Anterior Lumbar Interbody Fusion; A prospective, unmasked, non-randomized study of 240 patients utilizing a PEEK® Optima ALIF cage.

gold coast spine

BOND UNIVERSITY
BRINGING AMBITION TO LIFE

Associate Professor Matthew Scott-Young

4th International PEEK Meeting Washington DC

25-26th April 2019

Conflicts of Interest

ROYALTIES; DEPUY, PRISM

CONSULTANCIES; NIL

STOCKS (MEDICAL); NIL

OPTIONS; NIL

GRANT/RESEARCH SUPPORT; NIL

Background

- CLBP leading cause of work absenteeism, disability and QOL reduction
- >400,000 spinal fusions per year in the US
- 2017 - 83% of fusions in the US involved use of an IBF device

Why do we fuse?

Fundamental principle of treatment is spinal fusion surgery.

Fusion is directly correlated with improved patient outcomes.

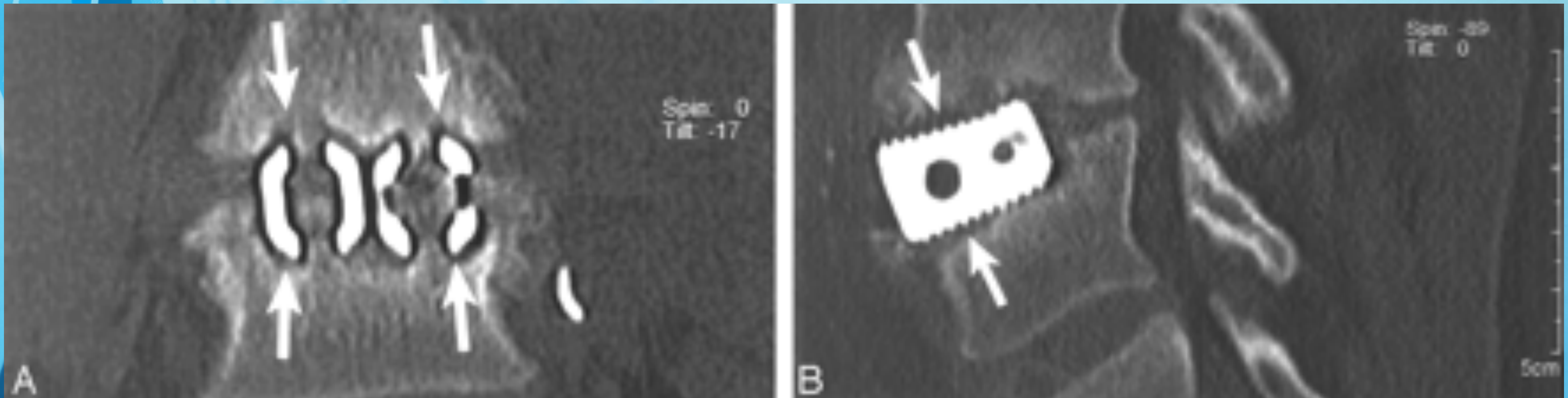
Background

- Most common materials used for interbody fusion devices are Titanium (Ti) and its alloys or polymer (polyetheretherketone-PEEK)

- IBF function is mechanical. Requires the addition of other materials to achieve bony fusion

Background

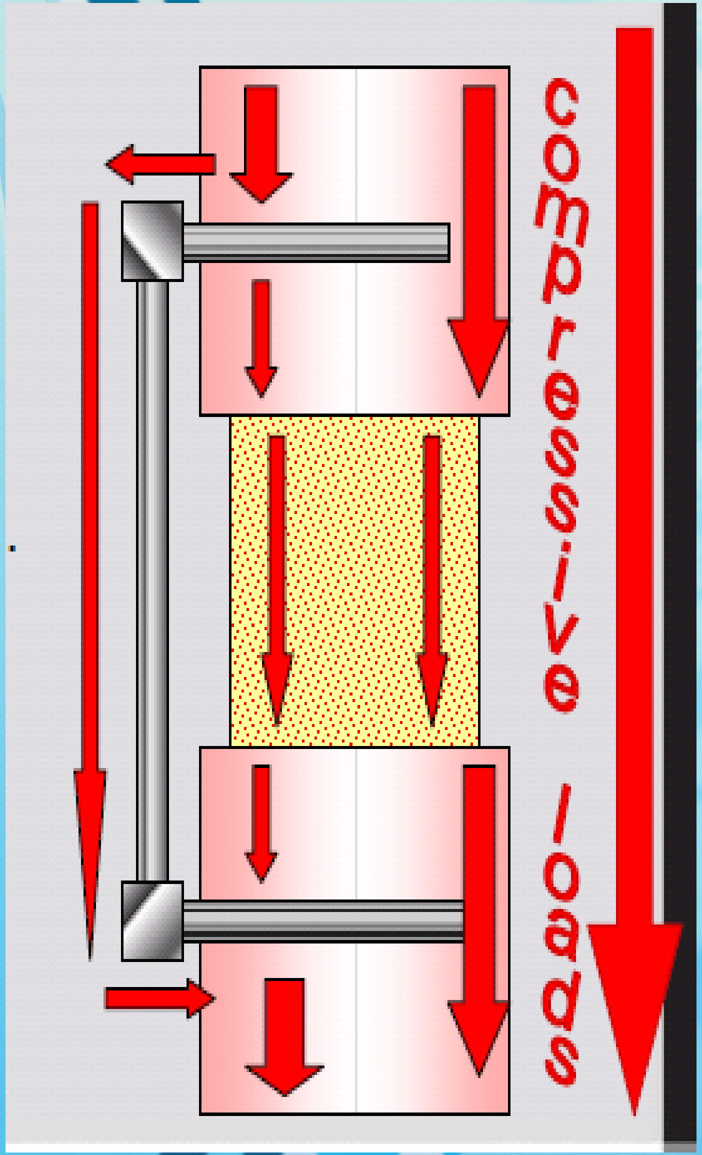
- **TiAlloy - Introduced in the 1980's**
  - **Positive**
    - **Results supportive of fusion but difficult to assess**
  - **Negative**
    - **Stress shielding = *Modulus Mismatch***
    - **Reports of high subsidence rates**



Background

- **Alternative material was sought for IBF devices that supported improved clinical outcomes**
    - **Improved fusion rates**
    - **Optimal post-op assessment of fusion mass**
    - **Reduced subsidence rates**
- **Introduced in the 1990s - PEEK**

Material History - PEEK

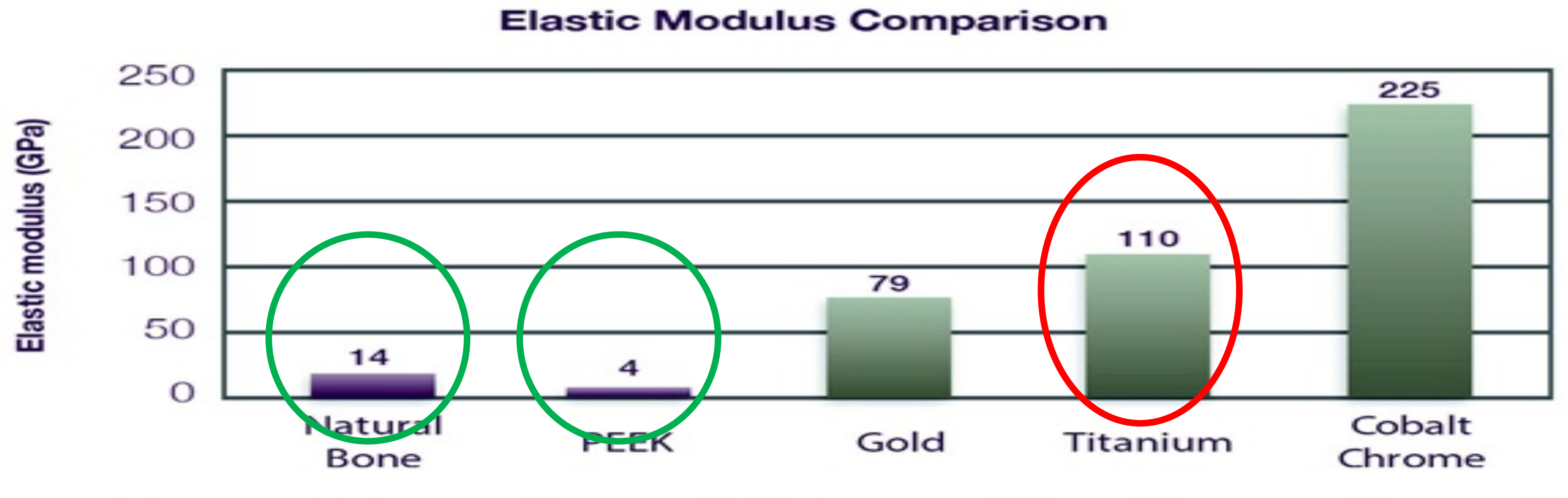


Wolff's Law

- **Excellent radiographic signature**
- **Modulus similar to human bone = Load sharing**

Material - PEEK vs TiAlloy

Property	Titanium	PEEK
Elasticity (Stiffness)	Higher	Lower
Radio-density	Radiopaque	Radiolucent
Modulus of Elasticity (Young’s Modulus)	103-110GPa	3-4GPa
Biocompatabilty (risk of allergic reaction)	Higher	Lower
Osseointegration	Higher	Lower



Rho, JY (1993). “Young’s modulus of trabecular and cortical bone material”. Journal of Biomechanics 26 (2): 111–119.

Material - PEEK vs TiAlloy

Journal of Clinical Neuroscience 44 (2017) 23–29

Contents lists available at ScienceDirect

Journal of Clinical Neuroscience

journal homepage: www.elsevier.com/locate/jocn

Review article

Titanium vs. polyetheretherketone (PEEK) inte...
Meta-analysis and review of the literature

Statistically significant subsidence rates

	Titanium	PEEK
Subsidence Rates	**16-35% (22%)**	0-28% (10.8%)
Fusion Rates	46.51-100% (82.5%)	76-100% (89.3%)

Author/year	Fusion Rate, n (%)		Subsidence, n (%)	
	Ti	PEEK	Ti	PEEK
Tanida, 2016	77 (82.8)	41 (80.4)	–	–
Nemoto, 2014	23 (100)	19 (76)	8 (35)	7 (28)
Chen, 2013	29 (100)	31 (100)	17 (34.5)	5 (5.4)
Cabraja, 2012	41 (93.2)	37 (88.1)	9 (20.5)	6 (14.3)
Niu, 2010	32 (86.5)	34 (100)	6 (16.2)	0 (0)
Chou, 2008	20 (46.51)	15 (100)	7 (25.9)	0 (0)

Material - PEEK vs TiAlloy

Li et al. BMC Musculoskeletal Disorders (2016) 17:379
DOI 10.1186/s12891-016-1234-1

BMC Musculoskeletal Disorders

RESEARCH ARTICLE Open Access

Is PEEK cage better than titanium cage in anterior cervical discectomy and fusion surgery? A r

Zhi-jun Li[1*†], Yao Wang[2†], (

	Titanium	PEEK
Fusion Rate 12/12	75% (31/124)	94.6% (5/91)
Subsidence Rate 12/12	15.6% (33/211)	5.9% (11/184)

Statistically significant subsidence rates

Eur Spine J (2013) 22:1539–1546
DOI 10.1007/s00586-013-2772-y

ORIGINAL ARTICLE

Comparison of titanium and polyetheretherketone (PEEK) cages in the surgical treatment of multilevel cervical spondylotic myelopathy: a prospective, randomized, control study with over 7-

Yu Chen · Xinwei V
Haisong Yang · We

	Titanium	PEEK
Fusion Rate	100%	100%
Subsidence Rate	34.5%	5.4%

Material - PEEK

- The use of PEEK in the anterior spine promoted both mechanical and radiological advantages.
- Combined with bone graft, excellent fusion results with statistically significant reduced subsidence rates.

So why are we trying to modify PEEK?

- Innovation in a space where there is a paucity of invention?

"Evidence doesn't matter. Everyone wants a set of new golf clubs.."

Why modify PEEK?

