

“Bare Bones”

© 2000 Francesca Pera

“Use of Systemic Osteoporosis Drugs in Select High Risk Patients Undergoing Spine Surgery”

30th Annual Metabolic Bone Disease
Society Meeting
Denver, CO
Oct 11, 2018

Kelly Krohn MD

Medical Director Bone Health
The CORE Institute

Chief, Center for Bone Health
Banner University Hospital

Orthopaedic and Spine Institute.

U of AZ College of Medicine
Phoenix, AZ

Disclosure

- Employee of Eli Lilly 2006-2016 with medical responsibility for TPTD
- Currently receive a retirement pension from Eli Lilly
- Speaker/Advisor for Radius
- Speaker for Alexion

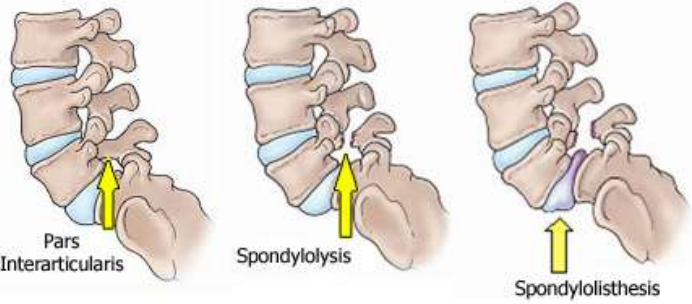
Topics

- Spine fusion surgery intro (lumbar)
- Bone related complications of spine surgery
- Pre-operative Bone Health Assessment
- TPTD/Bisphosphonate data

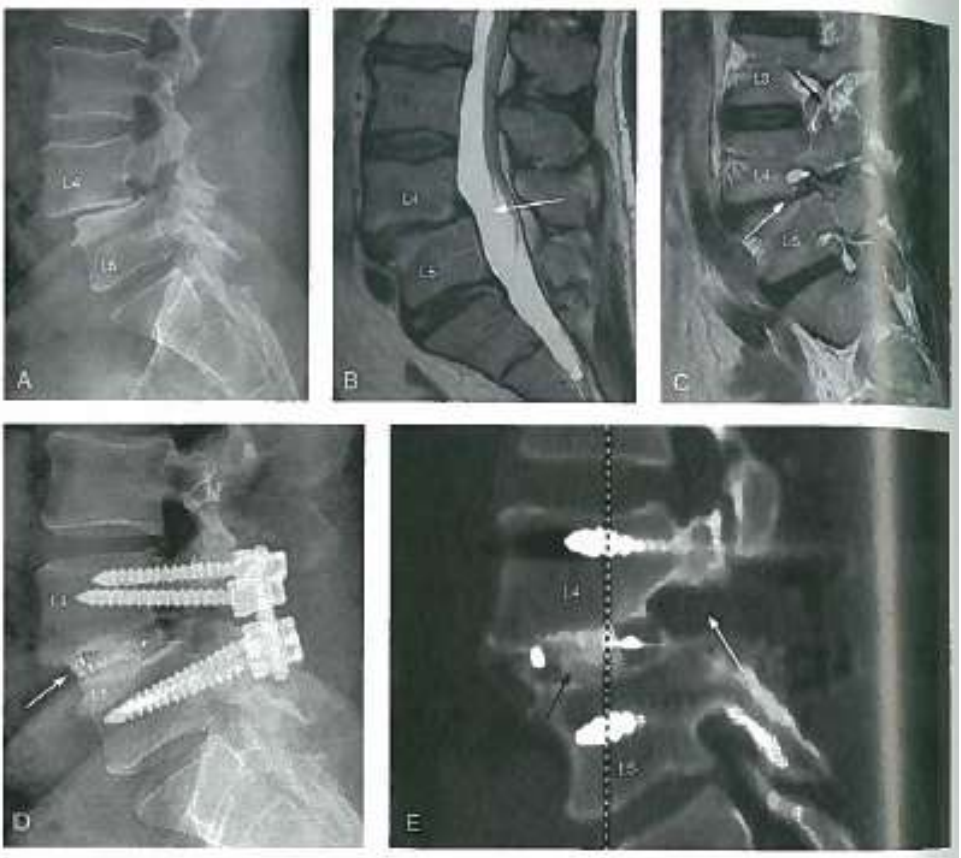
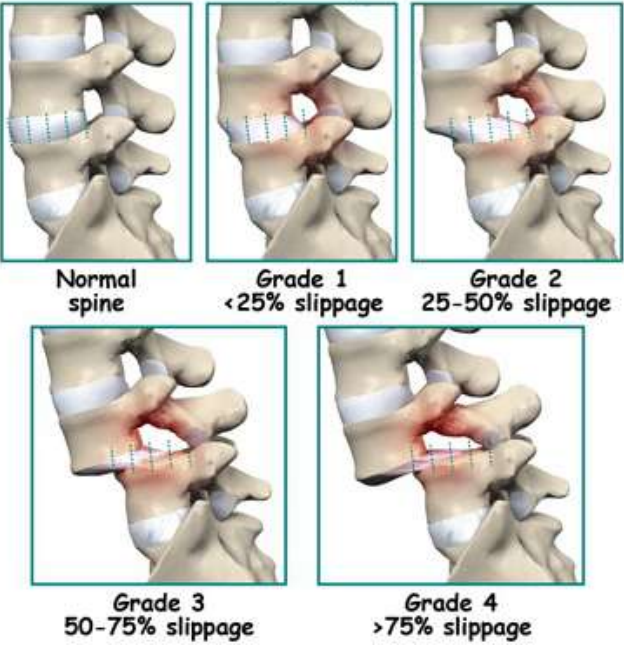
Spine Fusion: Definition

- Spine Fusion (arthrodesis):
 - A surgical procedure to provide internal stability of the spine, by facilitating bony interconnection between two or more of the vertebra, leading to absence of motion between these segments.
- Indications:
 - Degenerative diseases of the spine:
 - Instability, neurologic compression,
 - Deformity: scoliosis, kyphosis, spondylolisthesis
 - Trauma or tumor

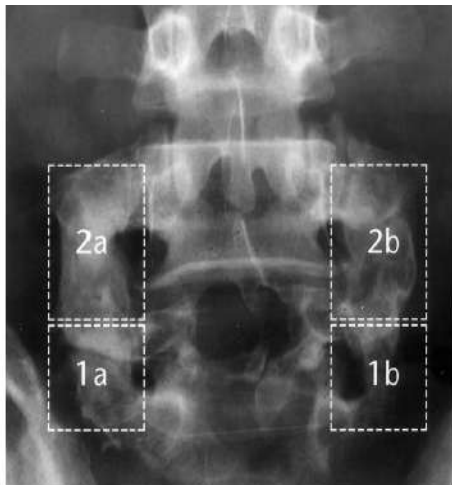
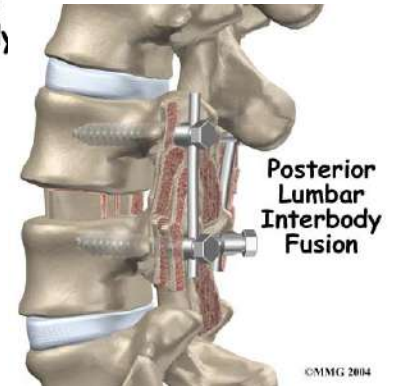
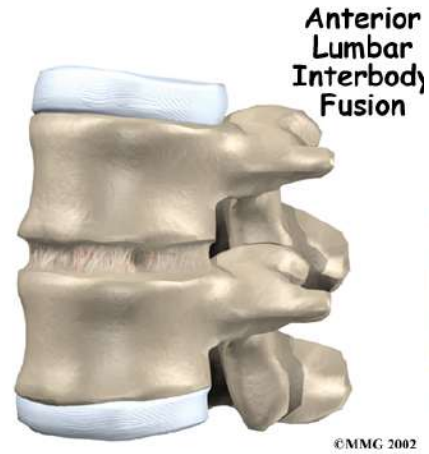
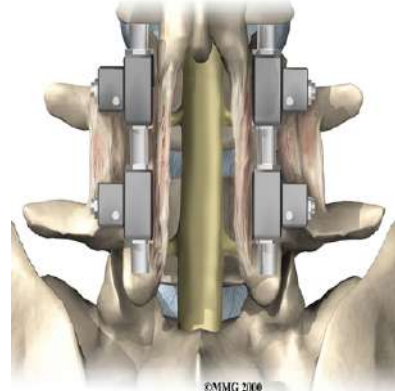
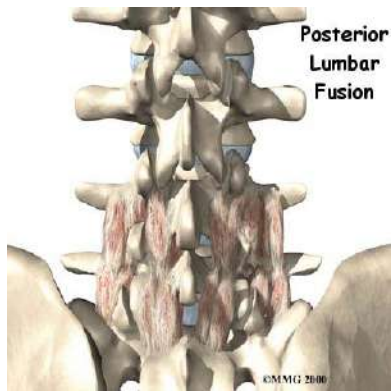
Spondylolisthesis



