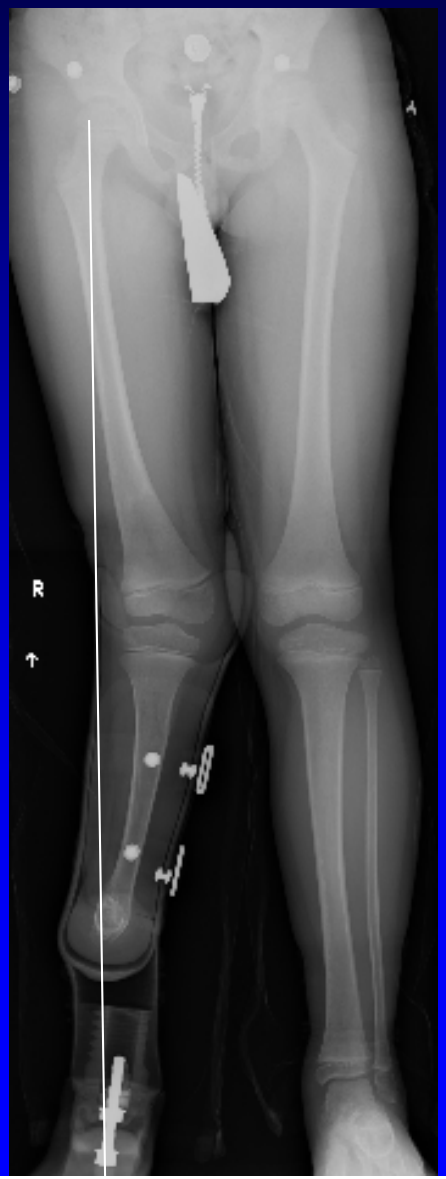
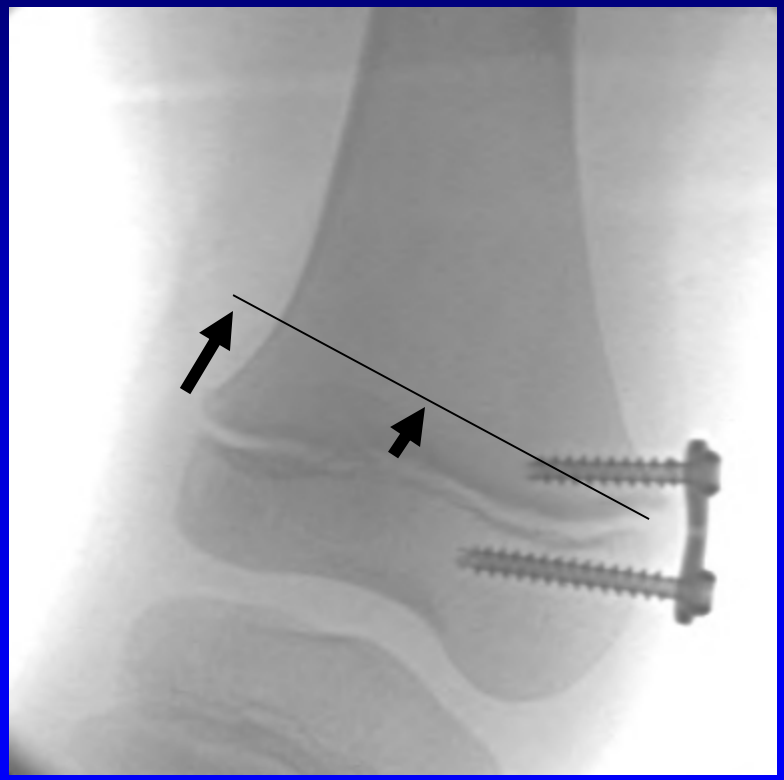
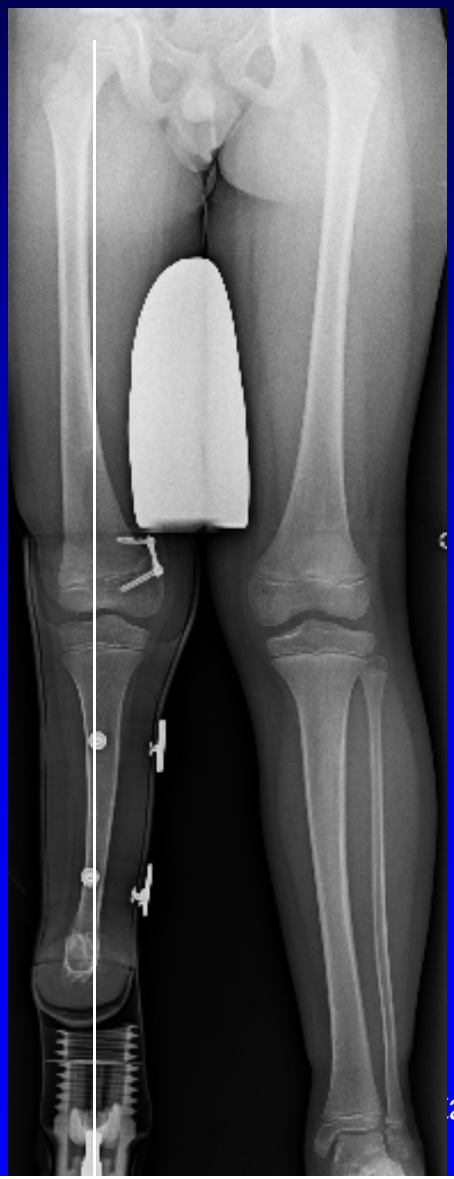
Long Bones…





Dist Femur: 10 mm/yr



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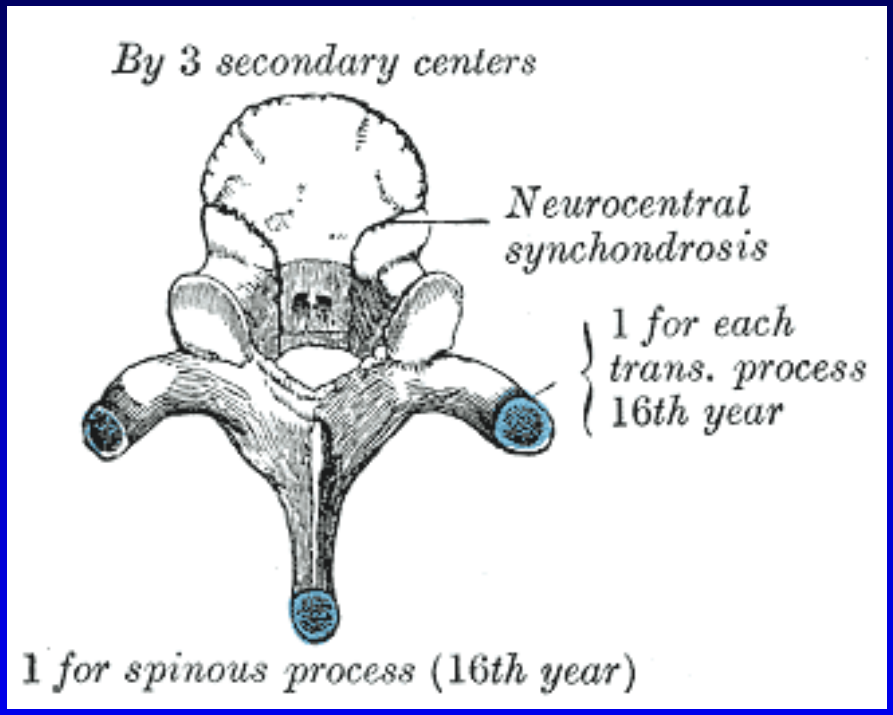
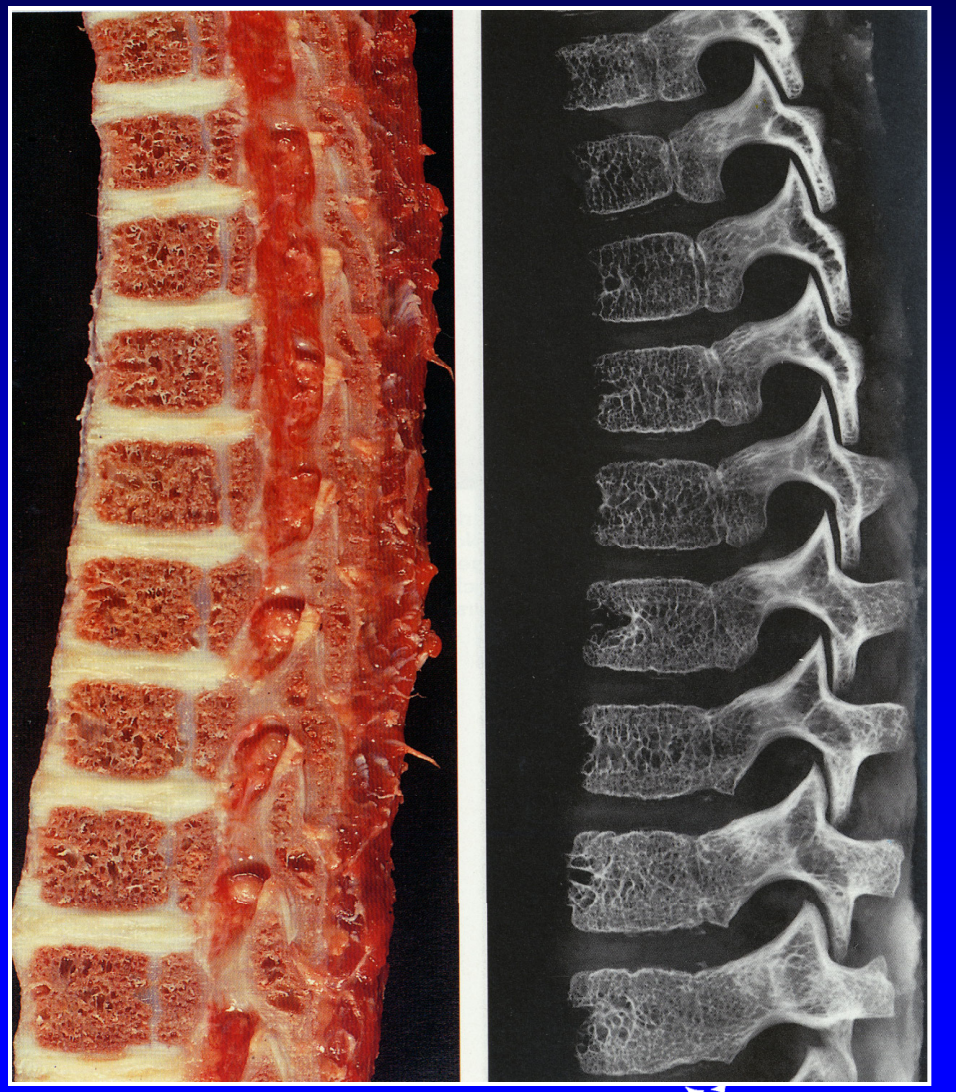
Spinal Growth





Thoracic Vert: 0.7 mm/yr

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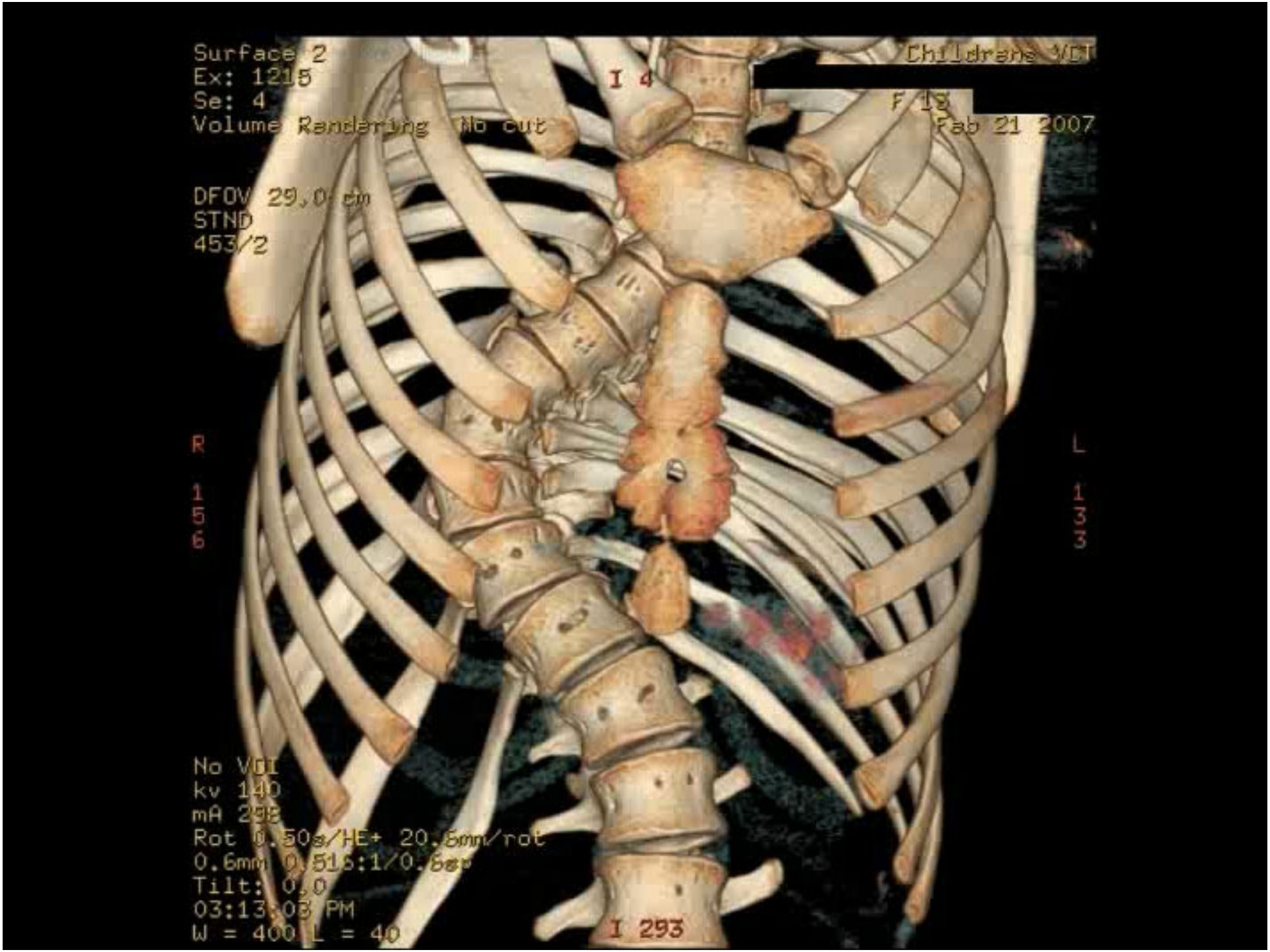
Idiopathic Scoliosis
"Disorder of Growth"

- Too much anterior spine, rotates out of plane to "shorten" the anterior column
- Thoracic curves
- Primary driver of all 3 planes of deformity

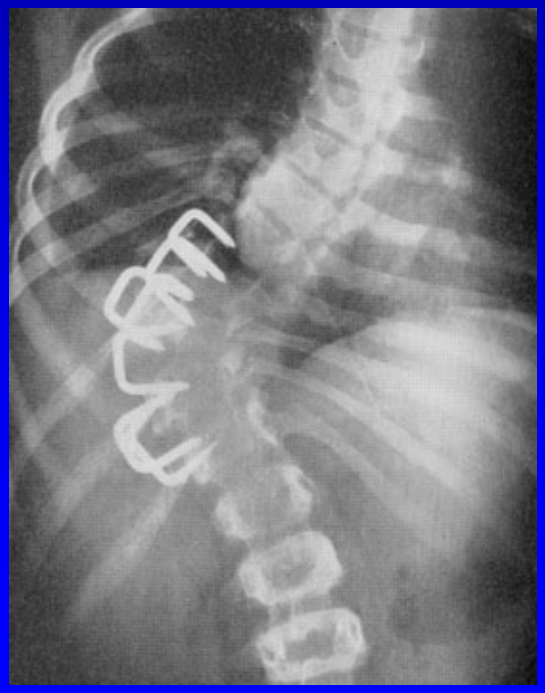

Surface 2
Ex: 1215
Se: 4
Volume Rendering No cut
Childrens MCT
I 4
F 13
Feb 21 2007
DFOV 29.0 cm
STND
453/2
R
156
L
133
No VOI
kv 140
mA 298
Rot 0.50s/HE+ 20.6mm/rot
0.6mm 0.516:1/0.6sp
Tilt: 0.0
03:13:03 PM
W = 400 L = 40
I 293

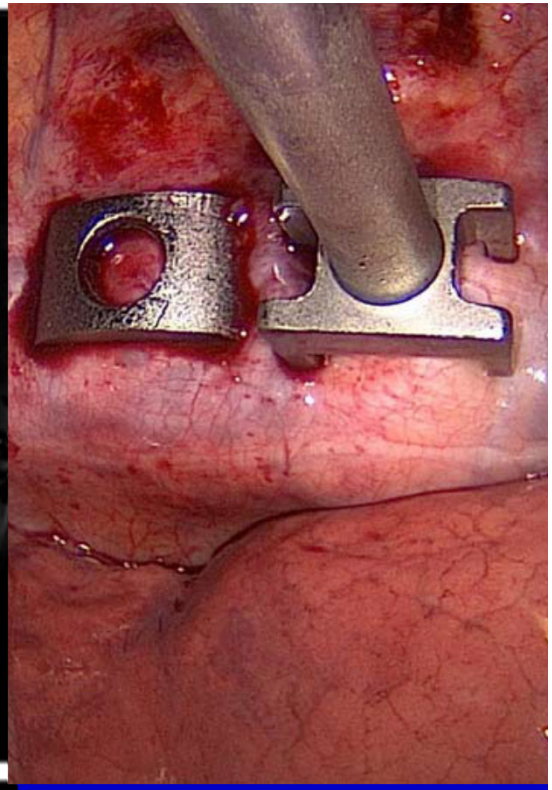
Potential Solutions

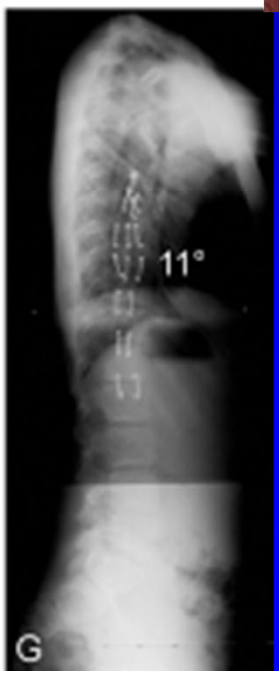
- Shorten the anterior column
- Lengthen posterior column
- Mechanically
- Biologically
- Over time (with growth as the engine…)

Vertebral Staples

- Traditionally used for long bone correction
- Historical results in spine disappointing
- Advances in staple design
- Nitinol – Alloy with shape memory properties



