Novel Surface Technologies In Spine

Innovasis Spine Symposium
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Louisville, KY

Disclosures

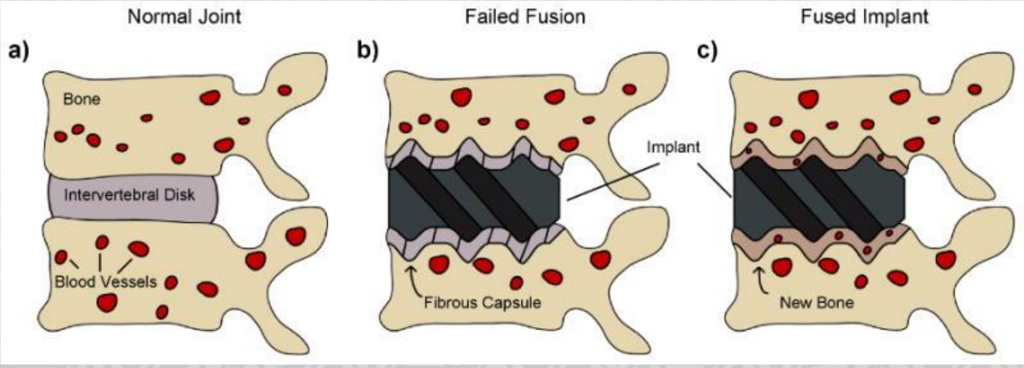
- Innovasis
- Baxter Pharmaceuticals

Surface Technology

- There is growing commercial and scientific interest in spinal implant surface technologies, with the emergence of nanoscale surface characteristics as the most promising.
- Biologically inspired surface features that can be "sensed" by individual cells to stimulate osteoblastic differentiation, ultimately leading to rapid bone formation and osseous integration.

Surface Technology

- Multiple reports of fibrous capsules around implants of metallic or polymeric nature
- Failure attributed to toxic wear debris phagocytosed by macrophages an other surrounding tissue
- Several cases of fibrous encapsulation without traces of debris resulting in aseptic inflammatory response that can lead to osteolysis
- Associated mainly with **smooth surfaces**



Surface Technology

- Experiences from the dental field demonstrated that controlling surface properties the fibrous layer can be avoided

Sul et al: Optimum surface properties of oxidized implants for reinforcement of osseointegration: Surface chemistry, oxide thickness, porosity, roughness, and crystal structure. Int J Oral Maxillofac Implants. 2005

- Process of osteointegration involves a complex chain of events
- Chain of events directly and indirectly affected by surface properties of device

Mendoca et al: Advancing dental implant surface technology--from micron- to nanotopography. Biomaterials. 2008.

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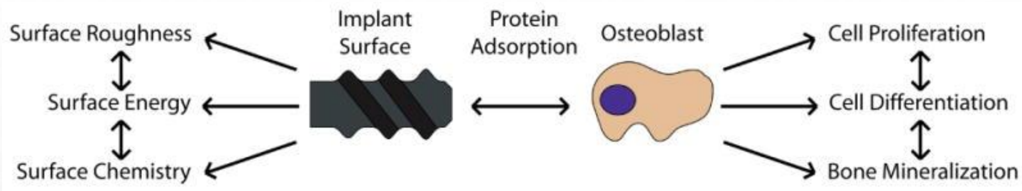
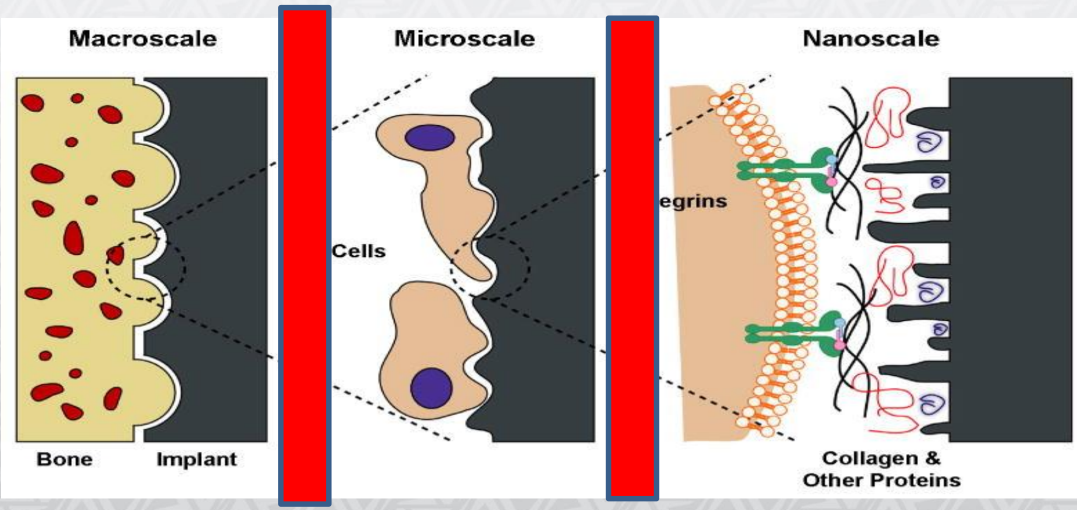
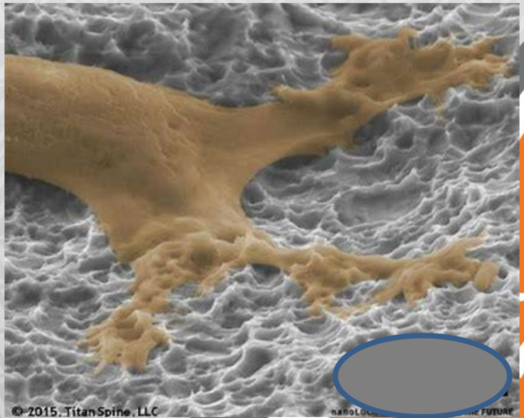
Hierarchy of Surface Technology



