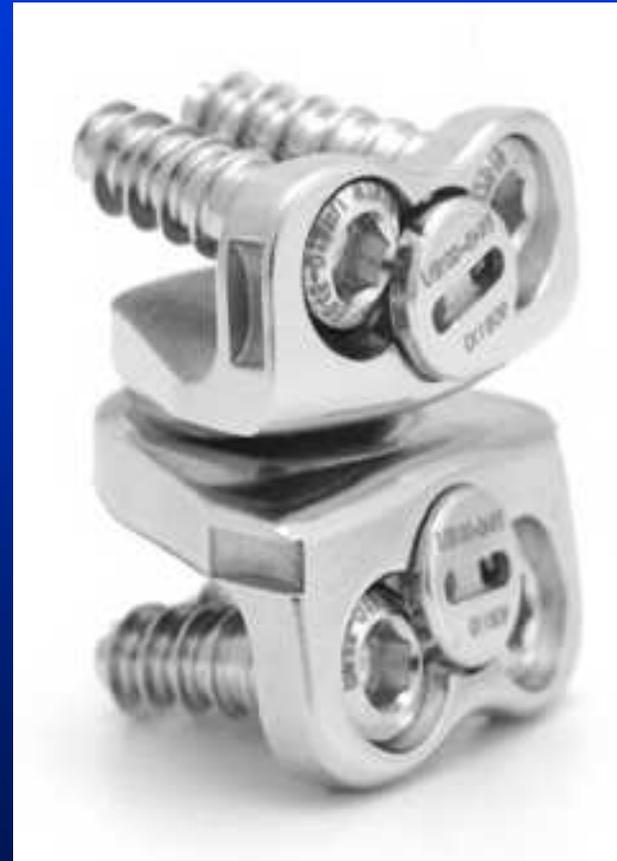
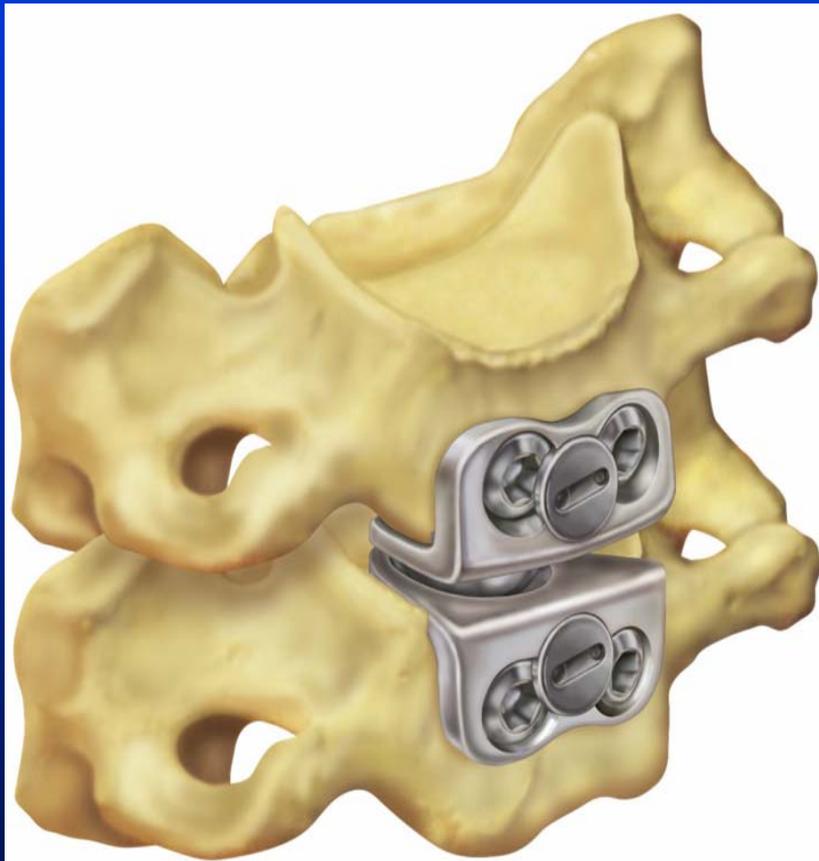


PRESTIGE® Cervical Disc

Orthopedic and Rehabilitation Device Advisory Panel Presentation

**Bailey Lipscomb, Ph.D.
Vice President, Clinical Affairs
Medtronic**

PRESTIGE® Cervical Disc



Cummins/Bristol Cervical Disc

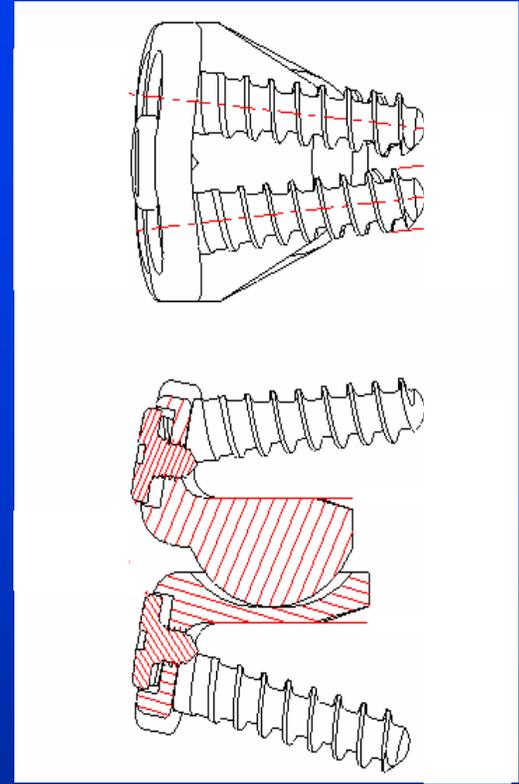


J Neurosurg 88:943-948, 1998

Surgical experience with an implanted artificial cervical joint

BRIAN H. CUMMINS, F.R.C.S., JAMES T. ROBERTSON, M.D., AND STEVEN S. GILL, F.R.C.S.