- **PEEK has recently attracted negative reports for its biologically inert or hydrophobic properties, thus limiting good integration with adjacent bone.**

"(PEEK)..may inhibit successful fusion"

Getting PEEK to Stick to Bone: The Development of [...] PEEK for Interbody Fusion Devices

F. Brennan Torstrick[1], David L. Safranski, Ph.D.[2], J. Kenneth Burkus, M.D.[3] [...] Chappuis, M.D., F.A.C.S.[4], Christopher S.D. Lee, Ph.D.[5], Robert E. Guldberg, [...] Gall, Ph.D[6], and Kathryn E. Smith, Ph.D.[2]

Technical Note

PEEK-Halo effect in interbody fusion

CrossMark

Kevin Phan[a,b], Jarred A. Hogan[b], Yusuf Assem[b], Ralph J. Mobbs[a,b,*]

[a] Neuro Spine Clinic, Suite 7a, Level 7 Prince of Wales Private Hospital, Barker Street, Randwick, NSW 2031, Australia
[b] NeuroSpine Surgery Research Group (NSURG), Sydney, NSW, Australia

Spine

SPINE Volume 40, Number 6, pp 399-404

EPIDEMIOLOGY

[...]nplant Materials Generate Different Peri-implant [...]flammatory Factors

Poly-ether-ether-ketone Promotes Fibrosis and Microtextured Titanium Promotes Osteogenic Factors

Rene Olivares-Navarrete, DDS, PhD,* Sharon L. Hyzy, MS,* Paul J. Slosar, MD,† Jennifer M. Schneider, MS,‡ Zvi Schwartz, DMD, PhD,*§ and Barbara D. Boyan, PhD*¶

Current Strategies to Improve the Bioactivity of PEEK

Rui Ma and Tingting Tang *

Material Evolution - PEEK

- **Methods to *"improve"* the osseointegration profile of PEEK have been hea**

Variant
HA coated PEE
Titaniu
Plasma
SiN Coa
HA enh
Porous

Material Evolution?

However, are our efforts as effective as intended?

Are we improving patient outcomes by modifying the physical, radiological and mechanical properties of PEEK?

Are the reported bio-inert properties of PEEK a 'real' clinical issue?

Evidence – Animal/In-vitro Studies

- **14 studies reviewed**
- **Results substantiated the improved osteoconductivity properties of modified PEEK devices compared to PEEK controls in animal/in-vitro studies**

= or ≠

Practical Efficacy

Evidence – Human Studies

Eur Spine J
DOI 10.1007/s00586-015-4353-8

CrossMark

REVIEW ARTICLE

Radiological and clinical outcomes of novel Ti/PEEK combined spinal fusion cages: a systematic review and preclinical evaluation

Yusuf Assem[1,2,3] · Ralph J. Mobbs[3,4,5] · Matthew H. Pelletier[2] · Kevin Phan[3,4] · William R. Walsh[2]

- **2015**
- **Conclusion**
  - **Clinical Outcomes = no significant difference b/w groups**
  - ***"Clinical studies at this stage exhibit similar fusion rates for Ti/PEEK compared to PEEK"***

Evidence – Human Studies

	Mobbs et al	Hoppe et al	Kotsias et al	Rickert et al	Phan et al	Sclafani et al	Chong et al
# of pts	15	42	50	18	47	44	25
Device	Composite PEEK/TI ALIF (Ti endplates)	Composite Ca/PEEK TLIF+PSF		Ti Coated PEEK TLIF+ PSF	Composite Ti-PEEK ACDF (Ti Endplates)	TiCoated PEEK ALIF ± PSF	Composite Ti-PEEK
Fusion Rate		93.6%		91.7%	96%	77%	
Subsidence Rate	15%	-	-	[illegible]	8.3%		
Patient Satisfaction	93% good-excellent	90.4% satisfied	88% good-excellent	-	92% good-excellent	-	92% good-excellent
Follow up	18 months	24-39 months	18 months	12 months	7.9 months	7.3 months (± 2.3)	12months

Conclusion; NO statistical significant difference

BMP & Allograft. 2 x PSF

Conclusion; NO statistical significant differences

75% subjects received PSF

All subjects received iliac crest BMA

Evidence – Human Studies

	Chong	Hoppe	Kotsias	Phan	Rickert	Sclafani	Mobbs
VASB pre					7.2		7.9
VASB final					3.6		1.8
VASB imp					3.6	5.2	6.1
MCID					2.5	2.5	2.5
VASN pre	7.1		[illegible]	[illegible]			
VASN final	2		[illegible]	[illegible]			
VASN imp	4.6		[illegible]	[illegible]			
VASL pre			[illegible]	[illegible]	6		
VASL final			[illegible]	[illegible]	3.7		
VASL imp			[illegible]	[illegible]	2.3	4.8	
MCID					2.5	2.5	
ODI pre					42		
ODI final					27		
ODI imp					15		34.3
MCID					12.8		12.8
NDI pre	44		38	47			
NDI final	26.4		12	22			
NDI imp	24.7		26	25			

?
Robust
Clinical
Data

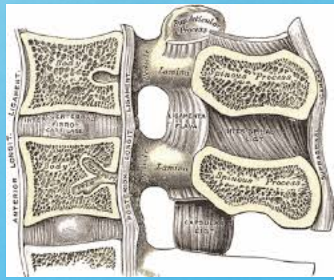
Evidence – Recent Studies

- **2019 UNSW Orthopaedic Research Labs presented at SSA 2019 (Walsh)**

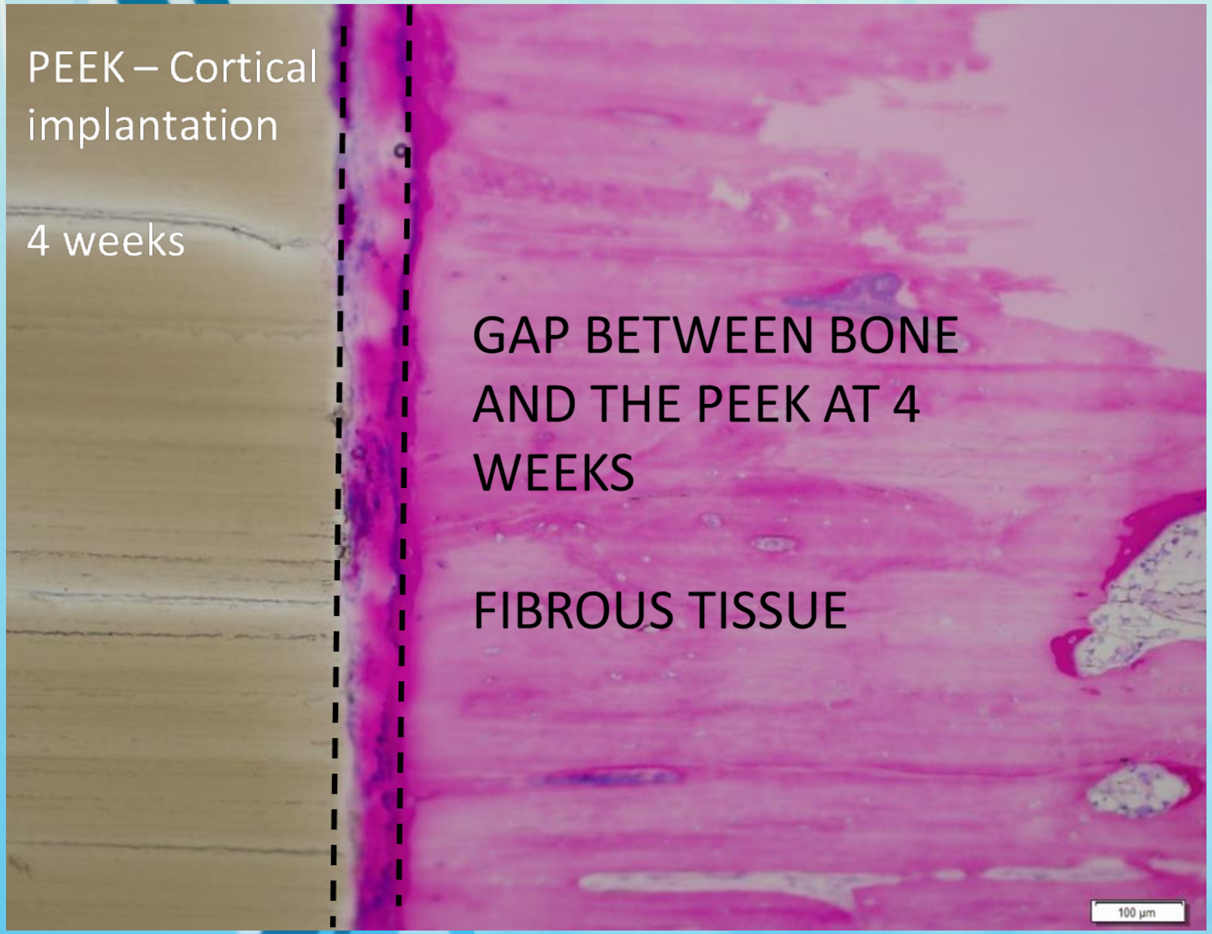
- **Ti-PEEK vs PEEK Pre-Clinical Ovine Long Bone Ongrowth Model (4, 12 and 26 weeks)**

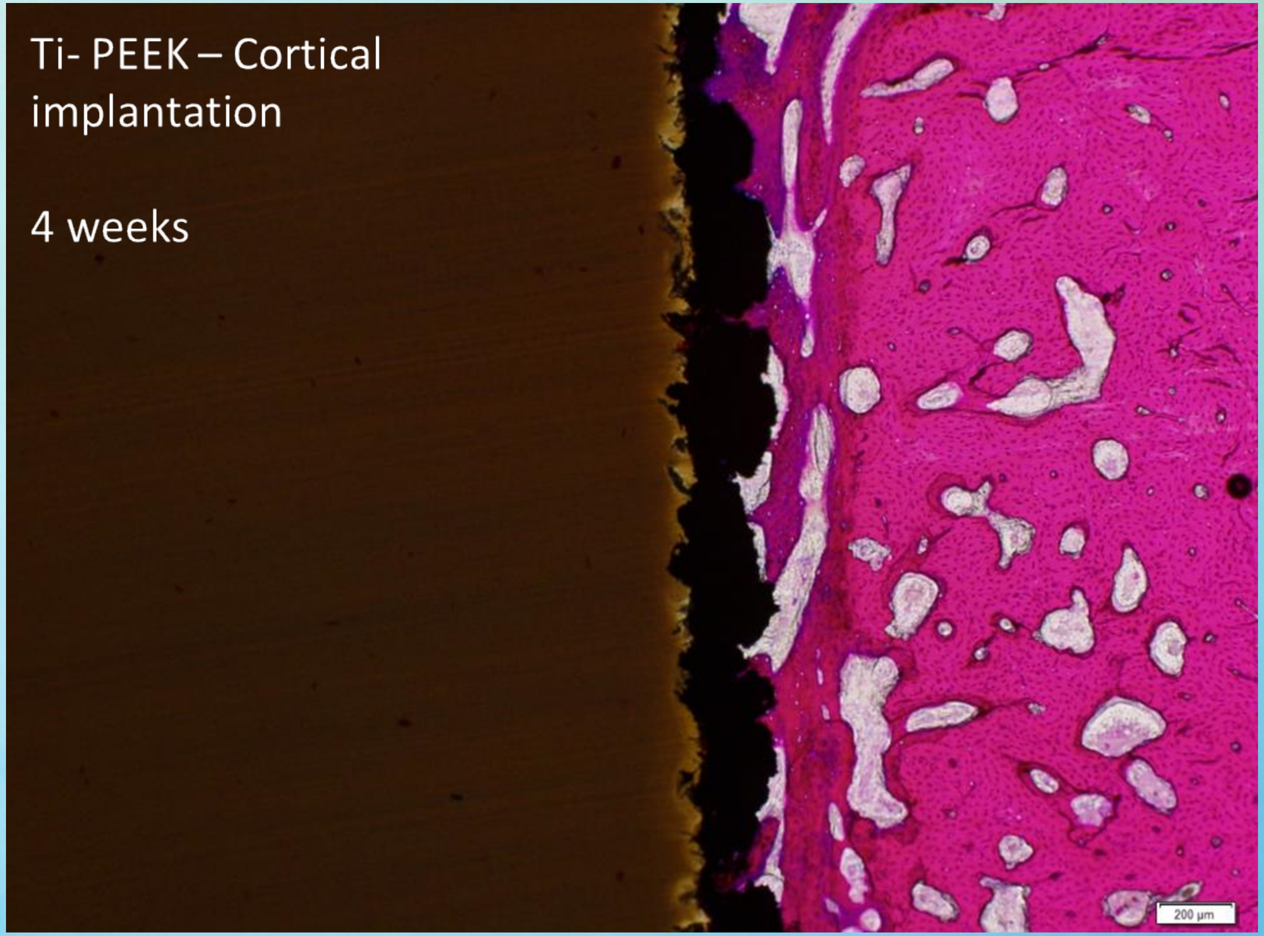
  - **To bond or not to bond to Bone?**

  - **Cancellous vs cortical model**
    - **Which one is predictive of human interbody fusion space?**

