

Safety and Efficacy of Bioabsorbable Cervical Spacers and Low-Dose rhBMP-2 for Multilevel ACDF



Kaveh Khajavi, MD, FACS
Alessandria Struebing, MSPH



Minimally Invasive Maximum Results

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Disclosures



- NuVasive, Inc.
 - Consultant
- FDA off-label usage
 - rhBMP-2 (INFUSE, Medtronic Sofamor Danek)
- All products discussed, spacer, infuse, and plate, all sold by Medtronic
- No relationship with Medtronic

Introduction



- Single-level ACDF:
 - high fusion rates, regardless of graft choice or instrumentation
- Multi-level ACDF:
 - variable fusion rates (56-100%)
 - Much higher failure rate, and complication rate
 - highly dependent upon graft choice, interbody spacer, instrumentation, # of levels, host factors, & definition
- Autograft is gold standard, but used less today
- Structural allograft used commonly but may result in lower fusion rates in multilevel cases

Other Spacer and Graft Options



- Synthetic spacers filled with graft material
 - Metal options
 - PEEK: most commonly used
 - ✦ Radiolucent
 - ✦ Modulus of elasticity similar to bone
- Bioabsorbable Spacer
- Many Graft options exist
 - Local bone
 - DBM
 - Ceramics
 - Tricalcium phosphate
- BMP

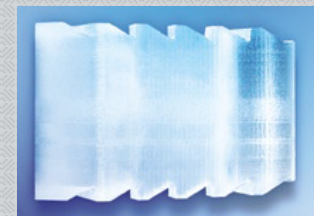
Bioabsorbable cervical spacers (BCS)



- Radiolucent; Modulus of elasticity similar to bone
- Rigid during implantation to provide immediate biomechanical stability, steadily degrades over time allowing gradual transfer of stresses to the graft material, degrades completely when fusion matured
- No issues with particulate debris or retained foreign body like PEEK
- The safety of polymers and their degradation products has been adequately demonstrated in the plastic surgery and orthopedic literature (suture, suture anchors, fracture fixation screws, etc.)



- Cornerstone HSR used in this study
 - Medtronic Sofamor Danek, Memphis, TN
 - Noncrystalline polylactide copolymer of polylactide, 70:30 poly (L-lactide) to poly (D,L-lactide)
 - Degraded slowly to lactic acid → pyruvic acid → (via Krebs cycle) is excreted as CO₂ and water



rhBMP-2



- rhBMP-2 (Infuse, Medtronic Sofamor Danek, Memphis, TN)
 - Achieves fusion at least as well as autograft
 - NOT FDA approved for use in the cervical spine
 - Significant complications have been reported

Methods

Study Overview



- Study Design
 - Prospective observational cohort
 - ✦ IRB approved, prospective registry (ProSTOS, PhDx)
- Inclusion Criteria
 - Consecutive patients treated between 2007-2012 ($n=72$)
 - Multi-level (2+) ACDF with BCS and low-dose rhBMP-2 (& local bone if available)
 - Failure of conservative treatments and available for follow-up

Methods



- 72 patients, 187 levels
 - 37 (51%) 2-level cases
 - 27 (38%) 3-level cases
 - 8 (11%) 4-level cases
- Primary Diagnosis:
 - Spondylosis: 40
 - Deformity/subluxation: 13
 - HNP: 8
 - Non-Union: 7
 - ASD: 4

Most (65%) patients had > 1 primary diagnosis

Methods

Patient Samples



	All (n=72)	2 Levels (n=37)	3+ Levels (n=35)	p-value
Follow-Up (months) – mean ± SD	13.8 ± 6.8	14.2 ± 7.0	13.3 ± 6.6	0.574
Age (years) – mean ± SD	55.3 ± 10.4	51.8 ± 9.5	59.0 ± 10.2	0.003*
Female – n (%)	51 (70.8)	26 (70.3)	25 (71.4)	0.977
BMI (kg/m²) – mean ± SD	28.4 ± 5.6	27.9 ± 5.6	28.8 ± 5.7	0.497
Tobacco Use – n (%)	24 (33.3)	16 (43.2)	8 (22.9)	0.067
Previous Cervical Surgery – n (%)	12 (16.7)	8 (21.6)	4 (11.4)	0.246

Methods

Surgical Summary



	All (<i>n</i> =72)	2 Levels (<i>n</i> =37)	3+ Levels (<i>n</i> =35)	p-value
Primary Indication – <i>n</i> (%)				---
CSM only	29 (40.3)	17 (45.9)	12 (34.3)	
Radiculopathy only	27 (37.5)	14 (37.8)	13 (37.1)	
Both CMS + Radiculopathy	15 (20.8)	6 (16.2)	9 (25.7)	
Neither	1 (1.3)	0 (0.0)	1 (2.9)	
rhBMP-2 (mg) – mean ± SD	0.58 ± 0.1	0.58 ± 0.1	0.58 ± 0.1	.0963
OR Time (min) – mean ± SD	144.4 ± 41.8	123.3 ± 33.0	171.3 ± 36.4	<0.001*
EBL (mL) – mean ± SD	49.0 ± 43.8	52.9 ± 57.0	44.6 ± 20.0	0.502
LOS (days) – mean ± SD	1.1 ± 0.6	1.2 ± 0.8	1.0 ± 0.0	0.109

Methods



- Clinical Outcomes
 - NDI
 - NRS (neck & arm, 0-10)
 - SF-36 (PCS & MCS)
 - Patient satisfaction

- Imaging Studies
 - Initial x-rays within 24 hours of surgery
 - AP and lateral x-rays at 4-6 weeks
 - Serial x-rays with flexion/extension at 3, 6, 12, 24 months
 - CT obtained only if uncertainty regarding fusion status

Methods



- Dysphagia Classification
 - Quantified if symptoms were unresolved by 2 weeks PO or hospital readmission and additional treatment were required
 - “Prolonged” dysphagia: present \geq 1 month po visit
 - “Persistent” dysphagia: present \geq 3 month po visit
- Analysis
 - Chi-squared/Fishers’ Exact tests and one-way ANOVA
 - Significance accepted for $p \leq 0.05$