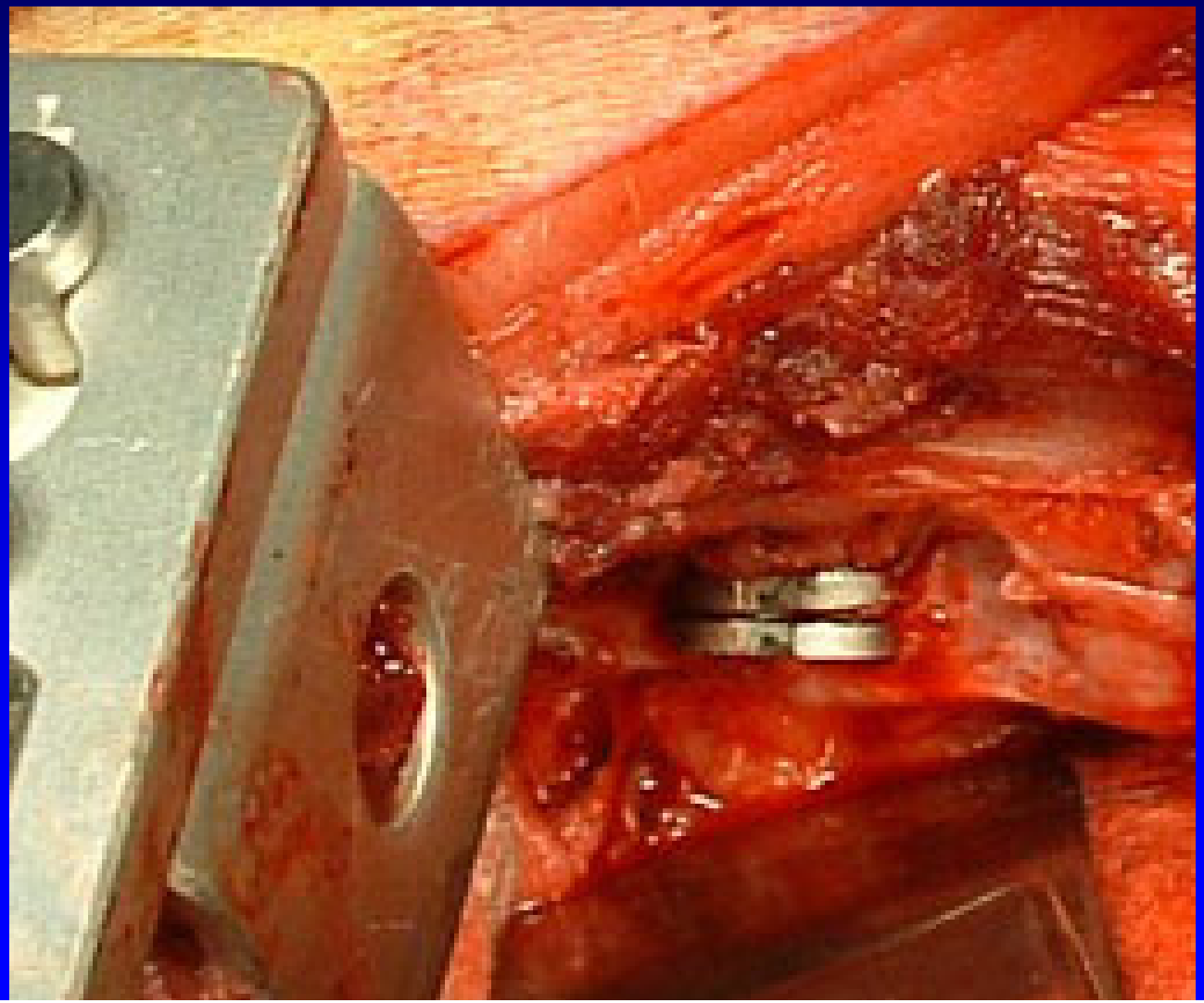


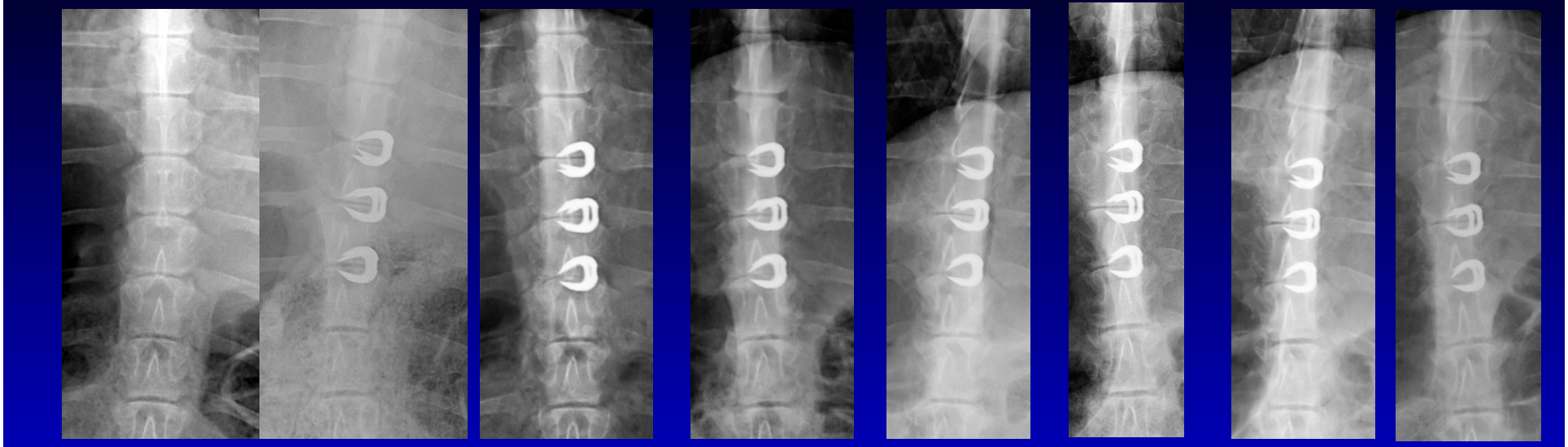


Betz et al.,
Spine 2003

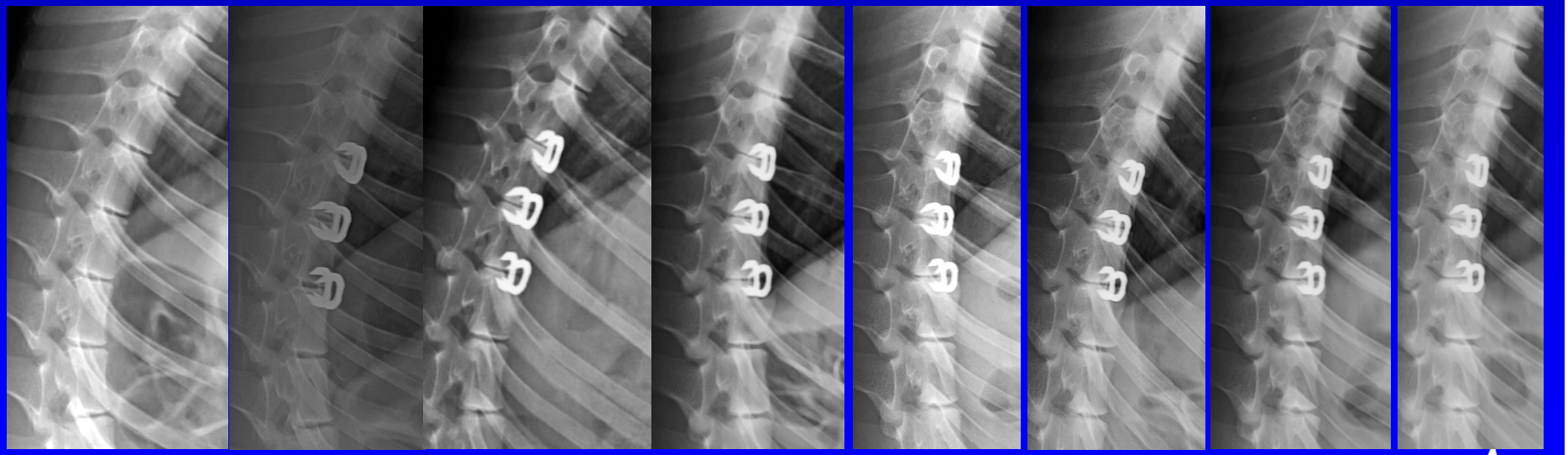
R Betz

Pig Model: Nitinol staples

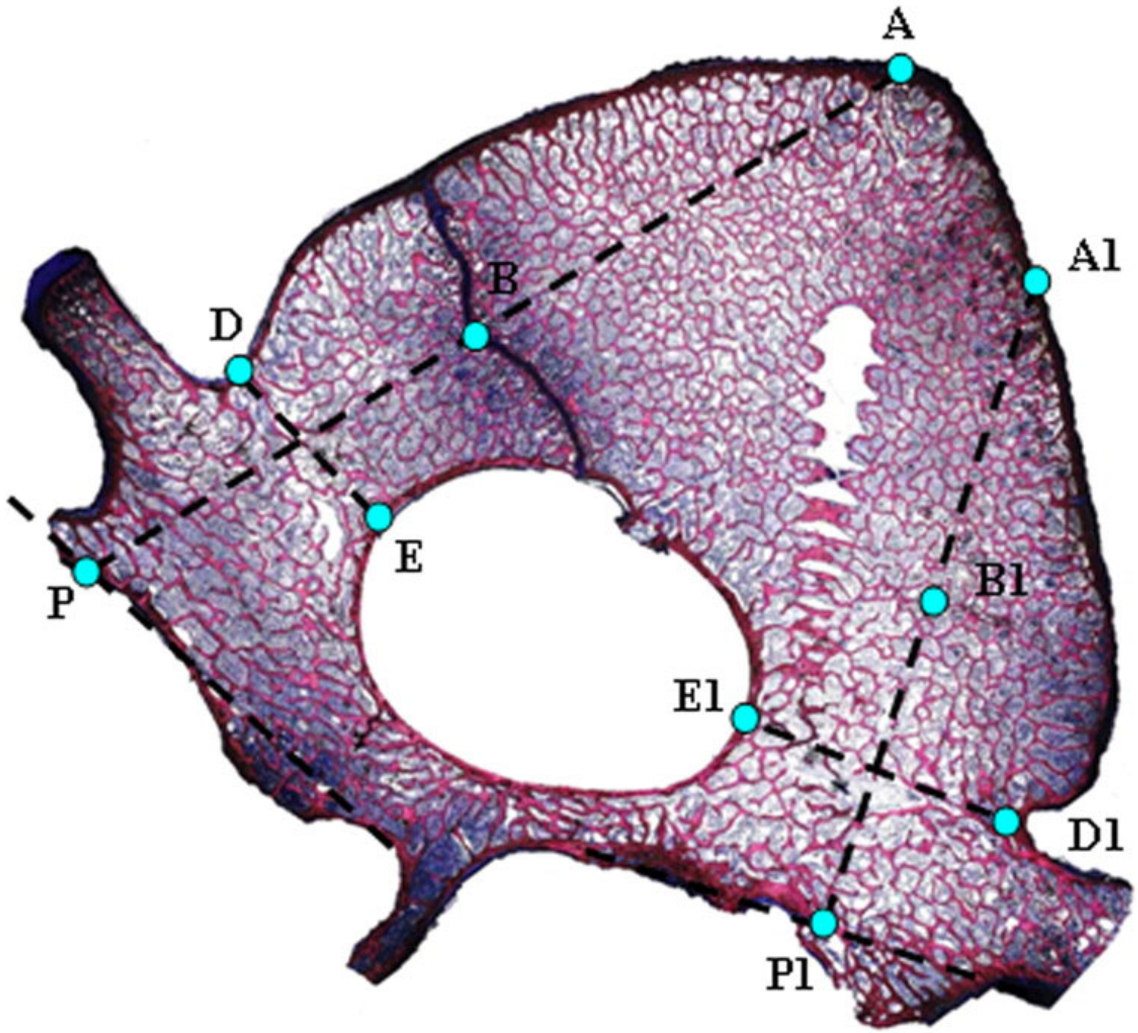




Pre-op Post-op 1 month 2 mos 3 mos 4 mos 5 mos 6 mos



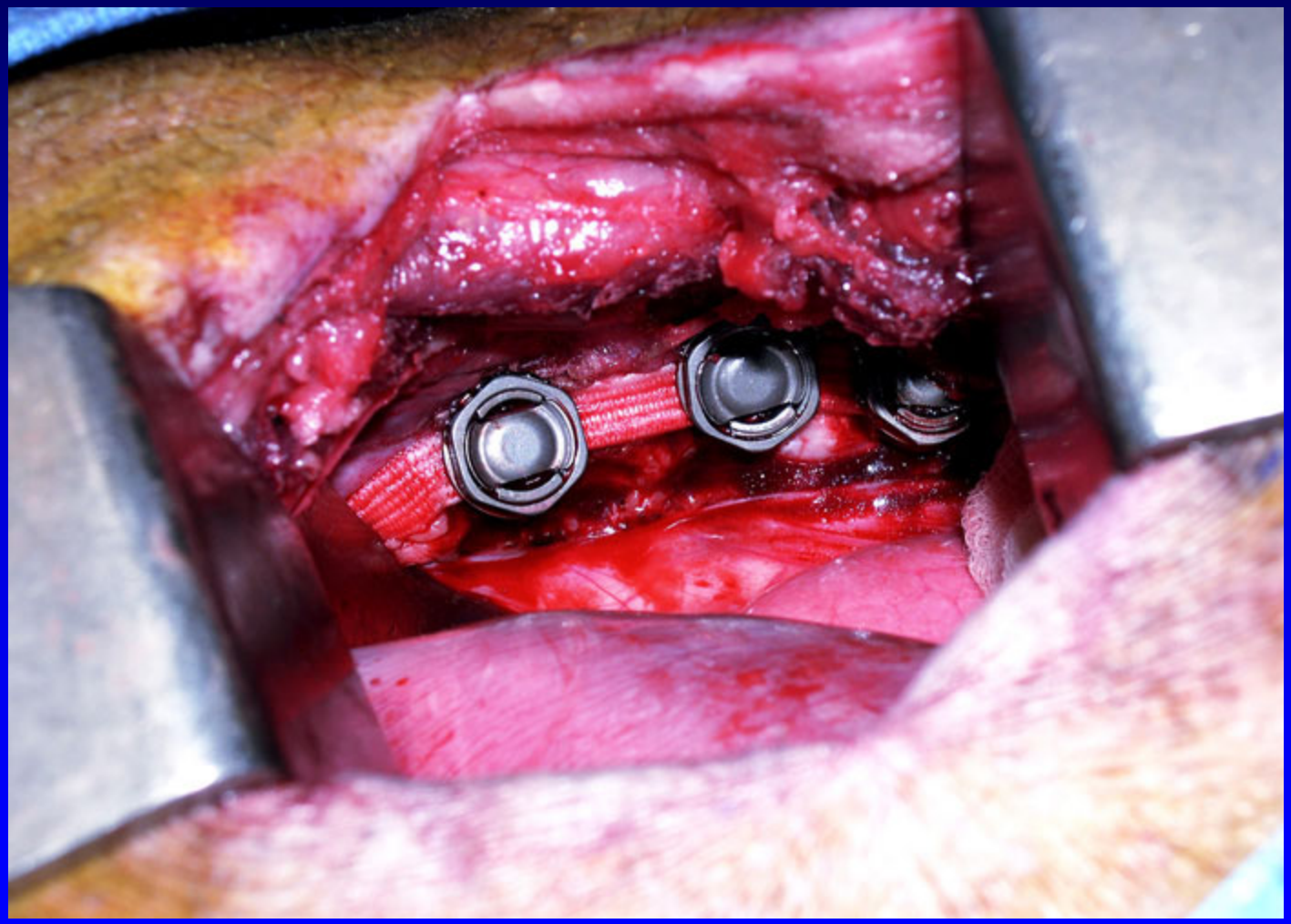
Synchondrosis closure



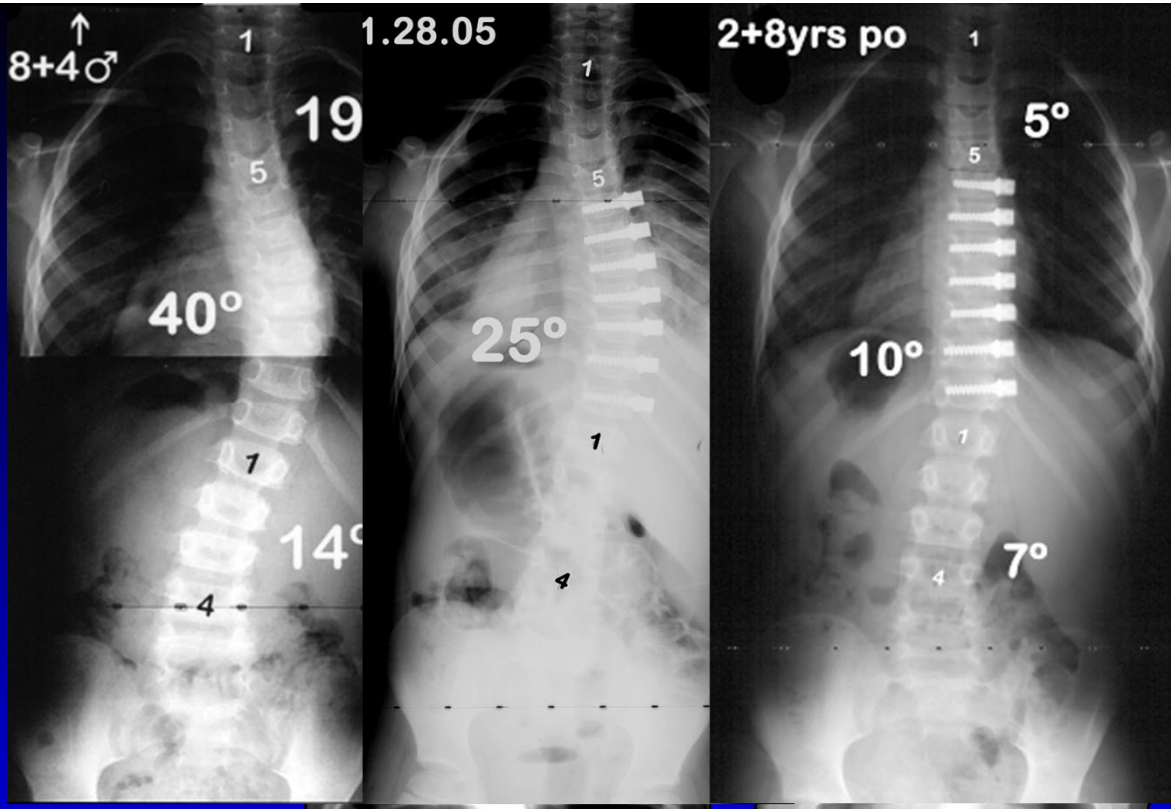
Left
Concavity

Right
Convexity
Screw side

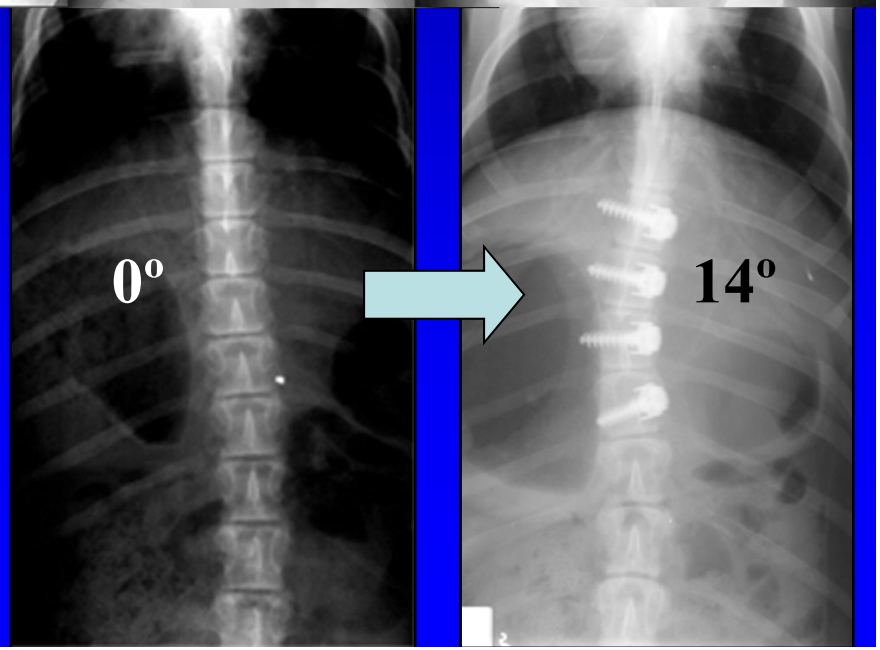
Anterior Spinal Tethering



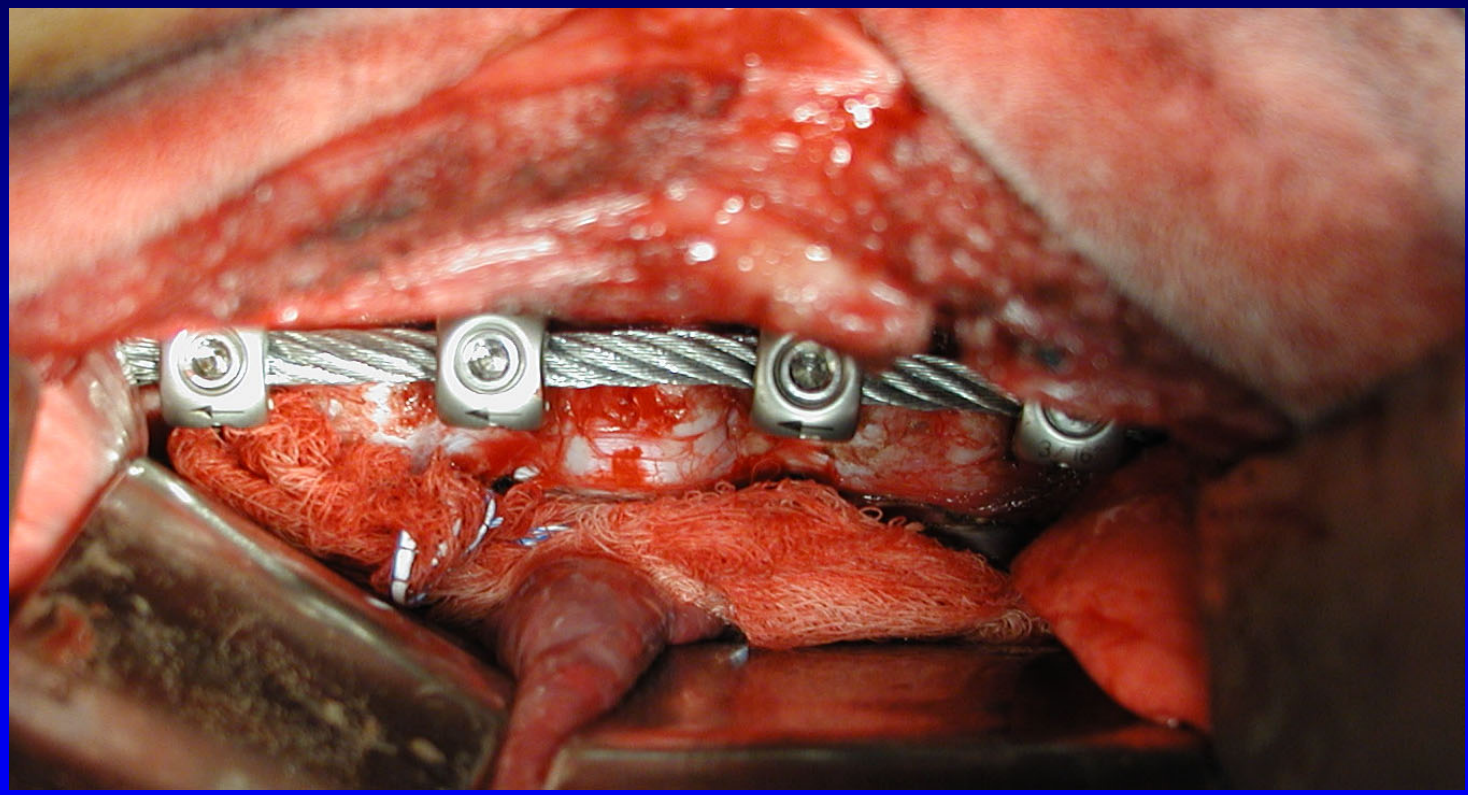
Clinical Application (Lenke case)