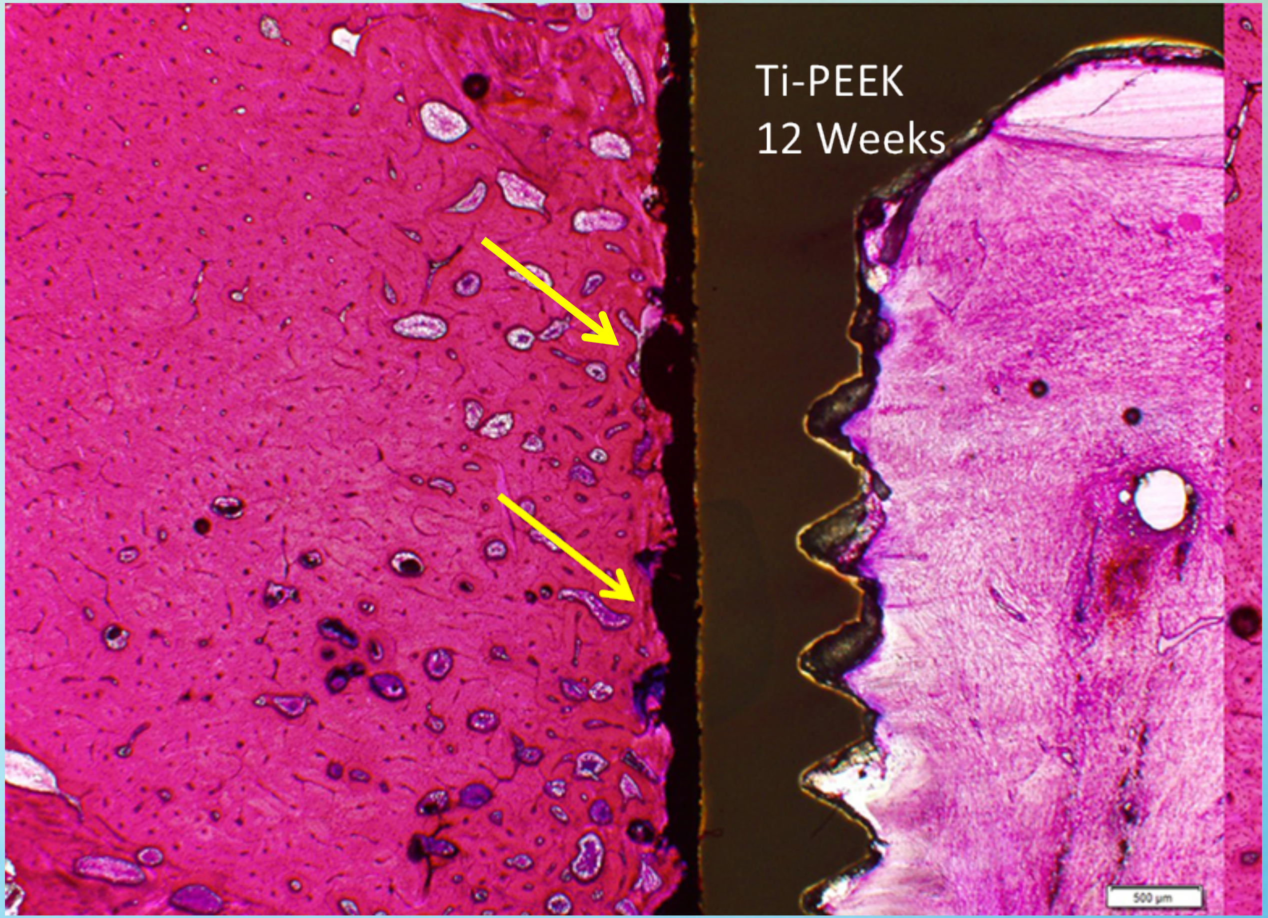


Histology - 4 weeks





Histology – 12 weeks



- In a cortical model bone CAN grow onto both PEEK and TiPEEK

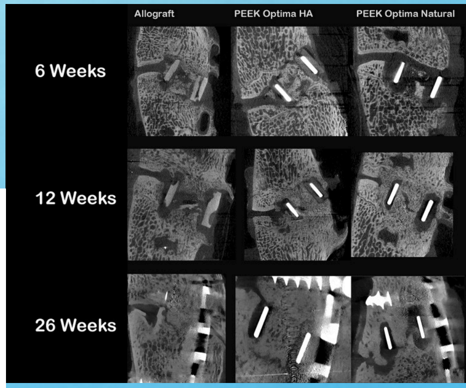
Histology – 26 weeks

Parameter	Group	6 weeks	12 weeks	26 weeks
New bone	Allograft	2.6 ± 0.9	2.0 ± 0.8	1.8 ± 1.0
	PEEK Optima HA	2.0 ± 0.8	2.8 ± 0.5	3.0 ± 0.0
	PEEK Optima Natural	1.0 ± 0.0	3.0 ± 0.0	3.0 ± 0.0
Quality	Allograft	1.2 ± 1.3	0.5 ± 0.6	0.8 ± 1.5
	PEEK Optima HA	1.0 ± 1.4	1.5 ± 1.3	1.8 ± 1.0
	PEEK Optima Natural	0.0 ± 0.0	0.8 ± 1.0	1.8 ± 1.5
Contact	Allograft	1.8 ± 1.3	1.3 ± 1.5	2.0 ± 1.2
	PEEK Optima HA	0.5 ± 0.6	1.5 ± 1.0	1.3 ± 0.5
	PEEK Optima Natural	0.0 ± 0.0	0.5 ± 0.6	1.0 ± 1.4

- **CT grading results**
- **All fusions remodelled with time and were mature by 26weeks**
- **Higher resorption rate with Allograft**

Does PEEK/HA Enhance Bone Formation Compared With PEEK in a Sheep Cervical Fusion Model?

William R. Walsh, PhD, Matthew H. Pelletier, PhD, Nicky Bertollo, PhD, Chris Christou, BVSc, PhD, andChris Tan, BVSc



Study comments…

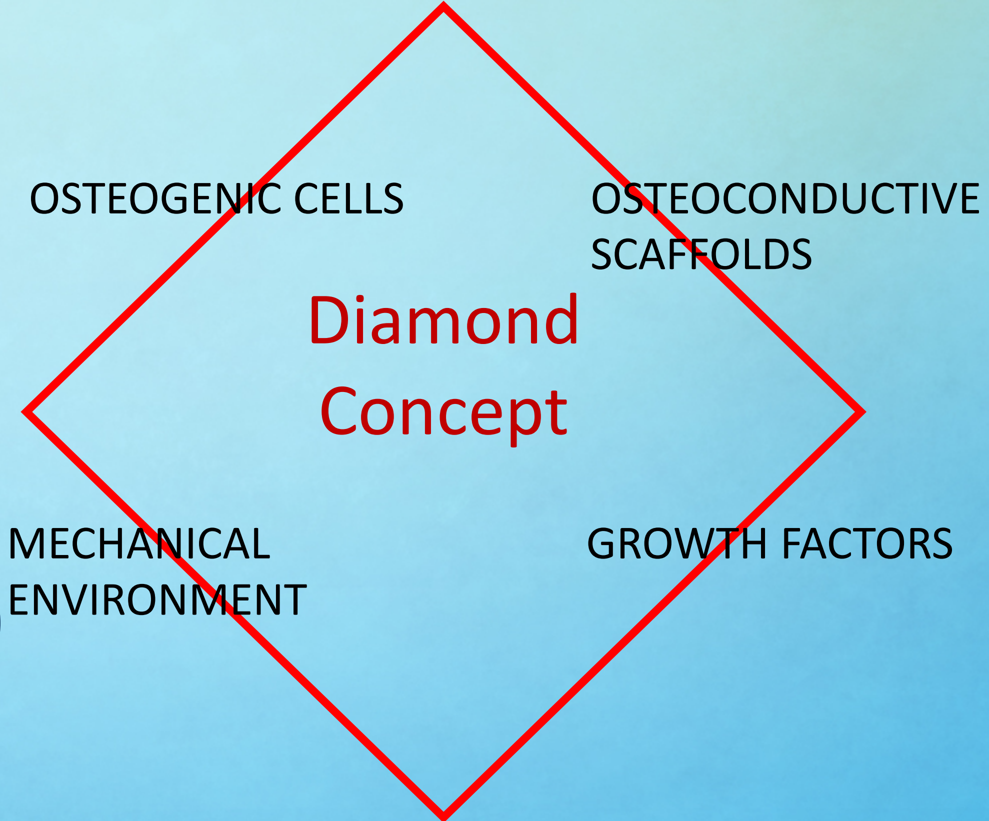
- **Anatomical site, surgical technique, graft material and loading play vital role in in-vivo response**
- **Cortical model limited in application to human pathology – implants contained in closed defect and are not under load.**
- **Bone ingrowth and fixation in cortical and cancellous sites in long bones DOES <u>NOT</u> translate directly to in-vivo interbody fusions.**
- **Bone remodeling process dictates where the bone will grow.**

Evidence - Context

- Animal/in-vitro evidence does not appear to support in-vivo evidence
  - 100% pre-clinical animal studies reviewed used long bone preparation sites (Tibia/Femur)
- Recent pre-clinical research
  - Testing conditions possibly not reflective of in-vivo interbody conditions
  - Full defect fill (dowel defect) and not under load
- Lack of human studies/data supporting "better" patient related outcomes or fusion rates

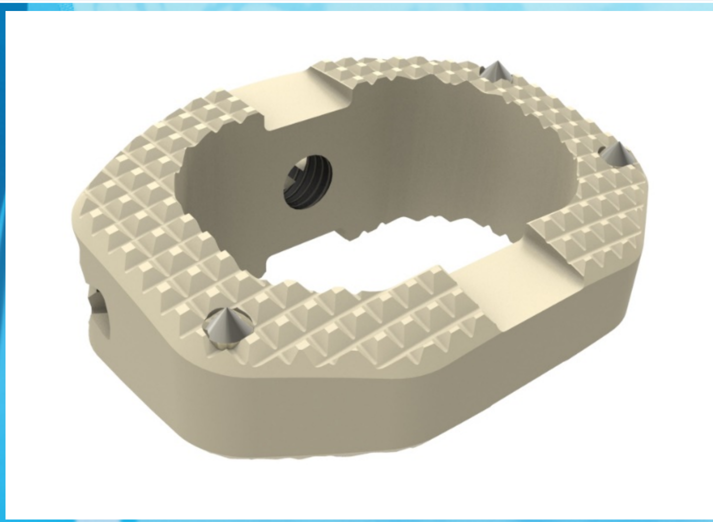
The GOLD Standard for successful fusion

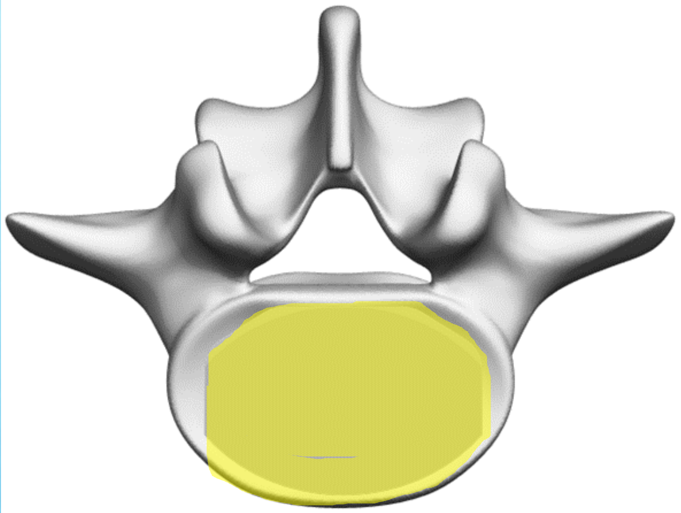
- Diamond Concept
    - **All 4 points are embraced for physiological healing**
- **Biological Environment**
    - **Patient factors**
    - **Surgical Preparation**
    - **Graft**
- **Mechanical Environment**
    - **Surgical Preparation**
    - **Patient factors**
    - **Device factors (material)**