Results

Adverse Events



	2 Levels (n=37)	3+ Levels (n=35)	Total (n=72)
Major	<ul style="list-style-type: none"> • RLL injury • Return to OR for symptomatic nonunion <p>2 (5.4%)</p>	<ul style="list-style-type: none"> • Excessive swelling (2) • Return to OR for seroma evacuation <p>3 (8.6%)</p>	5 (6.9%)
Minor	<ul style="list-style-type: none"> • COPD exacerbation • Readmit within 30 days PO for nausea <p>2 (5.4%)</p>	<ul style="list-style-type: none"> • AFIB exacerbation <p>1 (2.9%)</p>	3 (4.2%)

1 pt with symptomatic pseudoarthrosis (1.4%)

Results

Adverse Events: Dysphagia



- 38 patients (53%) had dysphagia that was not resolved by 2 week PO
 - 21 patients had their dysphagia symptoms resolved by 1 month
 - 13 patients had their dysphagia symptoms resolved by 3 months
 - 2 patient had their dysphagia symptoms resolved by 6 months
 - 2 patients had dysphagia 1 & 3 months then no dysphagia data/lost to f/u
- 2 of these patients required readmission and observation/IV steroids
- All resolved by 6 months

Prolonged dysphagia 17/72 = 24%

Persistent dysphagia 4/72 = 6%

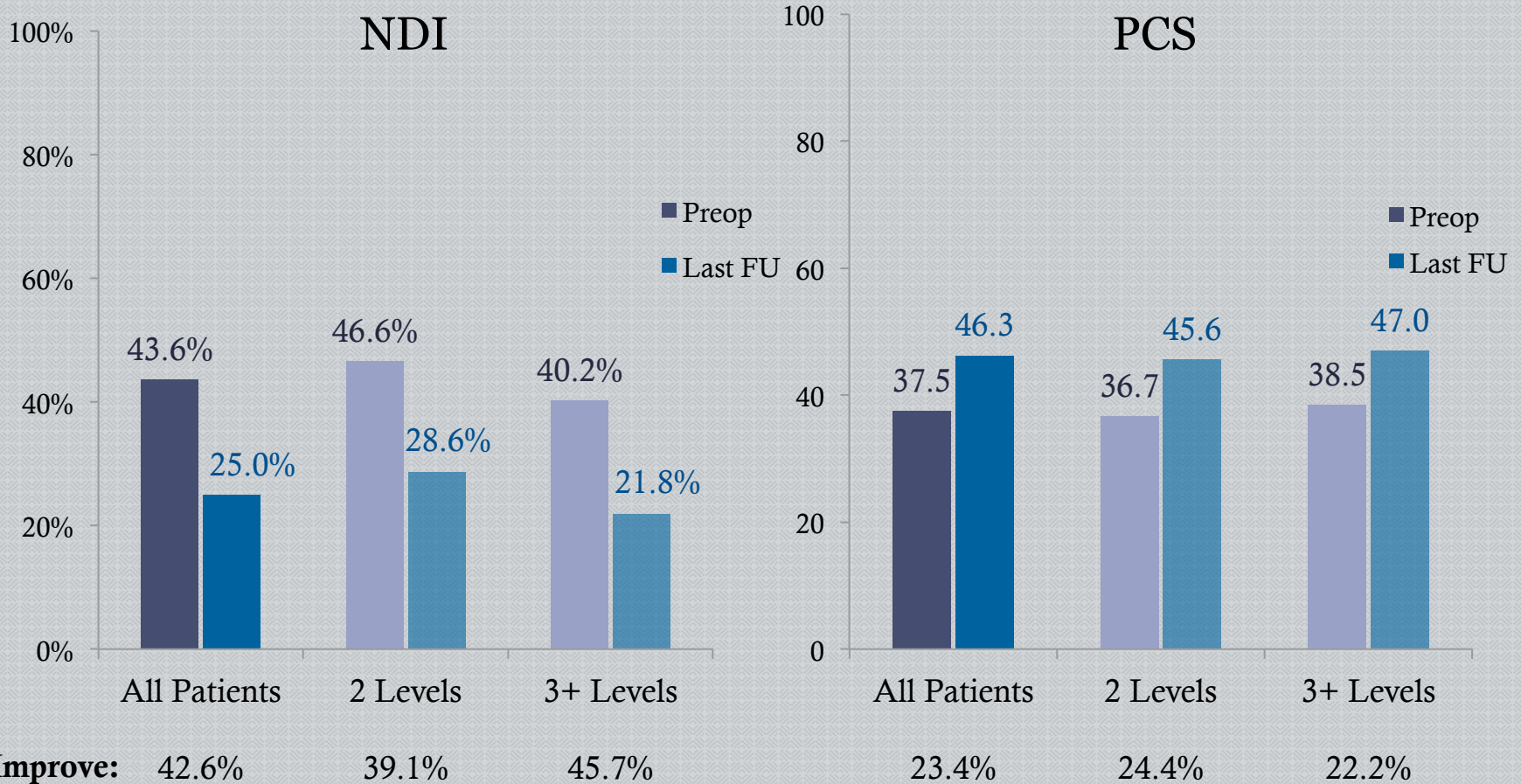


	Dysphagia	No dysphagia	Total
2 levels	18	19	37
3 levels	13	14	27
4 levels	7	1	8

P-value = 0.064

Results

Clinical Outcomes: NDI & SF-36 PCS

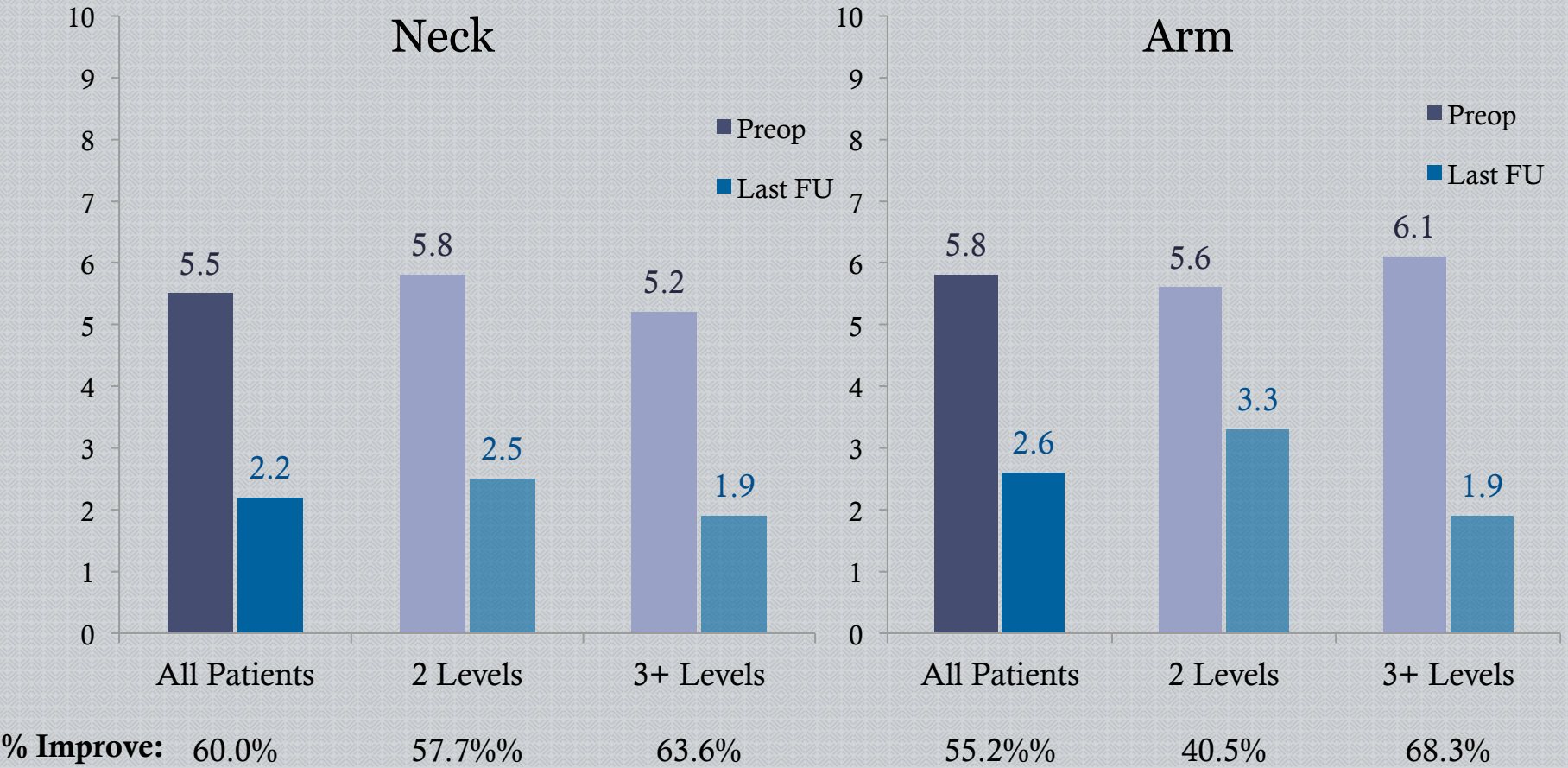




- It should be noted that the clinical indication for surgery was myelopathy in 40% of patients in the current series, and thus, the NDI, which contains questions mostly related to disability as a result of radicular symptoms, may not reflect the “true disability” for these patients.