Macro level (10^{-3}m) Micro level (10^{-6}m) Nano level (10^{-9}m)



- <u>nanotopography,</u> with its inherent biochemical information is signal that osteoblasts require when looking for a surface for new bone formation



Nanotopography

- **Microroughness**
  - Surfaces with complex microtopography more osteogenic
    - Peaks better than troughs
    - 30µm craters, 3µM peaks best response acid-etch + sand-blasted
    - Closely mimics nanoscale features left by osteoclast in remodeling

- **Net Bone Production**
  - **Up-regulate osteoblasts**

    TGF-B1, BMP-2, 4, 7
  - **Down-regulate osteoclasts**

    (Osteoprotegerin)

    TGF-B1
  - **Up-regulate angiogenesis**

    Angiopoietin-1,

    VEGF-A, FGF-2

Material Surface Nanotechnology

- Ti spontaneously forms a thin oxidized layer that inhibits further corrosion
- Ceramic in nature and mimics properties of hydroxyapatite in bone

- Subtractive
  - Titanium
  - Mechanichal or chemical
  - Best for stable robust microsurface
- Additive
  - Coating / 3D printing / incorporation
  - PEEK, Titanium, PEEK +Ti
  - **PEEK + HA**

Data demonstrate significant wear debris due delamination in PEEK implants
Ti coated (additive) while nanotechnology (subtractive) surfaces did not

Hydroxyapatite

- HA defined: $Ca_{10}(PO_4)6OH_2$
  - The main inorganic component of bone and tooth enamel
- Bone 70% HA, 25% organic , 5% water
- Bonfield, et al, 1881
  - HA mixed with polyethylene to create “artificial bone” void filler
  - 20-40% fractional volume demonstrated increased bone on growth in rabbit vs inert polyethylene
- 1990’s, Ti/HA hip implants, survivability 98% at > 20 years

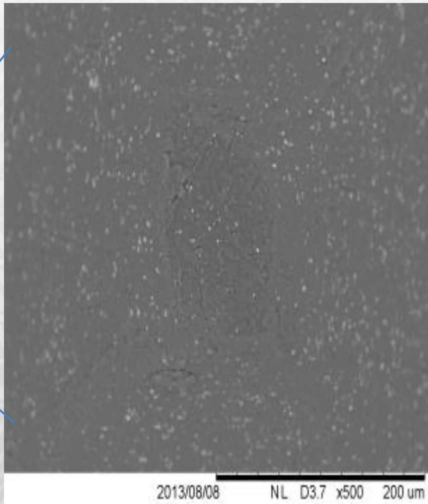
Polyetheretherketone (PEEK)

- Introduced in 1980’s by Victrex (Invibio)
- PEEK used in spinal fusion predominantly in the form of a load bearing interbody cage for approx 15 years
  - Advantages
    - Mechanical strength
    - MOE similar to cortical bone (3.5GPa)
    - Imaging compatibility
    - Biocompatibility
    - Ease of manufacturing
  - Disadvantages
    - Hydrophobic
    - Inert (no direct interaction at bone / graft interface)
    - Generation of a fibrous layer at B/G interface