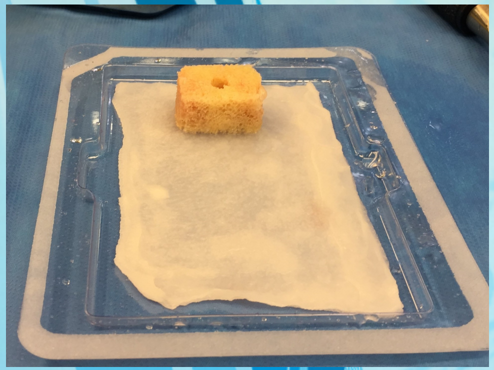
Mechanical - device design

Design Feature	Benefit
Large Footprint	Maximize vertebral endplate coverage – PL corners optimized
PEEK-Optima LT1	Optimal modulus elasticity = load sharing Optimal radiographic assessment of fusion
Minimal wall thickness	Optimize bone graft-endplate contact Optimize bone graft volume
Large Open Architecture – no strut	Optimize bone graft-endplate contact Optimize bone graft volume
Endplate Spikes	Initial stability/prevent migration





Tissue Engineering and product development



- Bone Restoration/Regeneration
  - ➢Osteoconductive – tricortical femoral head allograft
  - ➢Osteoinductive – Bone Morphogenic Proteins/Bone Growth factors
  - ➢Osteogenesis
- Mechanical environment
- Stability, proximity, viability

Methods/Materials

- Prospective, unmasked, non-randomized study
- 240 pts
  - 360 Fusion Levels
- 12mth f/up
- 1 independent centre, 2 surgeons
- Diagnosis
  - ➢ Clinical history
  - ➢ Clinical examination
  - ➢ Diagnostic imaging
  - ➢ Nerve Conduction Studies (EMG)
  - ➢ Baseline PROMs – ODI/VASB/VASB/RMDQ

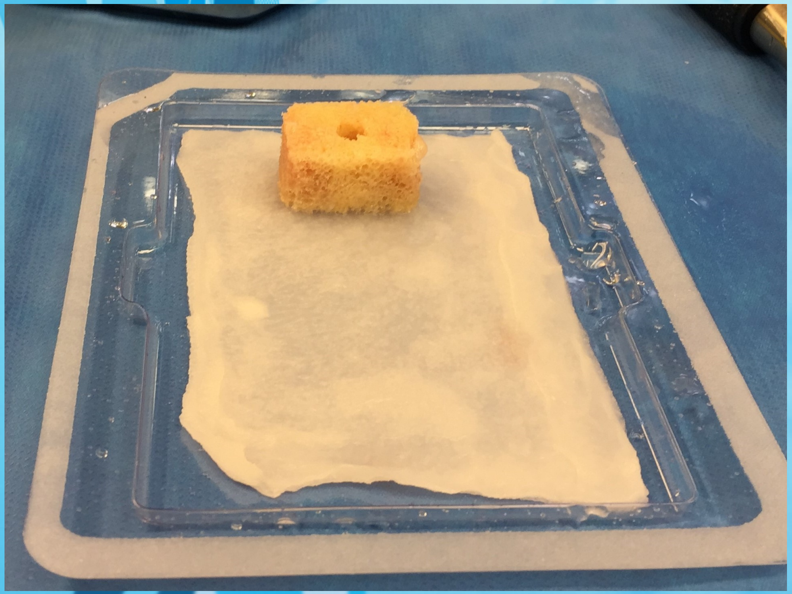
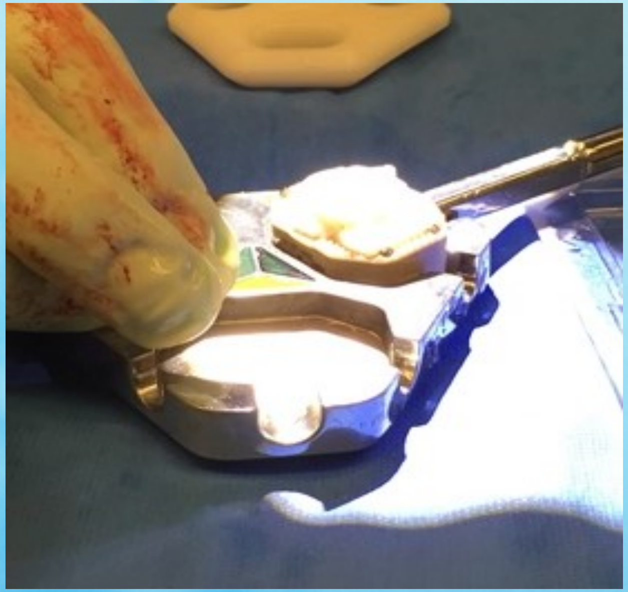
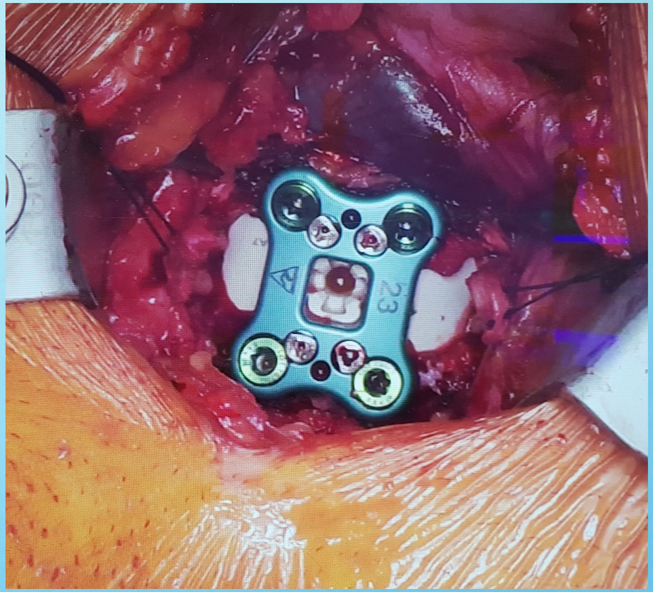
Methods/Materials

- Inclusion Criteria
  - >18 years/skeletally mature
  - L2-S1 operative pathology
  - Lumbar pathology at 1 or > levels with/out radicular pain
  - Failed conservative care >6 months
  - Willing/able to comply with f/up requirements

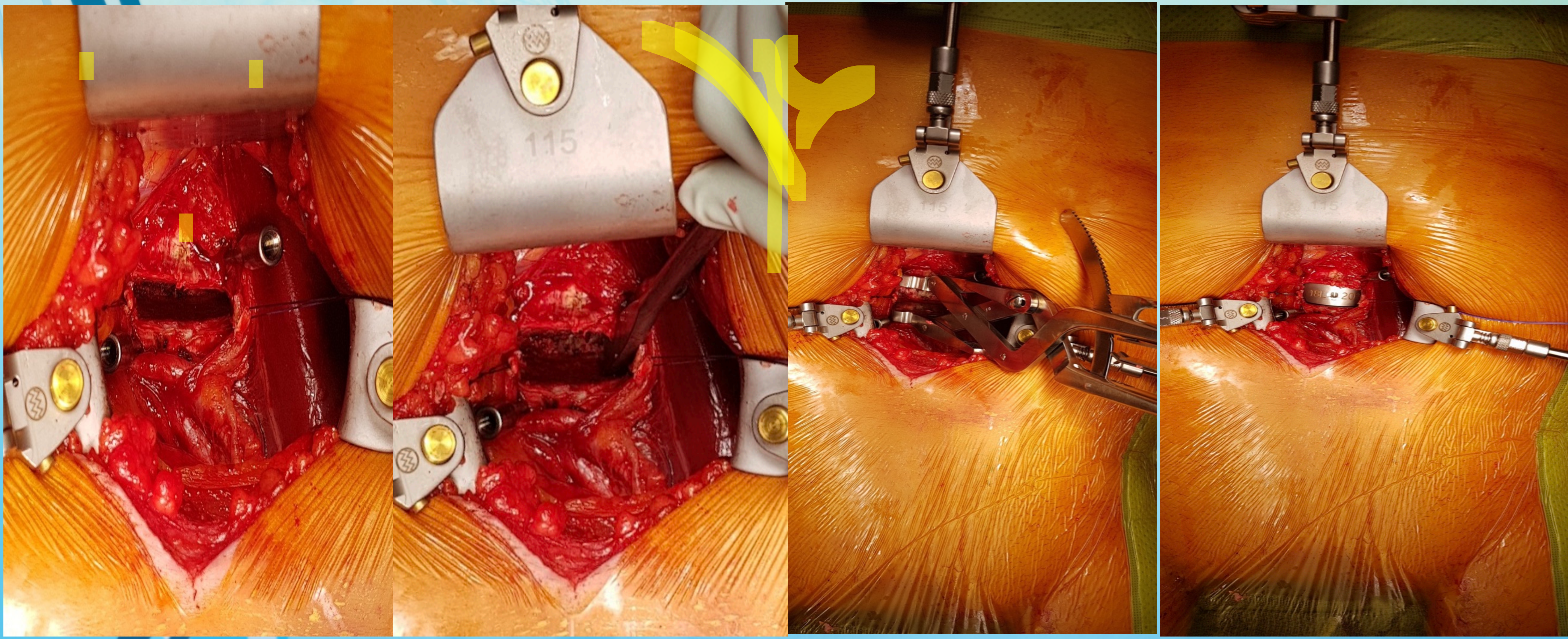
- Exclusion Criteria
  - Treatment outside L2-S1
  - Prior anterior spinal surgery
  - Local or systemic active infection
  - pregnancy

Methods/Materials

- **All pts –**
  - **Anterior Lumbar Interbody Fusion (Australis® ALIF cage + plate)**
  - **rhBMP-2 wrapped through and around pre-fashioned structural allograft (femoral head)**