Department of Neurosurgery, Frenchay Hospital, Bristol, United Kingdom; and Department of Neurosurgery, University of Tennessee Health Science Center, Memphis, Tennessee



PRESTIGE® Cervical Disc

IDE No. G010188

- **Prospective, randomized, controlled multi-centered clinical trial**
- **541 patients**
- **32 investigational centers**

PRESTIGE® Cervical Disc

IDE No. G010188

- **Cervical degenerative disc disease**
- **Single-level implantation**
- **PRESTIGE® device vs. ACDF**

PRESTIGE® Cervical Disc

PMA P060018

PRESTIGE® Cervical Disc FDA Panel Presentations

Device Design and Preclinical
Testing

Carl Stamp

IDE Clinical Results

J. Kenneth Burkus, M.D

Clinical Case Presentations

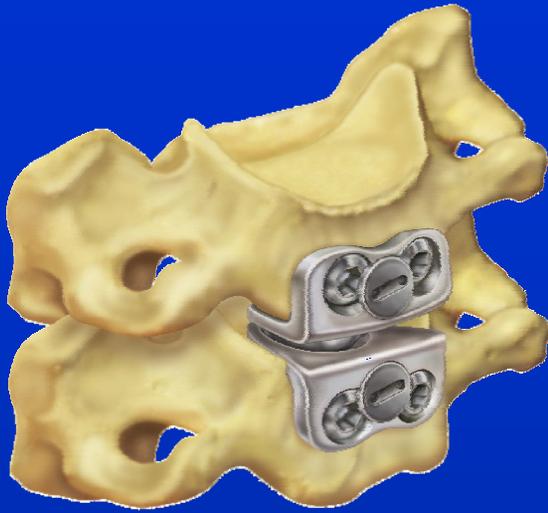
Vincent Traynelis, M.D.

Conclusion

Bailey Lipscomb, Ph.D.

Additional Resources

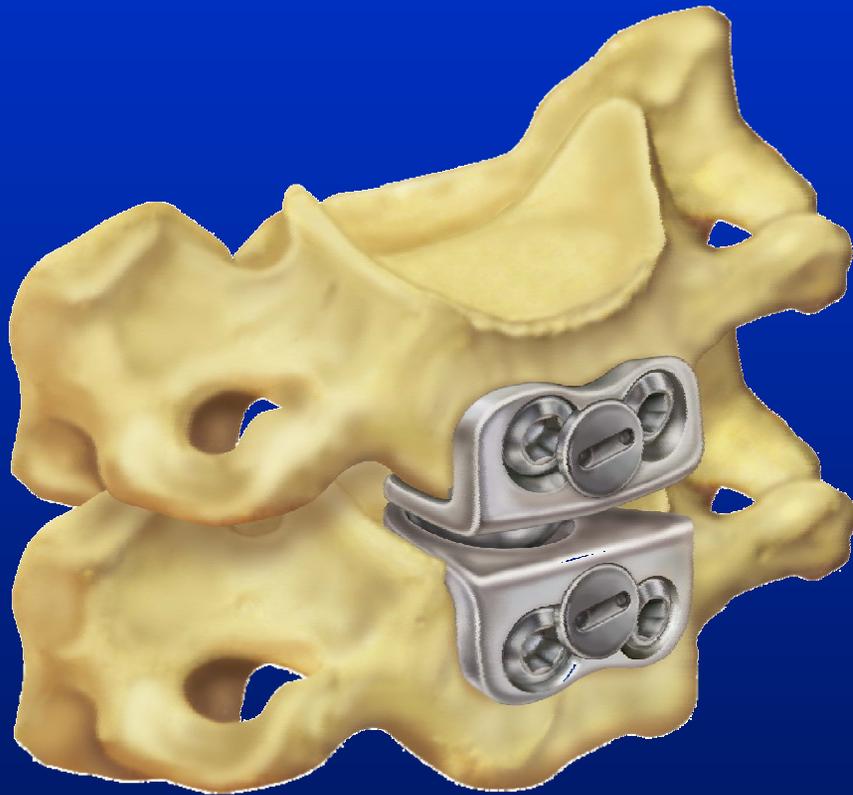
- Rick Sasso, M.D.
- Steve Papadopoulos, M.D.
- Hal Mathews, M.D.
- Josh Jacobs, M.D.
- Richard Herzog, M.D.
- Harry Genant, M.D.
- John Nemunaitis, M.D.
- J. T. Robertson, M.D.
- Donald Berry, Ph.D.
- Seth Greenwald, D.Phil. (Oxon)
- Jeffrey Toth, Ph.D.
- Steve Kurtz, Ph.D.
- Medtronic Staff