Experimental Application

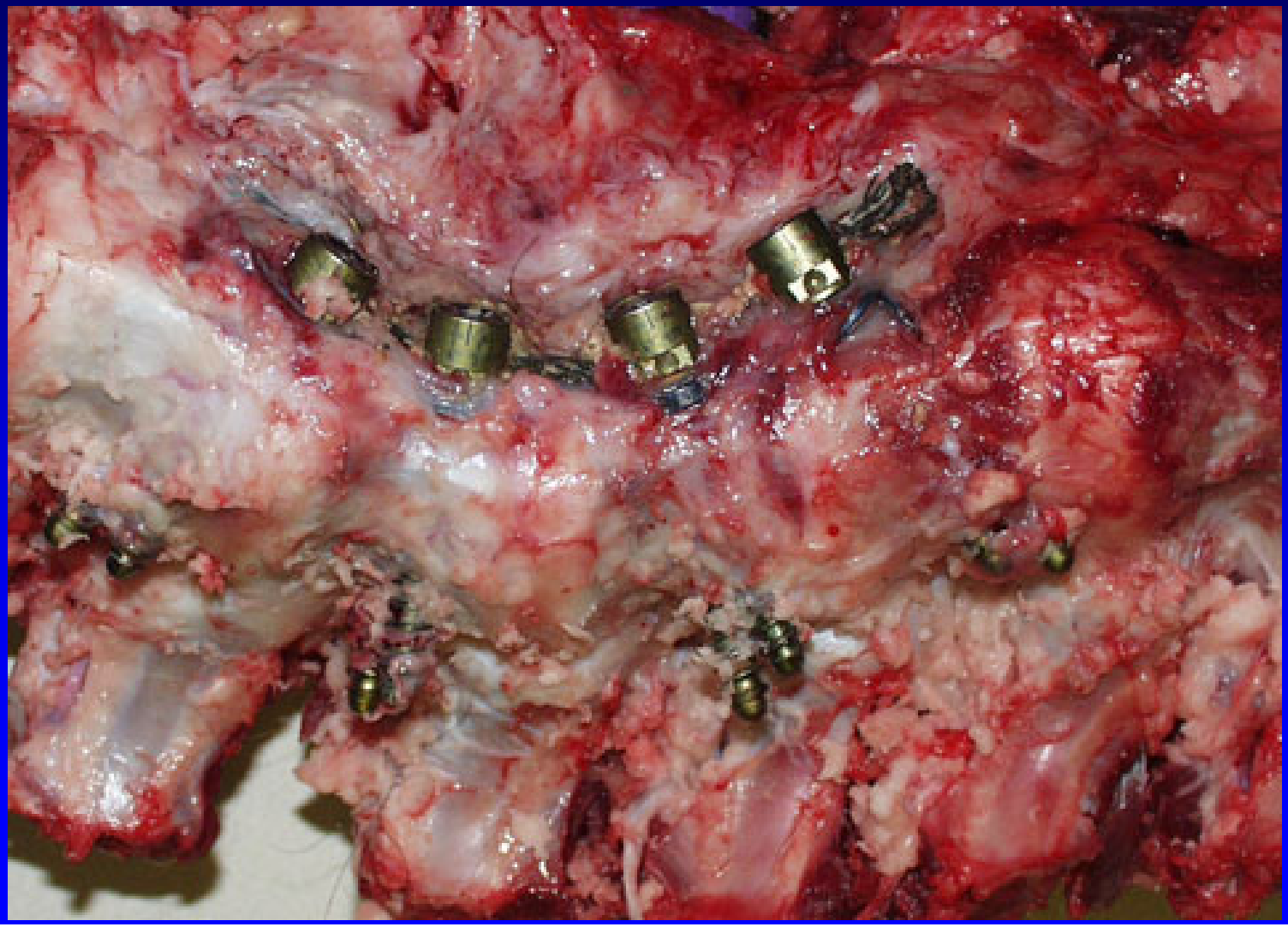


Bovine Model…



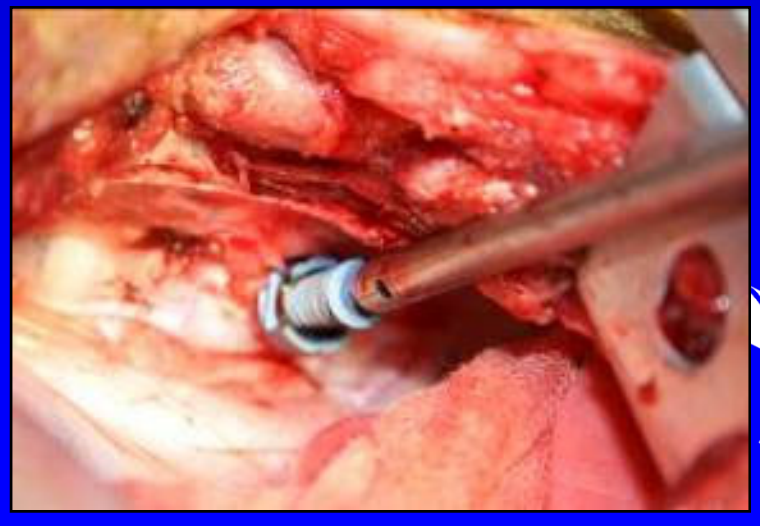
3/16” Cable from Home Depot (1990’s)

Big Deformity, Big Animal



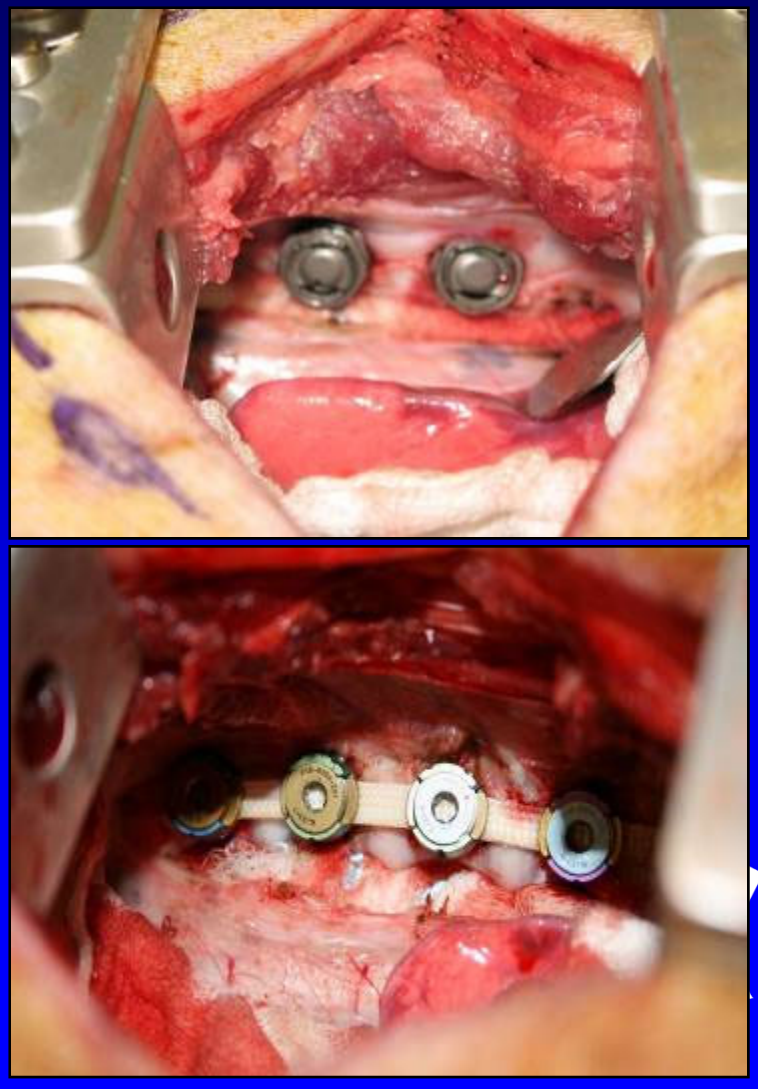
Yucatan Mini Pig Porcine Studies

- Twelve 7-month-old Mini-Pig
- Right sided double thoracotomy
- T8-T11 instrumented



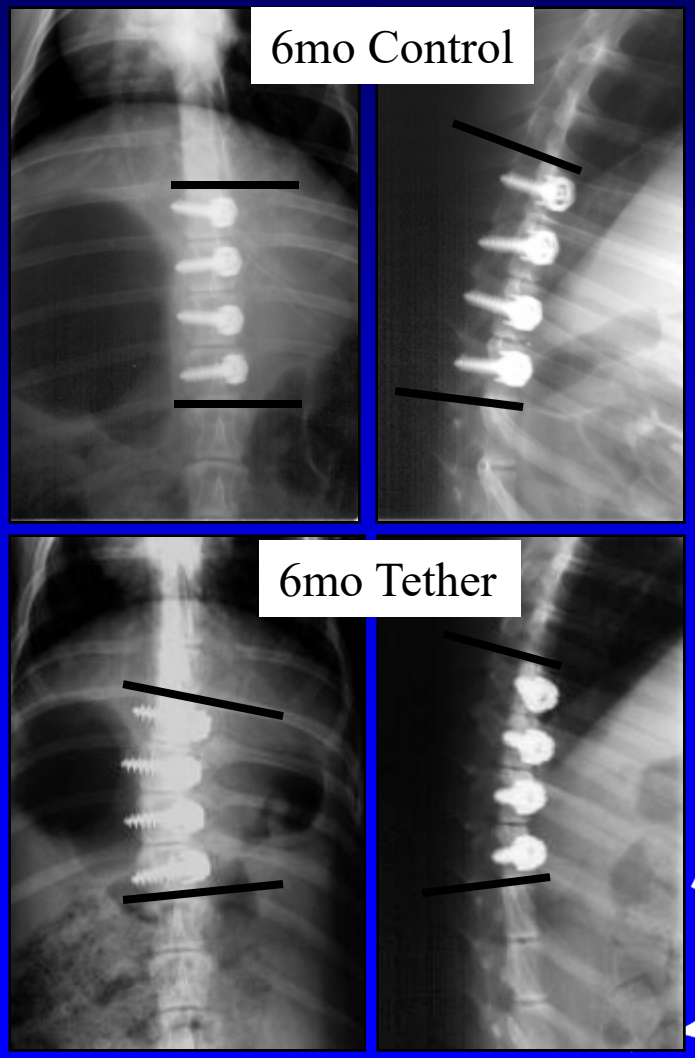
Control vs. Tether Groups

- **Control group (n=6):**
  - Sham surgery with only screws
- **Tether group (n=6):**
  - Tapered screw-staple design with a UHMWPE ribbon
- **6-month survival**



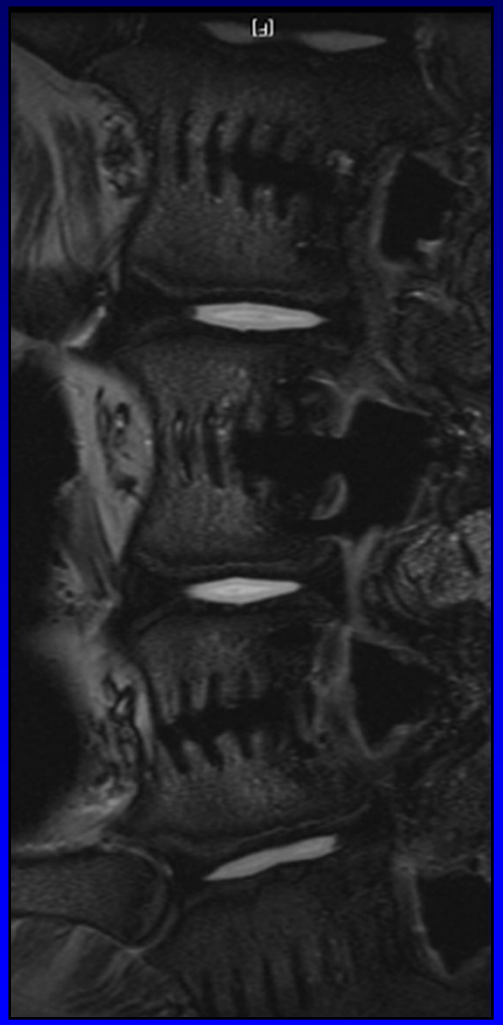
Radiographic Analysis

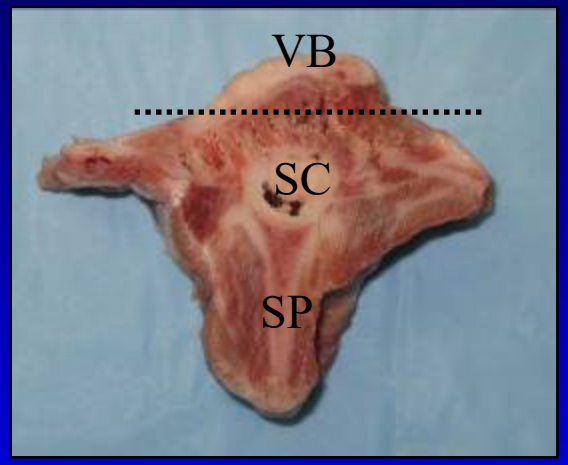
- **Assess deformity creation**
- **Radiographs**
  - Coronal Cobb
  - Sagittal Cobb
  - Vertebral body wedging
  - Intervertebral disc wedging
- **Computed Tomography**
  - Vertebral body and intervertebral disc heights
  - Vertebral body rotation

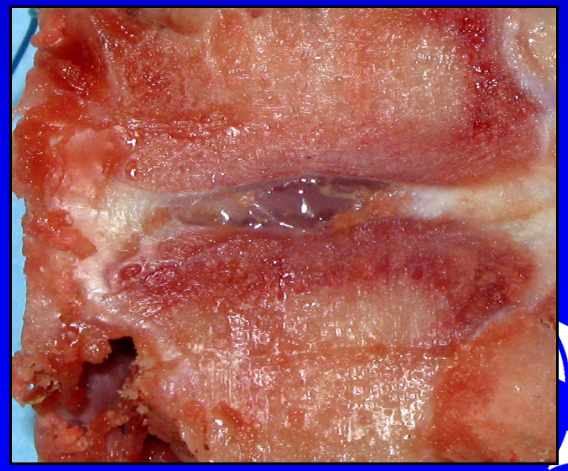


Qualitative Analysis

- **Magnetic resonance imaging**
- **Gross morphology**

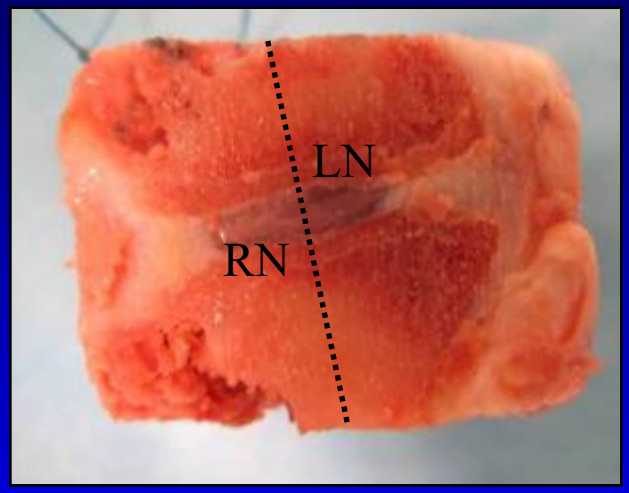


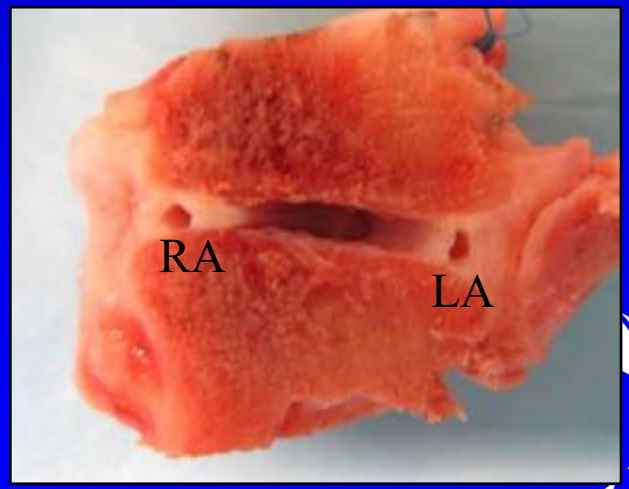




Biochemical Analysis

- **Percent Water**
- **Proteoglycan content (GAG assay)**
- **Collagen content (hydroxyproline assay)**
- **Cell Density (DNA assay)**

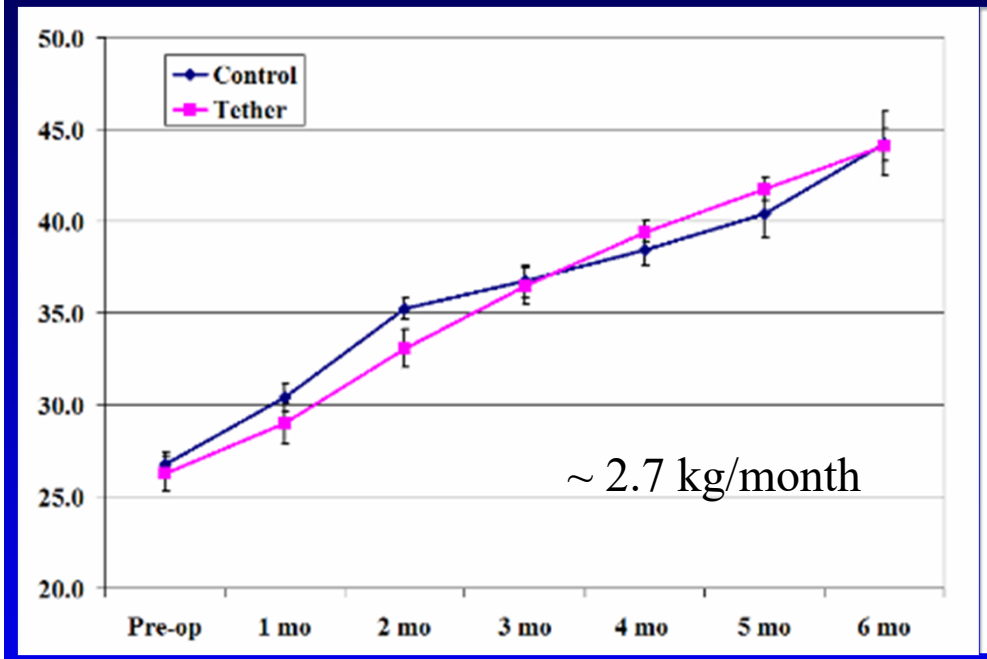


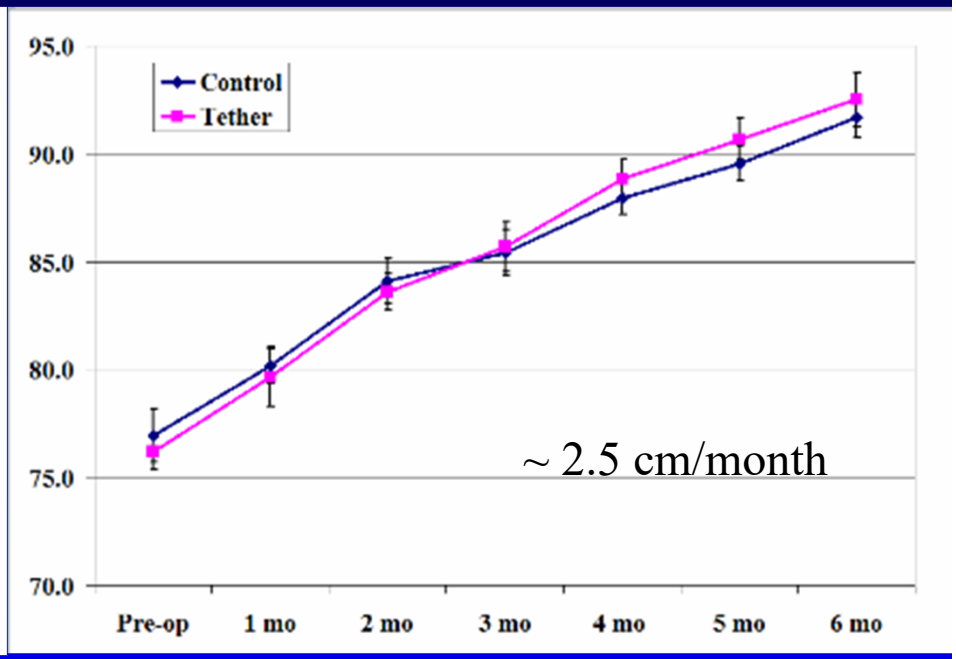


Statistics

- **ANOVA**
  - Radiographic data, CT measurements
- **Chi Square Analysis**
  - Thompson grade, MR grade, Histological grade
- **MANOVA**
  - Water content, GAG content, Hydroxyproline content, cell density
- **Bonferroni correction : $p < 0.0125$**

Porcine Growth

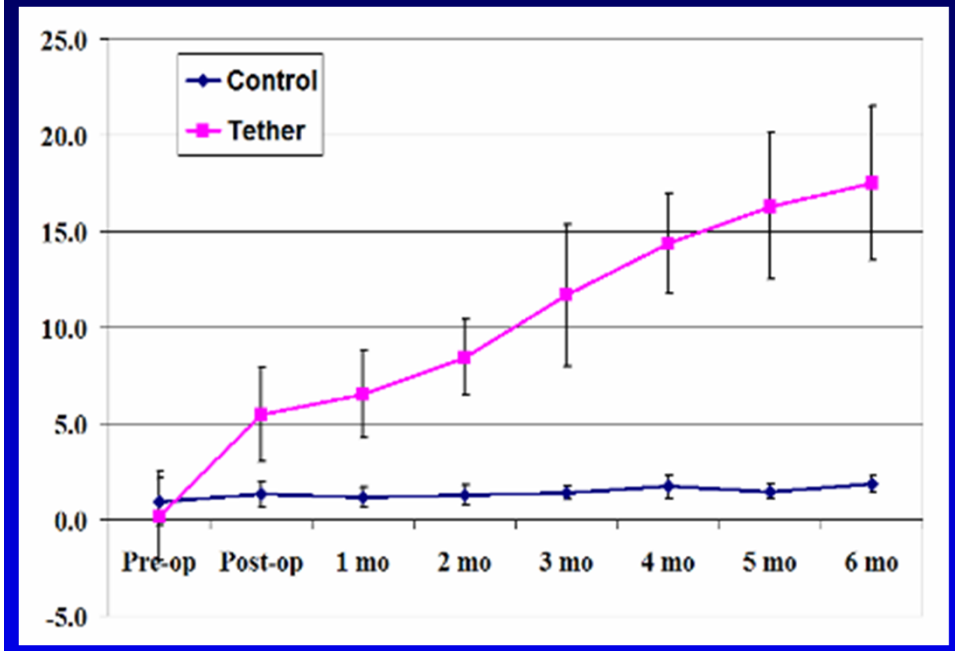


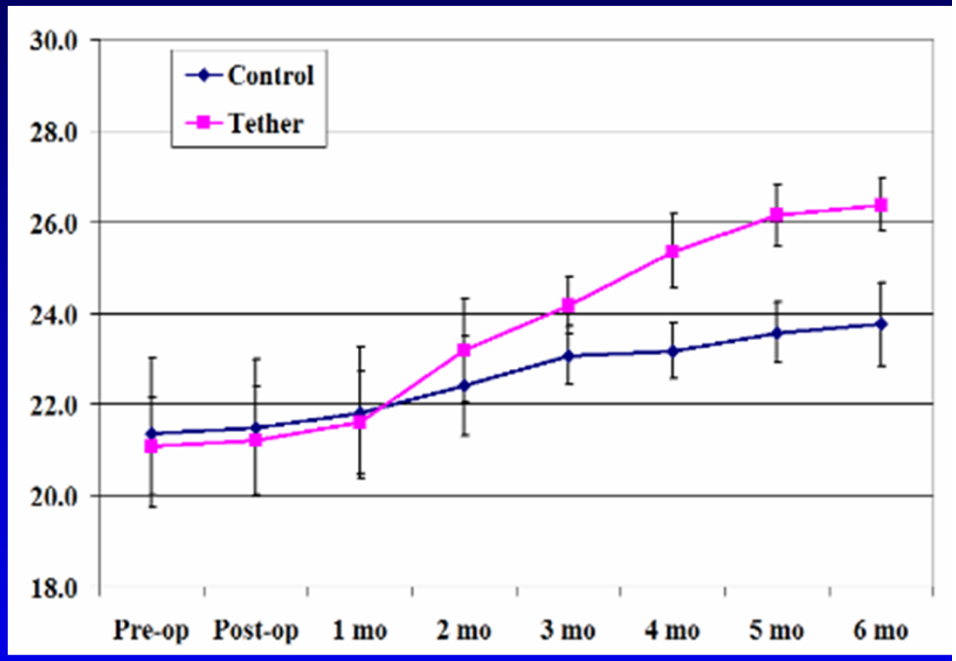


Weight (kg) **Length (cm)**

No significant differences in growth rate between the control and tether groups (p>0.73)