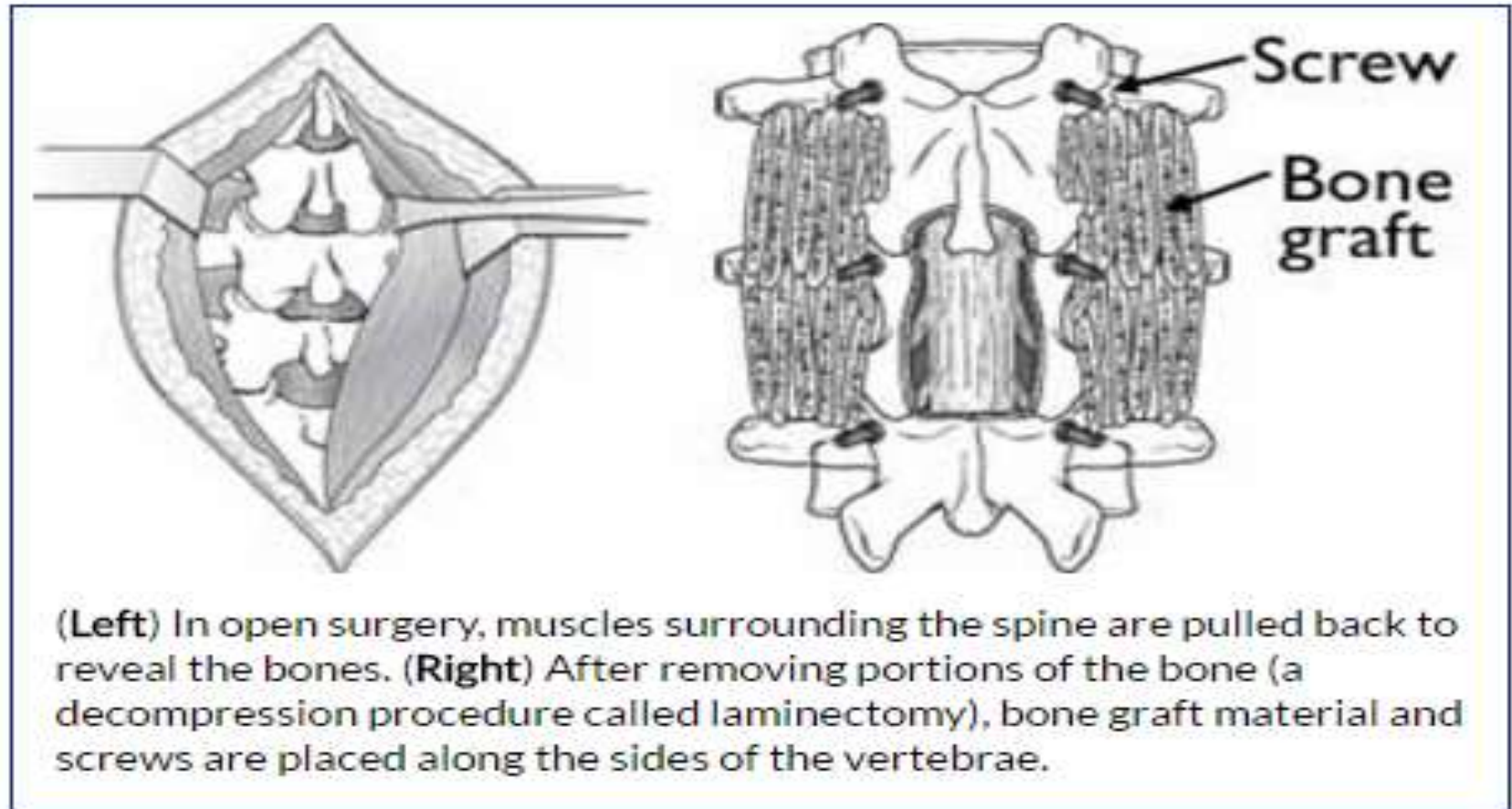
Grades of spondylolisthesis



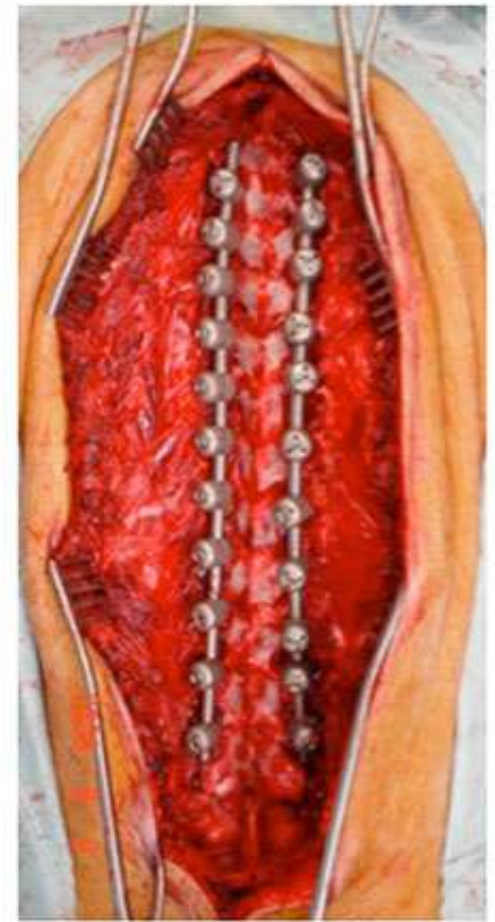
Spine Fusion: Fusion Types



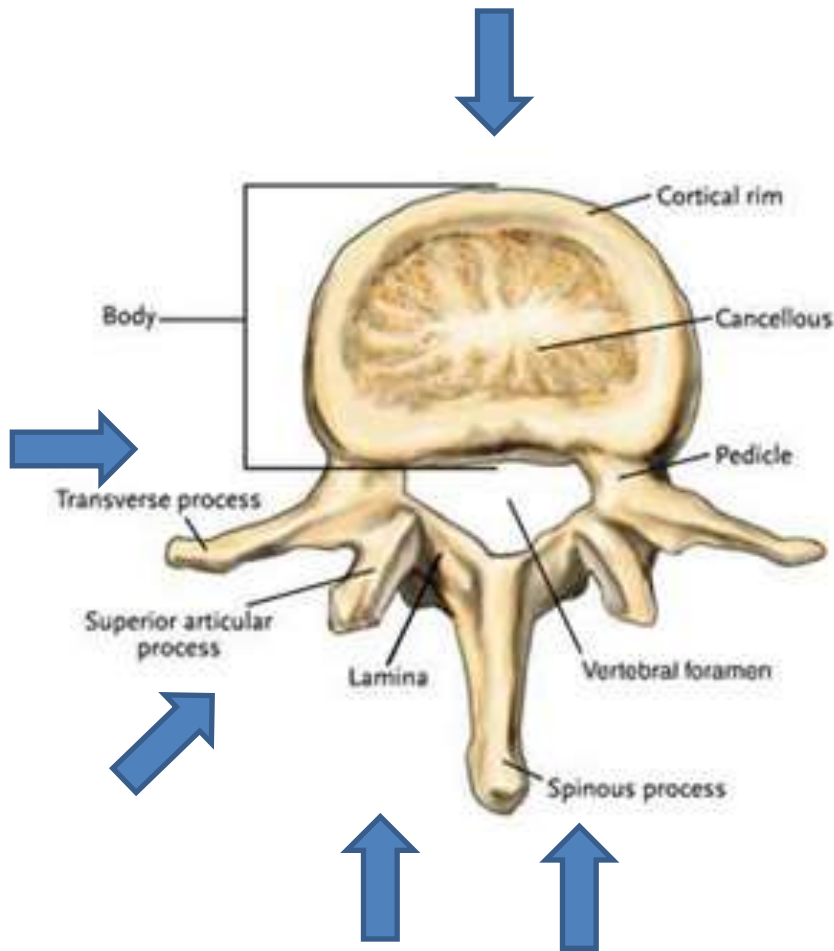
Classic Open Posterior Lateral Fusion



Scoliosis Correction through Posterior Approach



Spine Fusion Procedures



ALIF: Anterior lumbar interbody fusion

PLIF: Posterior lumbar interbody fusion

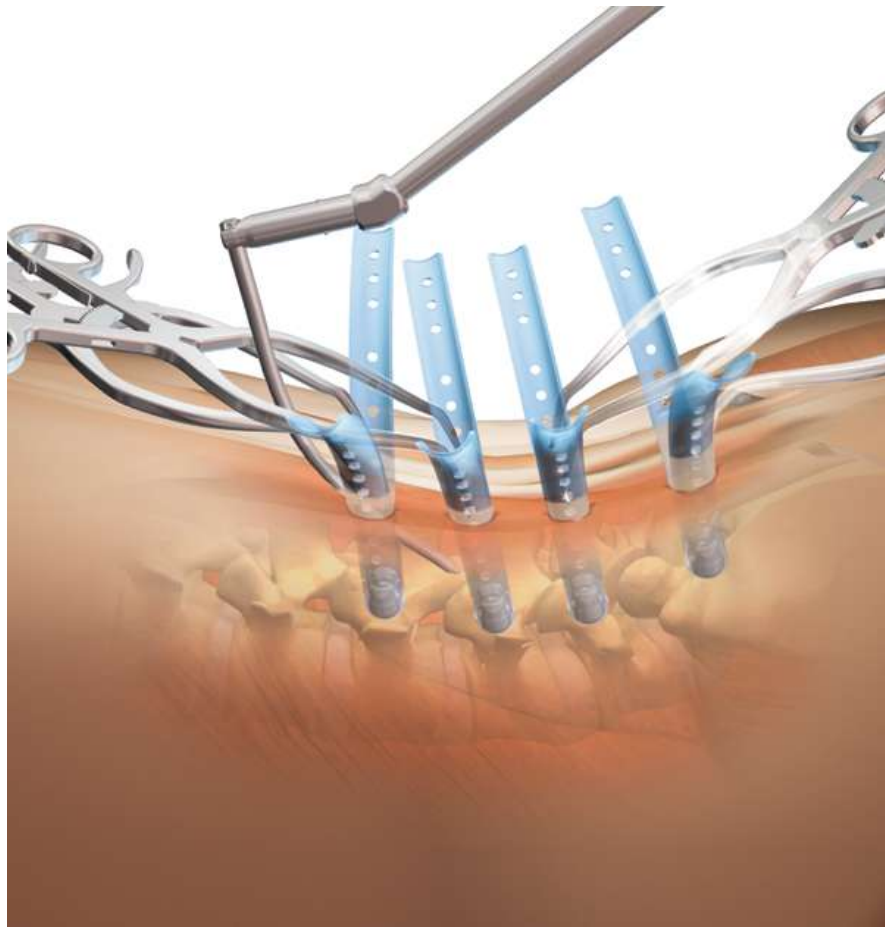
TLIF: Transforaminal lumbar interbody fusion

XLIF or LLIF: eXtreme lateral interbody fusion

PLF: Posteriolateral fusion

Circumferential fusion (**360°**): ALIF + PLF

MIS: Minimally invasive spine surgery



Minimally invasive spine surgery (MISS) is sometimes called less invasive spine surgery. In these procedures, doctors use specialized instruments to access the spine through small incisions.