Results

Clinical Outcomes: NRS Neck & Arm

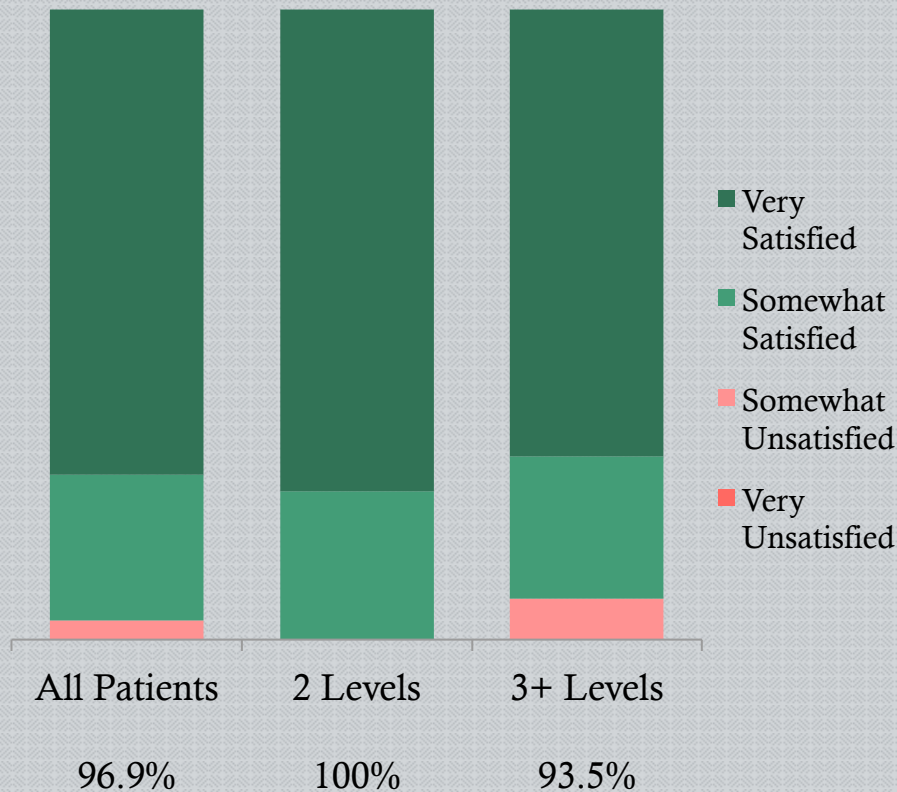


Results

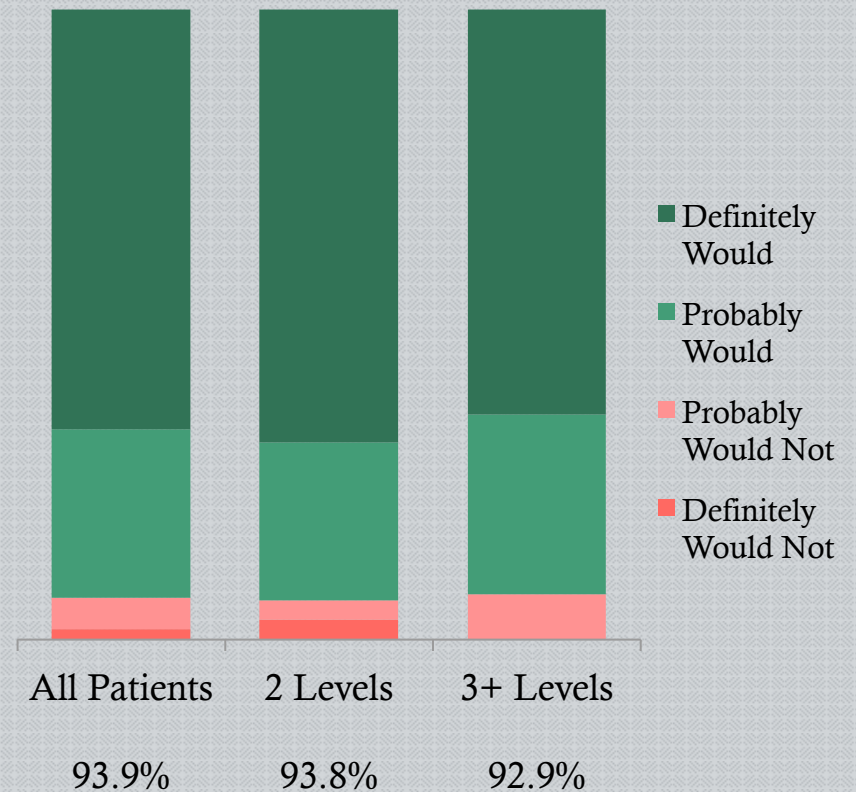
Patient Satisfaction



How satisfied are you with your surgical outcome?



Given your current condition, would you elect to have the same surgery again?