PEEK-OPTIMA HA Enhanced

PEEK-OPTIMA + Hydroxyapatite (HA)

Not a coating technology
Formed by heat extrusion into rods
Hydroxyapatite(HA) has a chemical and crystal structure similar to that found in bone
HA evenly distributed throughout PEEK



STRUCTURAL PROPERTIES OF PEEK +
THE OSTEOCONDUCTIVE PROPERTIES OF HA

PEEK-OPTIMA™ HA Enhanced

Typical Material Properties

20% fractional volume HA

Property	Impact (Notched) (KJ/m^2)	Flex Strength (Mpa)	Flex Modulus (Gpa)	Tensile Strength (Mpa)	Tensile Elongation at break (%)
PEEK-OPTIMA Natural	4.7	170	4.0	115	20
PEEK-OPTIMA®HA Enhanced	4.4	178	5.5	103	8
Cortical Bone	2-5 (un-notched)	173	18	80-150 (longitudinal)	1.4

Basic Science Study 1

- "Response of human osteoblast to nanoHA-PEEK – Quantitative proteomic study of bioeffectsof nano-HA composite"
  - Scientific Reports 3/2016 Zhao, et al
- Study looked at 40% by volume nano-HA coating
  - Found no toxicity of nano sized HA partiles
  - Cell attachement test demonstrated that the number of cells attached to n-HA/PEEK is significantly higher vs PEEK
  - Alk phosphatase activity increased signifying increased osteoblast differentiation

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Basic Science Study 2

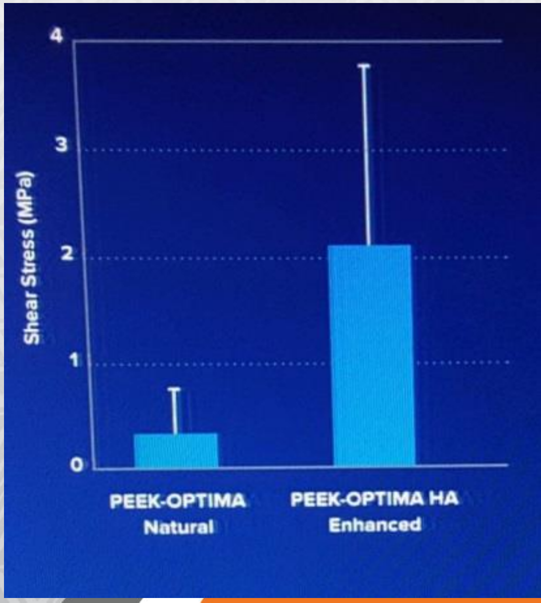
- "Preparation methods for improving PEEK's bioactivity for ortho and dental applications: A review"
  - IntJ of Biomaterials 2016 Almasi, et al
- Increasing the volume fraction of HA increases the Young's modulus, though strength and strain at fracture point decreases. Range 20 to 40%
- Best bioactivity approx 29%

Pre-Clinical Study 1

Ovine Study Design

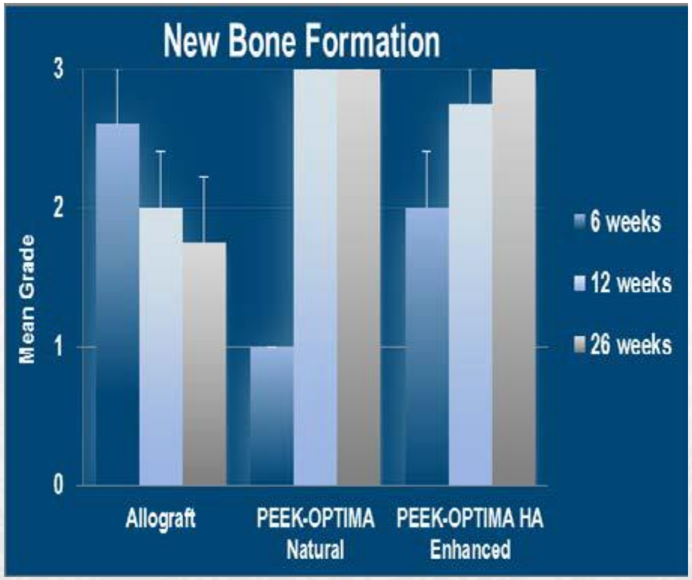
- **<u>Question</u>**: Does PEEK HA enhance bone formation compared with PEEK in a sheep cervical fusion model?"
  - CORR 11/2016 Walsh,etal
- **<u>Result</u>**: Incorporating HA into the PEEK matrix resulted in more direct bone apposition as opposed to the fibrous tissue interface with PEEK alone.