PRESTIGE[®] Cervical Disc Testing

Carl Stamp
Vice President of Global Operations
Medtronic Spine and Biologics

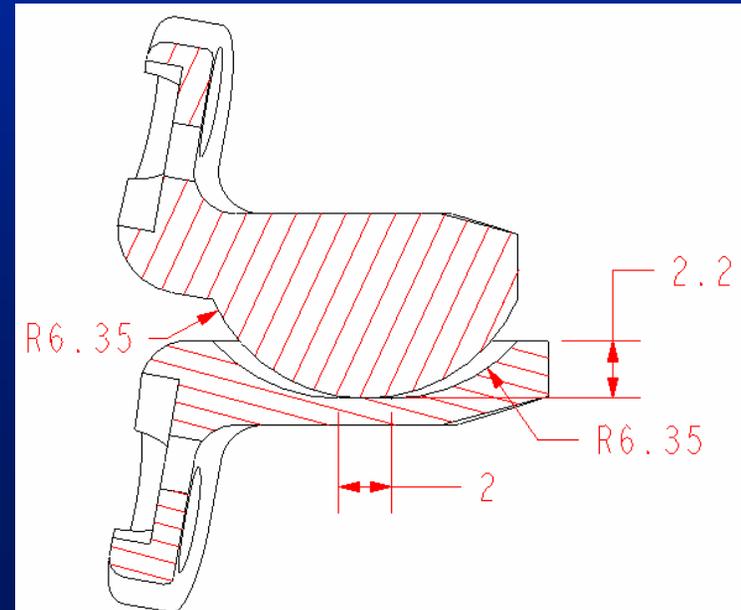
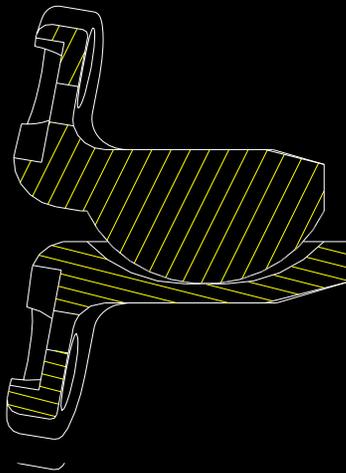
PRESTIGE[®] Cervical Disc



PRESTIGE[®] Cervical Disc Design Features

Anatomic Articulation

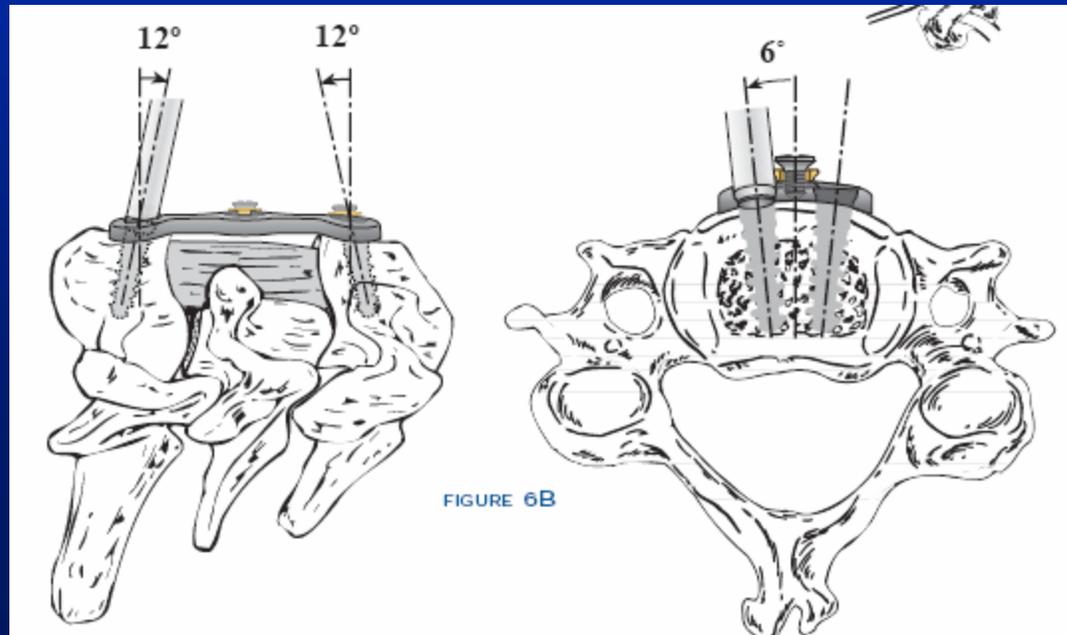
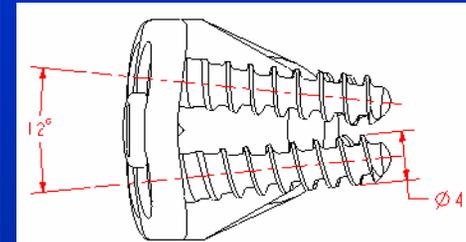
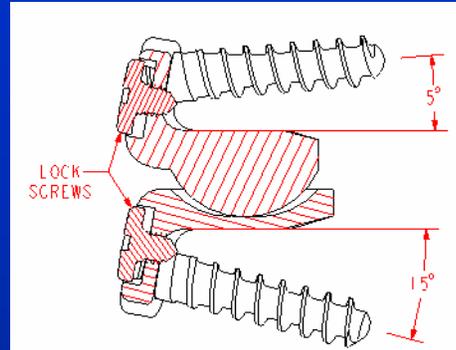
- Flexion/Extension: $> \pm 10^\circ$
- Lateral Bend: $> \pm 10^\circ$
- Axial Rotation: unconstrained
- A-P Translation: $\pm 2\text{mm}$
- Subluxation “jump height”: 2.2mm