Deformity Creation



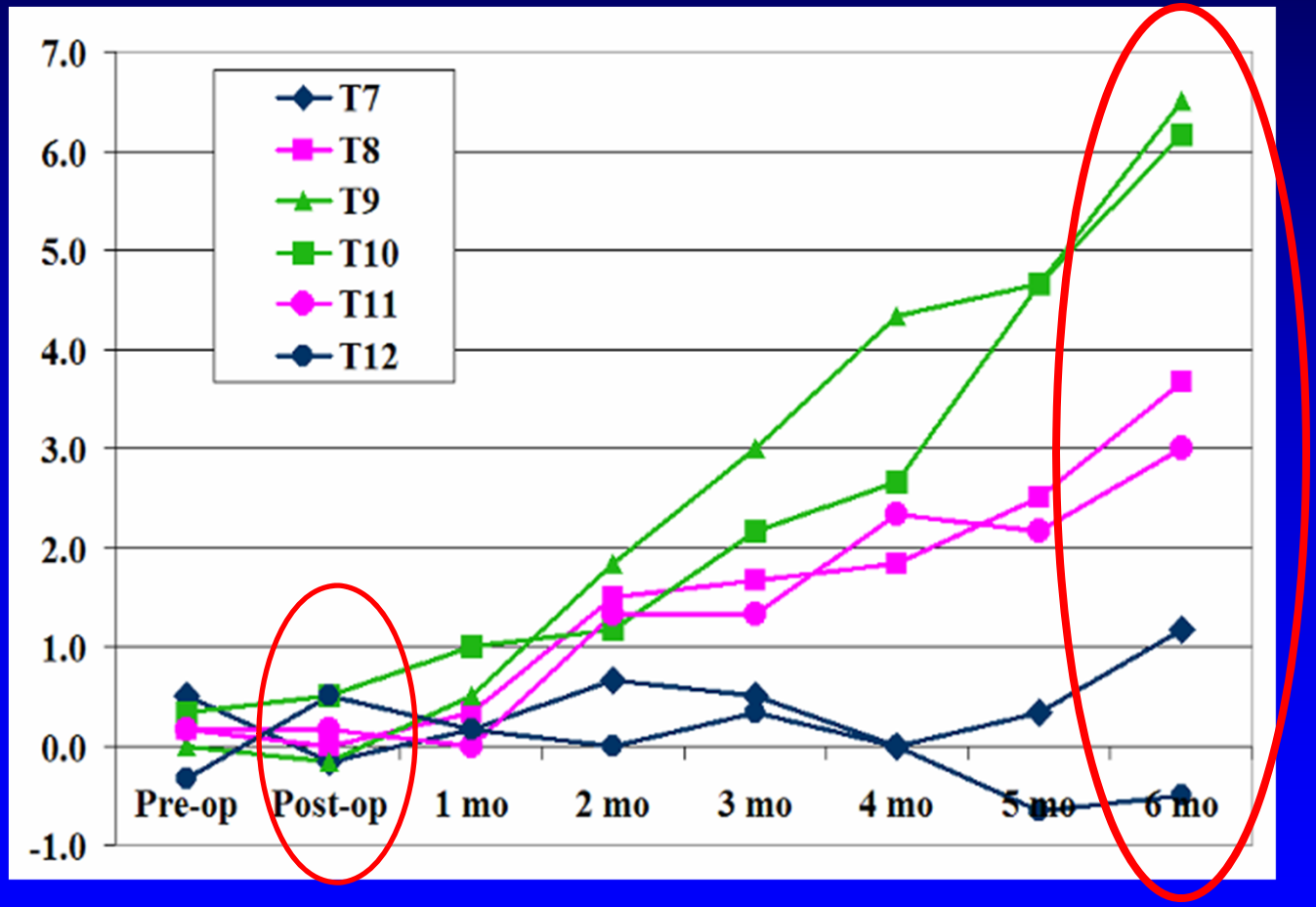


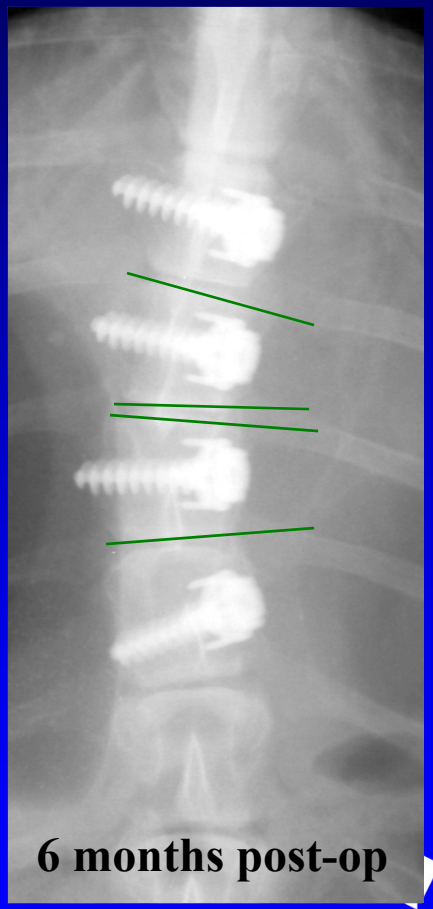
Coronal Cobb

Sagittal Cobb

Significant increase in the Coronal Cobb ($p<0.001$) and the Sagittal Cobb ($p<0.01$)