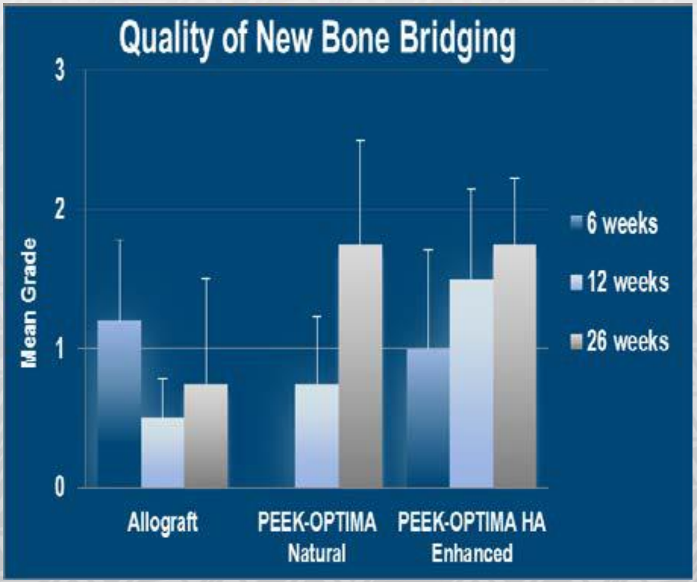
- **Test Group**
  - PEEK-OPTIMA HA Enhanced Polymer
  - *Implant in situ: 6mm x 25mm*
- **Control Group**
  - PEEK-OPTIMA Natural
- **Trabecular Bone**
  - Distal femur, proximal tibia
- **Cortical Bone**
  - Tibial diaphysis