ACDF x 2 for myelopathy



54 yo M CSM, Rt hemibody N/T 10 mo; inc DTRs, Hoffmans, clonus

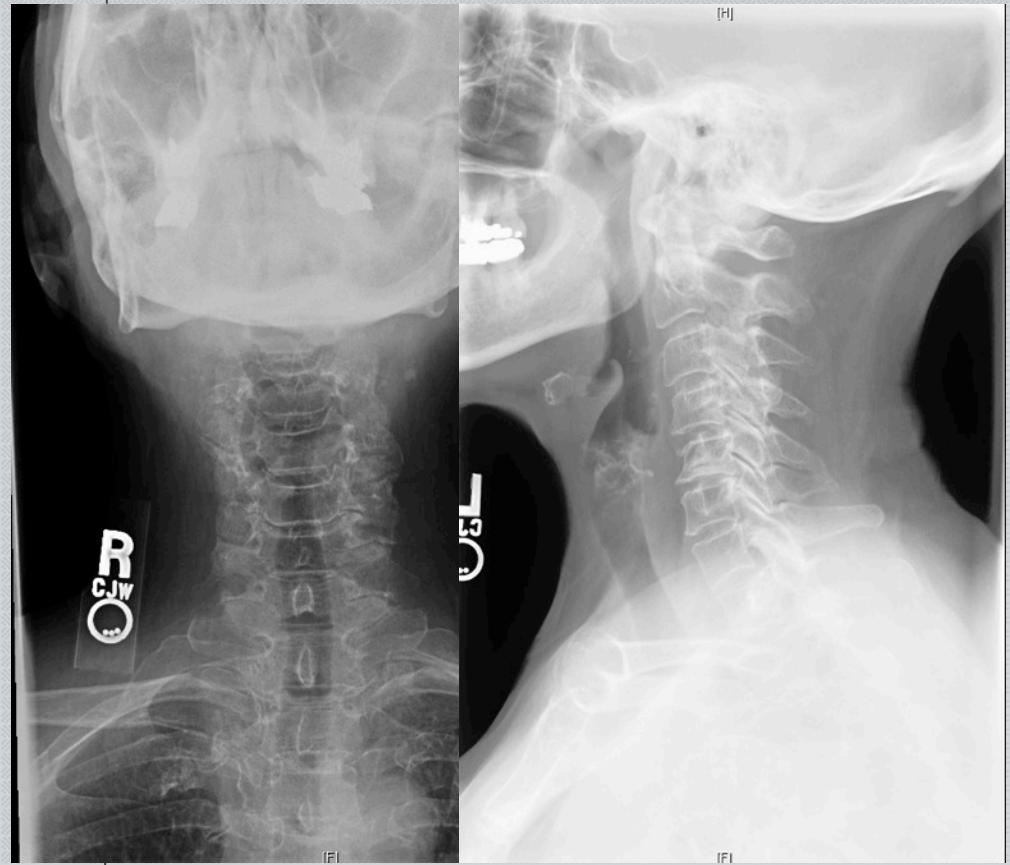


6 mo PO

ACDF x 2 for cerv radiculopathy

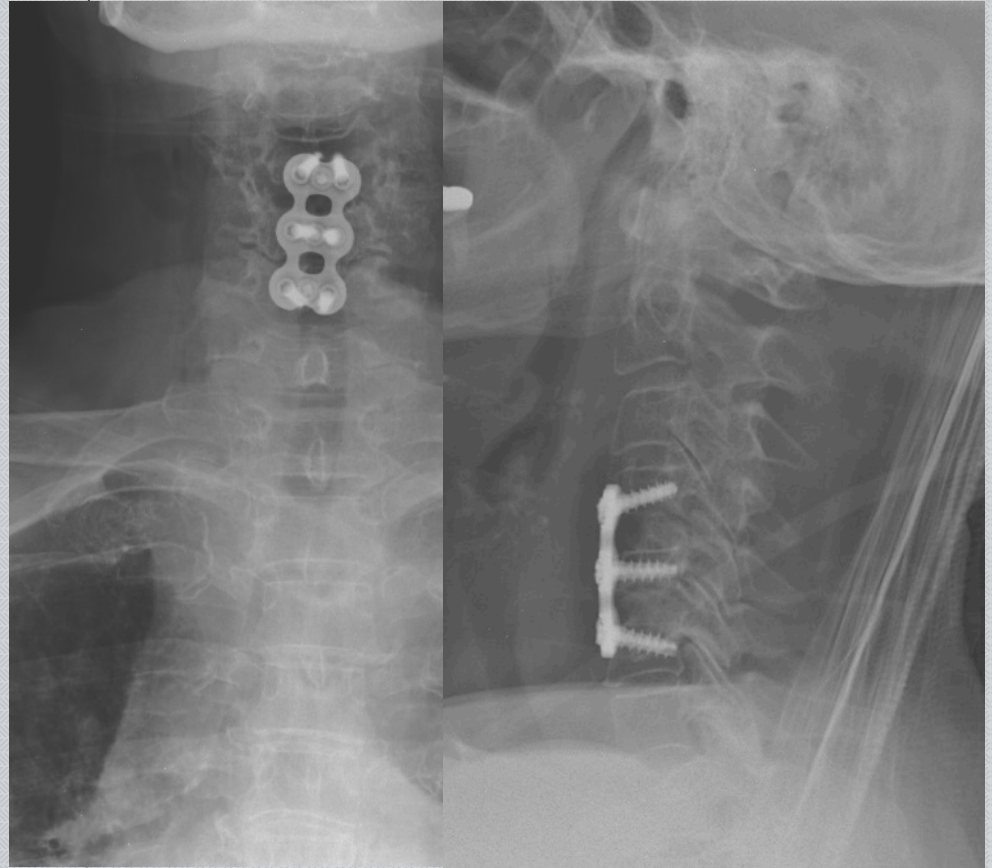


- 71 y/o female
- CC:
 - 3+ years neck pain + left C6 radiculopathy
 - Left 4+/5 deltoid weakness
 - Left 4/5 bicep weakness
 - Left 4-/5 BR and WE weakness
- Cervical radiculopathy
 - C4-5 DDD and subluxation
 - C5-6 severe DDD





- C4-6 ACDF
 - BCS
 - 0.5mg rhBMP-2 per level + crushed local autograft
 - C4-6 anterior cervical plating





- Expected dysphagia immediately PO, resolved by 2 weeks PO
- Clinical outcomes (24MO)
 - NDI 52 → 16
 - NRS Neck 8 → 0
 - NRS Arm 6 → 0
 - SF-36 PCS 41.4 → 59.1
 - SF-36 MCS 25.3 → 45.3
- Patient satisfaction
 - Very satisfied with surgical outcome
 - Would definitely do again