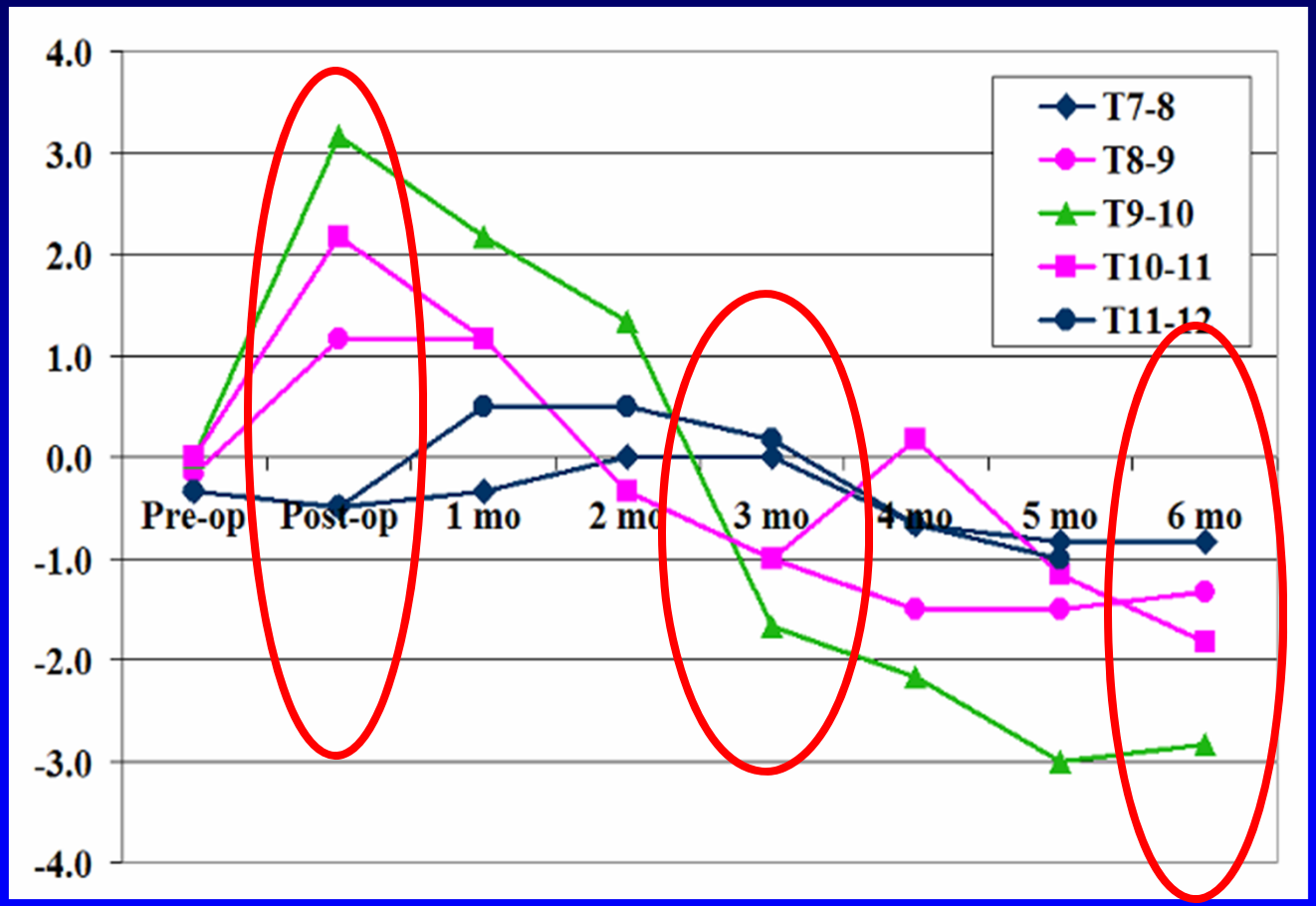
Effect of the Tether

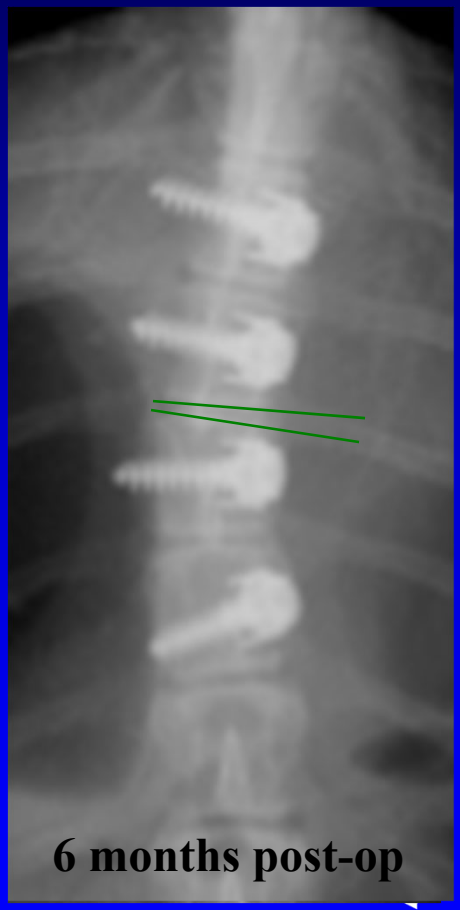




Vertebral Body Wedging

Effect of the Tether

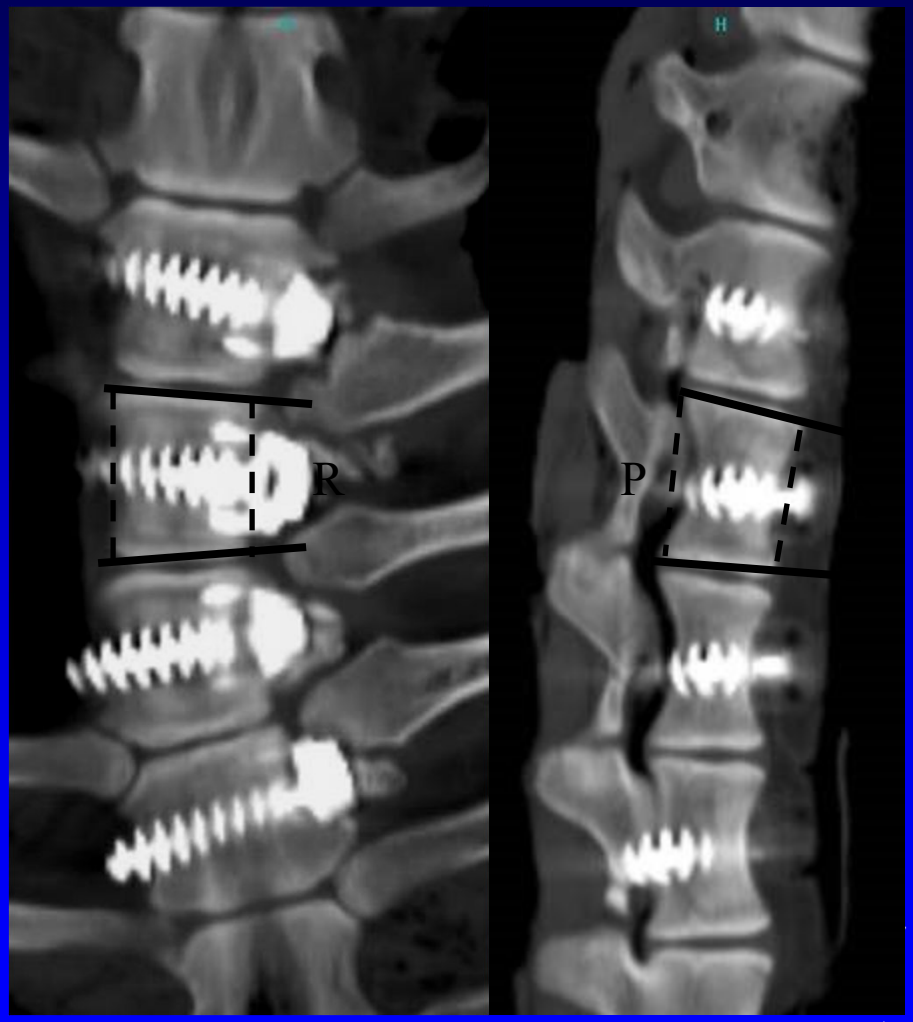




Intervertebral Disc Wedging

Computed Tomography

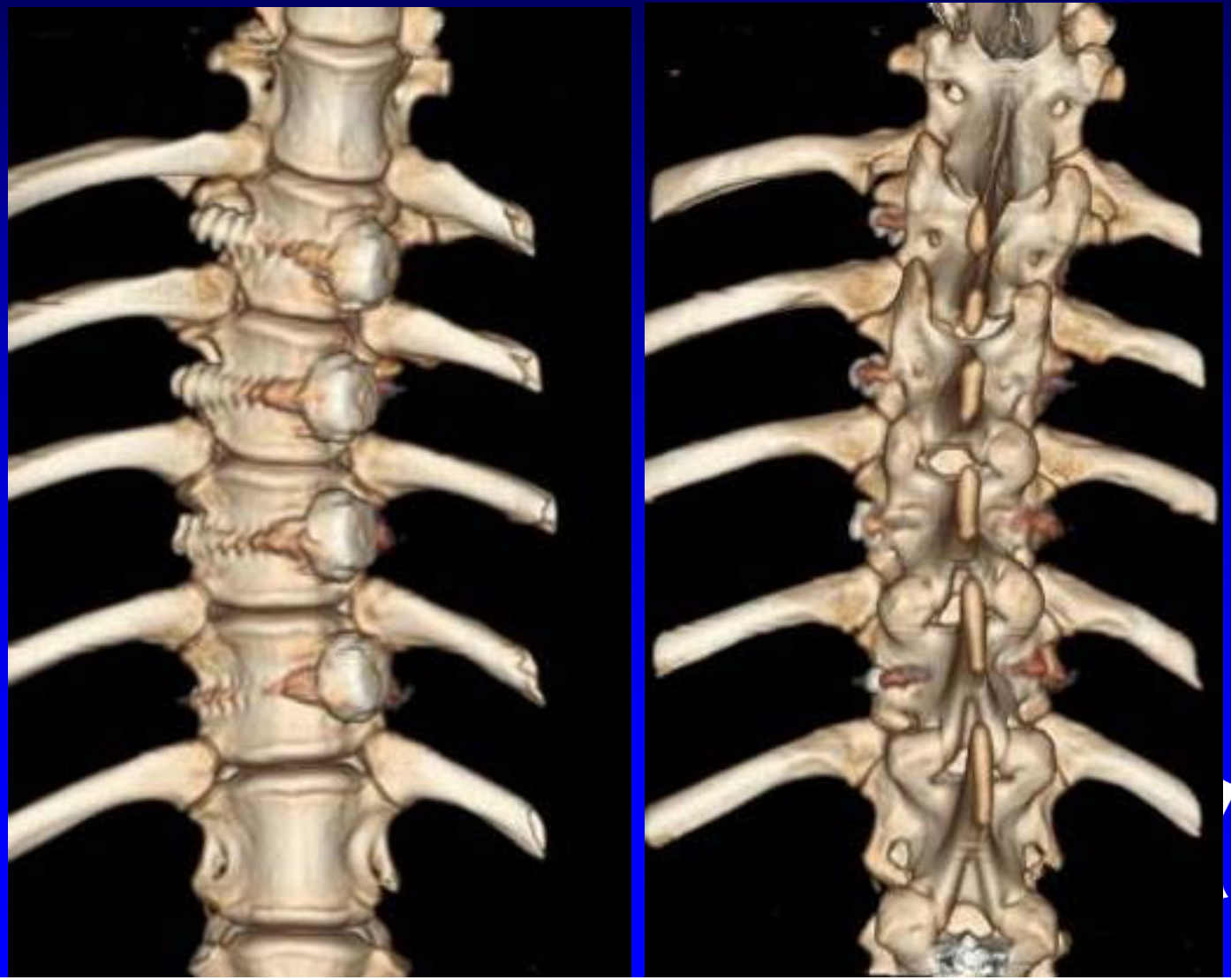
Control – 6 month post-op



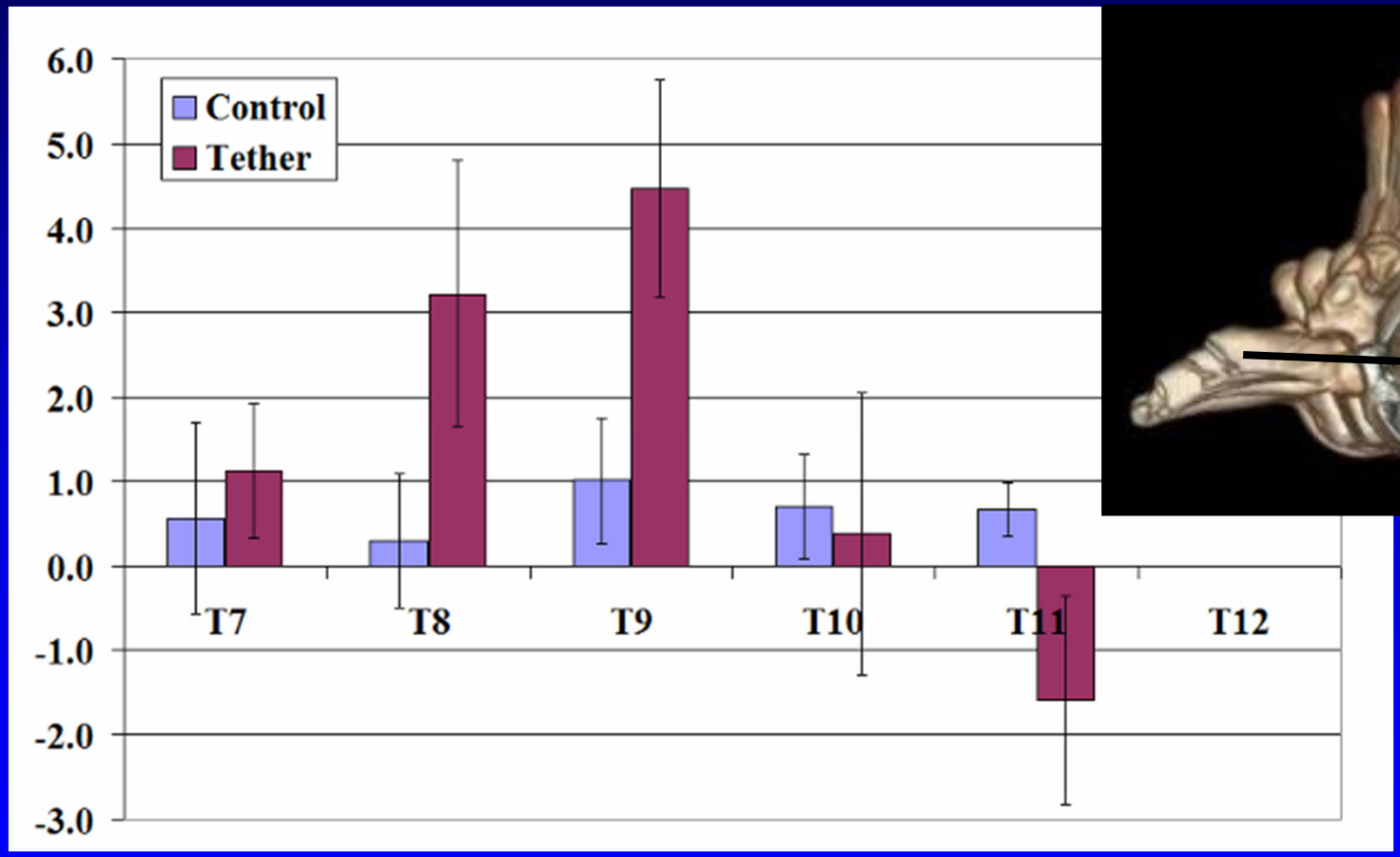
Tether – 6 month post-op

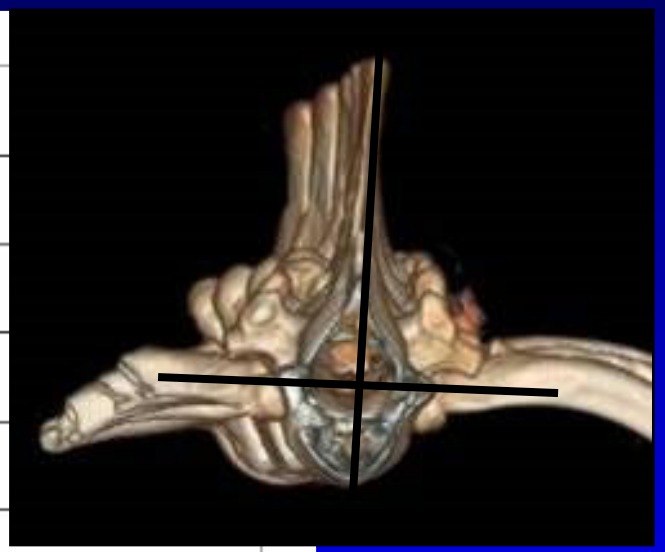
3D CT Reconstruction

Tether – 6 month post-op



Axial Plane Deformity





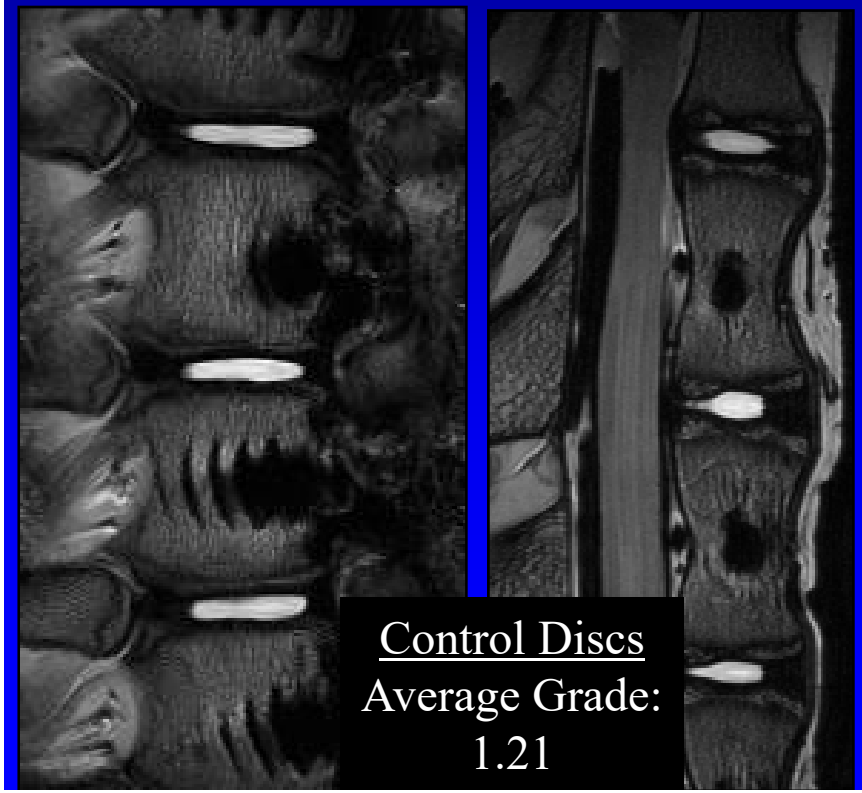
Vertebral Body Rotation

3T Magnetic Resonance Imaging

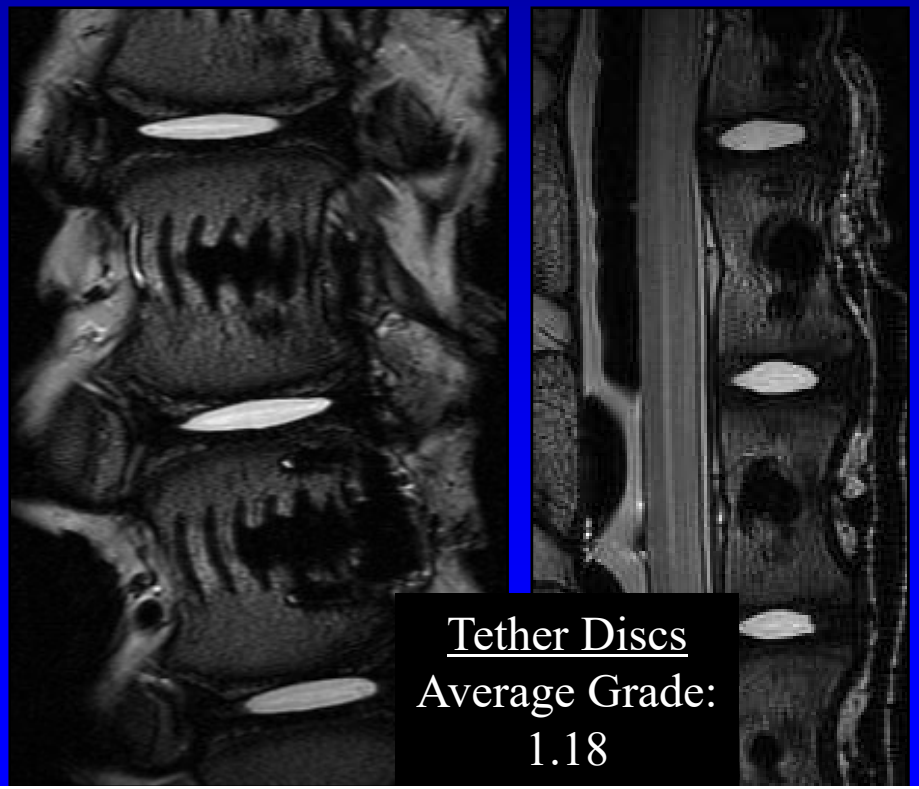
Classification of Disc Degeneration*

Grade	Structure	Distinction of Nucleus and Anulus	Signal Intensity	Height of Intervertebral Disc
I	Homogeneous, bright white	Clear	Hyperintense, isointense to cerebrospinal fluid	Normal
II	Inhomogeneous with or without horizontal bands	Clear	Hyperintense, isointense to cerebrospinal fluid	Normal
III	Inhomogeneous, gray	Unclear	Intermediate	Normal to slightly decreased
IV	Inhomogeneous, gray to black	Lost	Intermediate to hypointense	Normal to moderately decreased
V	Inhomogeneous, black	Lost	Hypointense	Collapsed disc space

* Modified from Pearce (cited by Eyre et al[9]).



Control Discs
Average Grade:
1.21



Tether Discs
Average Grade:
1.18

Gross Morphology

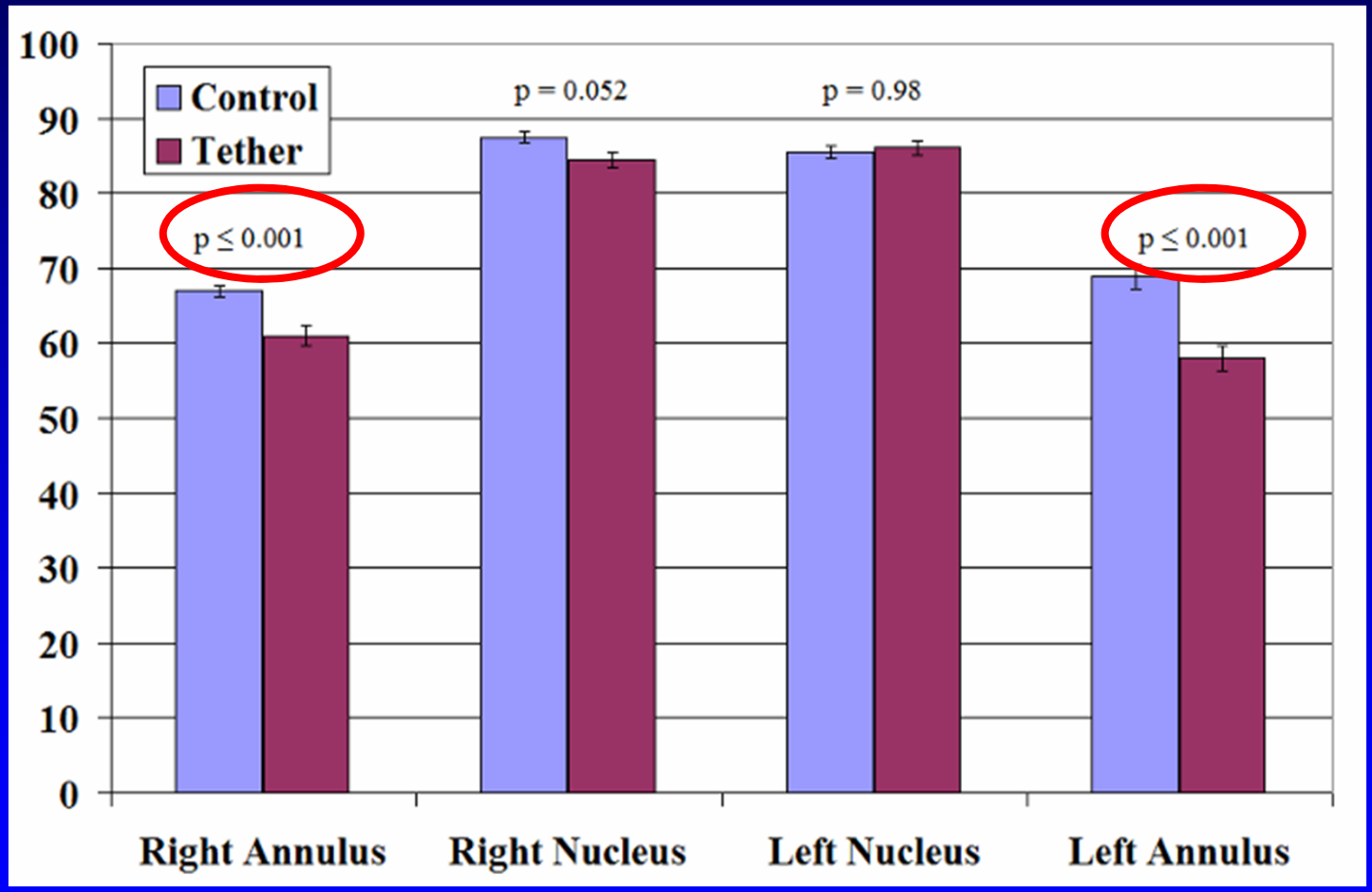
The Thompson grading scheme [42] for gross morphology of the human lumbar intervertebral disc

Grade	Nucleus	Annulus	Endplate	Vertebral body
I	Bulging gel	Discrete fibrous lamellas	Hyaline, uniformly thick	Margins rounded
II	White fibrous tissue peripherally	Mucinous material between lamellas	Thickness irregular	Margins pointed
III	Consolidated fibrous tissue	Extensive mucinous infiltration; loss of annular-nuclear demarcation	Focal defects in cartilage	Early chondrophytes or osteophytes at margins
IV	Horizontal clefts parallel to endplate	Focal disruptions	Fibro cartilage extending from subchondral bone, irregularity and focal sclerosis in subchondral bone	Osteophytes less than 2 mm
V	Clefts extend through nucleus and annulus	–	Diffuse sclerosis	Osteophytes greater than 2 mm

Control Discs
Average Grade:
1.46

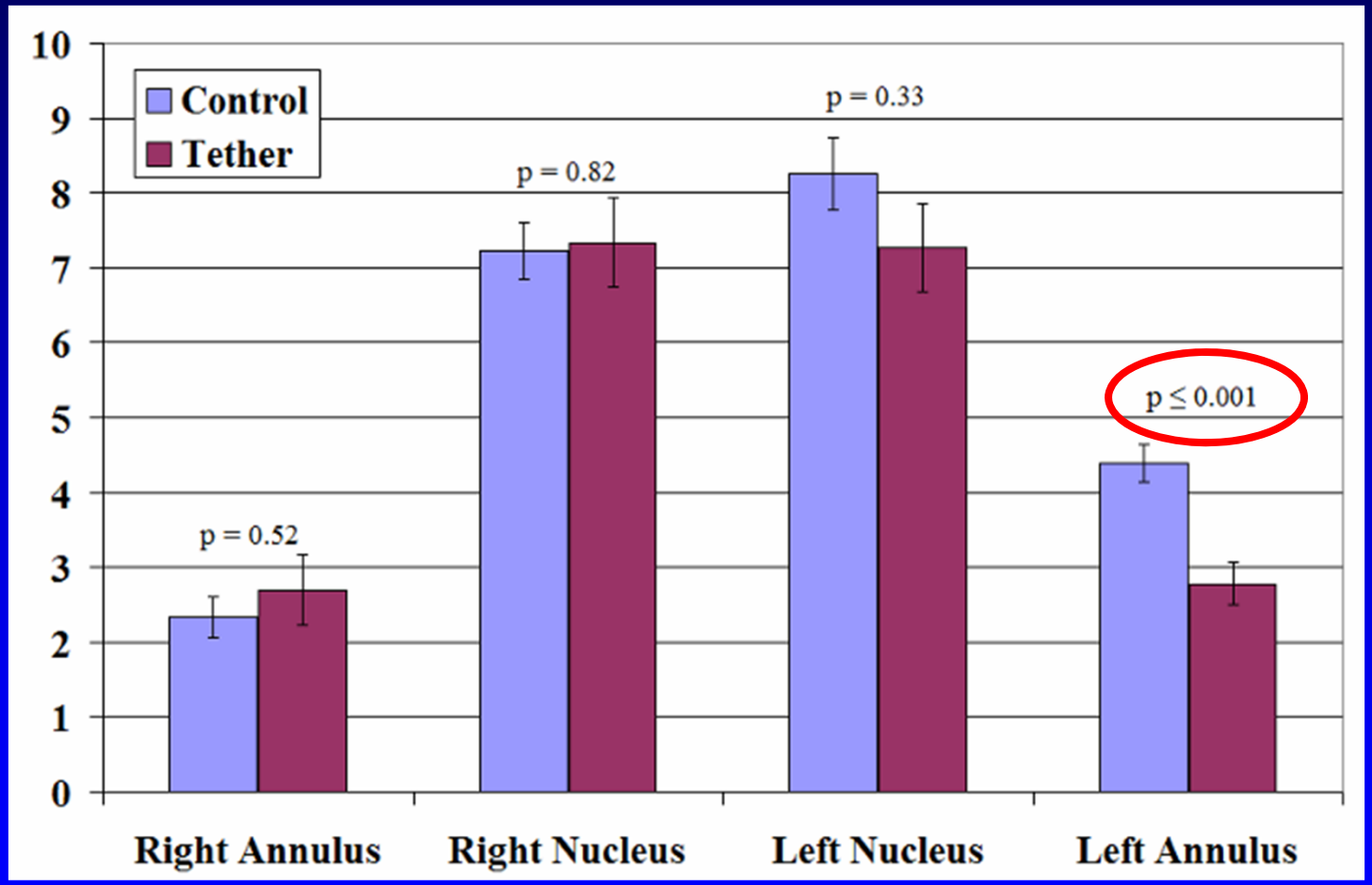
Tether Discs
Average Grade:
1.35

Biochemical Analysis



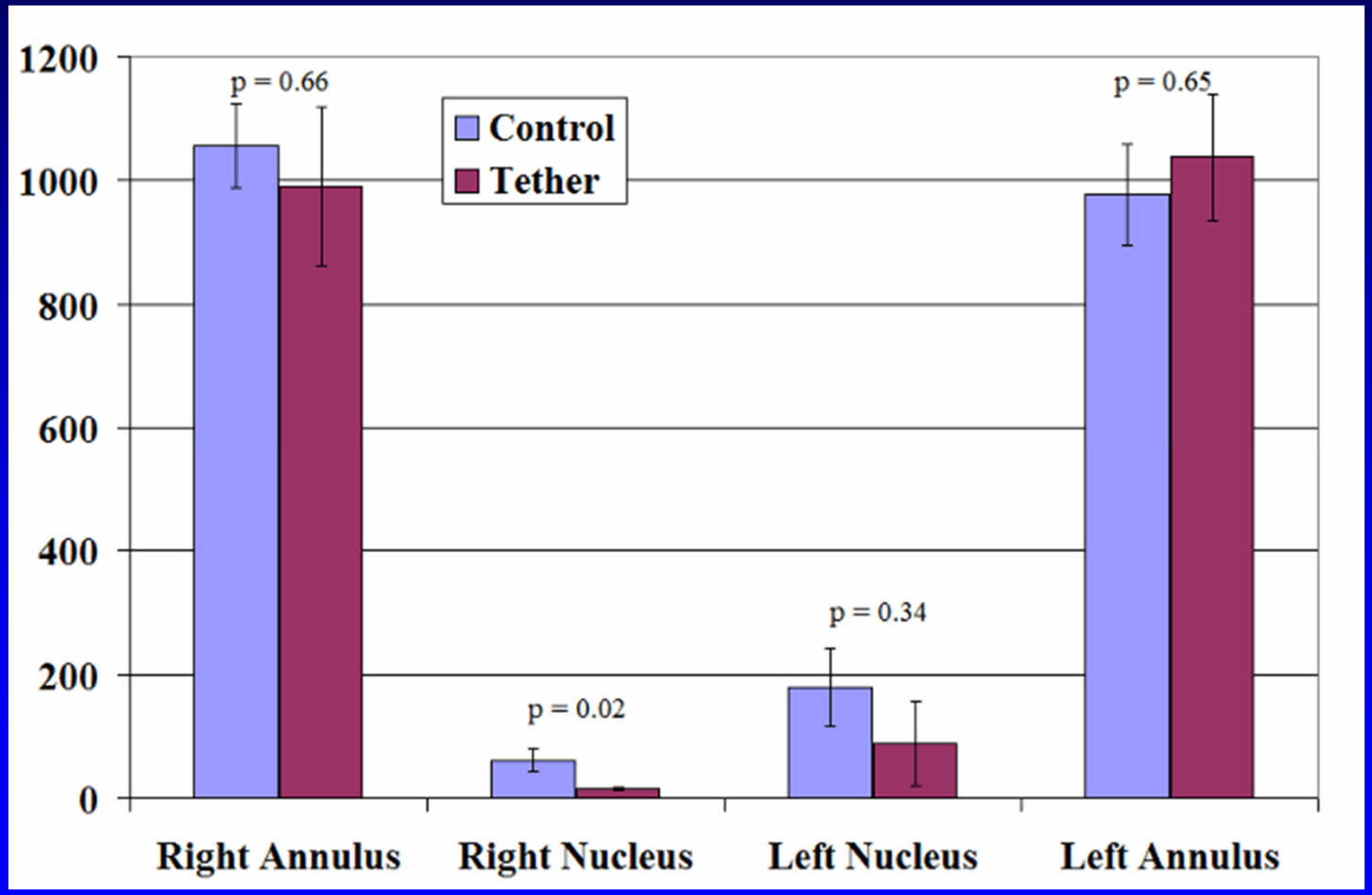
Water Content (%WW)

Biochemical Analysis



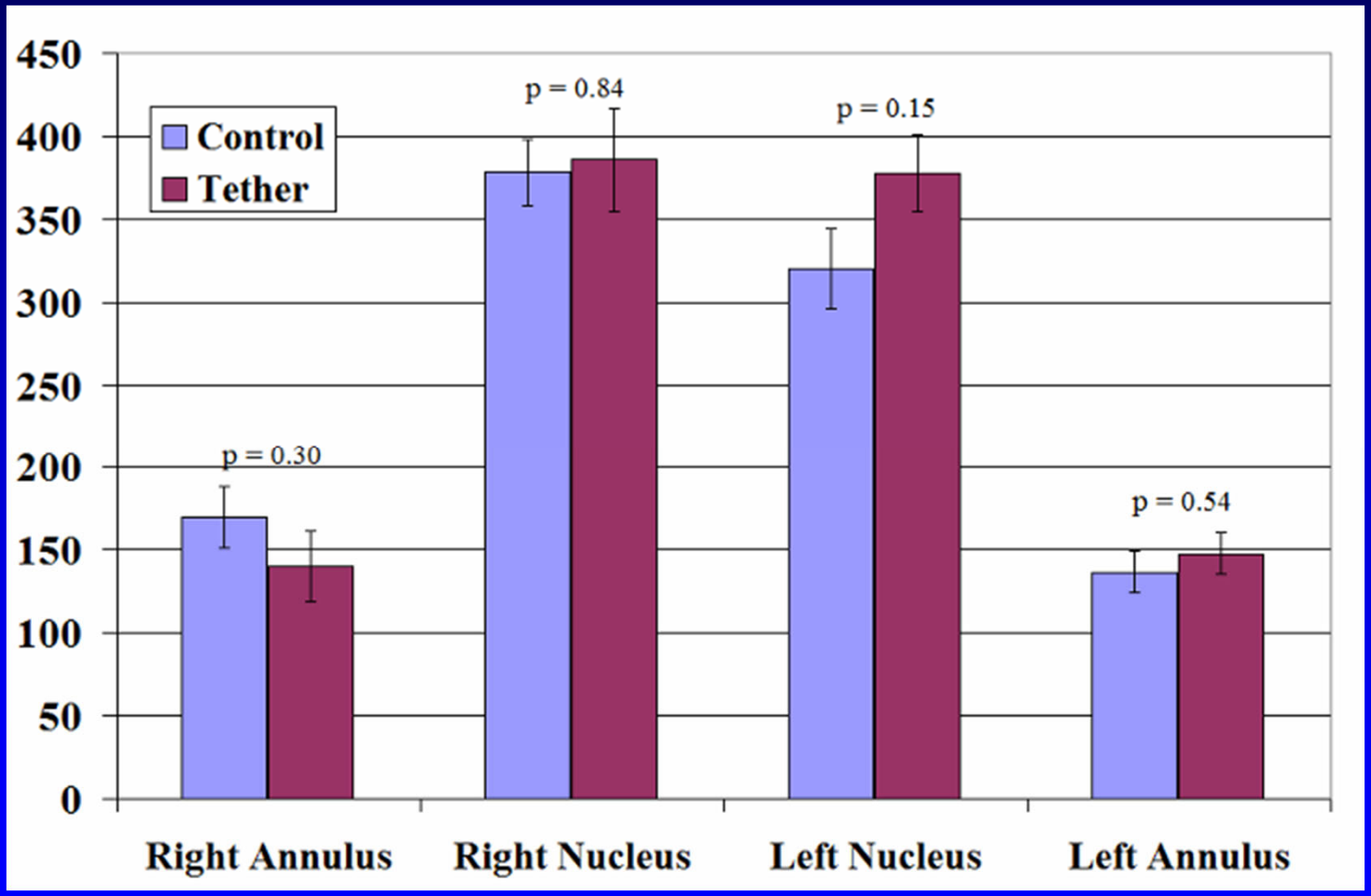
GAG Content (%WW)

Biochemical Analysis



Hydroxyproline Content (ug/ml)