Spine Fusion: Trends

Increase in spine fusion procedures in US (and other countries):

- Aging population, with desire to remain active
- Procedure improved and recovery time shortened

Highly specialized spine surgeons

- Fellowship trained (ortho and neuro) / Fusion procedure evolved: ALIF, PLF, PLIF, TLIF, XLIF, Mis-TLIF

Fusion success improved while concern remains

- Bone morphogenetic protein (BMP) experience
- ?systemic anabolic agents
- More ongoing research on osteosynthesis

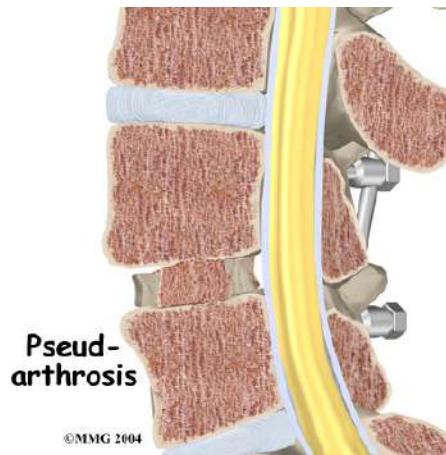
Competitive innovation in device, while no systemic agents are currently approved by FDA for spine fusion

- Device companies
- FDA device division and regulation

Potential Complications of Spine Fusion Related to Poor Bone Health

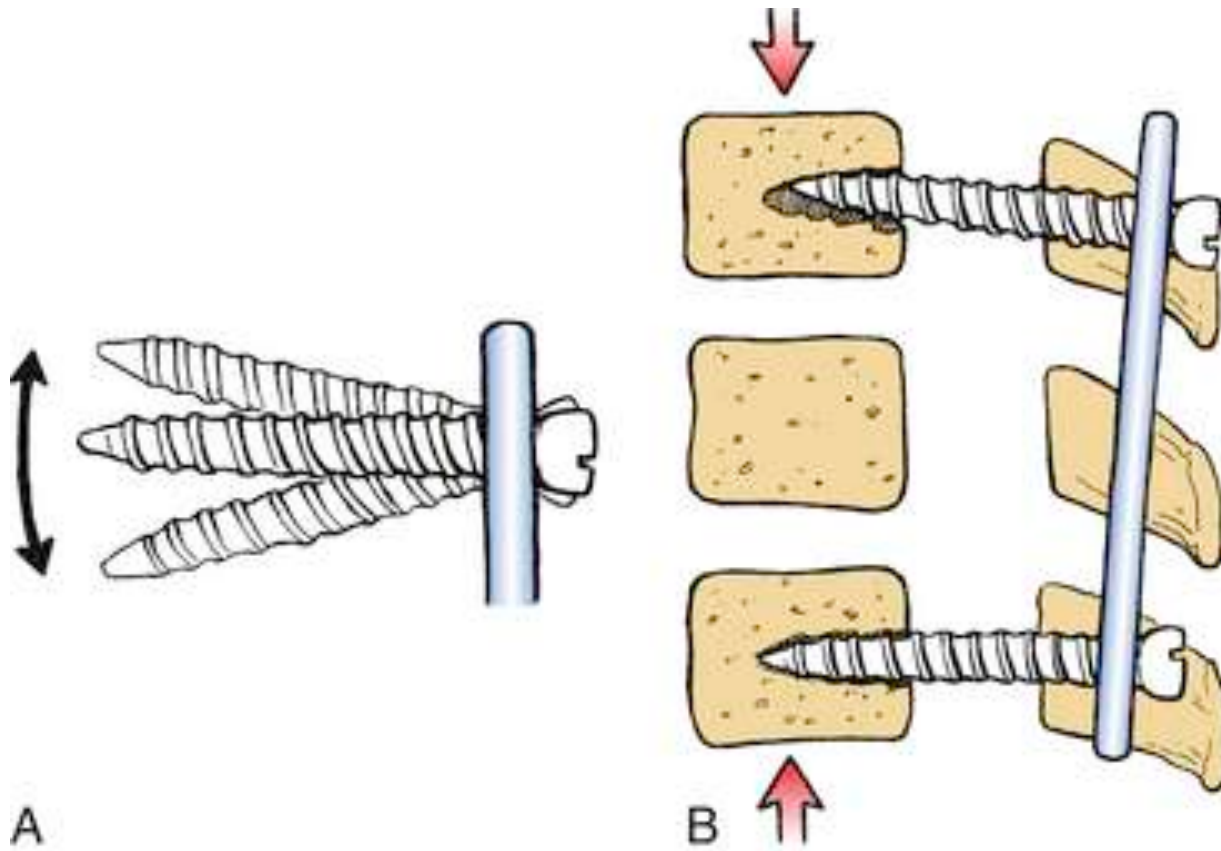
- Fusion Failure (pseudoarthrosis)
- Construct/Device failure (pedicle screw loosening, interbody device subsistence)
- Proximal Junctional Kyphosis due to compression fracture of adjacent vertebral level

Spine Fusion: Fusion Failure



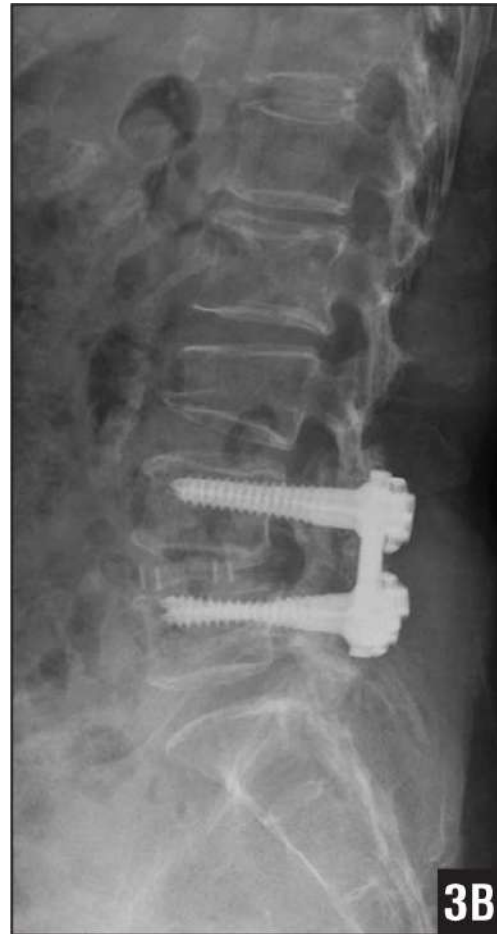


Failure of fusion
(pseudoarthrosis) that
results in significant
segmental movement
and eventual fracturing
of the rod



Pedicle screw loosening

Adjacent Segment Fracture (aka PJK)

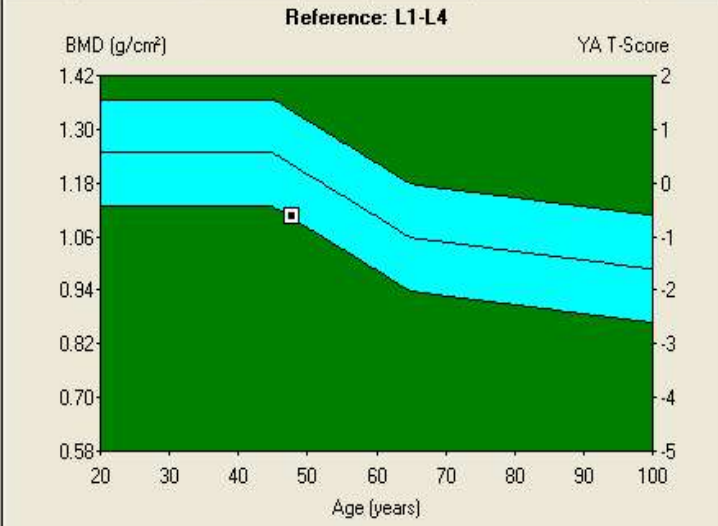
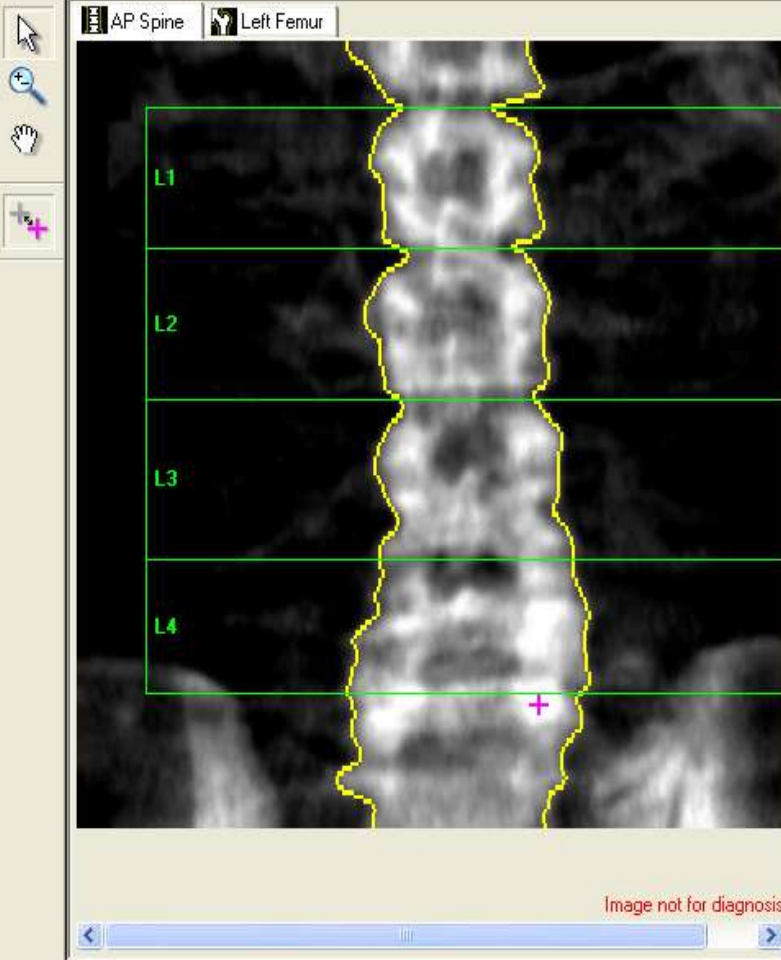


Spine Fusion Trend: US Device Market (projection)

Type	2009	2011	2013	2015	Trend ('10-'15)
Instrumented Thoracolumbar Fusion					
Degenerative	230,300	254,900	282,100	313,300	5.30%
Deformity	39,000	40,600	42,200	43,900	1.90%
Tumor/Trauma	33,300	37,400	41,900	47,200	5.90%
Total	302,600	333,000	366,300	404,400	4.90%
Lumbar Spine Fusion (traditional)					
Anterior plates	48,690	50,010	51,290	52,860	1.40%
Posterior pedicle screw (PLF)	230,950	256,360	284,280	316,000	5.30%
Lumbar Interbody Fusion (w/ or w/o pedicle screw)					
ALIF	52,990	54,560	55,260	55,590	0.60%
PLIF	43,050	43,150	41,450	37,610	-2.80%
TLIF	63,480	85,070	104,390	126,890	10.70%
LLIF	8,730	17,690	36,280	60,590	42.80%
Stand-alone IBD fusion (w/o pedicle screw)					
ALIF	18,547	22,370	24,314	25,016	-
PLIF	1,679	1,769	1,741	1,655	-
TLIF	2,158	3,063	3,862	4,949	-
LLIF	1,641	4,847	11,428	21,025	-

Pre-operative Bone Health Assessment Prior to Elective Spine Surgery

- *Maybe patients over 50? 65?*
- *Maybe younger in patients with glucocorticoid exposure*
- *Patients undergoing complicated surgery that will require decent quality bone to be successful*