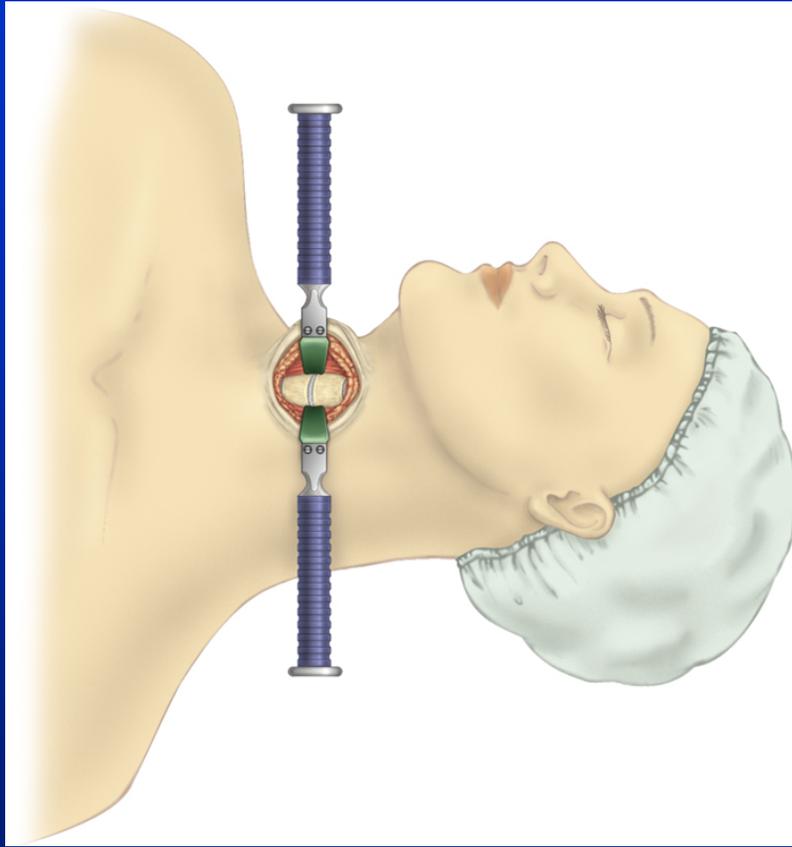






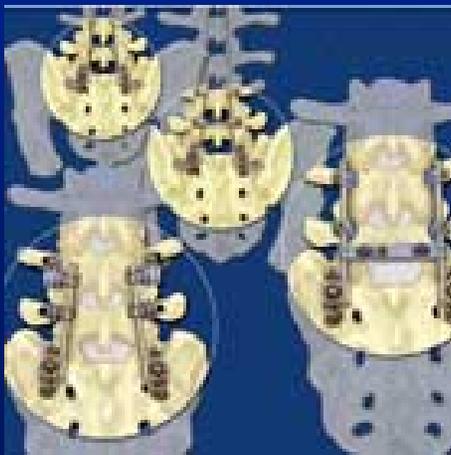
Screw Trajectory



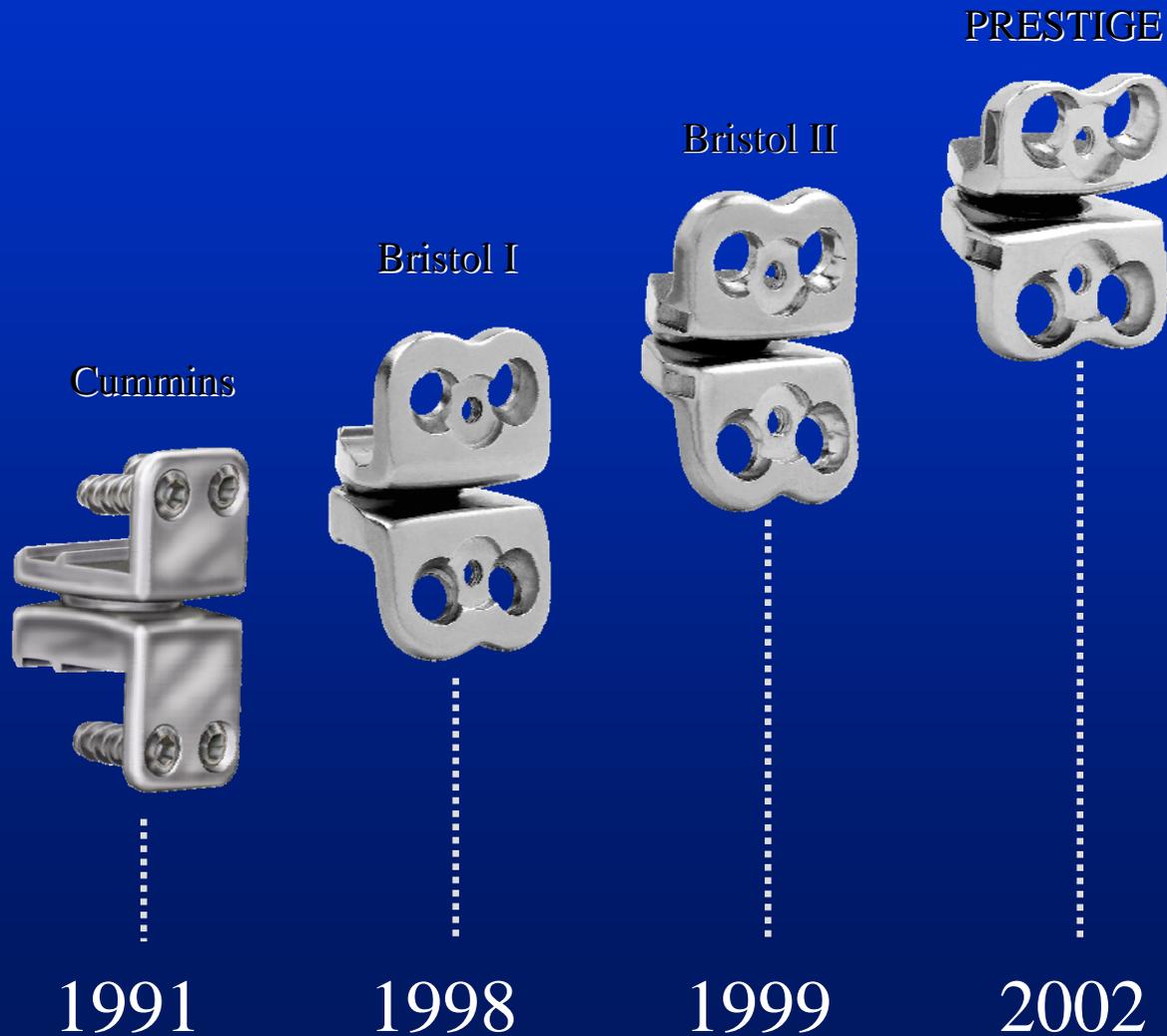




Stainless Steel Spinal Implants



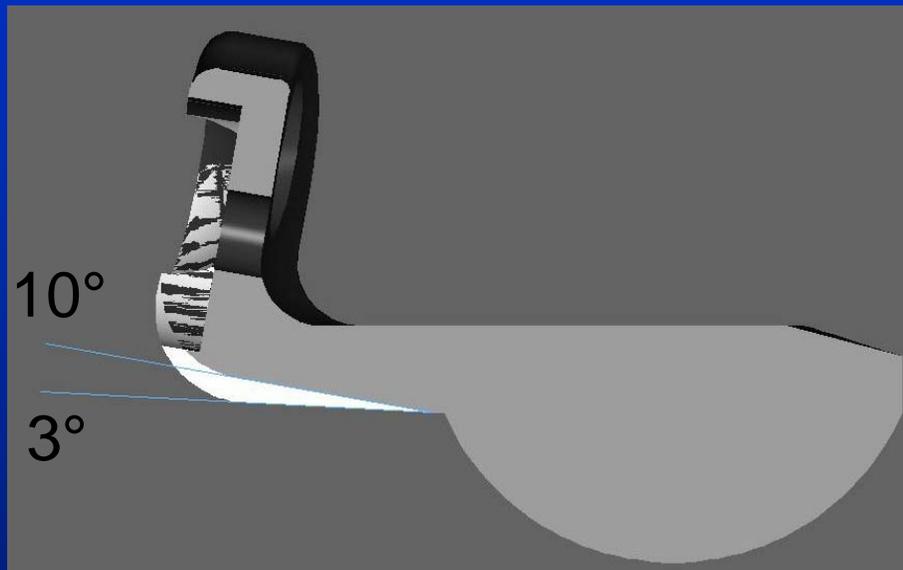