SURGICAL TECHNIQUE



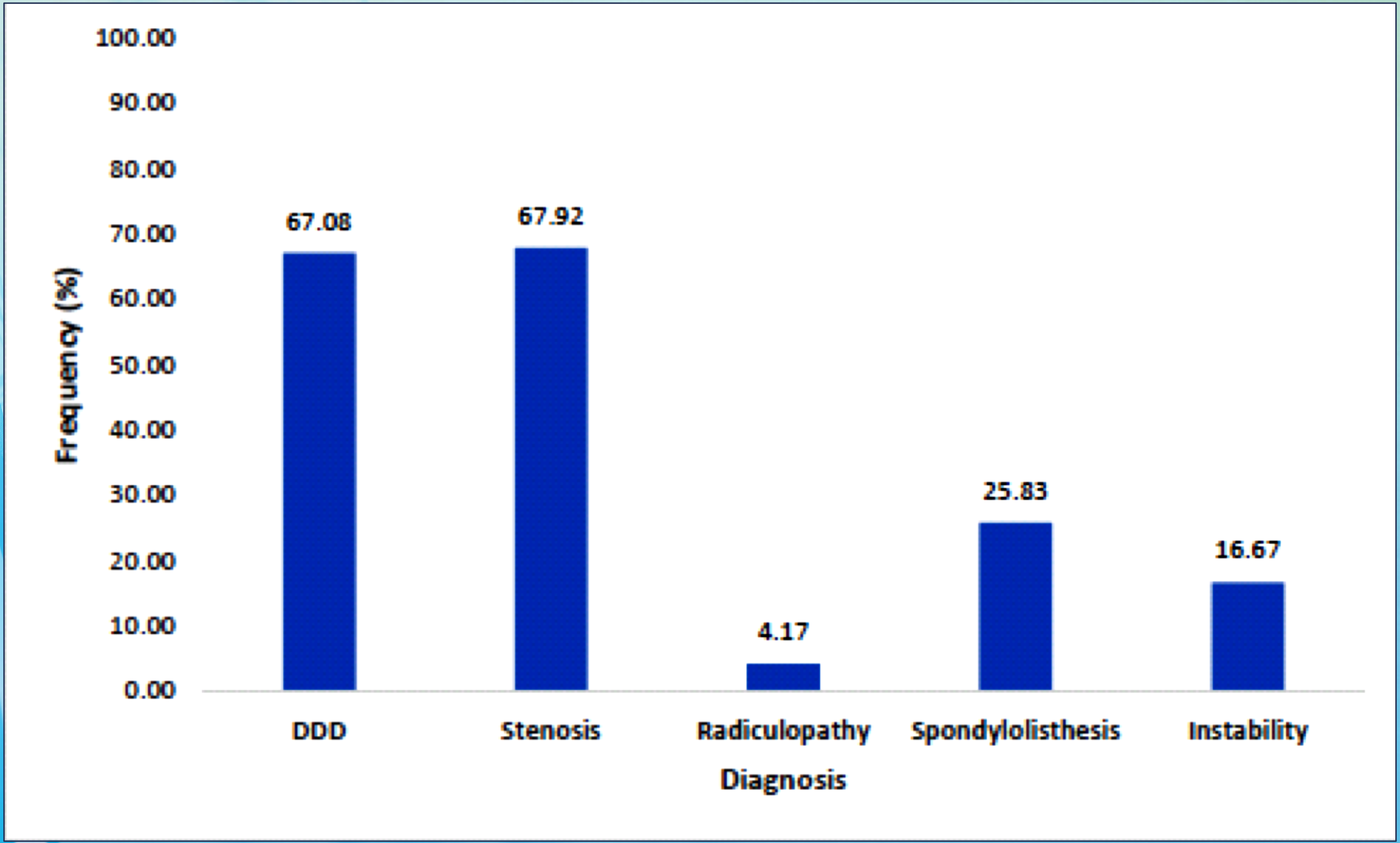
Methods/Materials

- **F/up baseline, 3, 6, 12 months**
- **Fusion acceptance criteria**
  - **Confluence of bridging bone by fine cut CT imaging**
  - **0° movement on flexion/extension films**
    - ***ALL PATIENTS MUST MEET BOTH CRITERIA TO QUALIFY***
- **Reoperation/ revision /removal / complication rates**

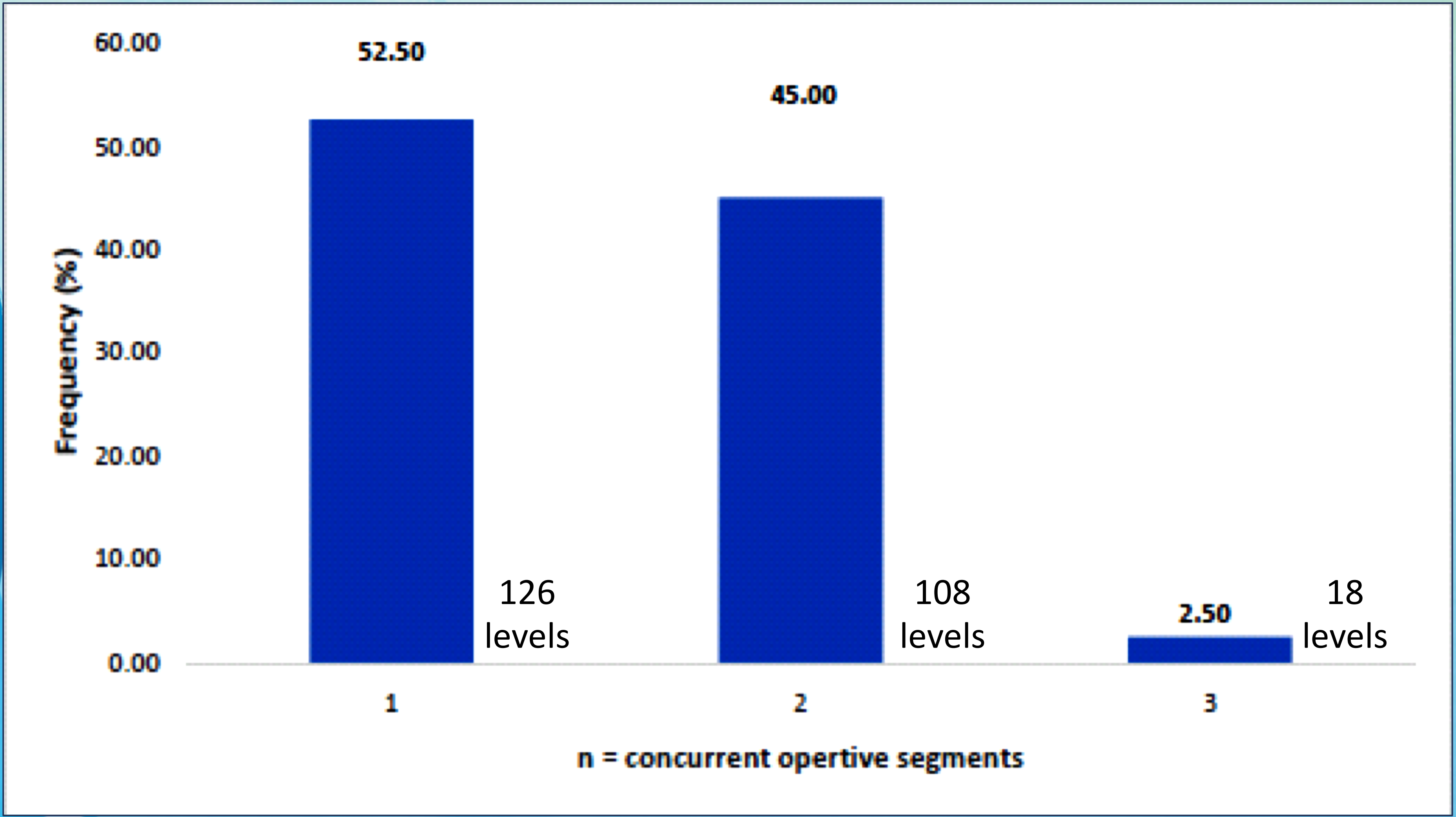
Statistical Analysis

- **Conducted on all PROMs using one-tailed paired Student's t-test**
- **Analyses and comparison at all timepoints 0-12 months**
- **Outcomes analyses for SS, MCID and SCB**
- **Raw data tabulated and graphical representation**