Reference

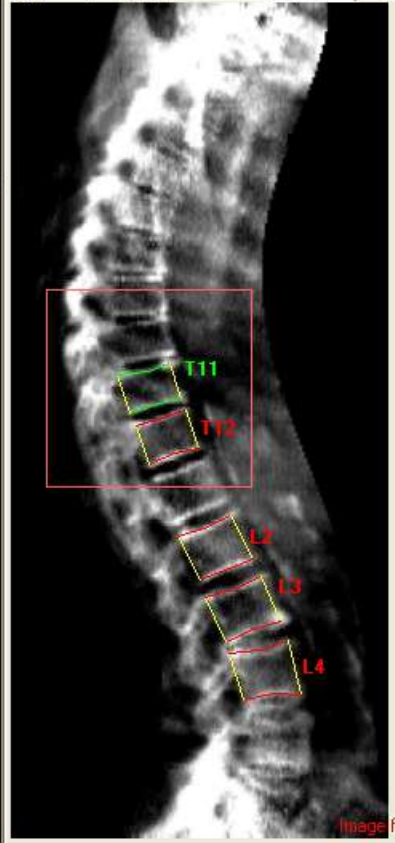
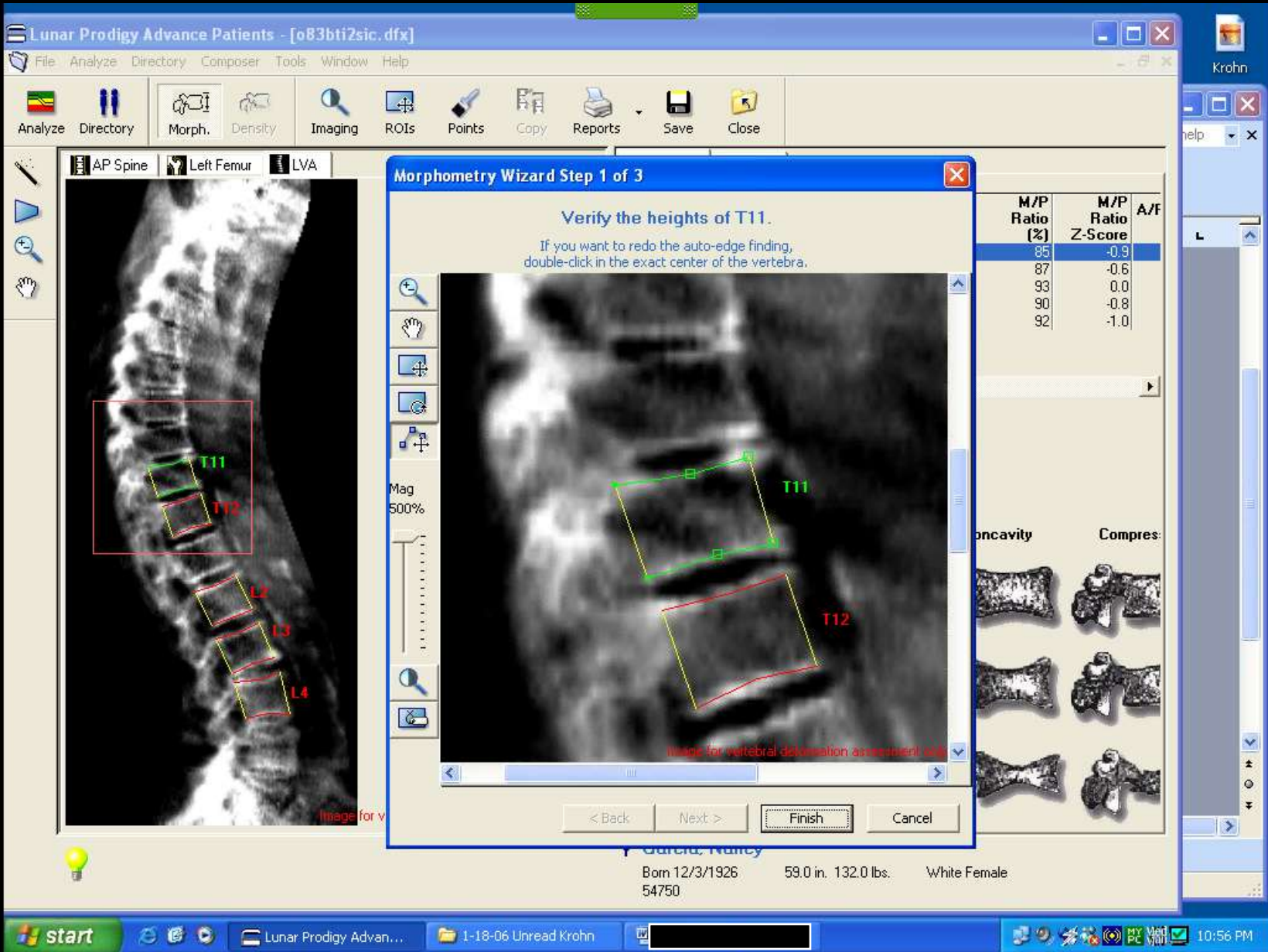
Region	BMD (g/cm³)	YA T-Score	AM Z-Score
L1	1.090	-0.3	-0.7
L2	1.093	-0.9	-1.2
L3	1.076	-1.0	-1.4
L4	1.156	-0.4	-0.7
L1-L2	1.091	-0.6	-1.0
L1-L3	1.085	-0.7	-1.0
L1-L4	1.106	-0.6	-1.0
L2-L3	1.084	-1.0	-1.3
L2-L4	1.110	-0.8	-1.1
L3-L4	1.117	-0.7	-1.0

Standard Results
 Select region: up/down arrows
 Results tab: left/right arrows
 Image tab: tab/shift+tab

Born 5/3/1958 62.2 in. 180.0 lbs. White Female
 31702



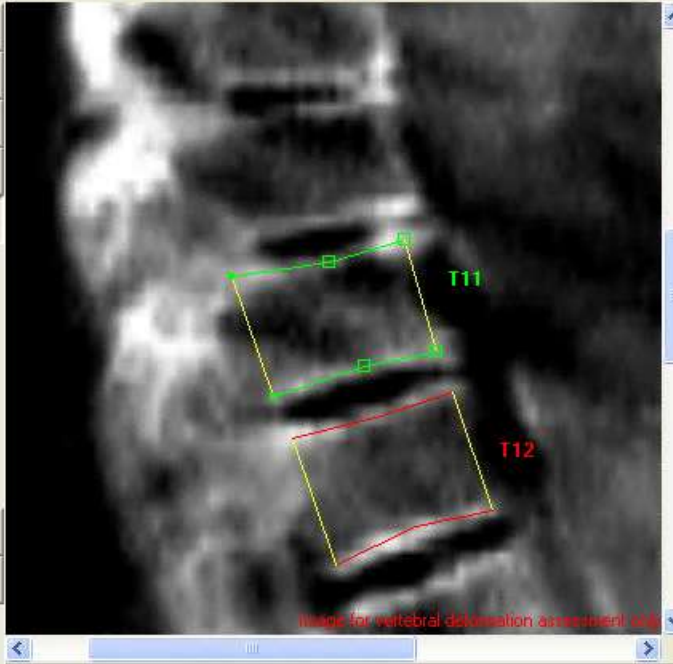
Severe scoliosis and rotation of thoraco-lumbar region



Morphometry Wizard Step 1 of 3

Verify the heights of T11.

If you want to redo the auto-edge finding, double-click in the exact center of the vertebra.

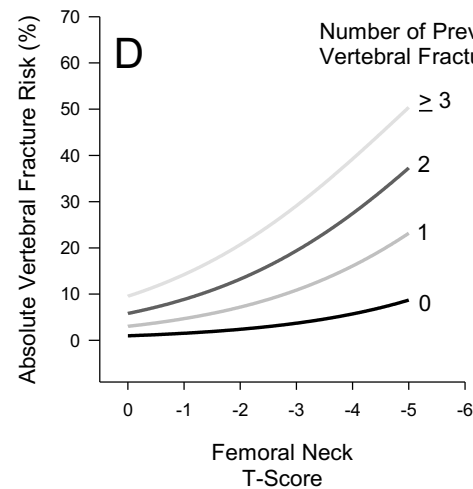
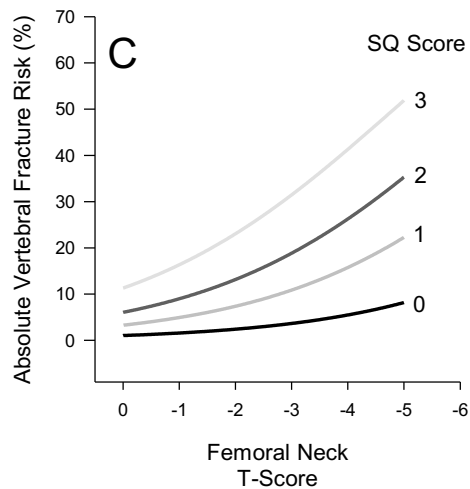
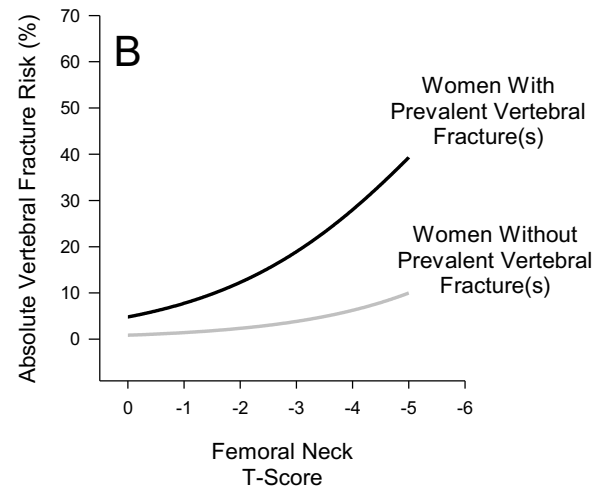
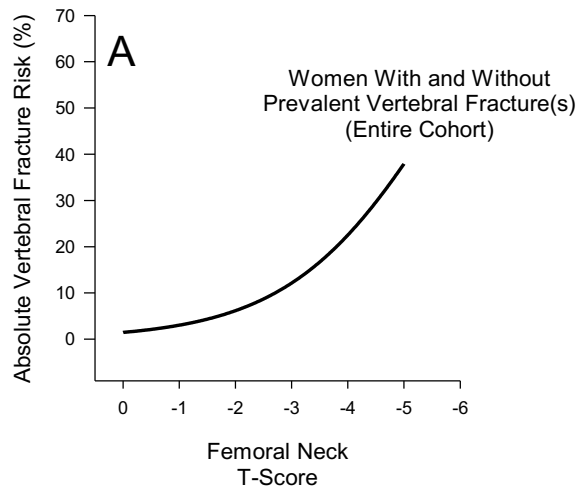