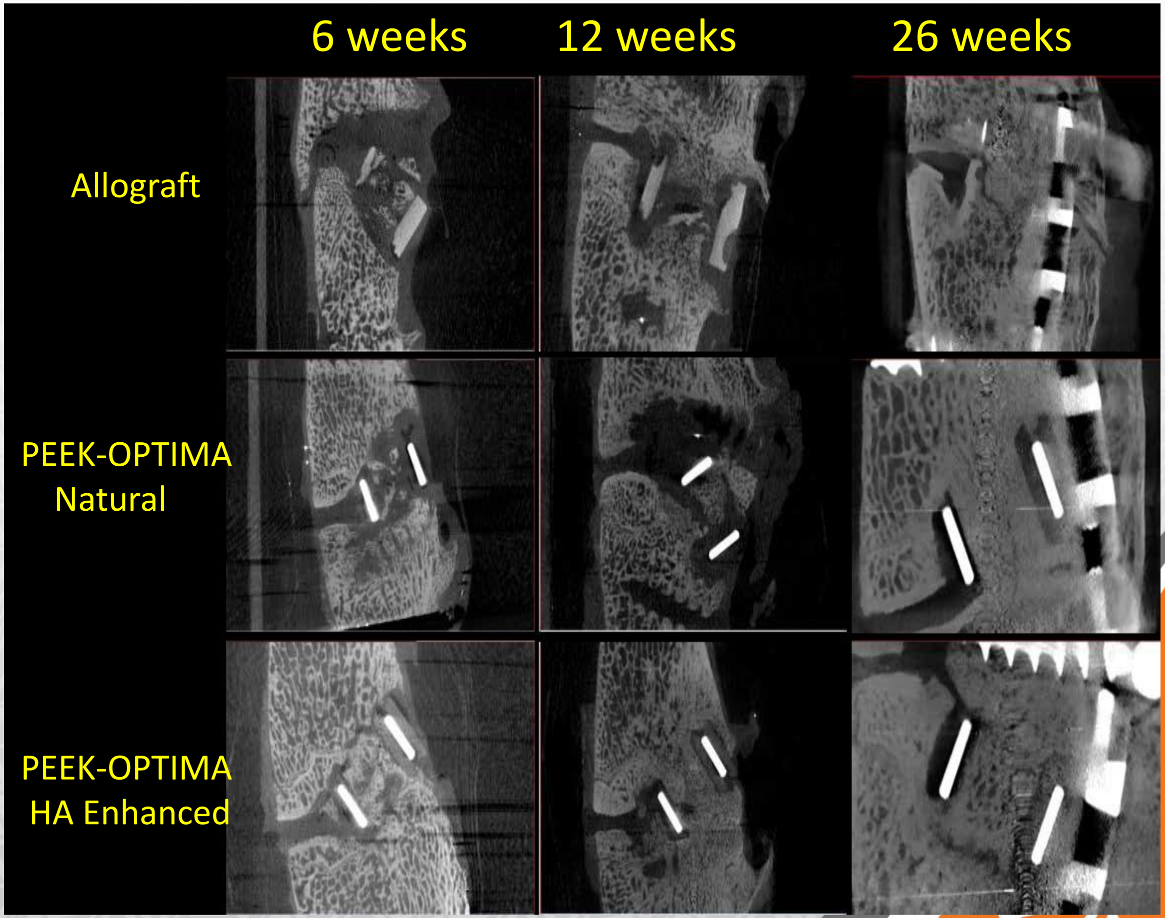


Pre-Clinical Study 1

Ovine Study Design







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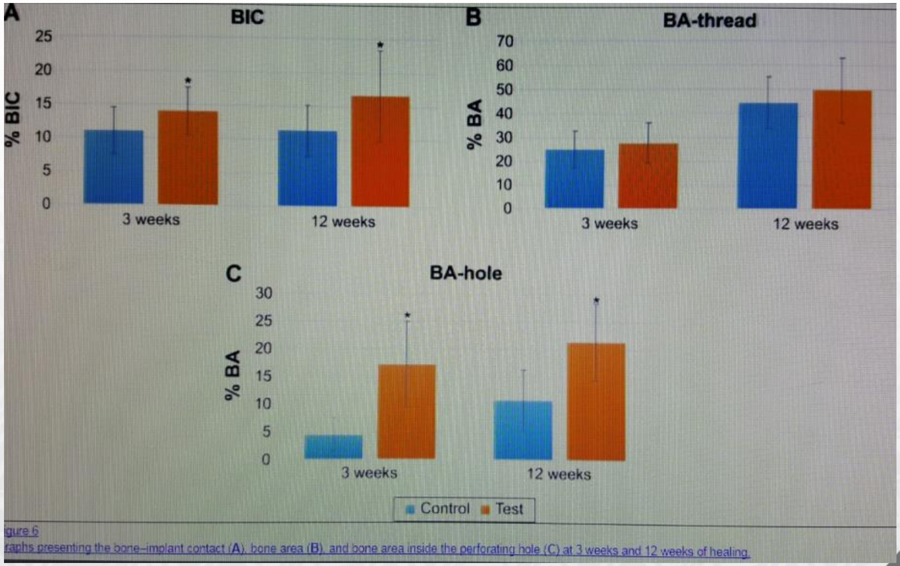
Pre-Clinical Study 2

- PEEK implants achieve increased bone fusion when coated with nano-sized HA: A histomorphometricstudy in rabbit bone”
  - Intj Nanomedicine11/2016 Johansson, et al
- Result: “Nano-sized HA coating on PEEK implants in rabbit femur significantly improved the bone-implant contact and demonstrated strong osteoconductiveproperties inside the implant”



Blue = control

Orange = test

TLIF Clinical Series

Tim Bassett, MD

- Patients treated with one and two level lumbar fusions between October 2015 and March 2017
- Purpose: To assess the 6 month post-op CT scan results in regards to the health of the interbodyfusion using PEEK-HA TLIF implants
- All patients had TLIF implants with iliac crest bone graft. No biologic adjuvants and no other graft sources were used
- Twenty total patients with 23 total fusion levels.

Demographics

Clinical

- Male 5 Female 15
- Total patients = 20
  - Tobacco 4
  - Opiates 13
  - DM 1
  - Steroids 1
- Age distribution
  - Age 30-39 2
  - Age 40-49 5
  - Age 50-59 5
  - Age 60-69 6
  - Age 70-79 2
- Pre-op diagnosis
  - Spondylolysis 1
  - DegenS-listhesis 7
  - Failed Lam/HNP 5
  - Discogenic, DDD 3
  - Failed fusion 2
  - Adjacent Segment 2

Surgical

- One level fusion 17 two level 3
- Total implant levels = 23
- Unilateral discectomy 15 bilateral 8
- Pedicle screws 14 ISP 3 Facet 3
- TLIF level distribution
  - L2/3 1
  - L3/4 4
  - L4/5 11
  - L5/S 17
- Primary vs Revision
  - Primary operation 11
  - Rev lam/disc 7
  - Rev fusion (implant) 2