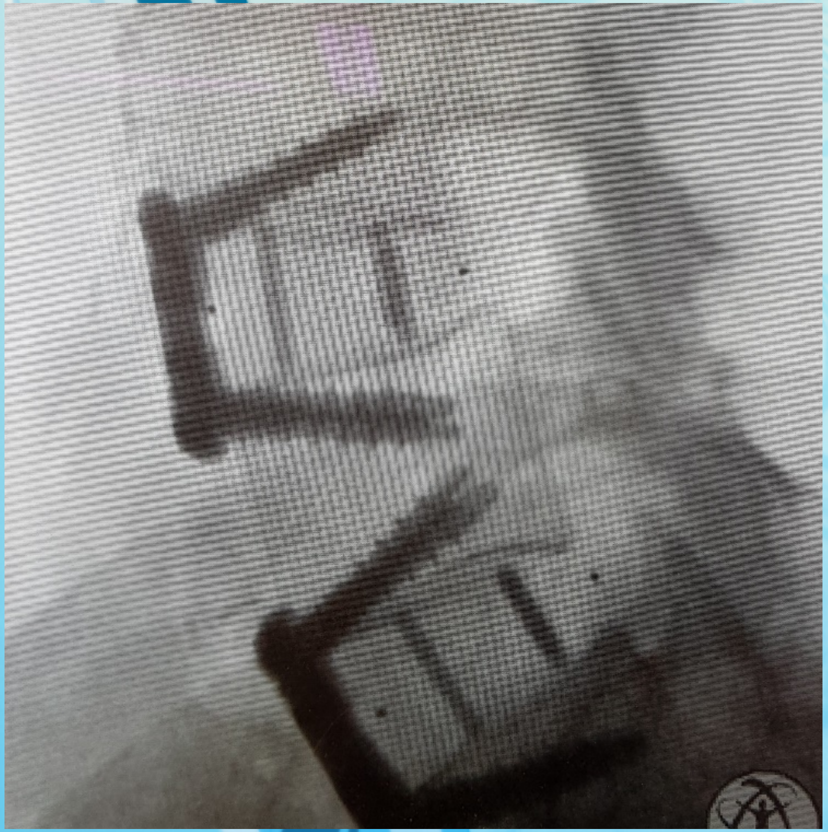
Primary Diagnosis

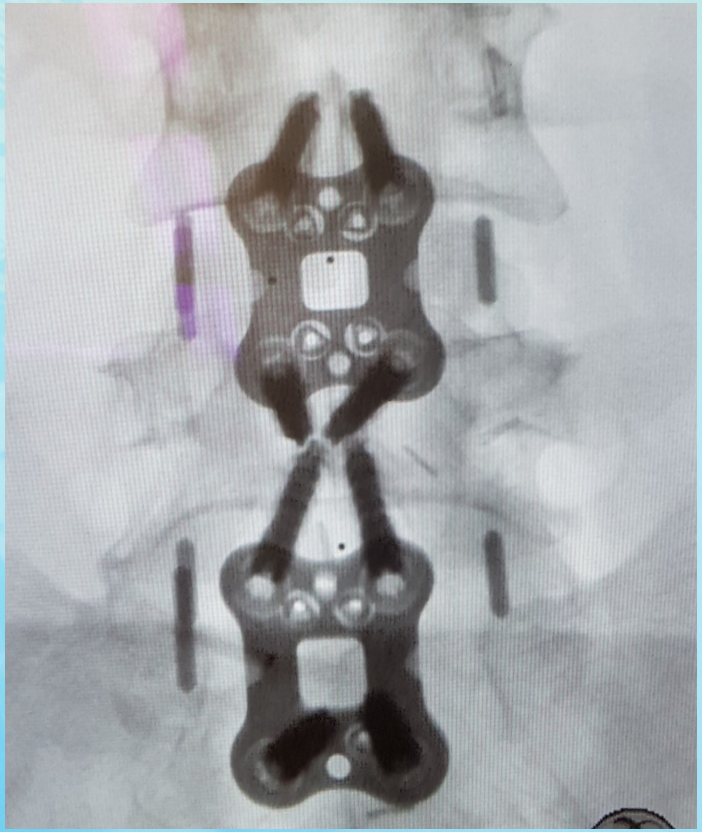


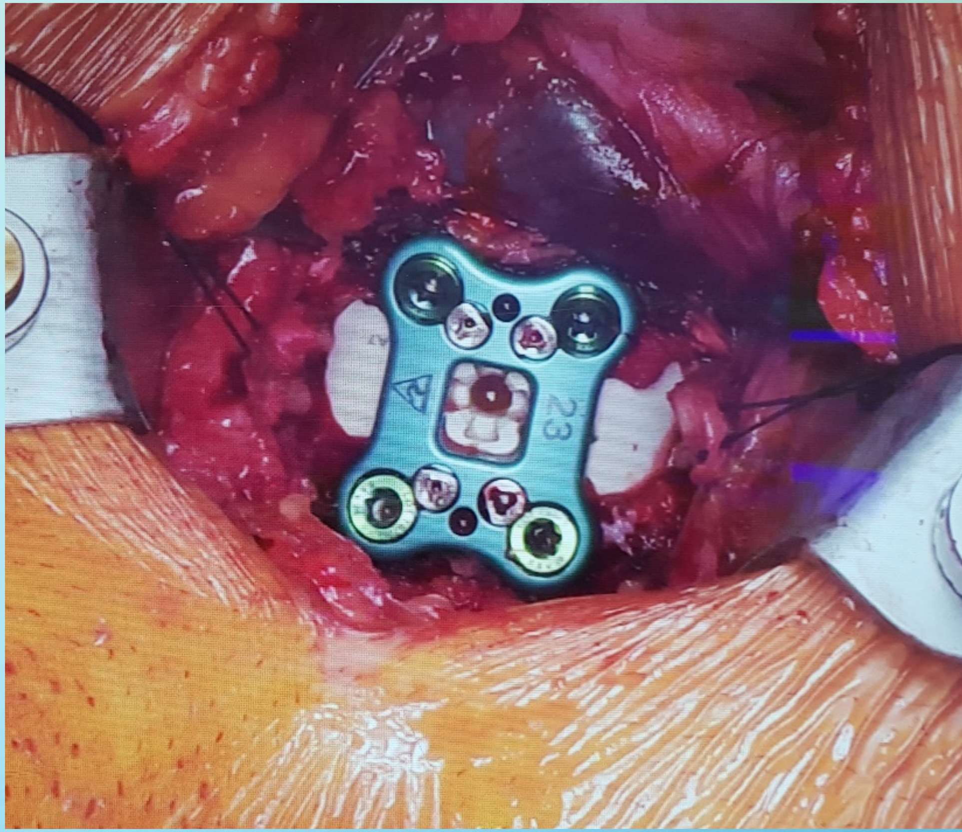
Operative Levels



Constructs







Mean VASB and VASL

VAS Outcome						
Back Pain						
Time Post-Surgery,	*n*	MEAN	*n*	MEAN Difference	95%CI	P score (<0.05)
0, Baseline	240	65.4	NA	NA	NA	NA
3 months	235	26.4	235	38.7	2.63	<0.0001
6 months	235	22.1	235	43	2.66	<0.0001
12 months	221	20.8	221	44.2	2.77	<0.0001
Leg Pain (combined R and L Leg)						
Time Post-Surgery,	*n*	MEAN	*n*	MEAN Difference	95%CI	P score (<0.05)
0, Baseline	240	38.4	NA	NA	NA	NA
3 months	235	15.6	235	22.2	2.04	<0.0001
6 months	234	12.3	234	25.7	1.98	<0.0001
12 months	219	11.9	219	25.4	1.96	<0.0001

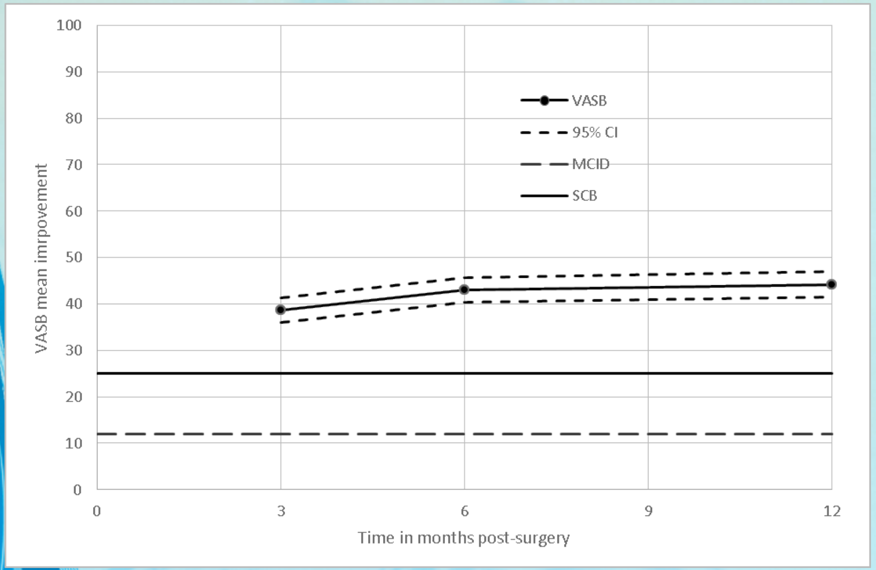
95% CI was calculated for the one-tailed Students T-test using the formula $x \pm z\ s/\sqrt{n}$ where 'x' is sample median, z score was 1.64 for a 90% CI, 's' was sample standard deviation and 'n' the number of participants.

Mean ODI and RMDQ

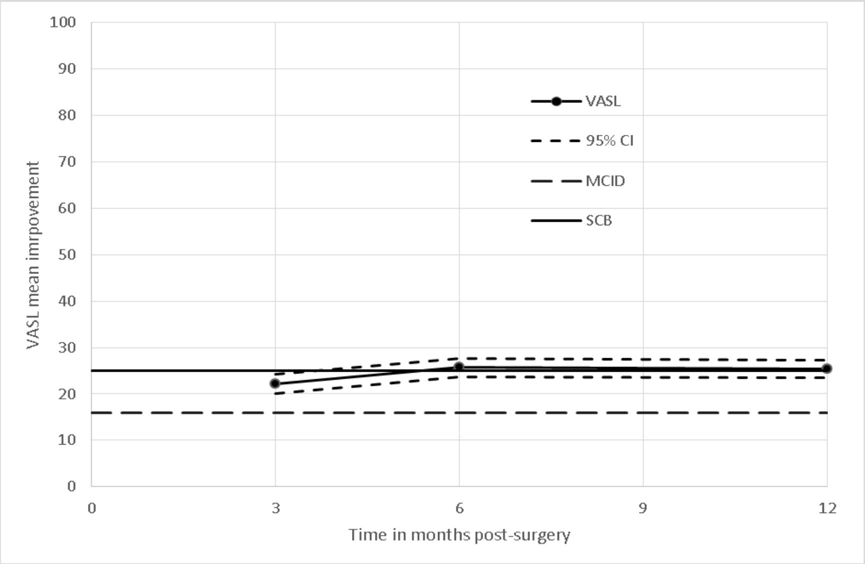
ODI						
Time Post-Surgery,	*n*	MEAN	*n*	MEAN Difference	95%CI	P score (<0.05)
0, Baseline	240	32.1	NA	NA	NA	NA
3 months	234	21.6	234	10.1	1.87	<0.0001
6 months	234	15.9	234	16.2	1.74	<0.0001
12 months	217	14	217	18.2	1.63	<0.0001
RMDQ						
Time Post-Surgery,	*n*	Mean	*n*	Mean Difference	95%CI	P score (<0.05)
0, Baseline	240	15.2	NA	NA	NA	NA
3 months	233	7.3	233	7.9	0.76	<0.0001
6 months	231	4.8	231	10.5	0.66	<0.0001
12 months	218	4	218	11	0.56	<0.0001

95% CI was calculated for the one-tailed Students T-test using the formula x±z s/√n where 'x' is sample median, z score was 1.64 for a 90% CI, 's' was sample standard deviation and 'n' the number of participants.

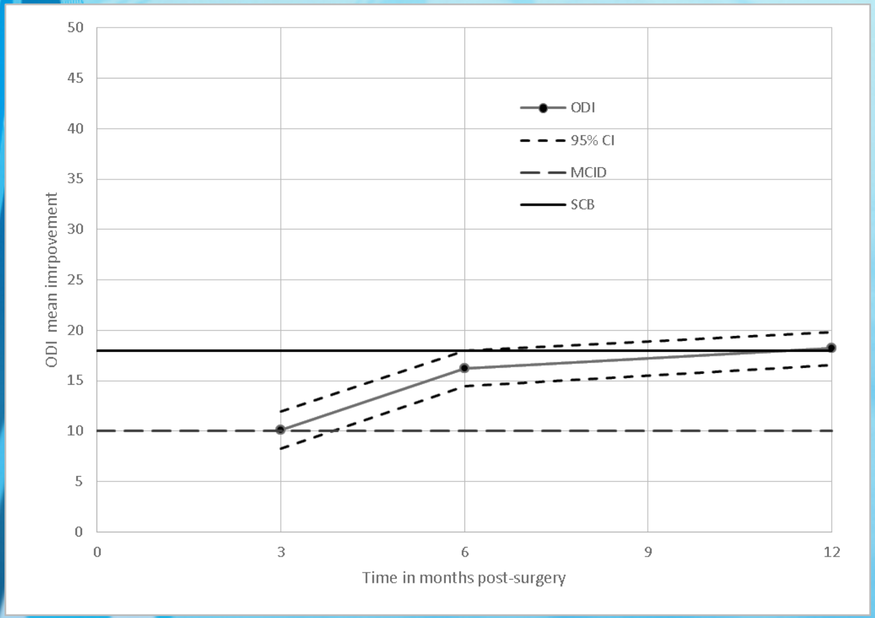
Results



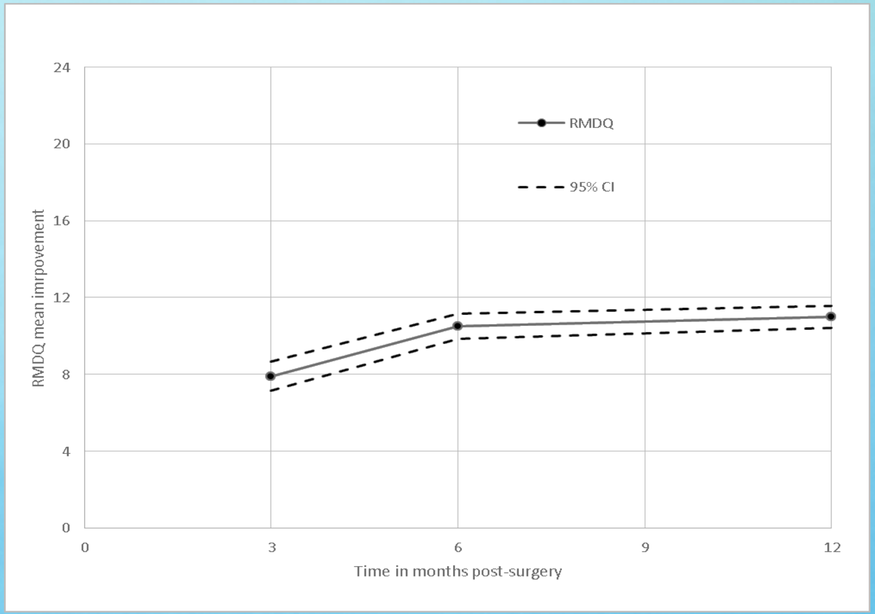
VASB
95% CI
MCID
SCB
VASB mean imrpovement
Time in months post-surgery