M/P Ratio (%)	M/P Ratio Z-Score	A/F
85	-0.9	
87	-0.6	
93	0.0	
90	-0.8	
92	-1.0	



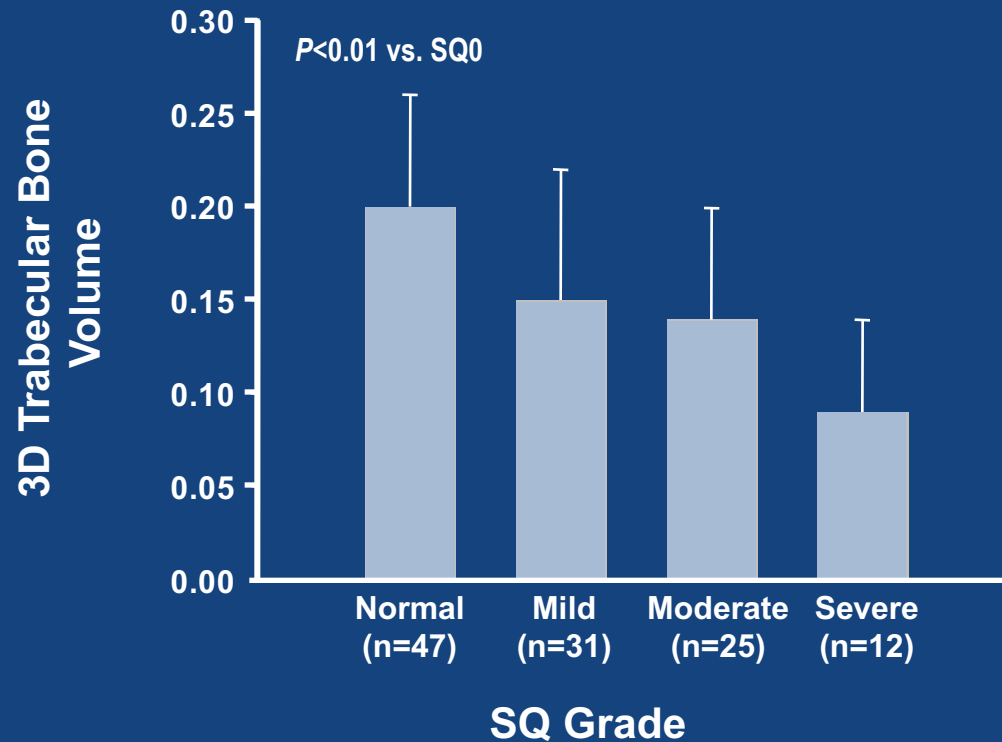
< Back Next > Finish Cancel

Garcia, Nancy
Born 12/3/1926 59.0 in. 132.0 lbs. White Female
54750



“Enhanced Prediction of Fracture Risk Combining Vertebral Fracture Status and BMD”
 Siris, Genant, Laster, Chen, Misurski and Krege
 Osteoporosis International Jan 2007

Relationship Between Vertebral Fracture Grade and Bone Biopsy Results¹



No Vertebral Fracture



Severe Vertebral Fracture



With kind permission from Springer Science and Business Media

Spine fracture status is related to bone biopsy results.

Data were adjusted for age, height, lumbar spine BMD

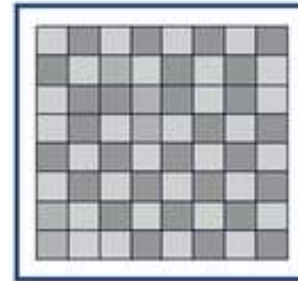
1. *Osteoporos Int.* 2007;18:69-76.

TBS a new parameter: Principles

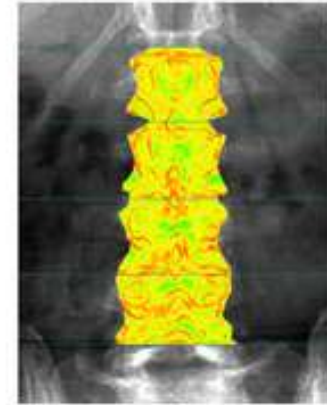
BMD= 0.972



Illustration of
Well-structured
trabecular bone



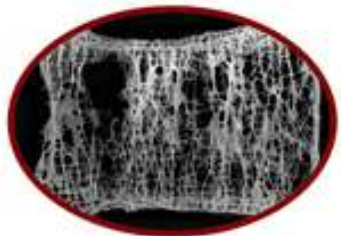
TBS= 1.459



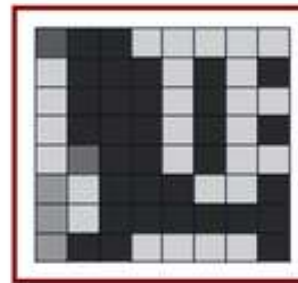
BMD= 0.969



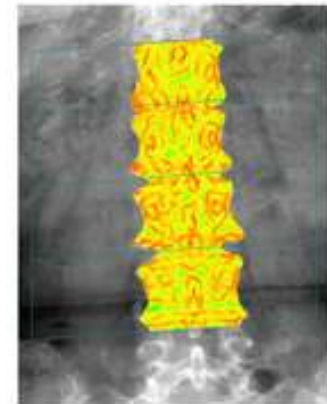
Illustration of
Altered
trabecular bone



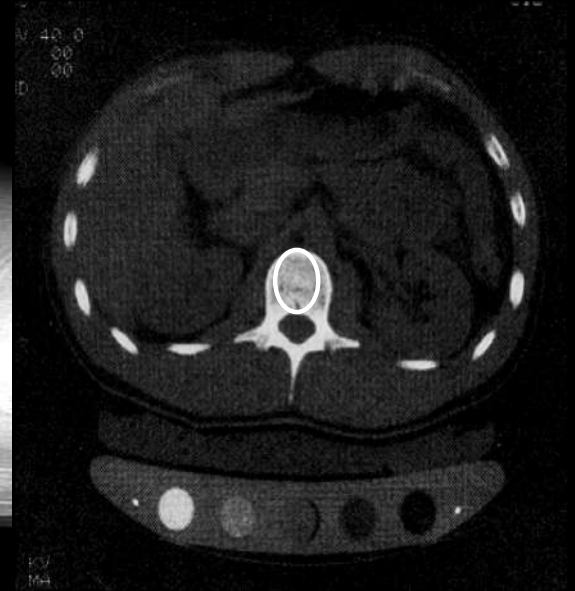
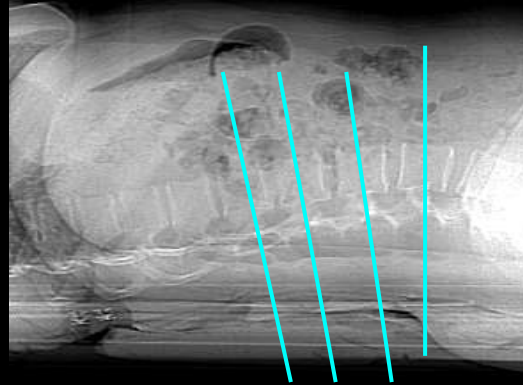
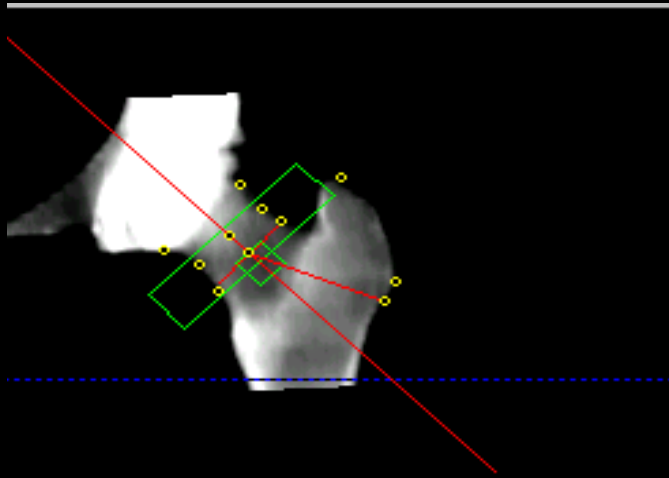
Experimental
variogram



TBS= 1.243



Quantitative CT: qCT



Projectional Hip Volume Scan

Any commercial CT scanner with appropriate software

Reference phantom

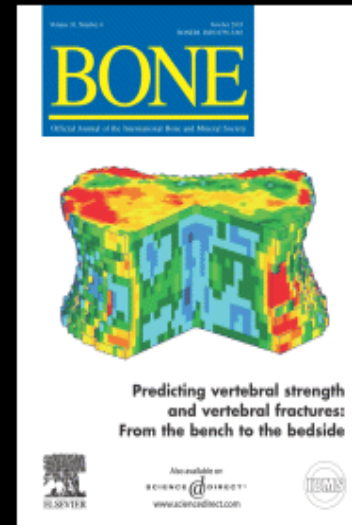
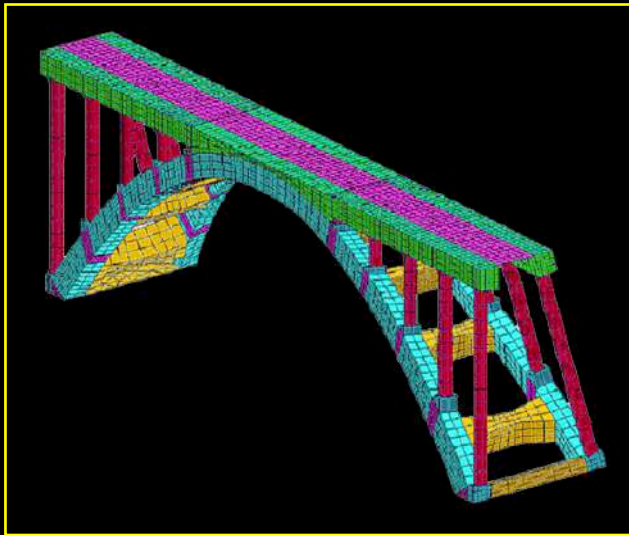
Able to isolate trabecular from cortical bone

Able to give volumetric BMD and geometrical parameters

Single Slice Spine Scan

Finite Element Analysis (FEA)