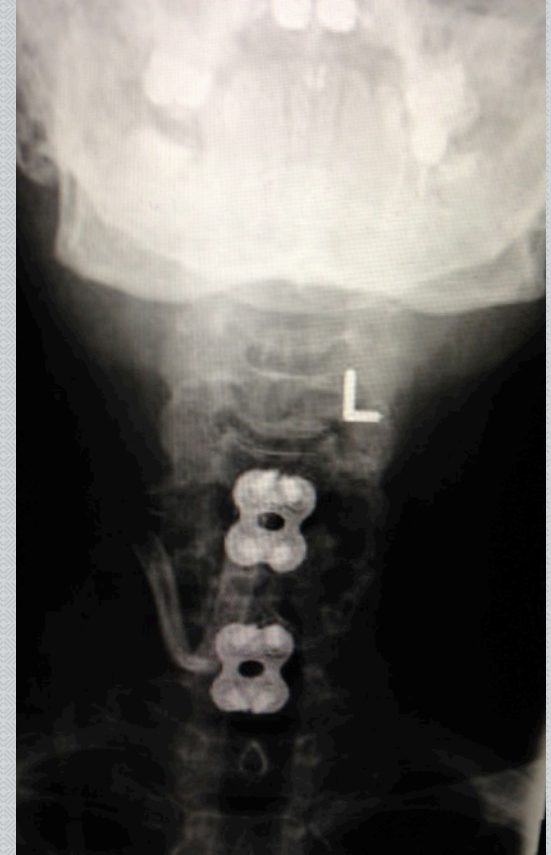


ACDF x 2 for pseudo and ASD

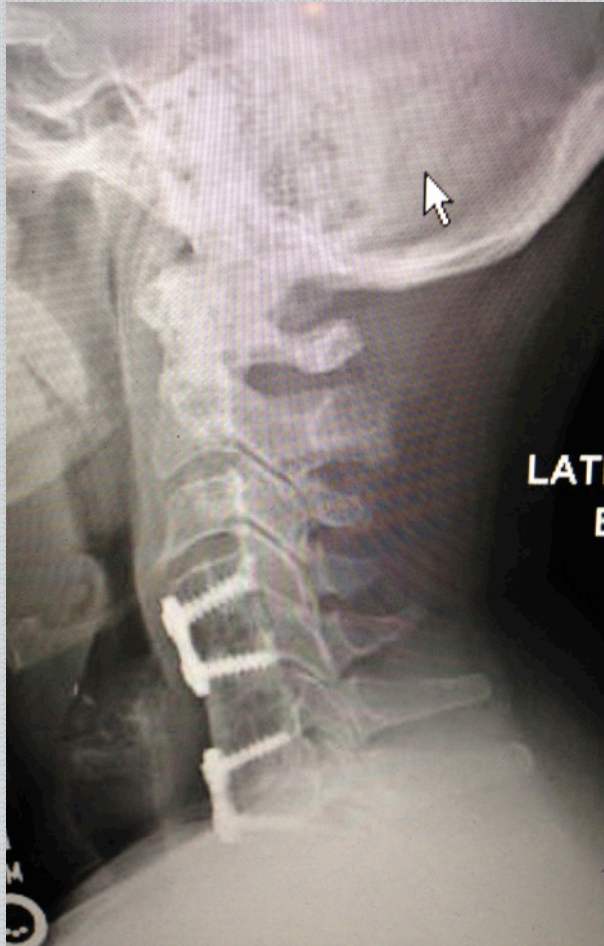


45 yo F s/p C5-6 ACDF 2004 , with chronic NP & Left C7 radic