VASL
95% CI
MCID
SCB
VASL mean imrpovement
Time in months post-surgery

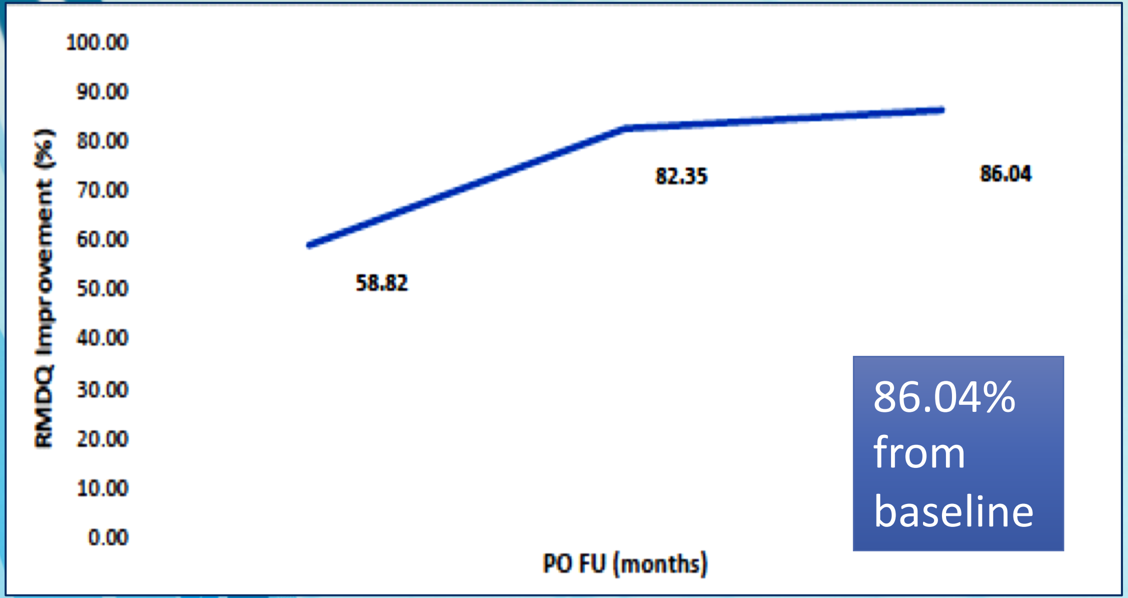


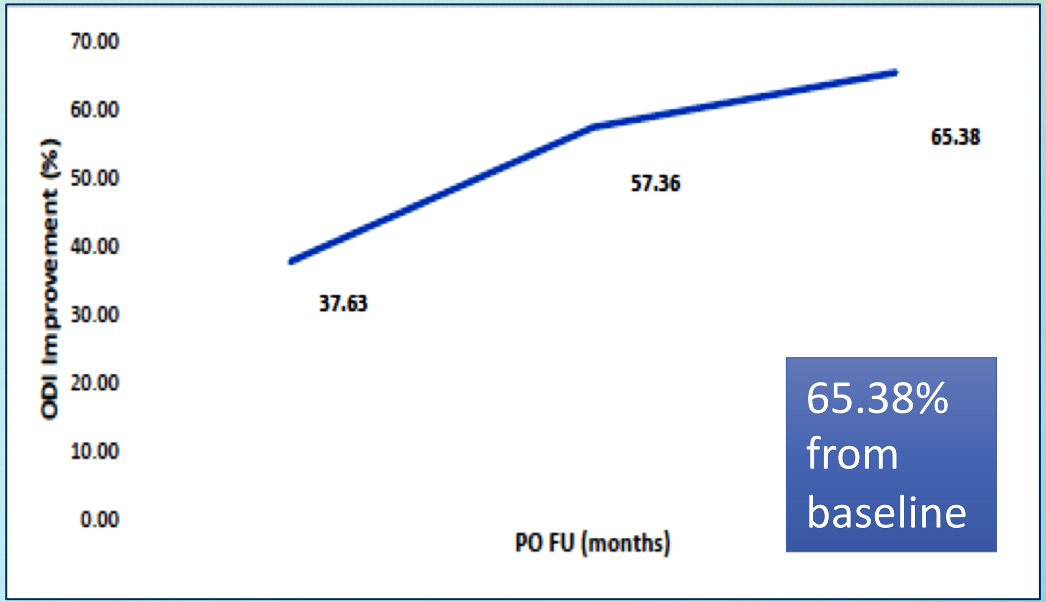
ODI
95% CI
MCID
SCB
ODI mean imrpovement
Time in months post-surgery

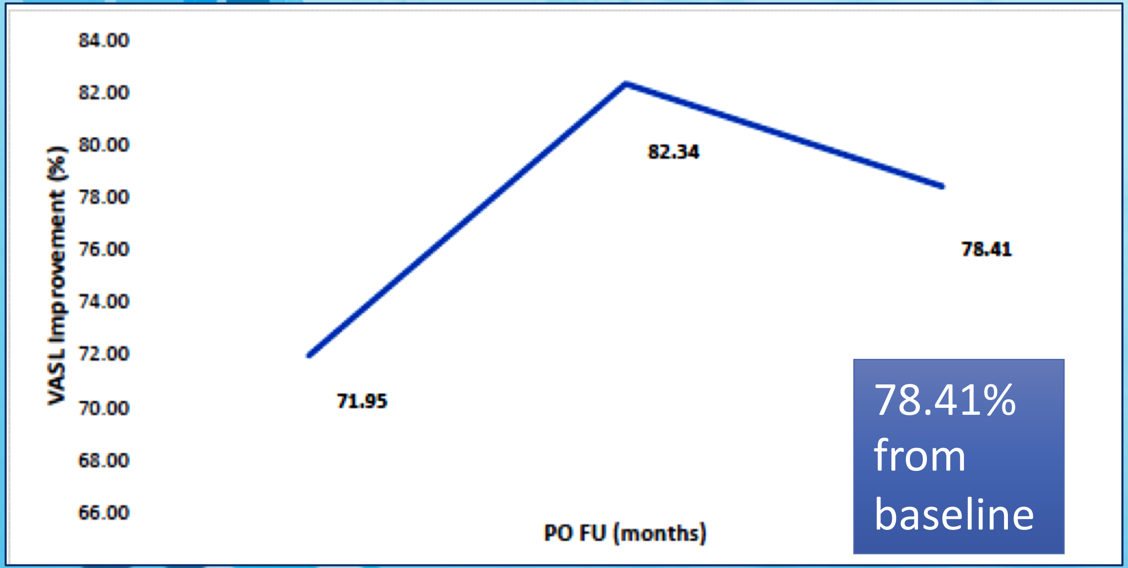


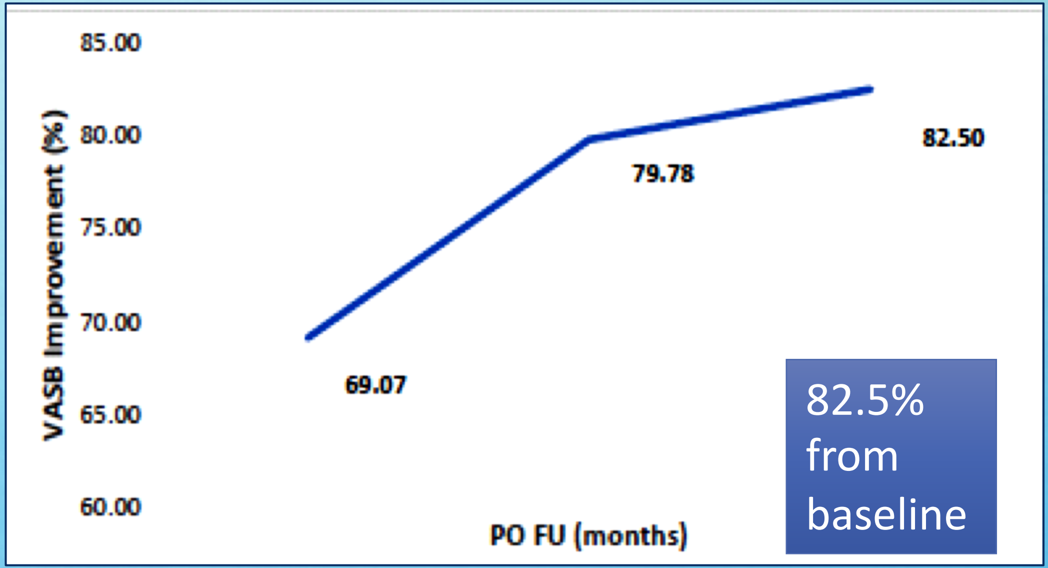
RMDQ
95% CI
RMDQ mean imrpovement
Time in months post-surgery