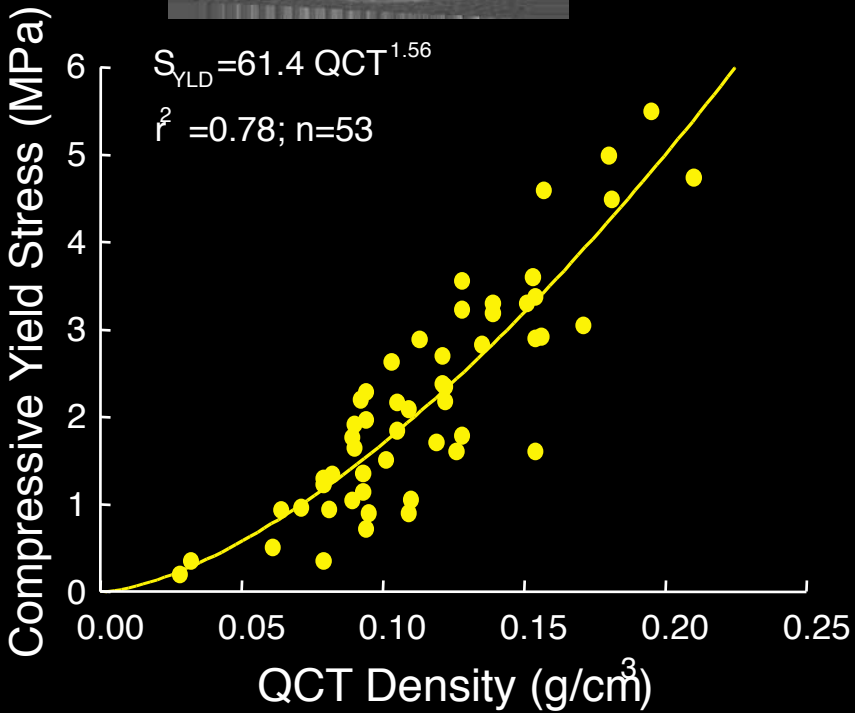
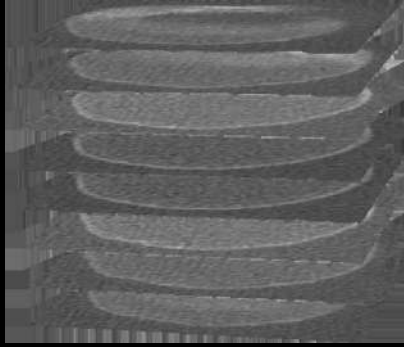
- Well-established method for analysis of complex structures
- Model structure as collection of “finite elements”
- Assign material properties to each element and external forces to whole model
- Compute strength or other structural performance



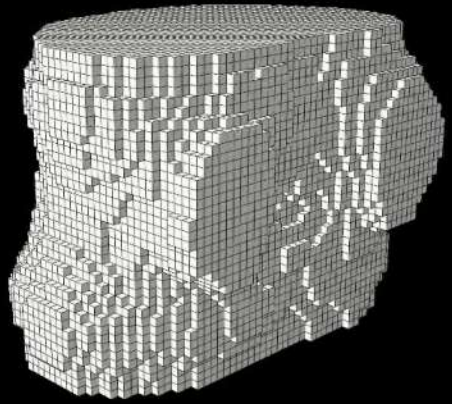
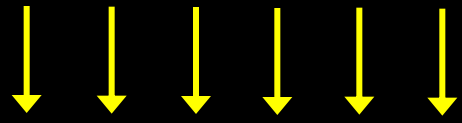
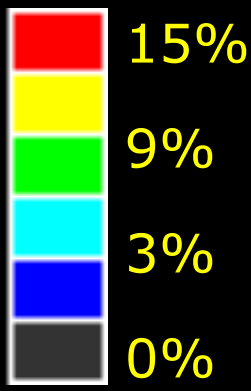
Crawford, Bone 2003

FEA and Vertebral Strength Assessment

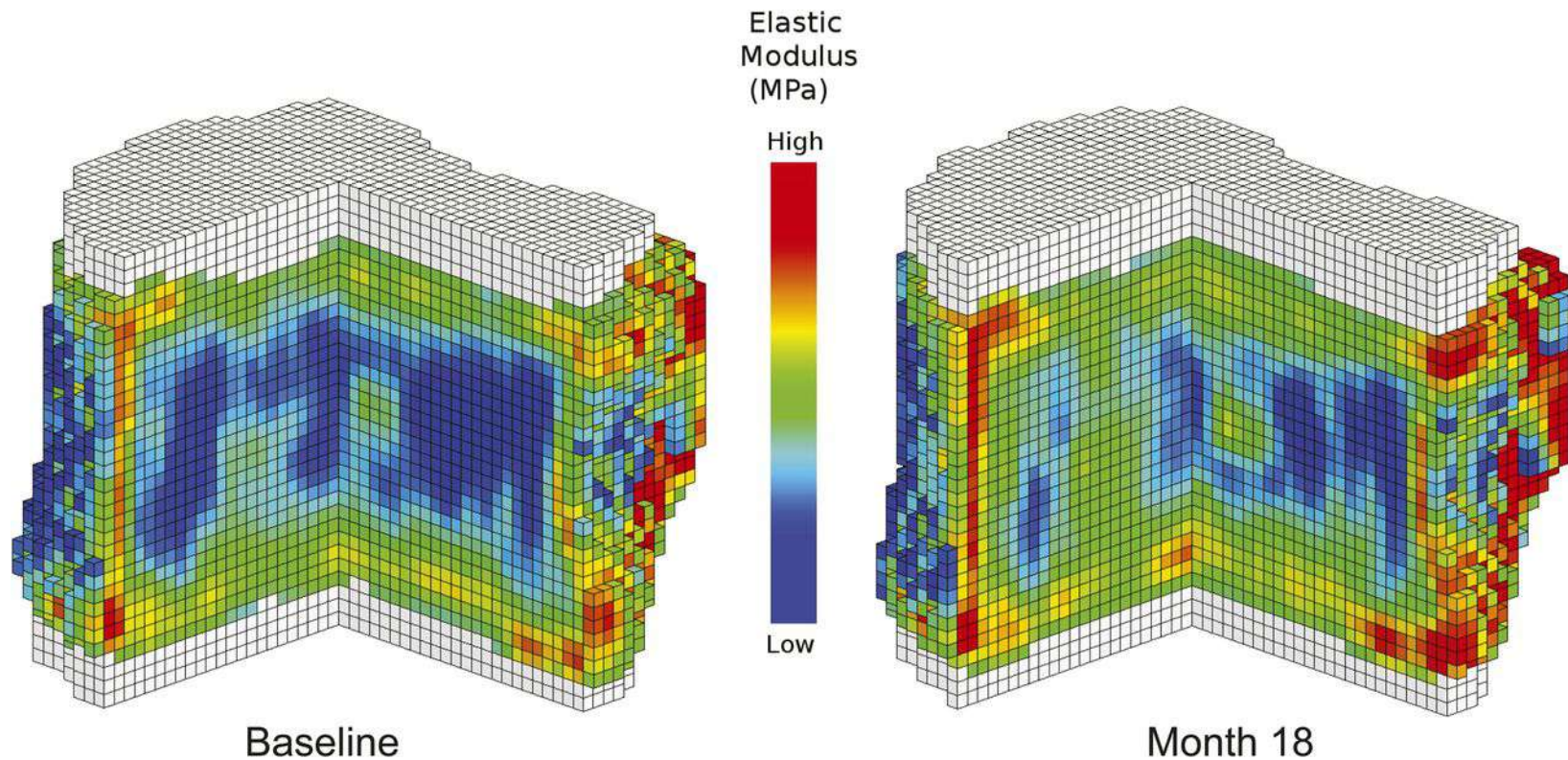
QCT Images (1 mm resolution)



Elastic Modulus

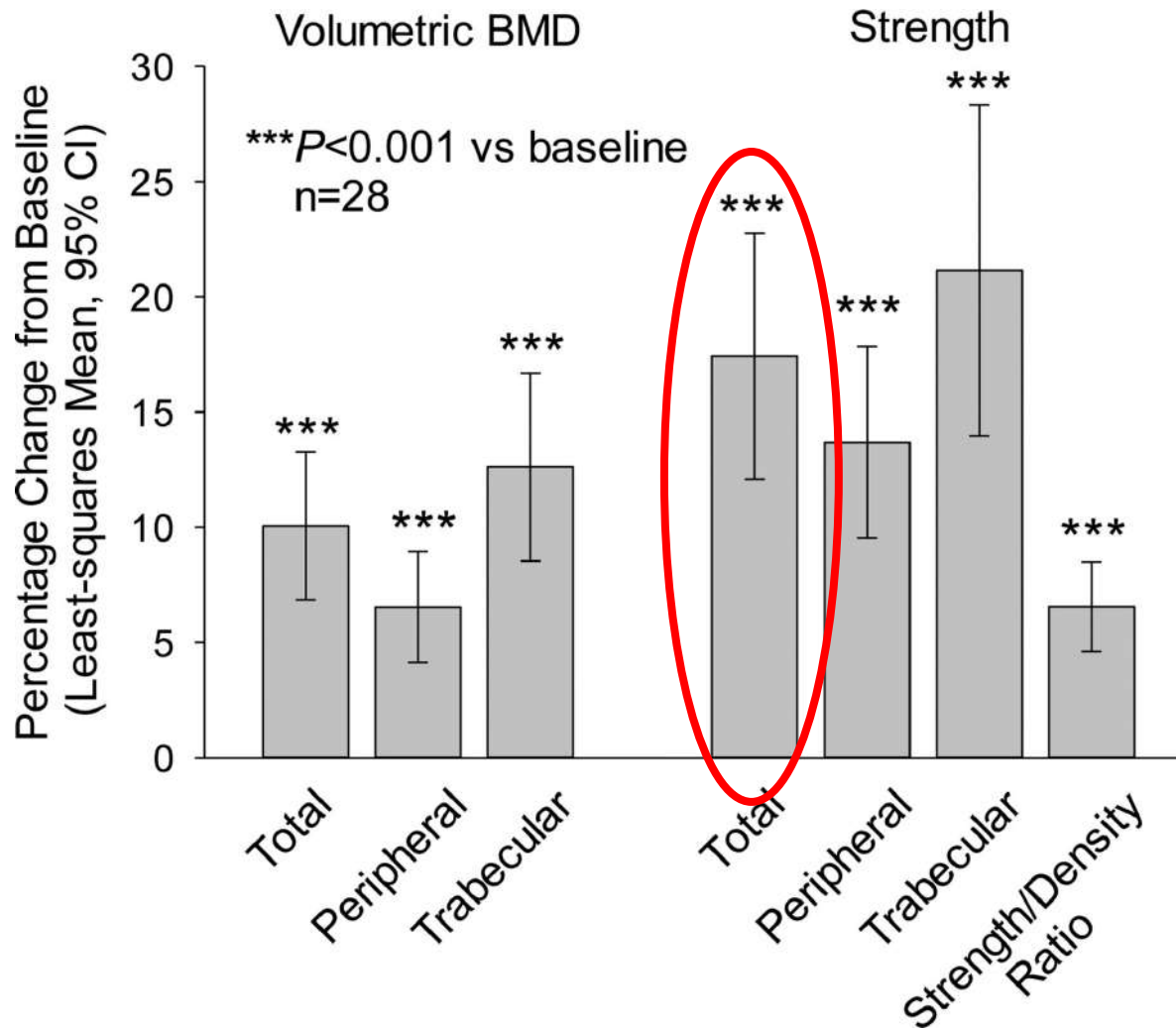


Quantitative CT-based finite element models of the L3 vertebra from a representative study subject before and after treatment with teriparatide.