ACDF C45, C6-7



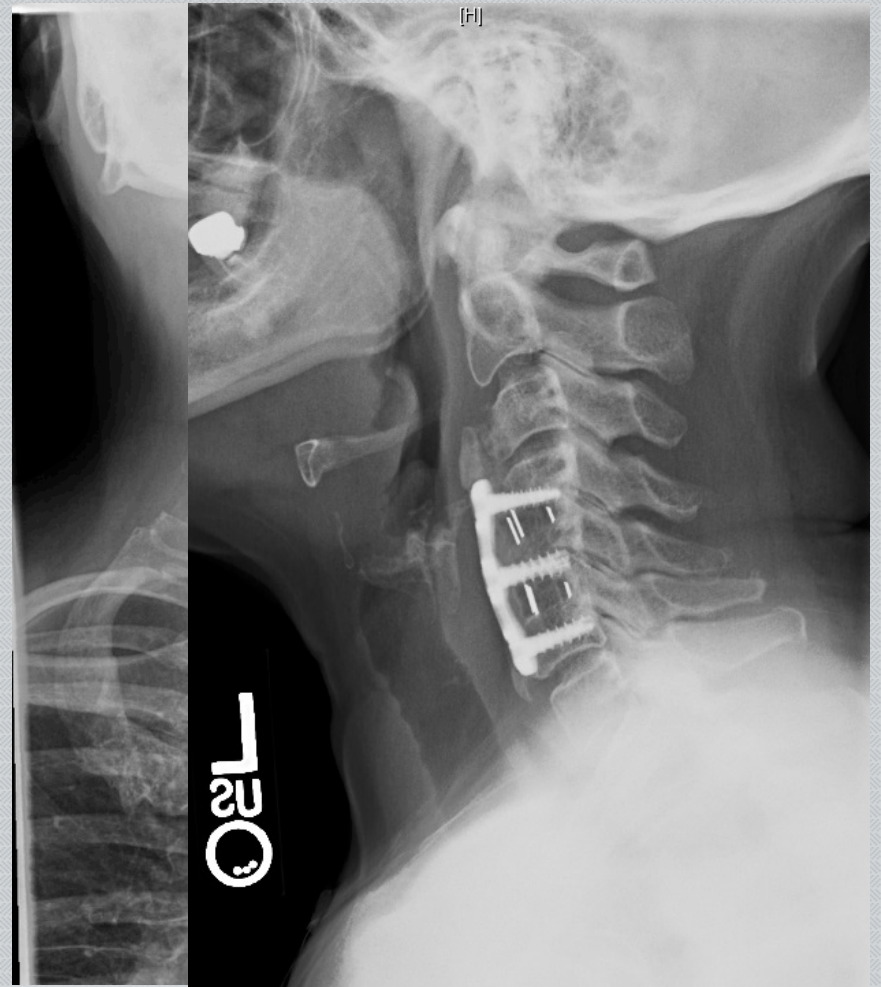
4 years PO



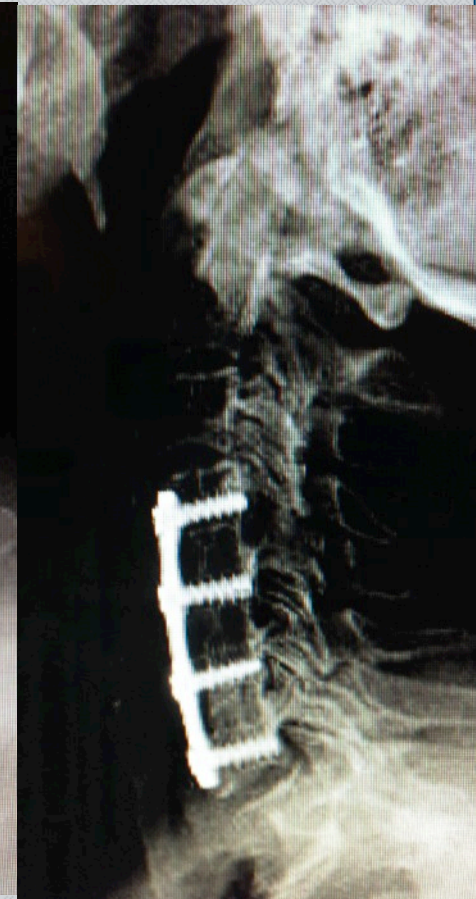
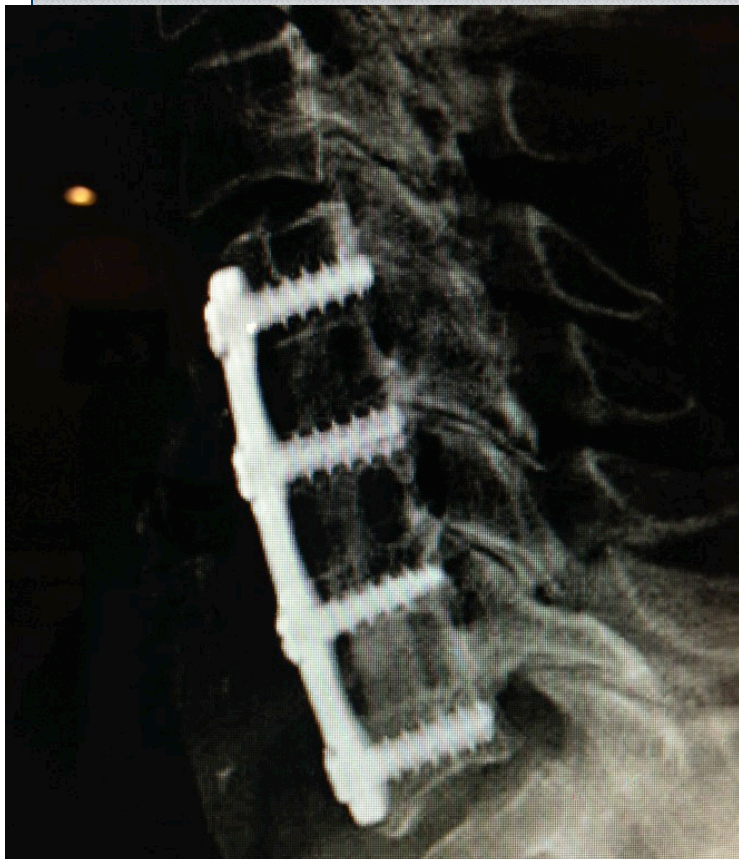
ACDF x 2 for ASD