Biochemical Analysis

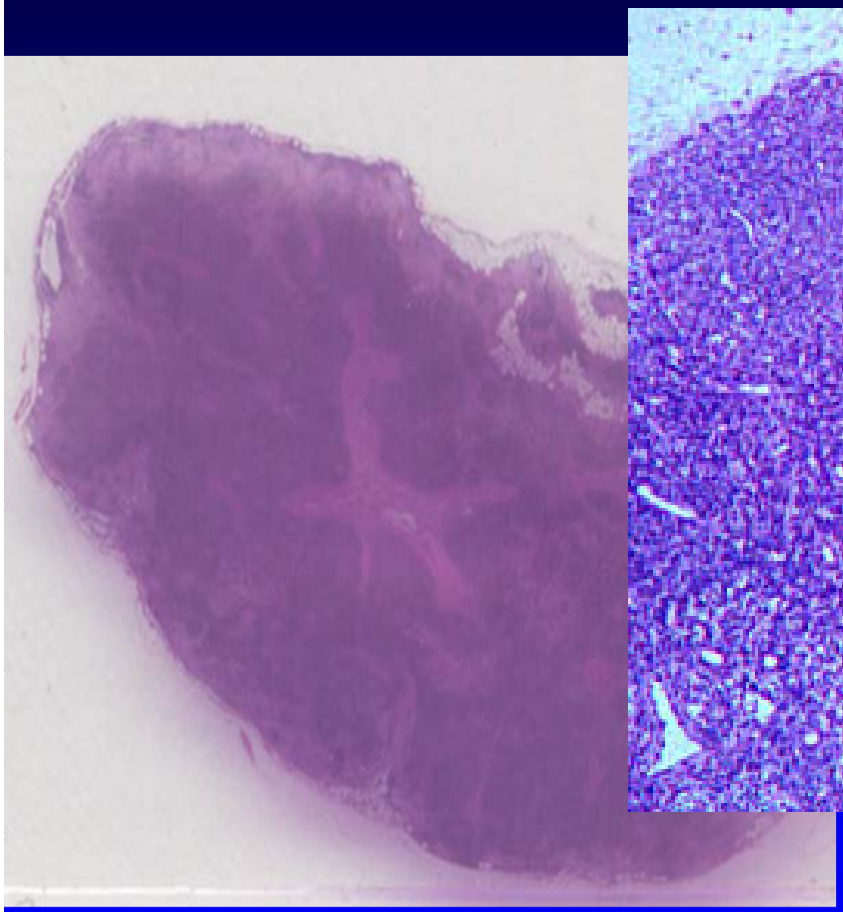


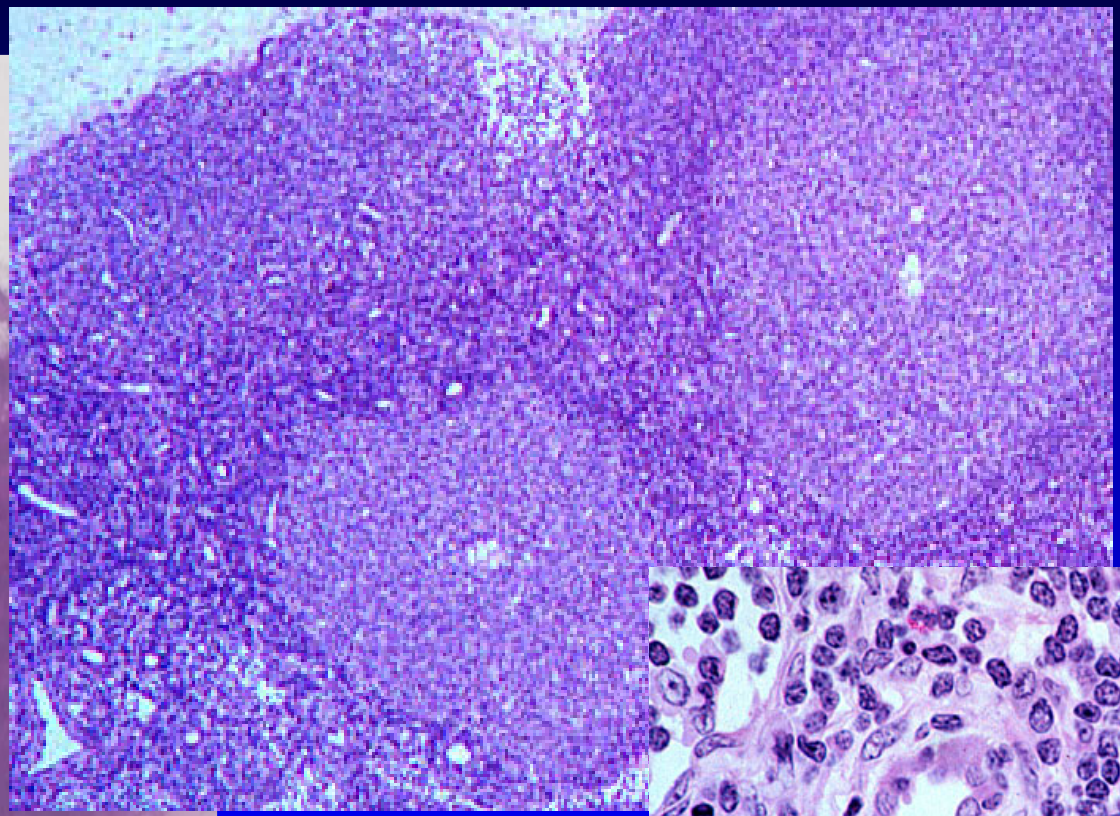
Cell Density (10^6 cells/g DW)

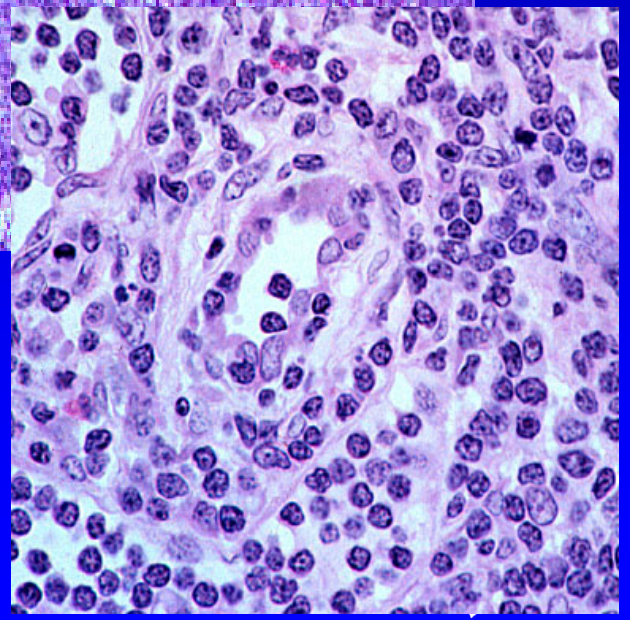
Bone-Screw Interface

No Fibrous Zone or Loosening

Lymph Nodes

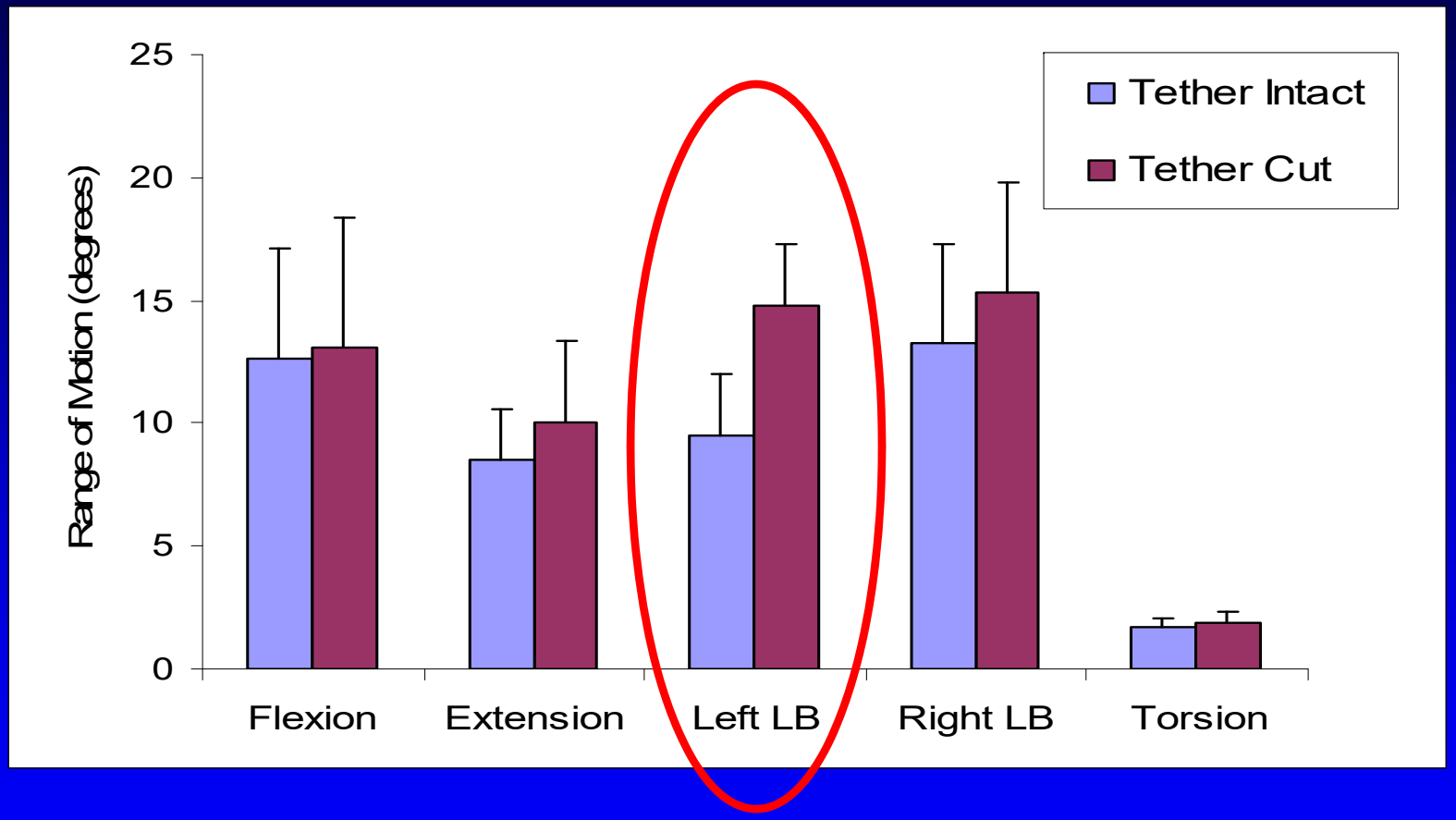






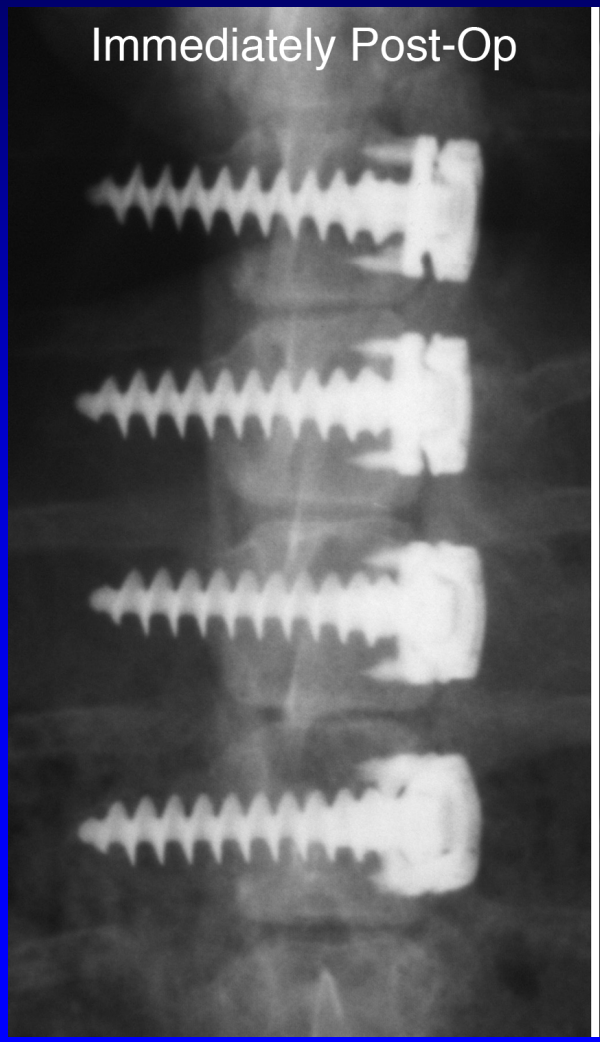
No Foreign Body Reaction

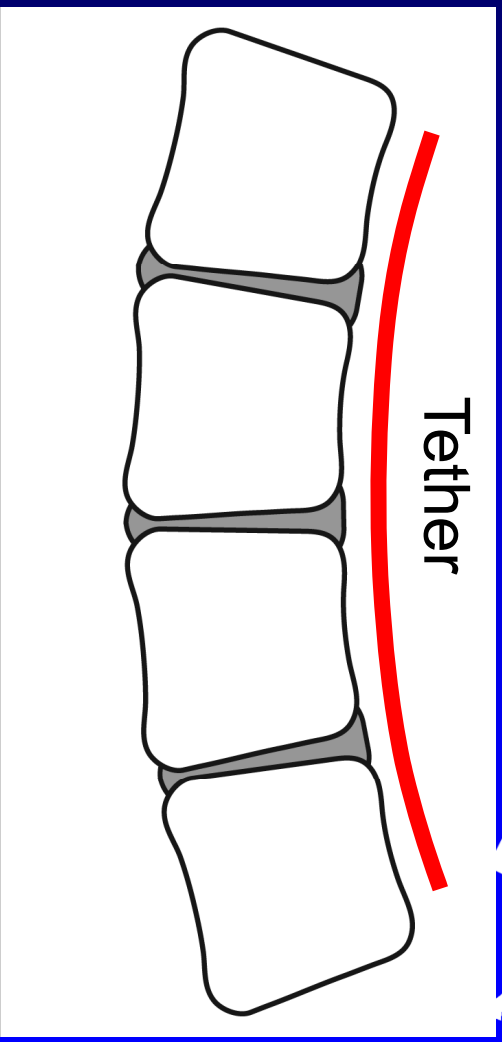
Range of Motion



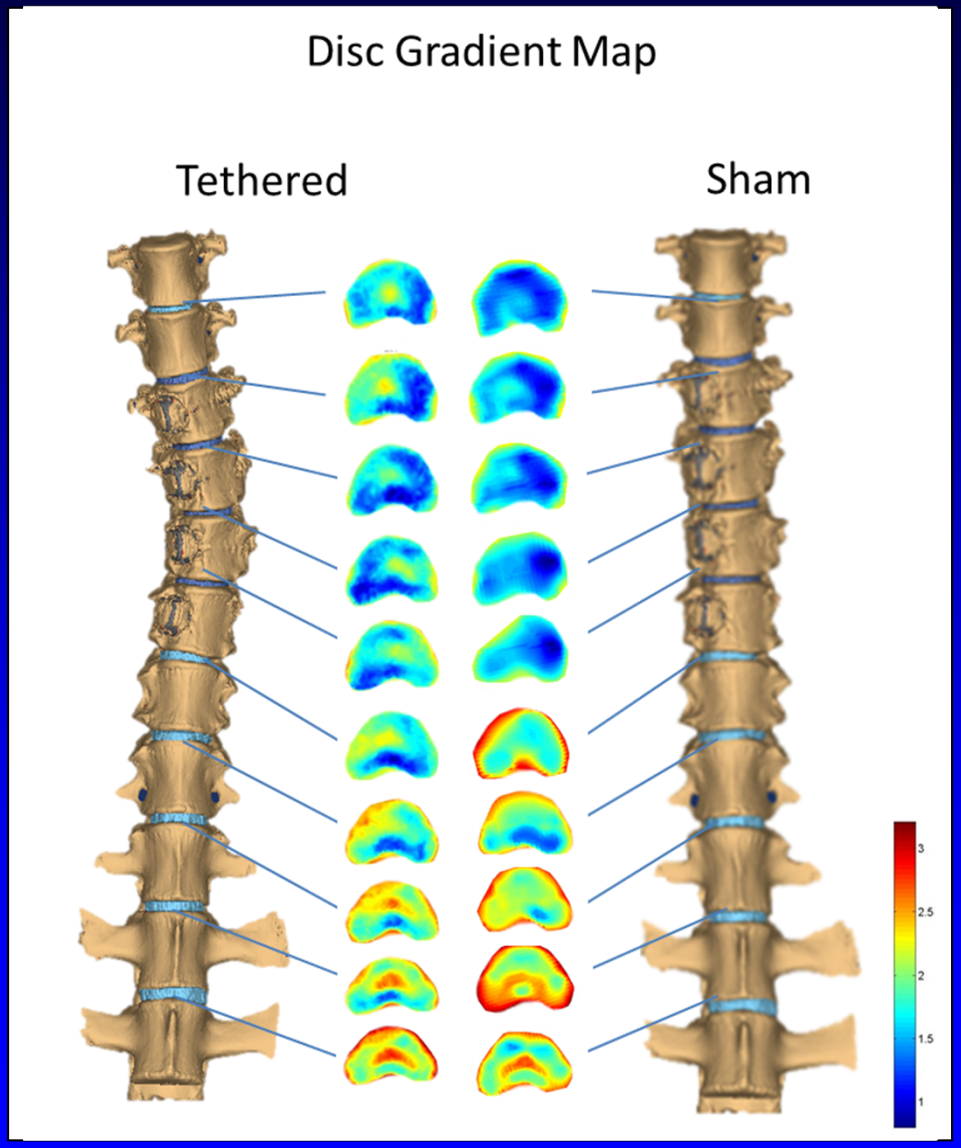
ROM significantly limited in lateral bending away from the tether. (p=0.01)

Discs wedged in the opposite direction to the vertebrae

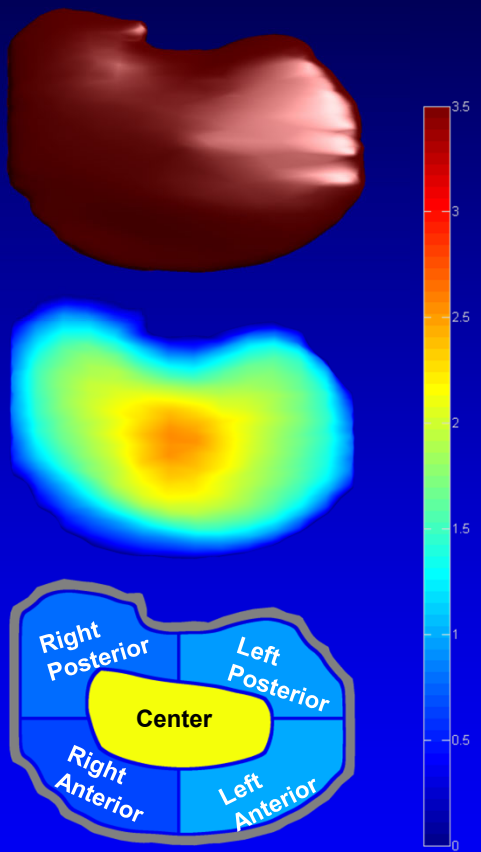




3D Spinal Deformation –MRI

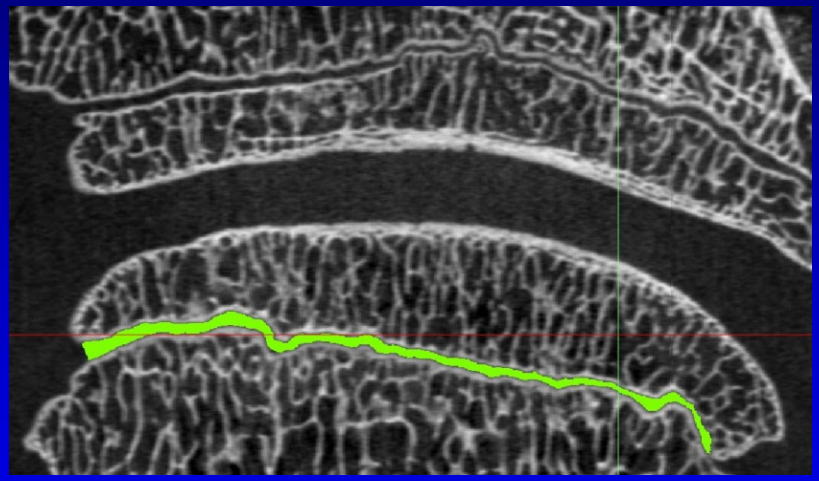


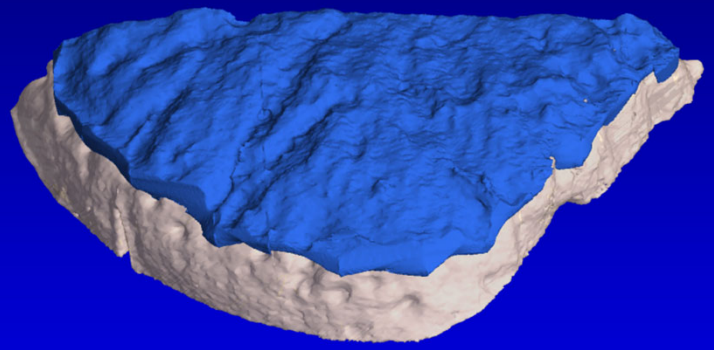
Disc (From MRI)