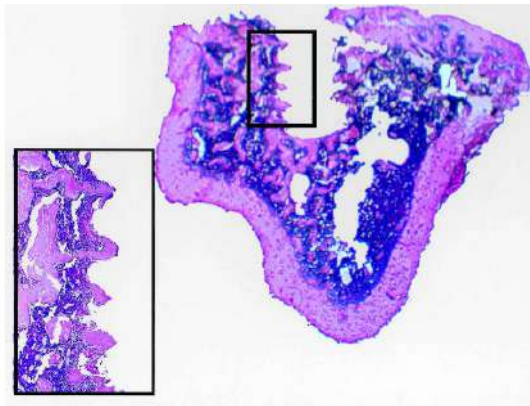
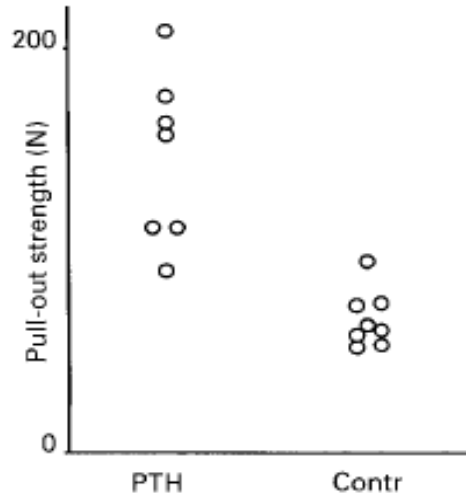
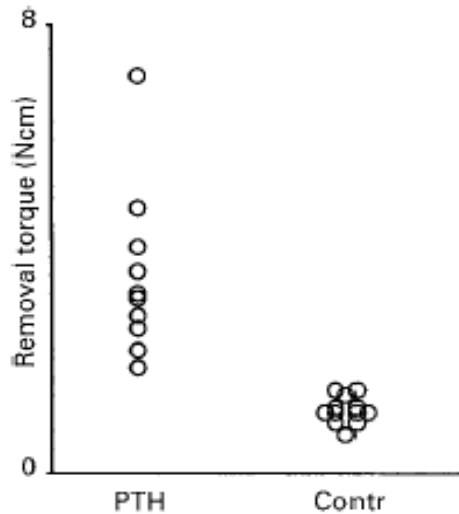
Kleerekoper M et al. J Bone Joint Surg Am 2014;96:e90

Vertebral outcomes for month-eighteen completers (full-set analysis).

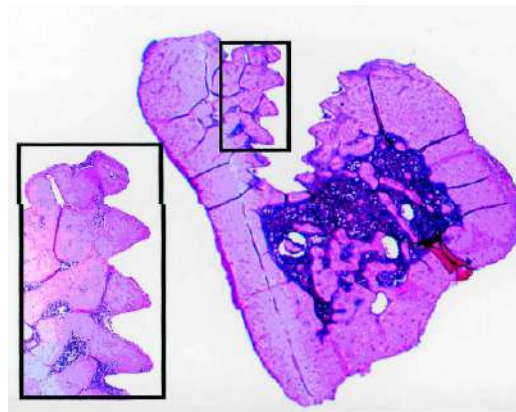


Kleerekoper M et al. J Bone Joint Surg Am 2014;96:e90

PTH on Implant Fixation in Rats



Control



PTH

- Stainless-steel screw were inserted in proximal tibia of 28 rats
- 14 rats, PTH(1-34) 60 ug/kg/day injection for 4 weeks
- 14 rats, vehicle daily injection for 4 weeks
- Histological examination showed that both groups had areas of soft tissue at the implant-bone interface, but these appeared less in the PTH group.
- **PTH may enhance the early fixation of orthopaedic implants**

More than 6 Months of Teriparatide Treatment Was More Effective for Bone Union than Shorter Treatment Following Lumbar Posterolateral Fusion Surgery

Seiji Ohtori, Sumihisa Orita, Kazuyo Yamauchi, Yawara Eguchi, Nobuyasu Ochiai, Kazuki Kuniyoshi, Yasuchika Aoki, Junichi Nakamura, Masayuki Miyagi, Miyako Suzuki, Gou Kubota, Kazuhide Inage, Takeshi Sainoh, Jun Sato, Yasuhiro Shiga, Koki Abe, Kazuki Fujimoto, Hiroto Kanamoto, Gen Inoue, Kazuhisa Takahashi

Department of Orthopaedic Surgery, Graduate School of Medicine, Chiba University, Chiba, Japan

Forty-five women with osteoporosis diagnosed with degenerative spondylolisthesis from one of the three treatment groups were evaluated based on: **short-duration treatment** (average, 5.5 months; n=15; daily subcutaneous injection of 20 µg teriparatide), **long-duration treatment** (average, 13.0 months; n=15; daily subcutaneous injection of 20 µg teriparatide), and **bisphosphonate treatment** (average, 13.0 months; n=15; weekly oral administration of 17.5 mg risedronate).

All patients underwent PLF with a local bone graft. Fusion rate and duration of bone union were **evaluated 1.5 years after surgery**.

Bone union rate and average duration for bone union were **92%** in the long-duration treatment group, **80%** in the short-duration treatment group, and **70%** in the bisphosphonate treatment group, respectively.

SURGERY

Comparison of Teriparatide and Bisphosphonate Treatment to Reduce Pedicle Screw Loosening After Lumbar Spinal Fusion Surgery in Postmenopausal Women With Osteoporosis From a Bone Quality Perspective

Seiji Ohtori, MD, PhD, Gen Inoue, MD, PhD, Sumihisa Orita, MD, PhD, Kazuyo Yamauchi, MD, PhD, Yawara Eguchi, MD, PhD, Nobuyasu Ochiai, MD, PhD, Shunji Kishida, MD, PhD, Kazuki Kuniyoshi, MD, PhD, Yasuchika Aoki, MD, PhD, Junichi Nakamura, MD, PhD, Tetsuhiro Ishikawa, MD, PhD, Masayuki Miyagi, MD, PhD, Hiroto Kamoda, MD, PhD, Miyako Suzuki, MD, PhD, Gou Kubota, MD, Yoshihiro Sakuma, MD, Yasuhiro Oikawa, MD, Kazuhide Inage, MD, Takeshi Sainoh, MD, Masashi Takaso, MD, PhD, Tomoaki Toyone, MD, PhD, and Kazuhisa Takahashi, MD, PhD

- 62 postmenopausal women undergoing decompression and 1-2 level fusion were given either risedronate 2.5 mg/d, TPTD 20 mcg/d or no medication for osteoporosis. **OP medications were given 2 months prior to surgery and 10 months post-operatively**
- The incidence of pedicle screw loosening in the teriparatide (X-ray-CT) **(7-13%)** group was significantly lower than that in the risedronate **(13-26%)** or the control group **(15-25%)**
- (P < .05)
- Conclusion: Our findings suggest that teriparatide increased the quality of the lumbar spine pedicle bone and reduced the loosening of pedicle screws compared with risedronate or control.

Teriparatide increases the insertional torque of pedicle screws during fusion surgery in patients with postmenopausal osteoporosis.

Inoue G¹, Ueno M, Nakazawa T, Imura T, Saito W, Uchida K, Ohtori S, Toyone T, Takahira N, Takaso M.

- Fusion surgery for the thoracic and/or lumbar spine was performed in 29 postmenopausal women with osteoporosis
- Patients were treated with teriparatide (n = 13) or not (n = 16) before the surgery
- Patients received preoperative teriparatide therapy as either a daily (20 µg/day, n = 7) or a weekly (56.5 µg/week, n = 6) injection for a mean of 61.4 days and a minimum of 31 days
- The mean insertional torque value in the teriparatide group was 1.28 ± 0.42 Nm (Newton meters), which was significantly higher than in the control group 1.08 ± 0.52 Nm, (p < 0.01).
- There was no significant difference between the daily and the weekly teriparatide groups with respect to mean insertional torque value (1.34 ± 0.50 Nm and 1.18 ± 0.43 Nm, respectively, p = 0.07).

Conclusion: Teriparatide injections beginning at least 1 month prior to surgery were effective in increasing the insertional torque of pedicle screws during surgery in patients with postmenopausal osteoporosis



ORIGINAL ARTICLE

Teriparatide improves volumetric bone mineral density and fine bone structure in the UIV+1 vertebra, and reduces bone failure type PJK after surgery for adult spinal deformity

M. Yagi^{1,2} · H. Ohne¹ · T. Konomi¹ · K. Fujiyoshi¹ · S. Kaneko¹ · T. Komiyama¹ · M. Takemitsu¹ · Y. Yato¹ · M. Machida¹ · T. Asazuma¹

Forty-three patients who started TPTD therapy immediately after surgery and 33 patients who did not receive TPTD were enrolled in this prospective case series. These patients were female, over 50, surgically treated for ASD, and followed for at least 2 years. Preoperative and postoperative standing whole spine X-rays and dual-energy X-ray absorptiometry scans, and multidetector CT images obtained before and 6 months after surgery were used to analyze the bone strength in the vertebra above the upper-instrumented vertebra (UIV+1).

After 6 months of treatment, mean hip-bone mineral density (BMD) increased from 0.721 to 0.771 g/cm² in the TP group and decreased from 0.759 to 0.729 g/cm² in the control group. The bone volume/tissue volume ratio increased from 46 to 54 % in the TP group, and the trabecular bone thickness and number increased by 14 and 5 %, respectively.

At the 2-year follow-up, the PJK type 2 incidence was significantly lower in the TPTD group (4.6%) than in the control group (15.2%; $p=0.02$).

Conclusions: Prophylactic TPTD treatment improved the volumetric BMD and fine bone structure at UIV+1 and reduced the PJK-type 2 incidence

Does Systemic Administration of Parathyroid Hormone after Non-instrumented Spinal Fusion Surgery Improve Fusion Rates and Fusion Mass in Elderly Patients Compared to Placebo in Patients With Degenerative Lumbar Spondylolisthesis?

Jespersen AB^{1,2}, Andresen ADK^{1,2}, Jacobsen MK^{1,2}, Andersen MØ^{1,2}, Carreon LY^{1,2}.

Patients with degenerative spondylolisthesis scheduled for non-instrumented posterolateral fusion were randomized to receive 90-day subcutaneous injections with 20 µg teriparatide (N = 41) or placebo (N = 46) in a 1:1 fashion. Fusion volume and quality was evaluated using 12 month postoperative fine cut CT scans.