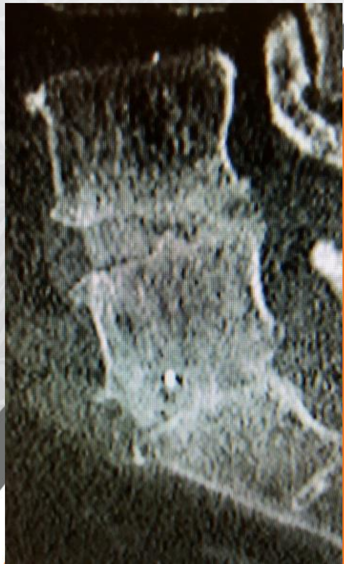
Data Evaluation

Clinical

- VAS Back pain % reduction
- VAS Leg pain % reduction
- Opiate Usage at 6 months

Surgical

- CT average = 189 days post-op (6 month,6 days)
- Volume of nucleus filled
- Gap size between implant/endplate
- Gap size between implant/bone graft
- Subsidence of implant



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Clinical Results

- Lumbar pain VAS % reduction (n=20)
  - 100 % 15
  - 75 % 1
  - 50 % 4
  - 25 % 0
- Leg pain VAS % reduction (n=16)
  - 100 % 15
  - 75 % 0
  - 50 % 1
  - 25 % 0
- Opiate Usage
  - Pre-op 13
  - 6 month 1
- Complications:
  - 1 graft site
  - 1 lumbar incision wound dehiscence treated dressing changes only

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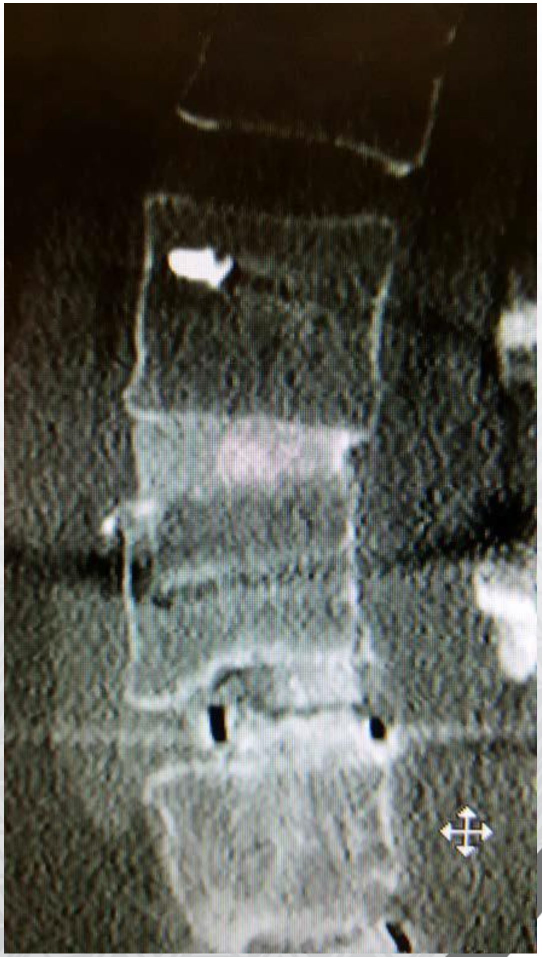
CT Scan Results

- Nucleus volume filling (n=23)
  - 100 % 18
  - 75 % 3
  - 50 % 2
  - 25 % 0
- Implant/endplate gap (n=23)
  - <0.5 mm 18
  - 0.5-2 mm 5
  - >2mm 0
- Implant/graft gap (n=23)
  - <0.5mm 19
  - 0.5-2mm 4
  - >2mm 0
- Subsidence (n=23) 1



14/23

Complete fusion (n = 17)

Incomplete fusion (n = 6)

Conclusion

- From the basic science, pre-clinical animal studies, and from personal surgical experience, it would appear that the addition of HA to PEEK interbody implants improves the early stability of the implants, possibly enhancing an earlier and more robust fusion
- In the series presented on TLIF PEEK HA implants, 15 of the 20 patients having complete back pain relief. Leg pain relief occurred completely in 15 of 16 preoperatively symptomatic patients.
- Absolute fusion at 6 months average was confirmed on CT scan in 17 pt, meeting all parameters.
- 14 of 23 levels showed robust dense bone formation at the immediate margins of the implant.
- Since October 2015
  - 95 TLIF patients with 124 levels
  - 26 ACDF patients with 45 levels
  - 3 single level ALIF stand alone.
- One revision. Zero planned revisions