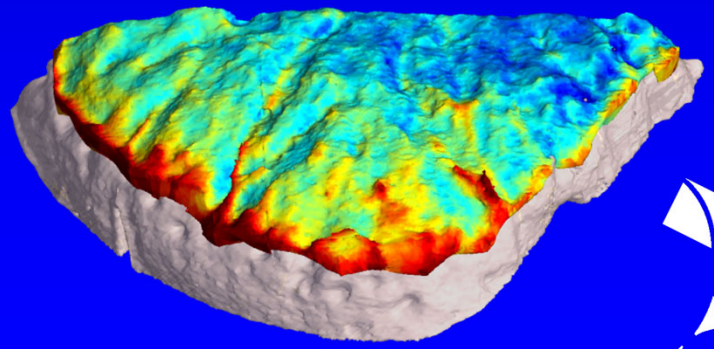


Disc Regions for analysis

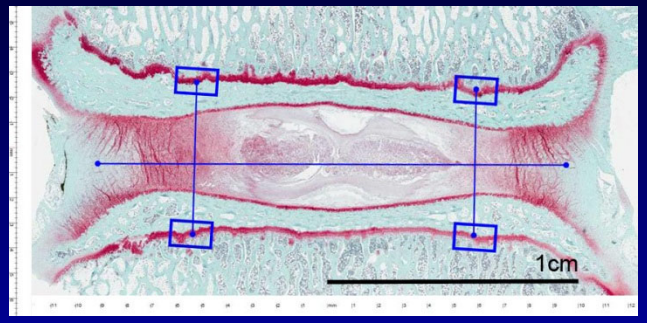
3D Spinal Deformation – Physis



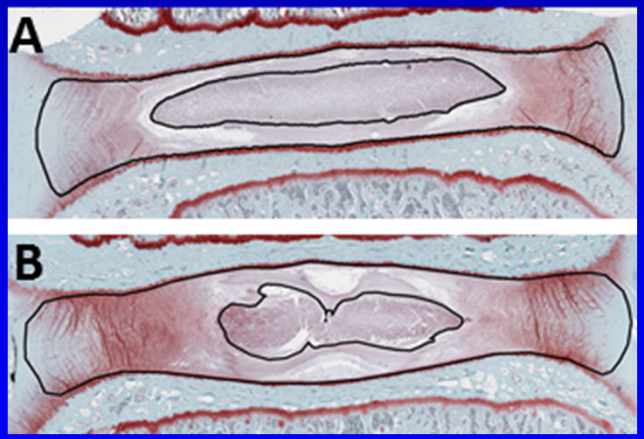




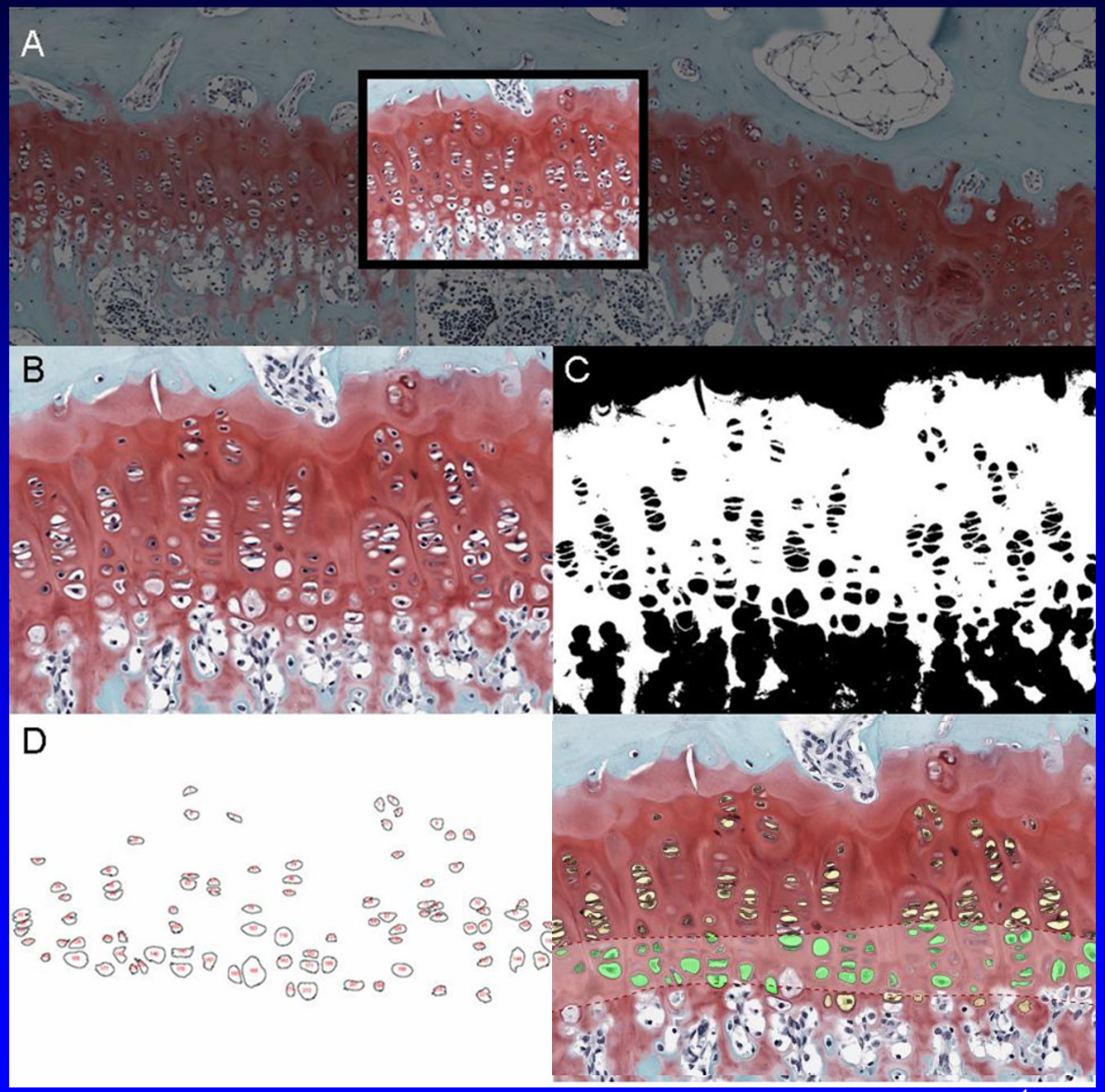
3D Spinal Deformation –Histology



Physis: Cell and Zonal Analysis

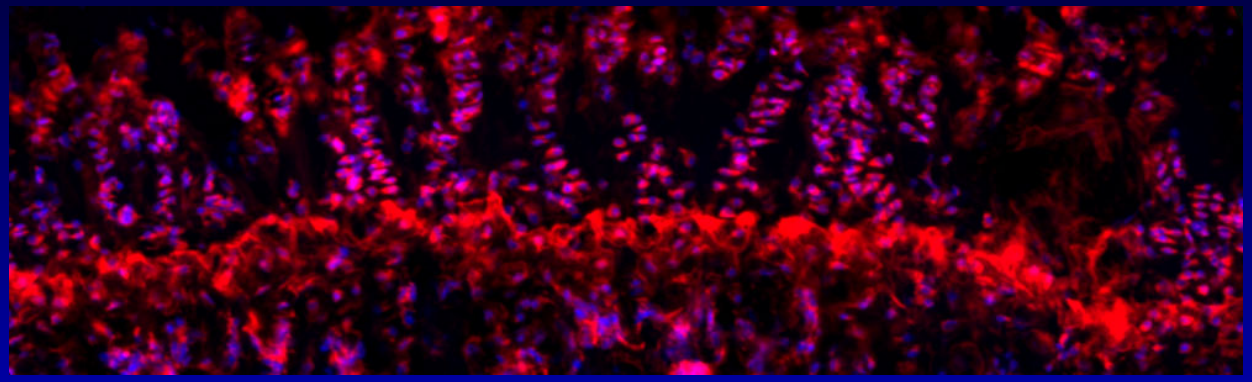


Disc: Shape, Nuclei-to-Disc Ratio, Circularity, Area-to-Volume Analysis

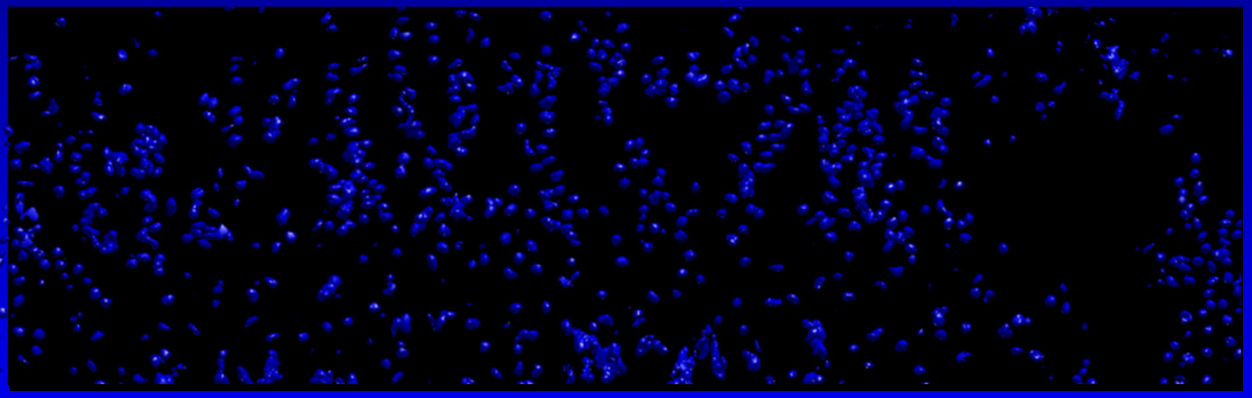


3D Spinal Deformation Analysis –Confocal

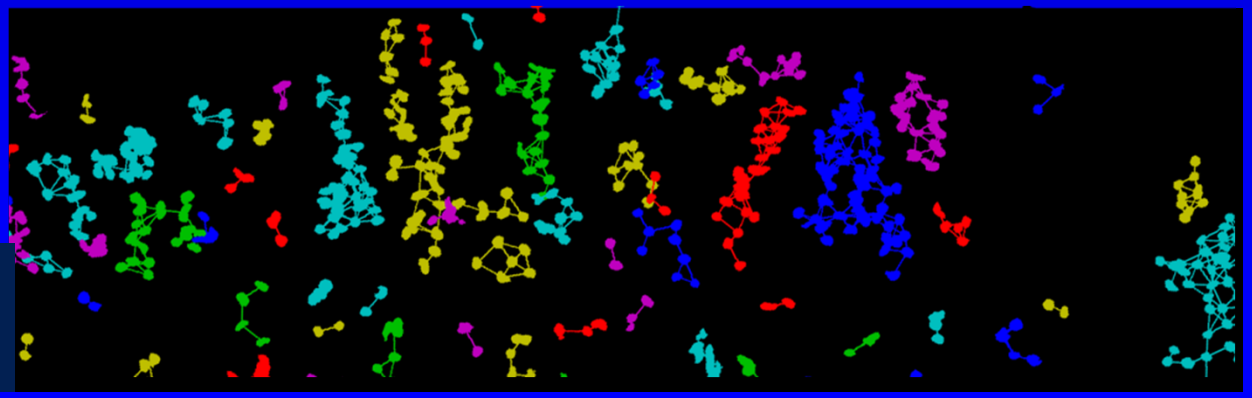
Projection Plane



Nuclei Reconstruction

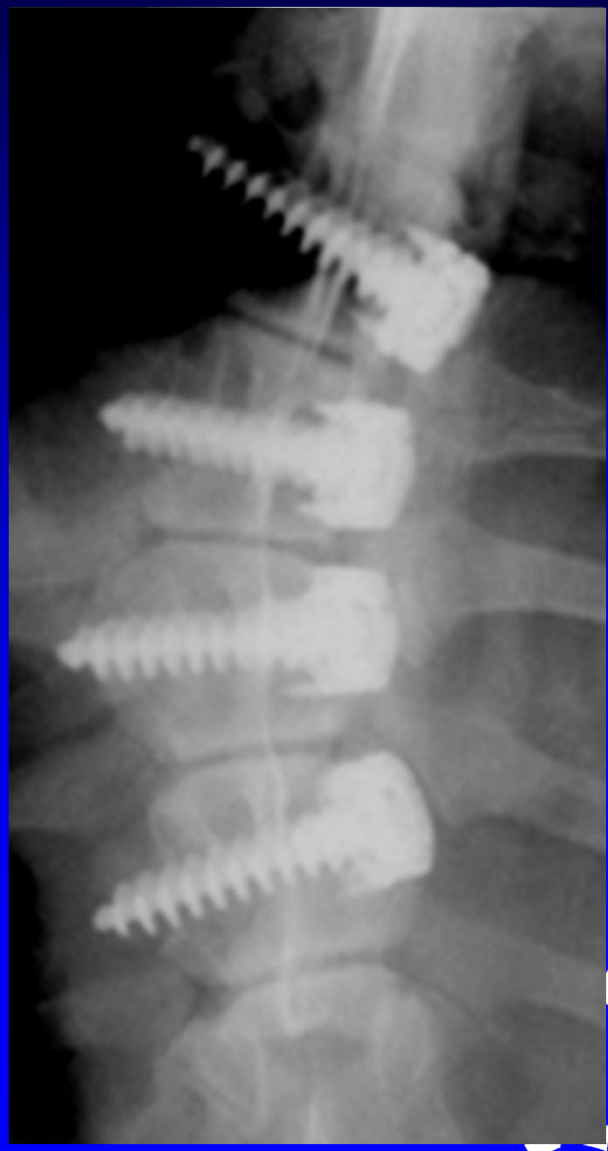


GP Stacks Analysis



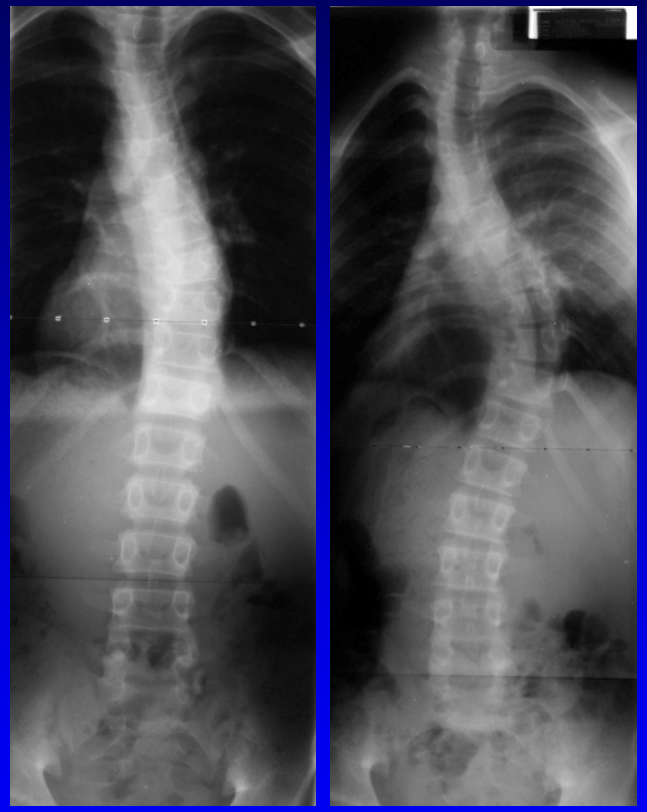
Conclusion

- **Consistent growth modulation.**
- **Disc Motion maintained**
- **Disc metabolism maintained**



Clinical Tethering?

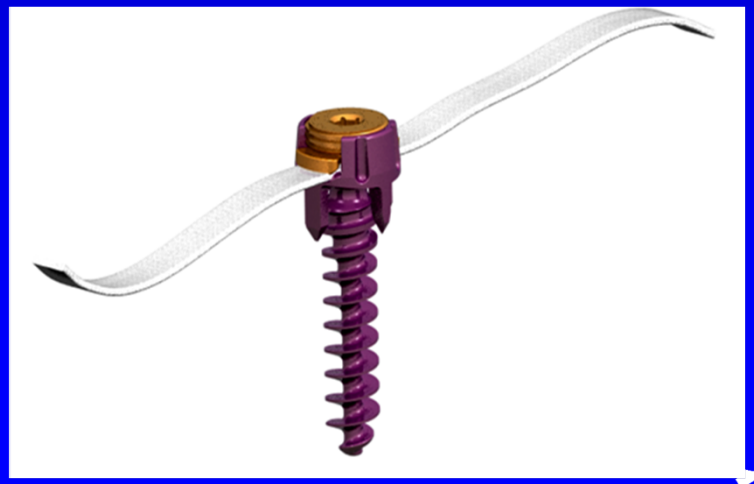
- Cautious optimism
- Potential shift in treatment
- Data supports a clinical trial

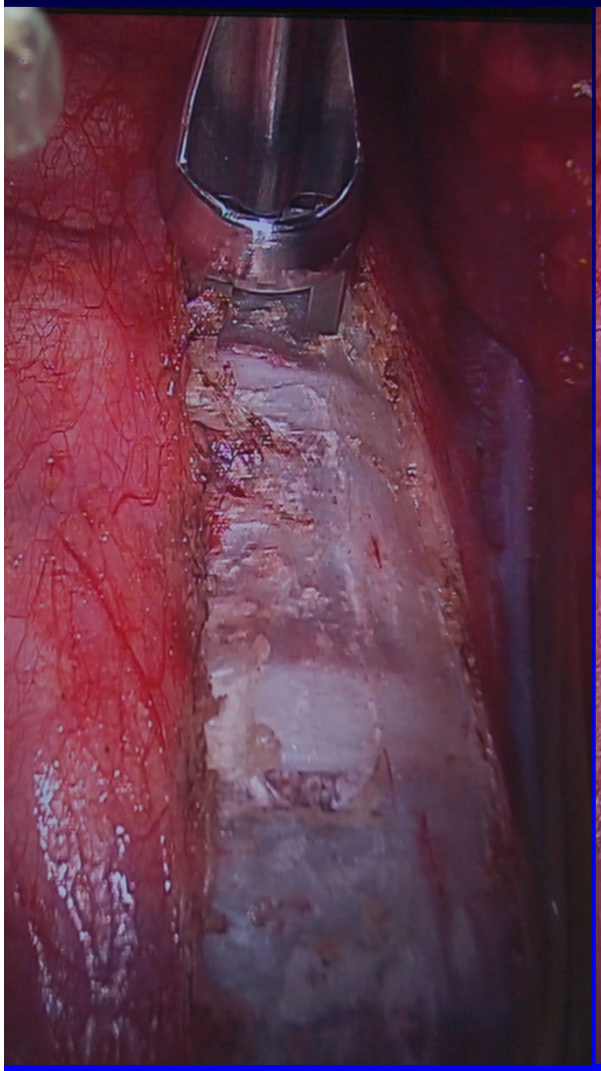


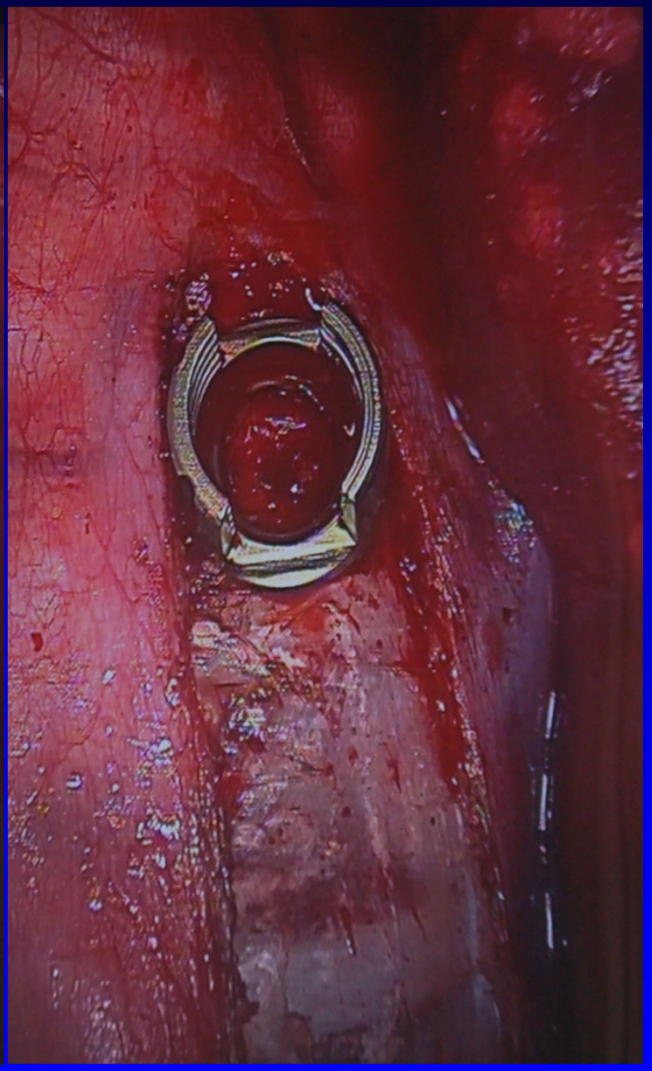
Non-Fusion Correction

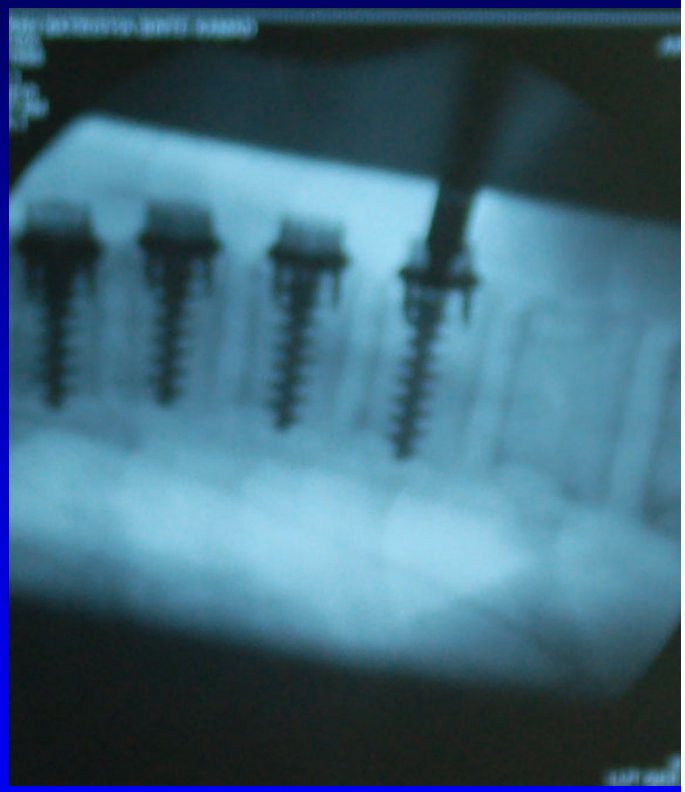
Pilot Trial – Hee Kit Wong

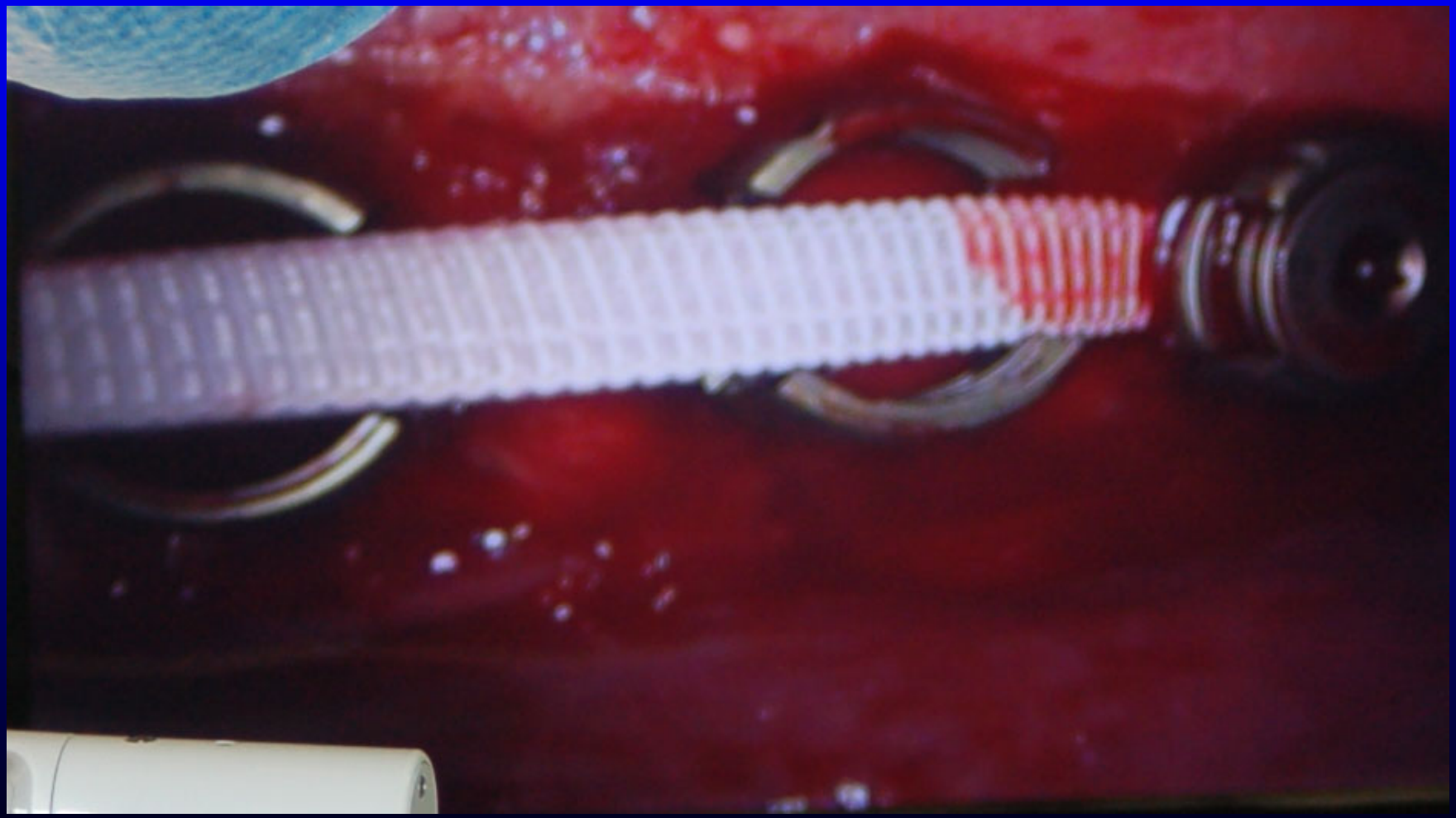
- Male and female
- 8 to 15 years of age
- juvenile or adolescent idiopathic scoliosis
- Major thoracic curve of 35° to 55° who are at high risk for progression
- At least three years of estimated growth remaining based on hand/wrist radiograph assessment of bone age (less than or equal to 11 for girls, less than or equal to 13 for boys.)