PRESTIGE[®] Cervical Disc Clinical Experience with S.S.



PRESTIGE® Cervical Disc Sizing

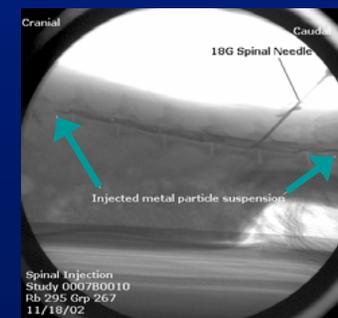
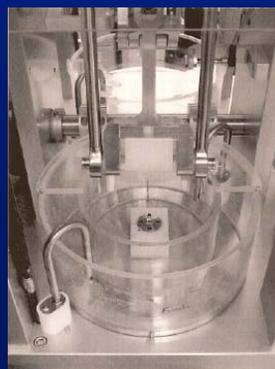
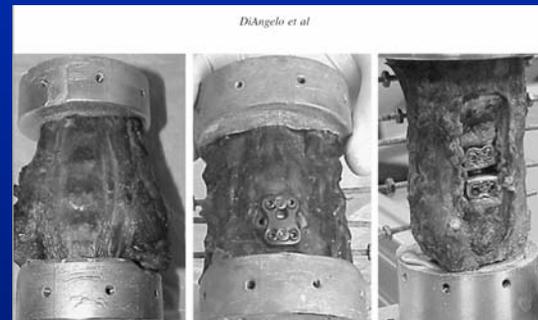
 Height Depth	6	7	8
12	X	X	
14	X	X	X
16	X	X	X
18		X	X