RESULTS:

The two groups were comparable in terms of age, gender and numbers of levels operated. PTH treatment was well tolerated but provided no additional benefit versus placebo. Fusion rates, the mean volume and robustness of the fusion mass were similar between the PTH and placebo groups.

CONCLUSIONS:

90-day subcutaneous administration of 20 µg teriparatide did not increase fusion volume or improve the quality of the fusion mass in elderly patients compared to placebo after non-instrumented spinal fusion surgery for degenerative spondylolisthesis.

Does alendronate disturb the healing process of posterior lumbar interbody fusion? A prospective randomized trial

Clinical article

KEN NAGAHAMA, M.D.,¹ MASAHIRO KANAYAMA, M.D.,¹ DAISUKE TOGAWA, M.D.,¹ TOMOYUKI HASHIMOTO, M.D.,¹ AND AKIO MINAMI, M.D.²

¹Spine Center, Hakodate Central General Hospital, Hakodate; and ²Department of Orthopaedic Surgery, Hokkaido University, Sapporo, Hokkaido, Japan

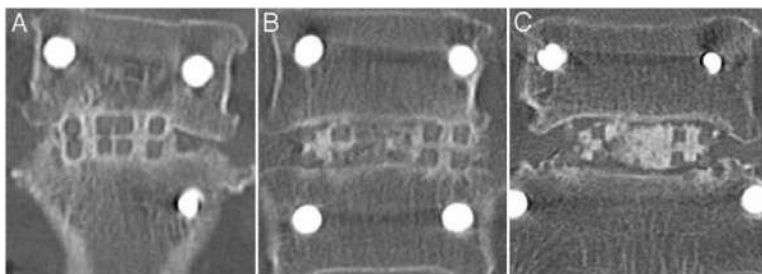


FIG. 1. Computed tomography evaluation of bridging bone formation. Coronal multiplanar reconstructed CT was used to evaluate bridging bone formation. Bridging bone formation was graded into 3 categories, illustrated in panels **A**, **B**, and **C**, respectively: Grade A (bridging bone through bilateral cages), Grade B (bridging bone through unilateral cage), or Grade C (incomplete bony bridging).

- 40 patients randomized to ALN 35 mg/wk vs Vit D
- Single level PLIF with cage device
- CT bridging across levels graded A, B and C
- Followed for one year
- Also looked at vertebral fractures and cage subsistence

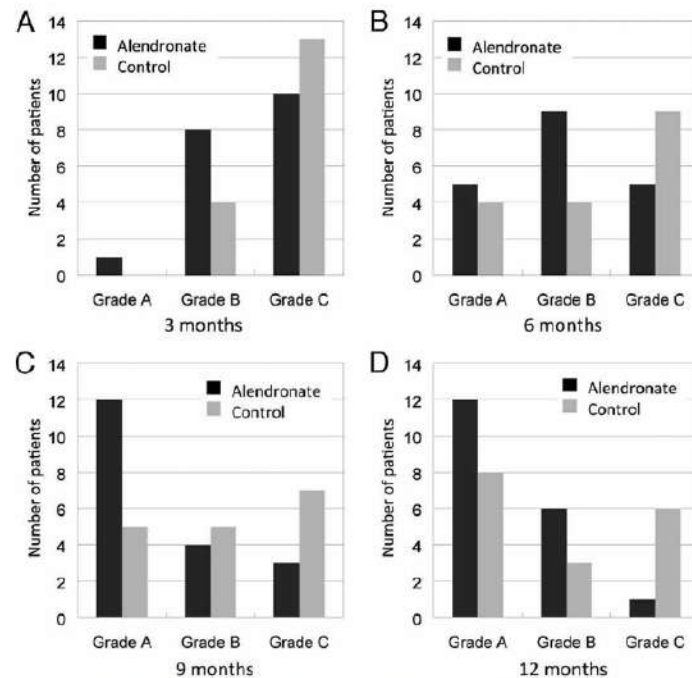


FIG. 2. Bridging bone formation. Bridging bone formation (Grade A or B) was more frequently observed in the alendronate group at all postoperative periods. At 12 months postoperatively, 18 (95%) of 19 patients in the alendronate group and 11 (65%) of 17 patients in the control group had bridging bone formation. The fusion rate was significantly higher in the alendronate group than in the control group ($p = 0.025$, Mann-Whitney U-test).

Does alendronate disturb the healing process of posterior lumbar interbody fusion? A prospective randomized trial

Clinical article

**KEN NAGAHAMA, M.D.,¹ MASAHIRO KANAYAMA, M.D.,¹ DAISUKE TOGAWA, M.D.,¹
TOMOYUKI HASHIMOTO, M.D.,¹ AND AKIO MINAMI, M.D.²**

¹Spine Center, Hakodate Central General Hospital, Hakodate; and ²Department of Orthopaedic Surgery, Hokkaido University, Sapporo, Hokkaido, Japan

Results Continued:

- There was **no pedicle screw loosening reported in either arm**
- There were **fewer adjacent fractures in the ALN arm zero vs 4 in Vit D arm**
- **Cage subsistence was seen in one ALN patient and 5 Vit D patients**
- No significant difference in the Oswestry scores between groups. 3 in ALN group did poorly and 4 in D group did poorly (less than 20% improvement)...in those that did poorly pseudoarthrosis and vertebral compression fractures were common

Conclusion: Treatment with ALN in patients with OP undergoing spine fusion reduces subsequent vertebral compression fractures and cage subsistence. The mechanical circumstances of ALN treatment postop may overcome any potential detrimental biological effect on bone healing.

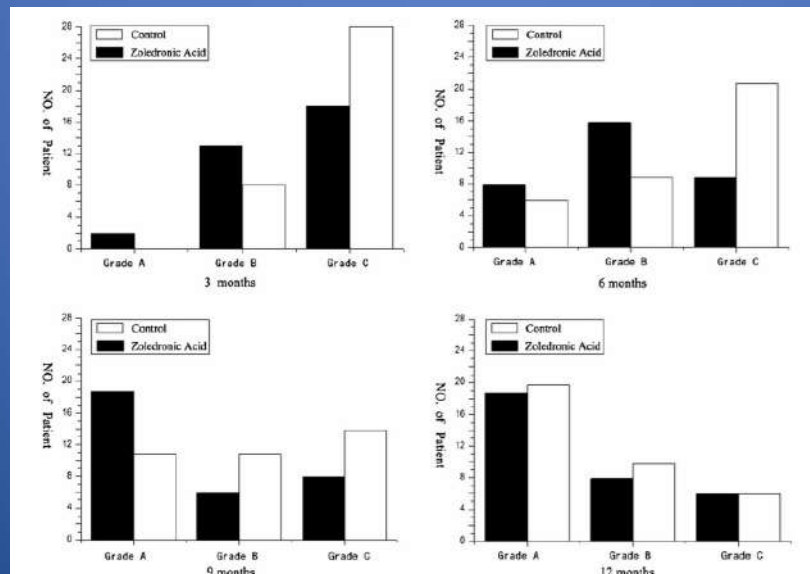
Effects of zoledronic acid on bone fusion in osteoporotic patients after lumbar fusion

F. Chen¹ · Z. Dai¹ · Y. Kang¹ · G. Lv¹ · E. T. Keller^{3,4,5} · Y. Jiang^{2,3,5}

Seventy-nine patients were randomized to zoledronic acid (5 mg) or saline. Infusions were done 3 days after surgery.

65 women and 14 men were randomized and 69 patients completed the 12 month follow-up. All patients had single level degenerative spondylolisthesis and had OP by DXA BMD of -2.5 SD or lower at hip or spine. Patients underwent decompression and the disc material was removed. Local bone and allograft was packed space into the disc. Pedicle screws and rods were placed from a posterior approach.

Radiographic bone bridging was graded A (complete), B (bridging with one body) or C (incomplete bone bridging)



Effects of zoledronic acid on bone fusion in osteoporotic patients after lumbar fusion

F. Chen¹ · Z. Dai¹ · Y. Kang¹ · G. Lv¹ · E. T. Keller^{3,4,5} · Y. Jiang^{2,3,5}

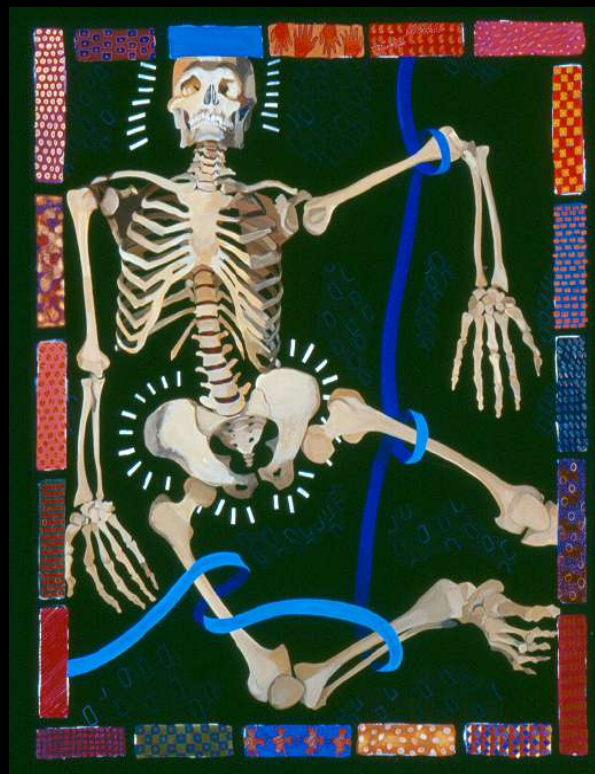
Results Continued:

- BMD was preserved in the zol arm and there was generally loss of BMD (hip) in the saline arm
- There were no adjacent vertebral fractures in the zol arm and 6 patients (17%) had fractures in the saline arm
- There was no pedicle screw loosening in either arm
- Oswestry scores were significantly better in zol compared to saline at 9 and 12 months post-surgery

Conclusion: Treatment with zol in osteoporosis patients with spinal fusion shortens the time to **radiographic fusion**, prevents subsequent vertebral compression fractures and improves clinical outcomes.

Conclusions

1. Older patients undergoing elective spine surgery have considerable risk for bone related complications
2. We can assess who is at highest risk for these complications....much like we do for standard OP fracture risk assessment with emphasis on vertebral fractures
3. Anabolic drugs appear to reduce complications and possibly improve fusion success. Anti-resorptive agents do not appear to reduce fusion success and may reduce complications like screw failure and adjacent segment fracture.



krohnkelly@yahoo.com

“Bare Bones”

© 2000 Francesca Pera

Q & A