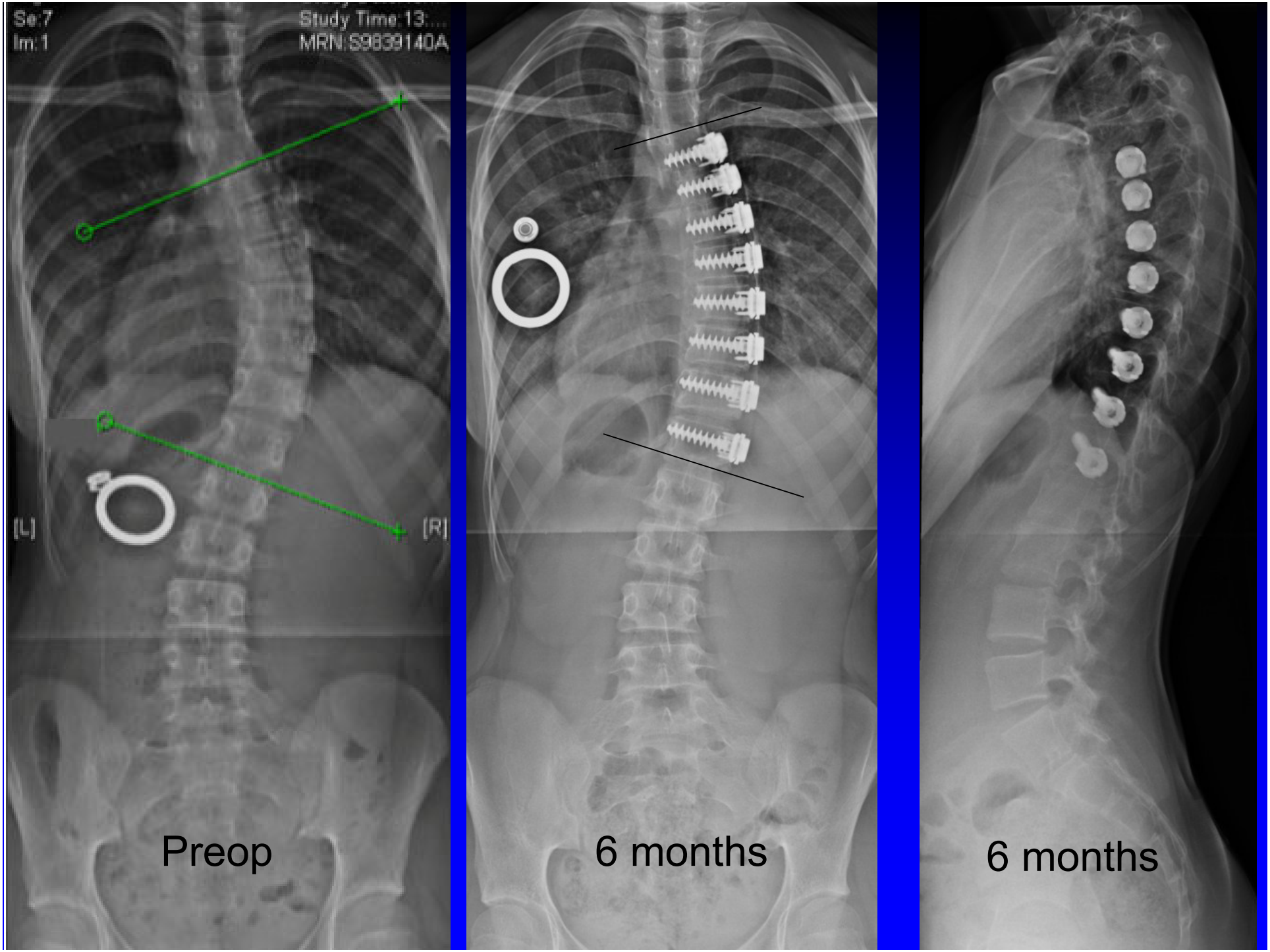


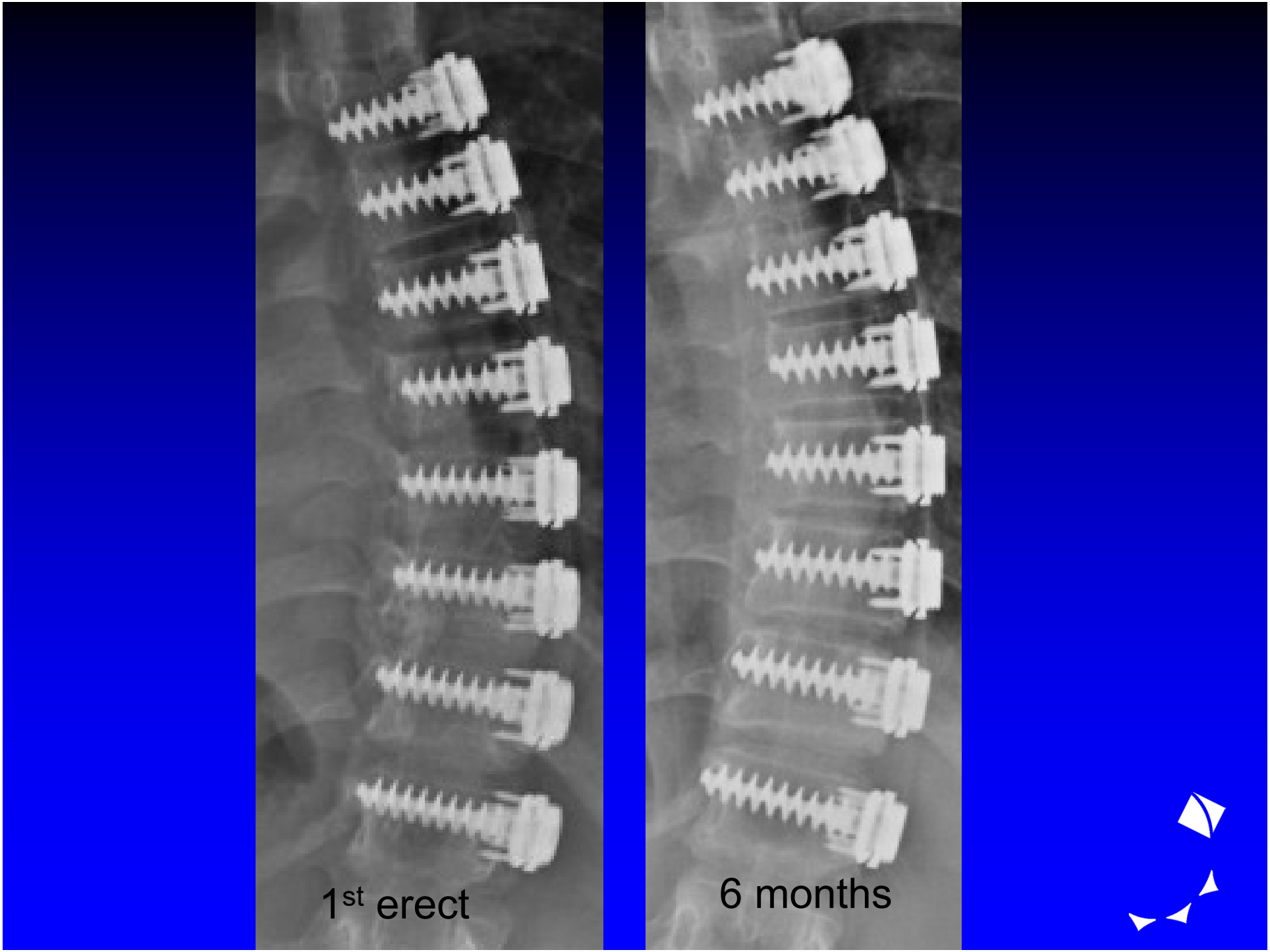




Subject 01

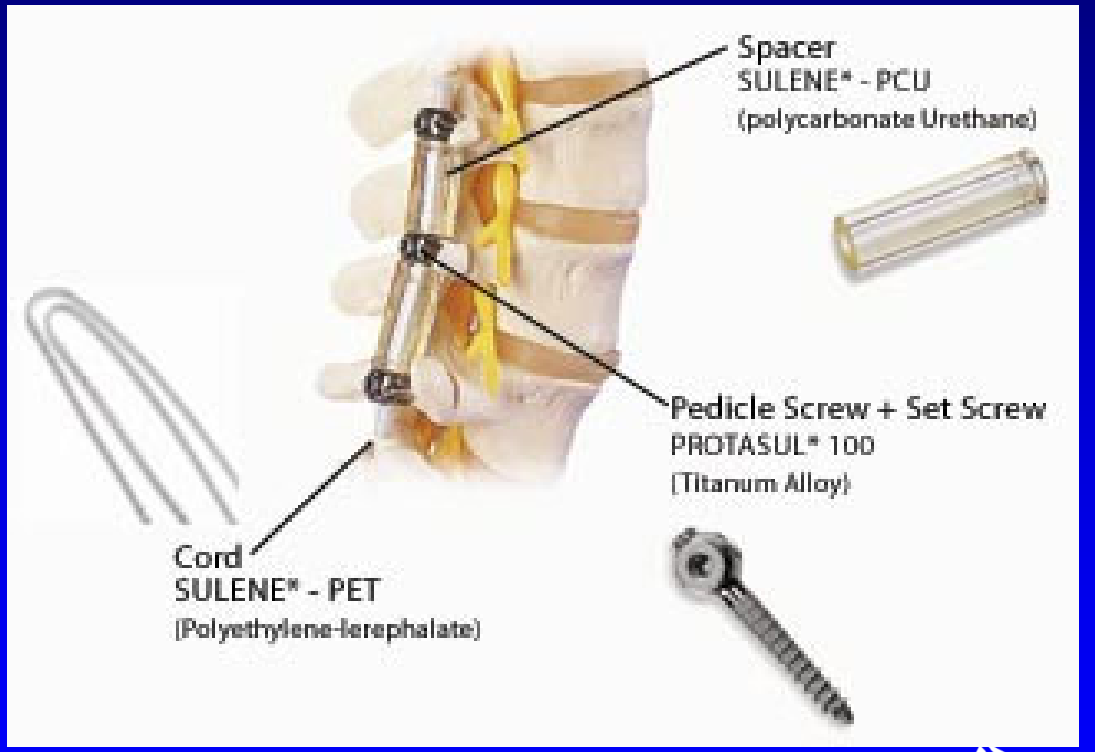
- 13 year old female
- Risser 0
- Cobb Angle 45 degrees
- Instrumentation T5 – T12

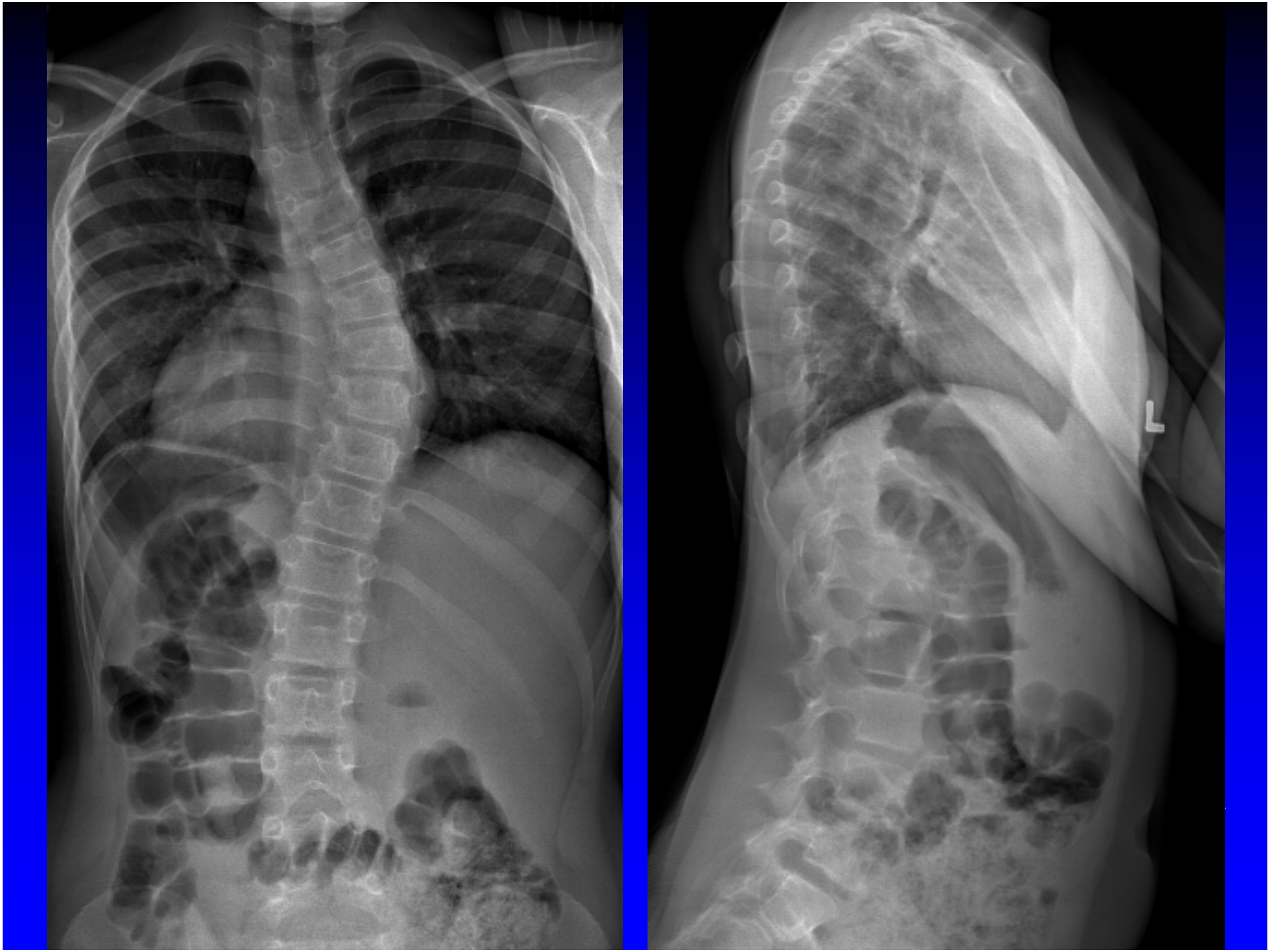

Se:7
Im:1
Study Time:13:...
MRN:S9839140A
[L]
[R]
Preop
6 months
6 months


1st erect
6 months

Off Label Dynesys Anterior

- 9 y/o male
- Prader-Willi
- Progression in brace

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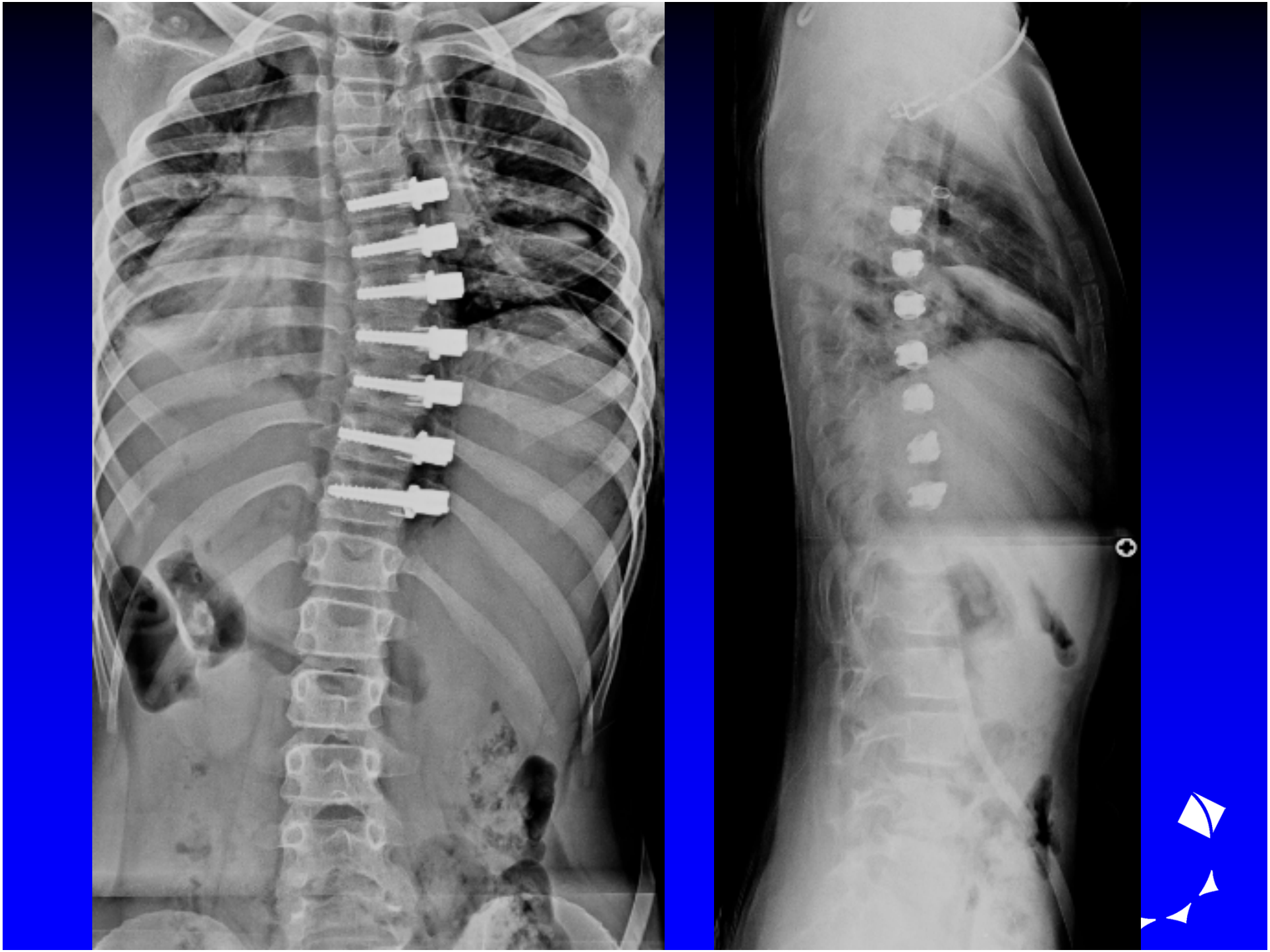
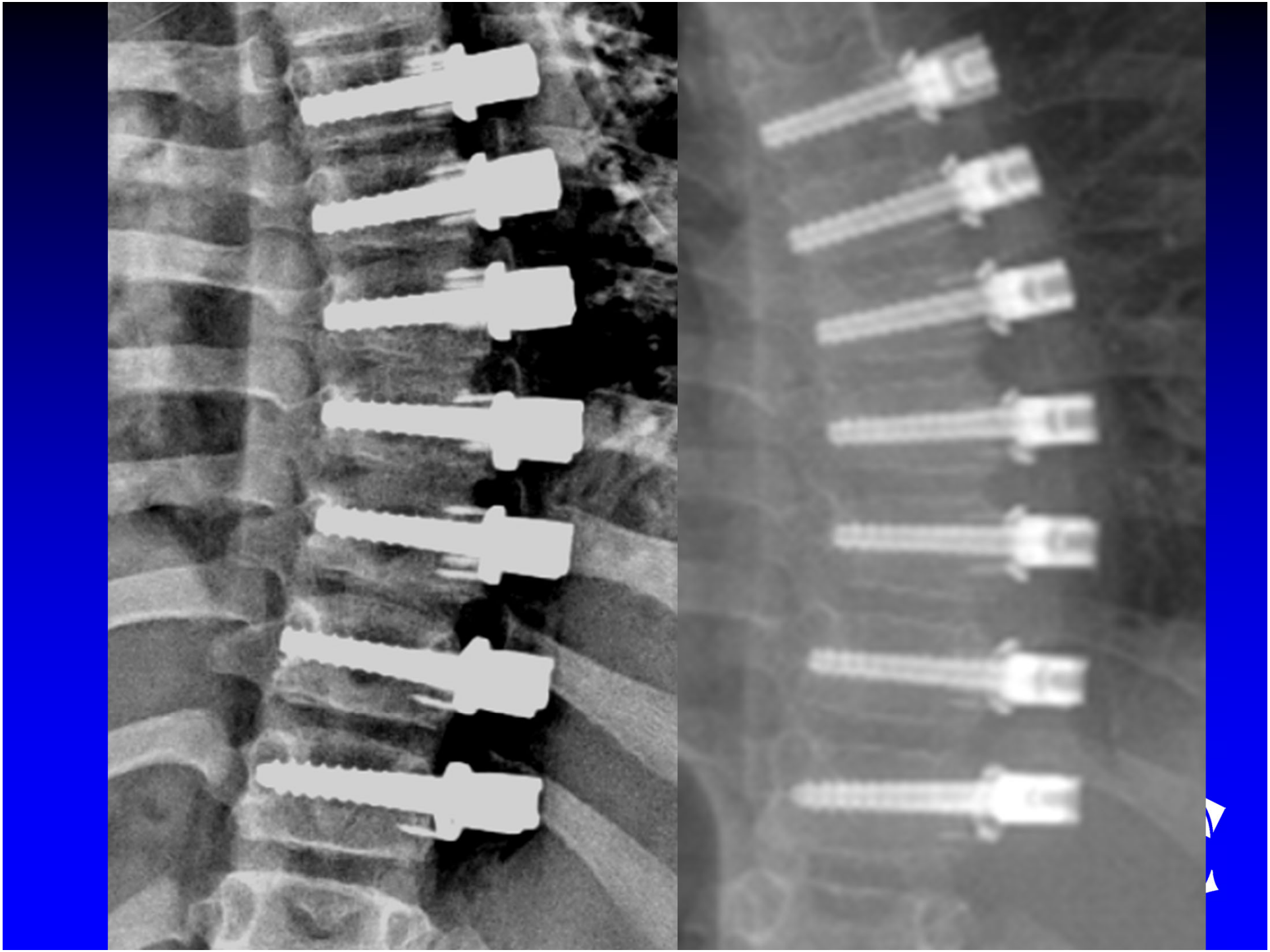



6 weeks
L



Stay tuned…

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  - Aileen Laurente
  - Molly Moor
  - Joanna Roocroft
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- **Biomechanical Studies – Diana Glaser, PhD**
  - Josh Doan, MS
  - Chaitanya Nandipati
- **Harms Study Group – Michelle Marks, MS**
  - Maty Petcharaporn
  - Caitlyn Schulte
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- **UCSD Research Residents – Drs Fricka, Upasani, Varley, Carreau**
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