Maximum Flexion Angle

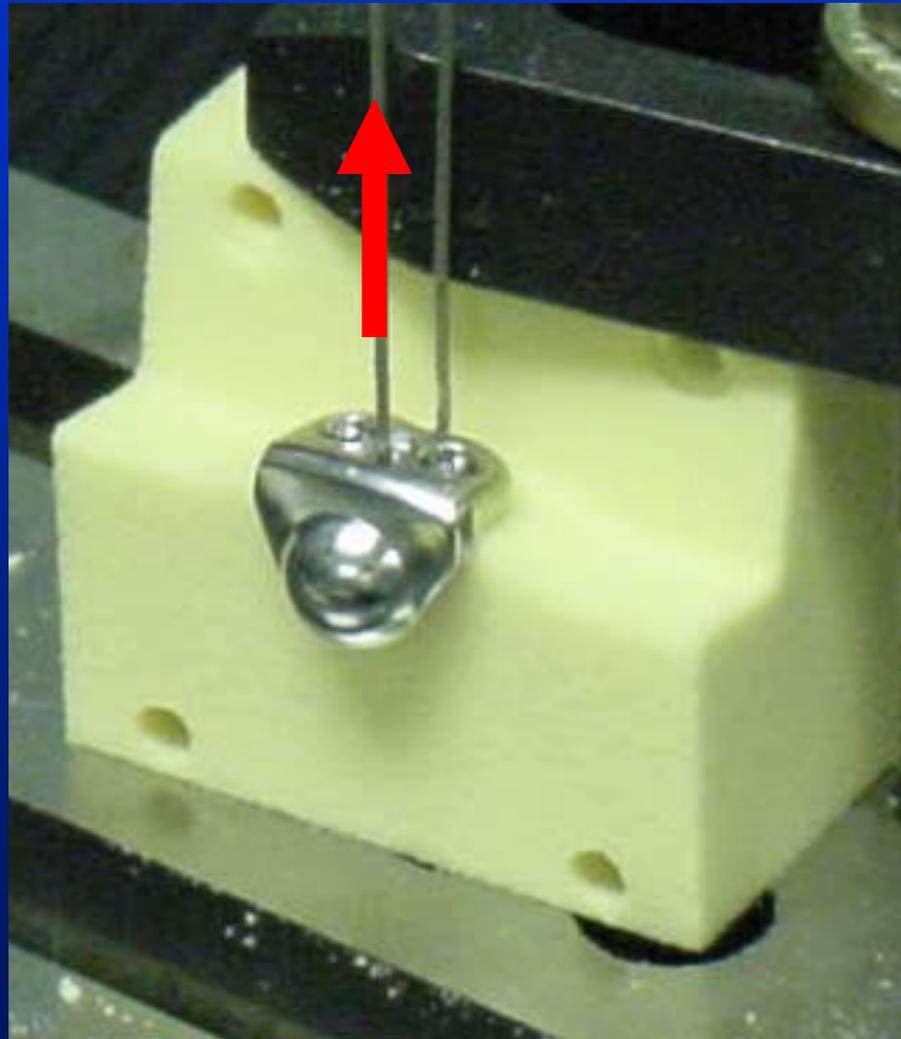


PRESTIGE[®] Testing Summary

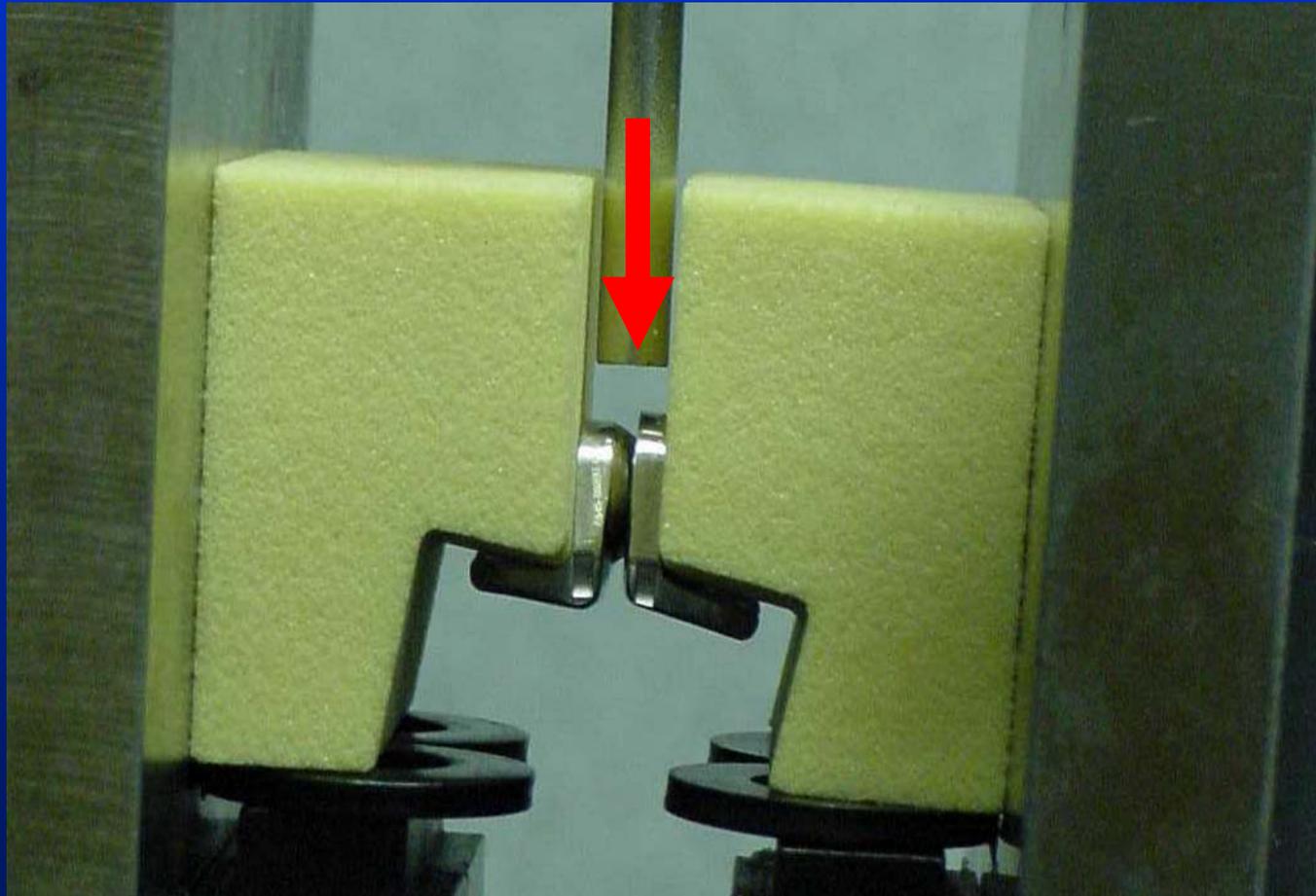
- Mechanical
 - Static
 - Dynamic
- Biomechanical
 - Cadaver
- Wear
- Animal



Pull Out (w/ Screws)