% improvements

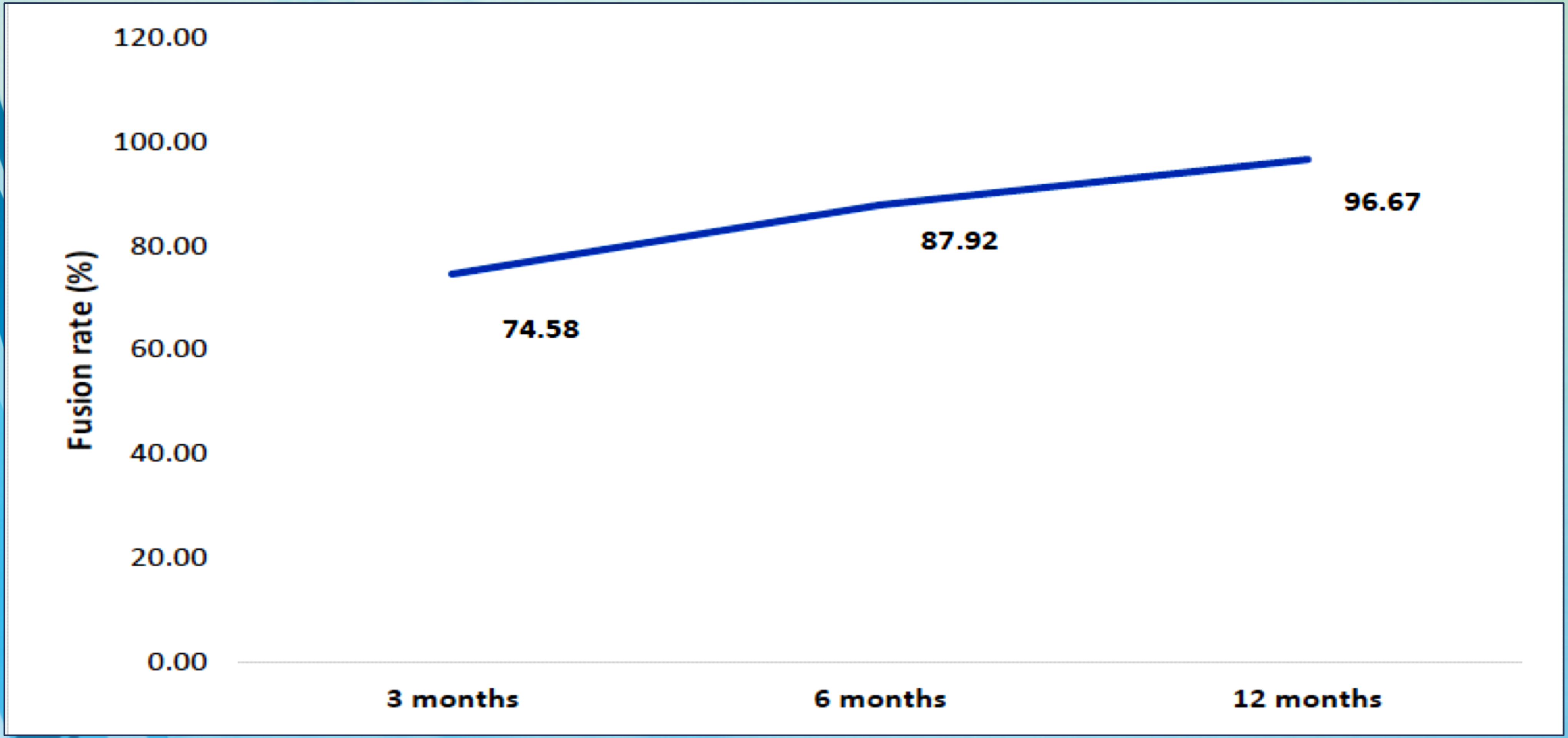








Fusion% n = 240



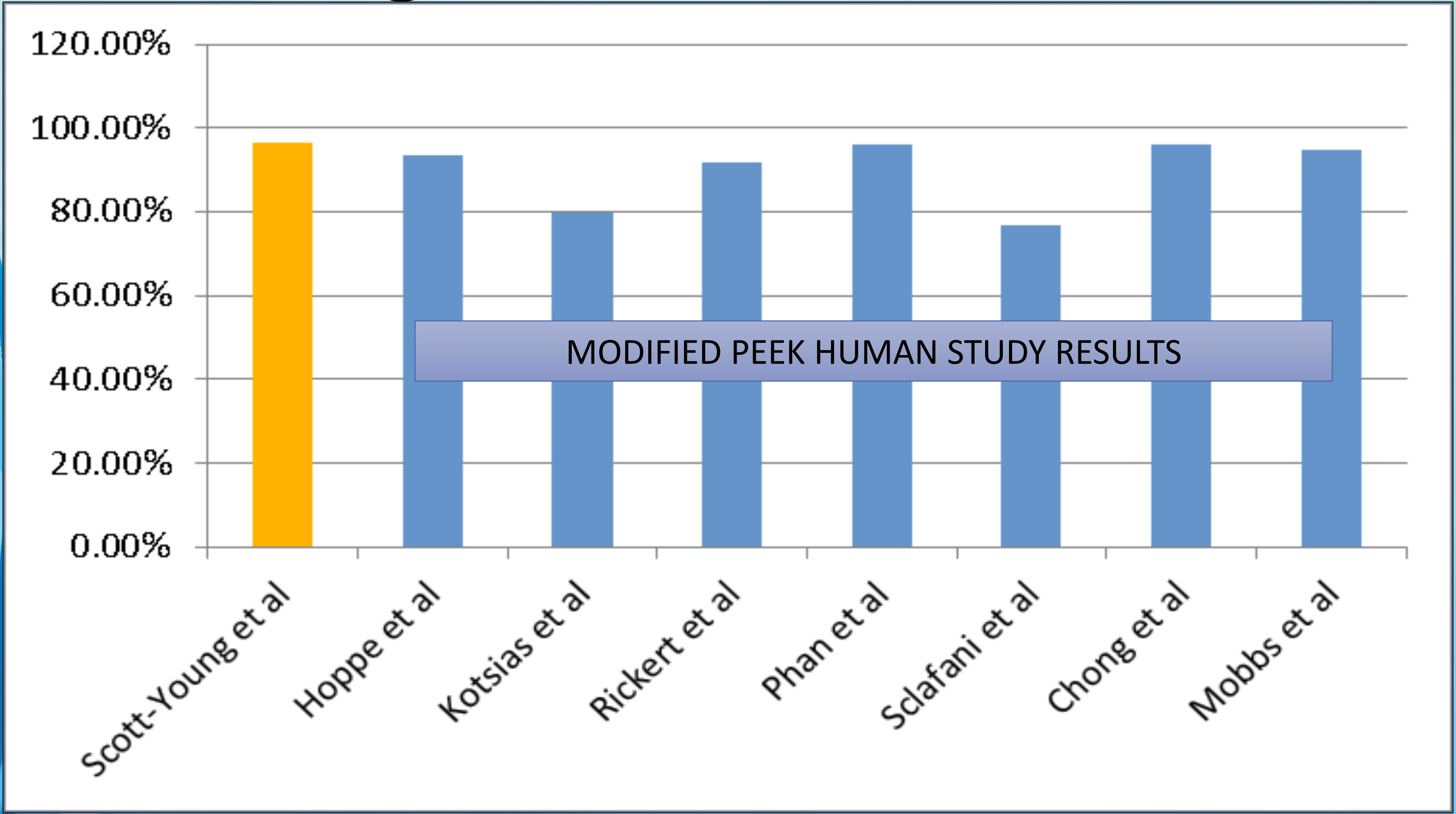
- **8 patients did not meet solid fusion criteria by 12 months at all operative levels.**

Results

AE/Complication	Total AE/Complication	Total % (n = 240)
Vessel Injury	2	0.83%
#ALIF cage - intraoperative	1	0.41%
#Plate Lock – intraoperative	1	0.41%
Subsidence <5mm	1	0.41%
TOTAL	**4**	**2.08%**

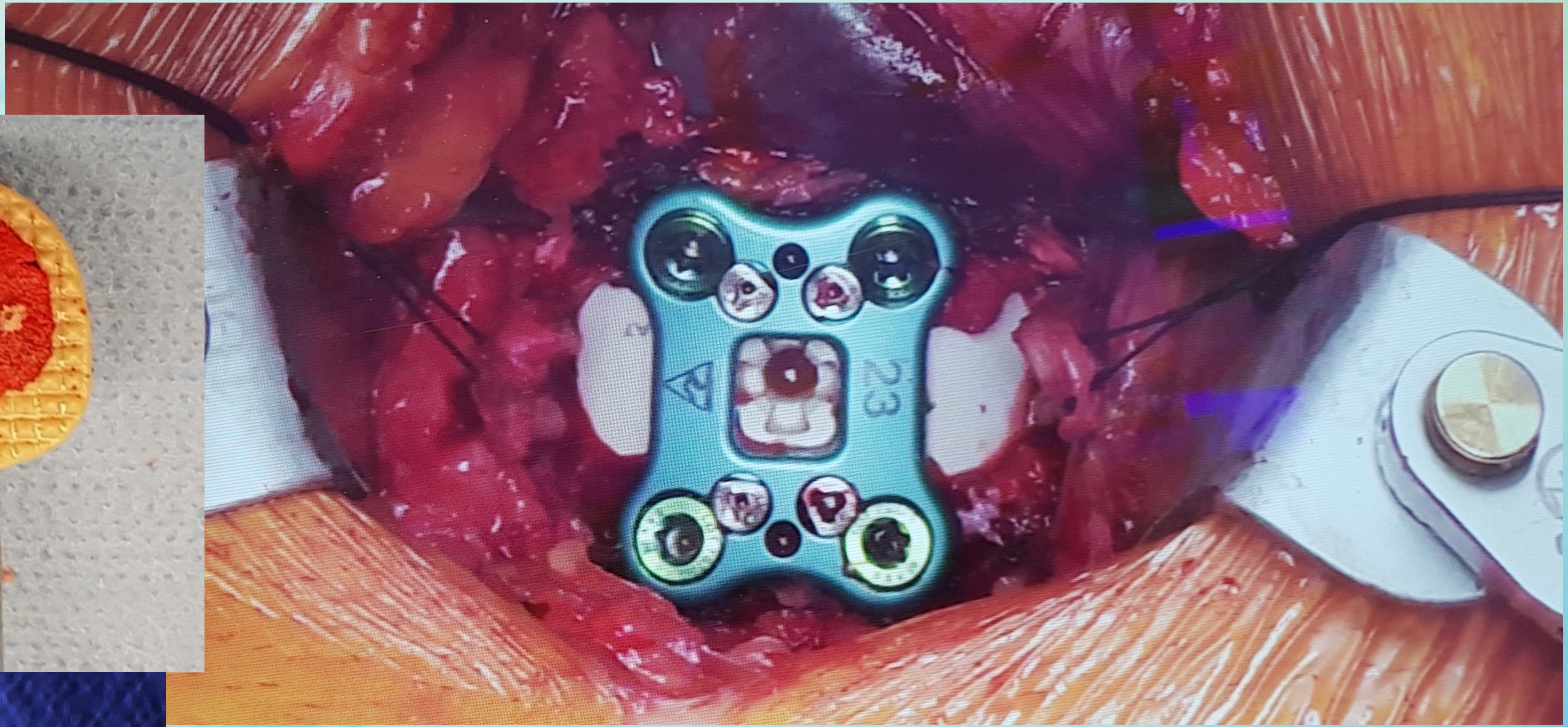
- **No post op revisions of primary constructs**
- **No post op reports of cage migration or construct failure**
- **Total loss to f/up = 7.9% (n=19)**

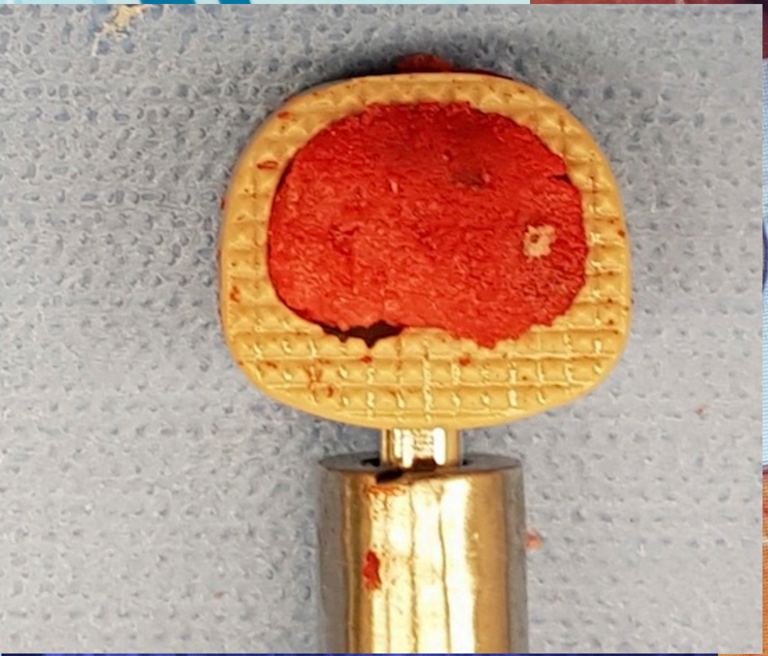
Scott-Young et al vs Evidence - %Fusion

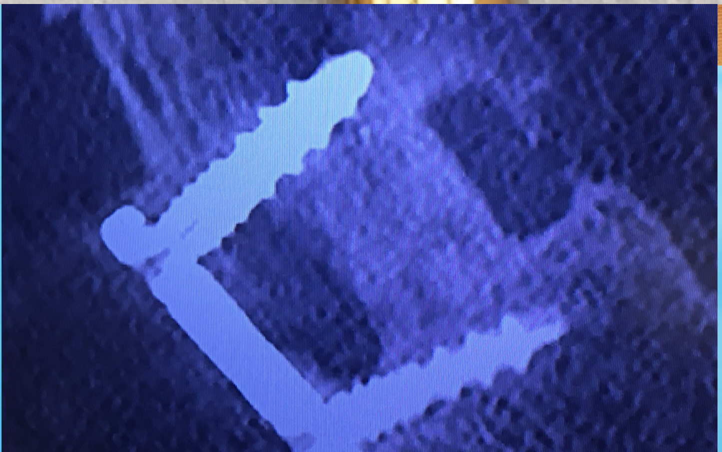


- Methods of radiographic analysis are not homogenous and often poorly defined.

Scott-Young et al - Fusion



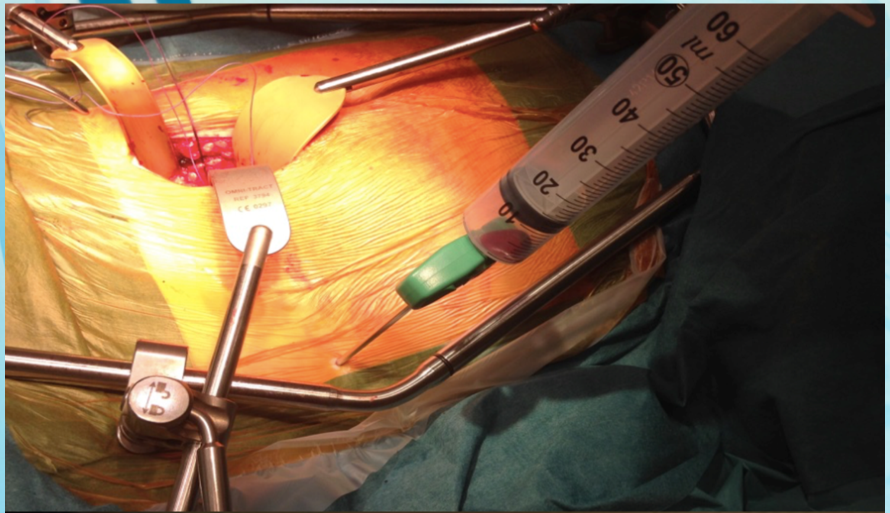




UK cohort - ISASS2018

- ***Northumbria NHS Trust, Mr A Kasis, Mr C Jensen***
- **Shortage of BMP led to alternative source**
- **Same meticulous surgical technique**
- **ALIF PEEK cage with ALIF Plate**
- **Same grafting technique based on Diamond Concept**
  - **Meticulous surgical technique**
  - **Structural femoral head allograft**
  - **BMP substituted with Autograft (ICBG) – MIS harvesting technique using Jamshidi needle**

UK Cohort - Results



- **50 consecutive patients**
- **53 levels in total**
- **L4-S1 ALIF**
- **Results**
  - **98% radiological fusion (52 levels)**
  - **No complications from donor site reported**

Conclusion

- **Look for robust data to support clinical interventions = EBM**
- **Currently a paucity of evidence to support the clinical effectiveness of modified PEEK devices**
- **In-vivo assessment methods can vary results – difficult to compare outcomes**
- **Literature Review - No statistical significance was demonstrated between groups – Study vs Control**
- **Current study demonstrates robust fusion results @96%/12mths with statistically significant PROMs**
- **Diamond concept = successful fusion and patient related outcomes**
- **When modifying devices patient related improvements should be paramount**

gold coast spine

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THANK YOU