- 63 y/o female
- PMHx
 - 2 years post C4-6 ACDF with PEEK cages 2009
- Presents 2010 with increasing NP, L shoulder pain
- In 2011 develops Left C7 radic



ACDF x 3 for myelopathy & radiculopathy



79 yo F with CSM & radic

ACDF x 4 for CSM



77 yo F CSM, N/C hands 5 yrs, lermittes, intrinsic hand weakness, hoffmans signs

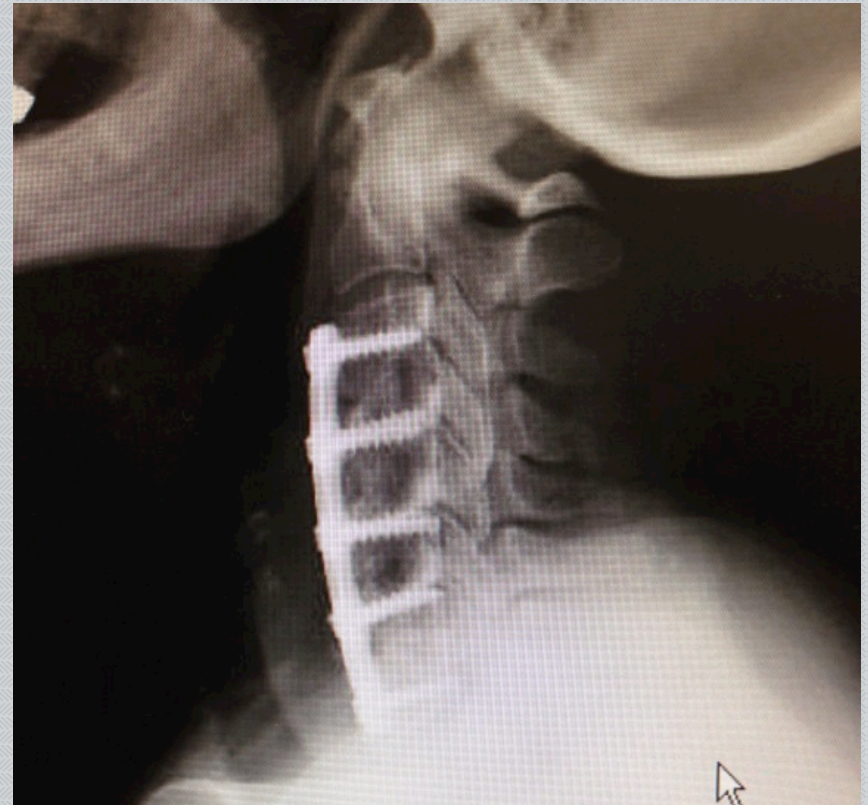
Immediate PO





1 year PO

5 years PO



Only case of symptomatic non-union



May 2010

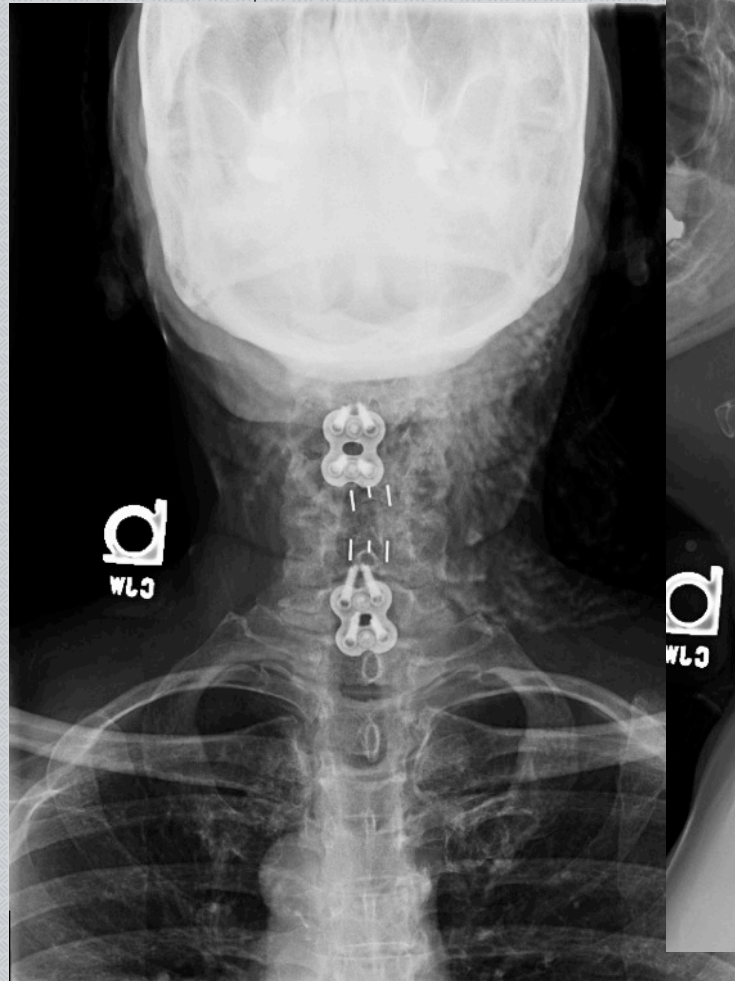


May 2011





- Felt she had ASD C3-4 and C6-7
- C3-4/C6-7 ACDF July 2011
 - BCS
 - 0.5mg rhBMP-2 per level + crushed local autograft