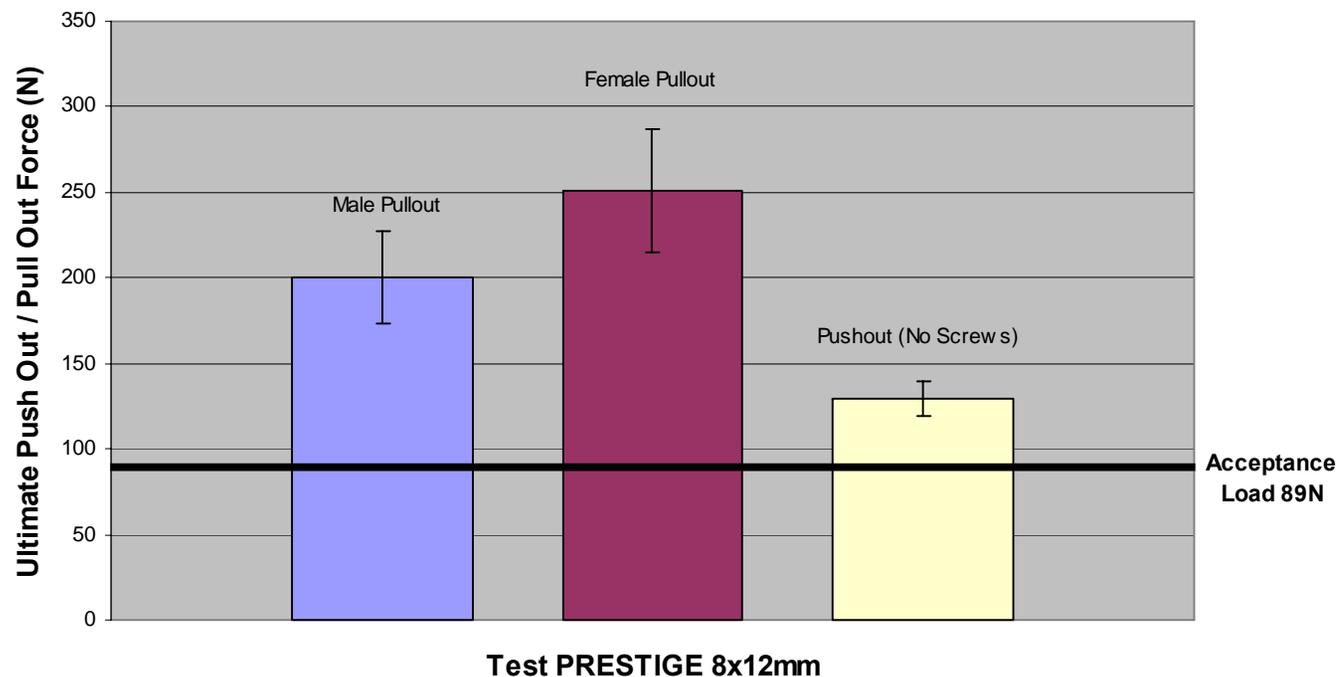


Push Out w/o Screws

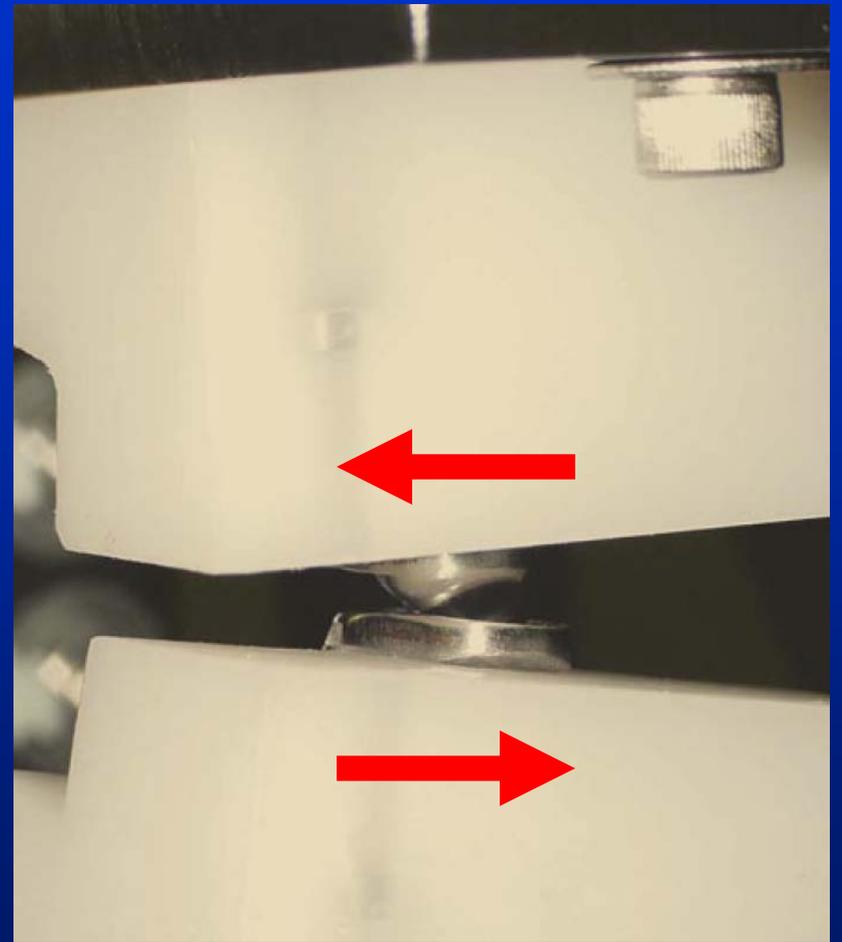