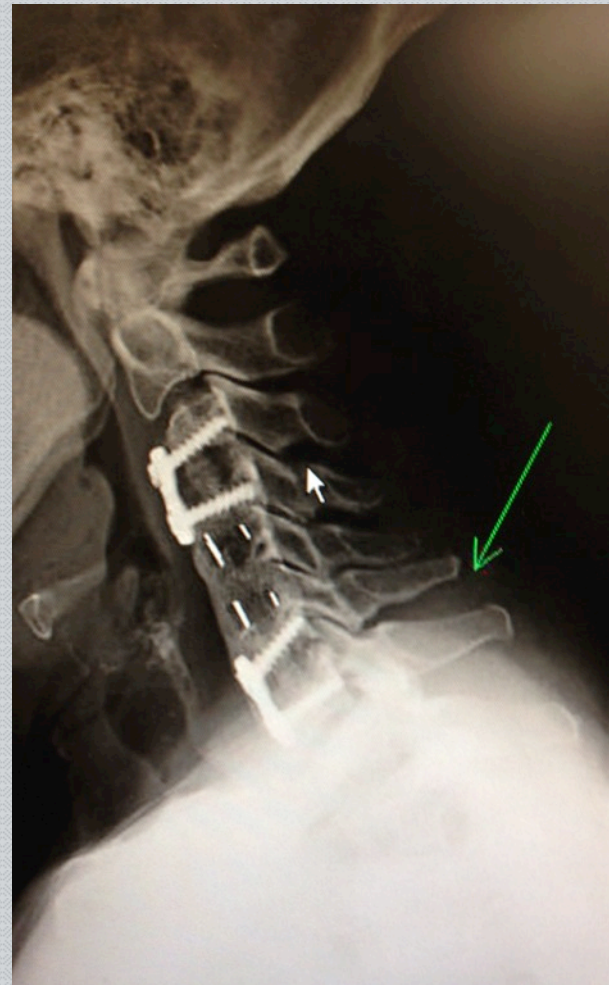




- Mild, transient prolonged dysphagia resolved by 1MO PO
- 6 MO PO
 - Solid C3-4 fusion
 - C6-7 symptomatic pseudoarthrosis
 - Tried external electrical stim unit



Note splay of spinous processes





- Return to OR 11MO PO for repair of C6-7 nonunion
 - C6-7 posterior arthrodesis
 - C6-7 instrumented lateral mass screw rod fixation
- Solid fusion by 6 months PO



Solid fusion achieved



Discussion: Comparative Studies

Fusion rates vs other graft/spacer options



- Current study: BCS + low-dose rhBMP-3, 2-4 levels
 - 98.6% fusion rate: 1 pt with symptomatic pseudoarthrosis (1.4%)
- Fountas KN, Kapsalaki EZ, Nikolakakos LG, et al. Anterior cervical discectomy and fusion associated complications. *Spine (Phila Pa 1976)* 2007;32:2310-7.
 - Retrospective, autograft or allograft, +/- plate, 1-3 levels, 1015 patients
 - 94% fusion rate for 2-level cases, 91% for 3-level cases
- Miller LE, Block JE. Safety and effectiveness of bone allografts in anterior cervical discectomy and fusion surgery. *Spine (Phila Pa 1976)* 2011;36:2045-50.
 - Systematic literature review, 20 studies, almost 2000 pts
 - Allograft or autograft: fusion rate = 91% levels treated

Discussion

Comparative Studies: Fusion rates vs other BCS papers



- Current study: BCS + low-dose rhBMP-3, 2-4 levels
 - 98.6% fusion rate; 1 pt with symptomatic pseudoarthrosis (1.4%)
- Lanman TH, Hopkins TJ. Early findings in a pilot study of anterior cervical interbody fusion in which recombinant human bone morphogenetic protein-2 was used with poly(L-lactide-co-D,L-lactide) bioabsorbable implants. *Neurosurg Focus* 2004;16:6.
 - BCS + rhBMP-2, 100% fusion rate (x-ray & CT), 3 mo f/u

Discussion

Comparative Studies: Complications / Dysphagia Rates



- Current study: BCS + low-dose rhBMP-3, 2-4 levels
 - 11% complication rate (7% major, 4% minor)
 - 24% prolonged & 6% persistent dysphagia rate (all resolved by 6 months)
- Fountas KN, Kapsalaki EZ, Nikolakakos LG, et al. Anterior cervical discectomy and fusion associated complication. *Spine (Phila Pa 1976)* 2007;32:2310-7.
 - 1-3 levels, 9% complication rate, 11% prolonged dysphagia rate
- Riley LH, Skolasky RL, Albert TJ. Dysphagia after anterior cervical decompression and fusion. *Spine* 2005;30:2564-9
 - Retrospective review, 454 pts/23 sites, telephone interviews
 - Dysphagia at 3 mo: 20% 1 level, 33% 2 levels, 39% for 3+ levels

Study Strengths / Limitations



- Strengths
 - All consecutive patients included
 - Outcomes all prospectively collected
- Limitations
 - 72 pts/187 levels still small, short f/u
 - Fusion definition based on x-rays
 - Dysphagia self reported. Telephone interviews may yield a higher % of patients with persistent dysphagia
 - Did NOT use myelopathy outcome measures (MDI, JOA, Nurick, etc)

Conclusions



- Multilevel ACDF can be a very effective treatment for symptomatic cervical spondylosis, although complications rates, particularly dysphagia, can be high, as can pseudoarthrosis rates
- Although the use of rhBMP-2 is both off-label and controversial, the results of the current study suggest that the combination of low-dose rhBMP-2 with a BCS seems to be a useful treatment option with acceptable complication rates, high fusion rates, and good clinical improvements in patients undergoing multi-level ACDF

Thank you!



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Maximum Results

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