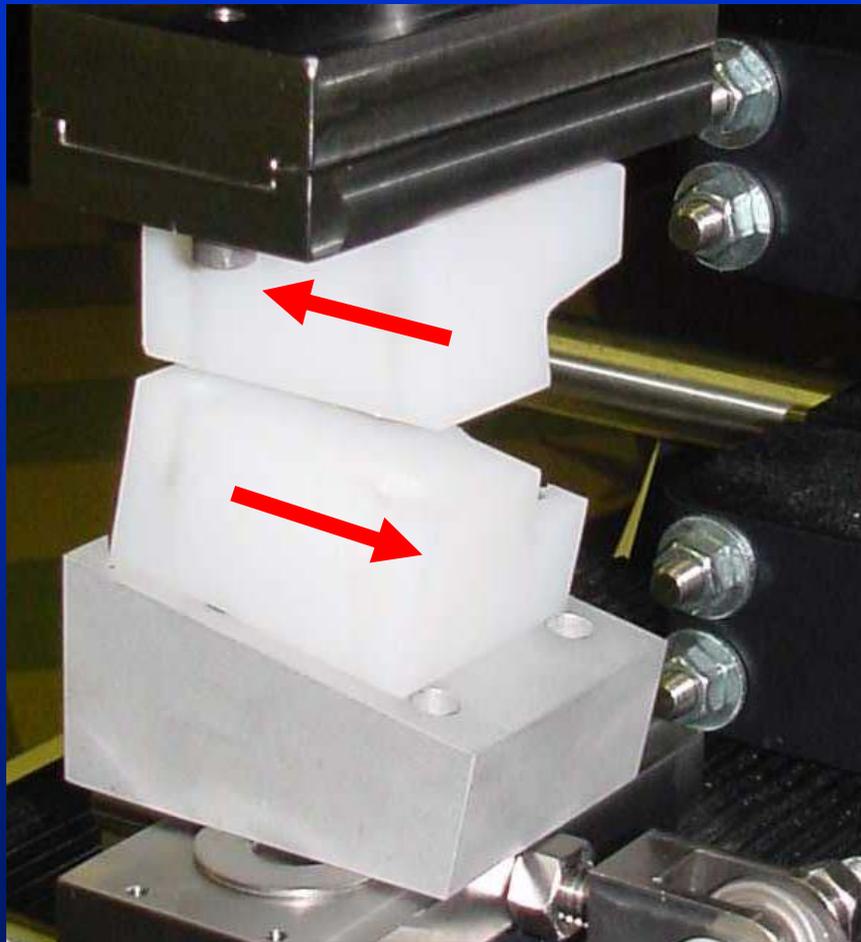


Push Out and Pull Out Testing Results

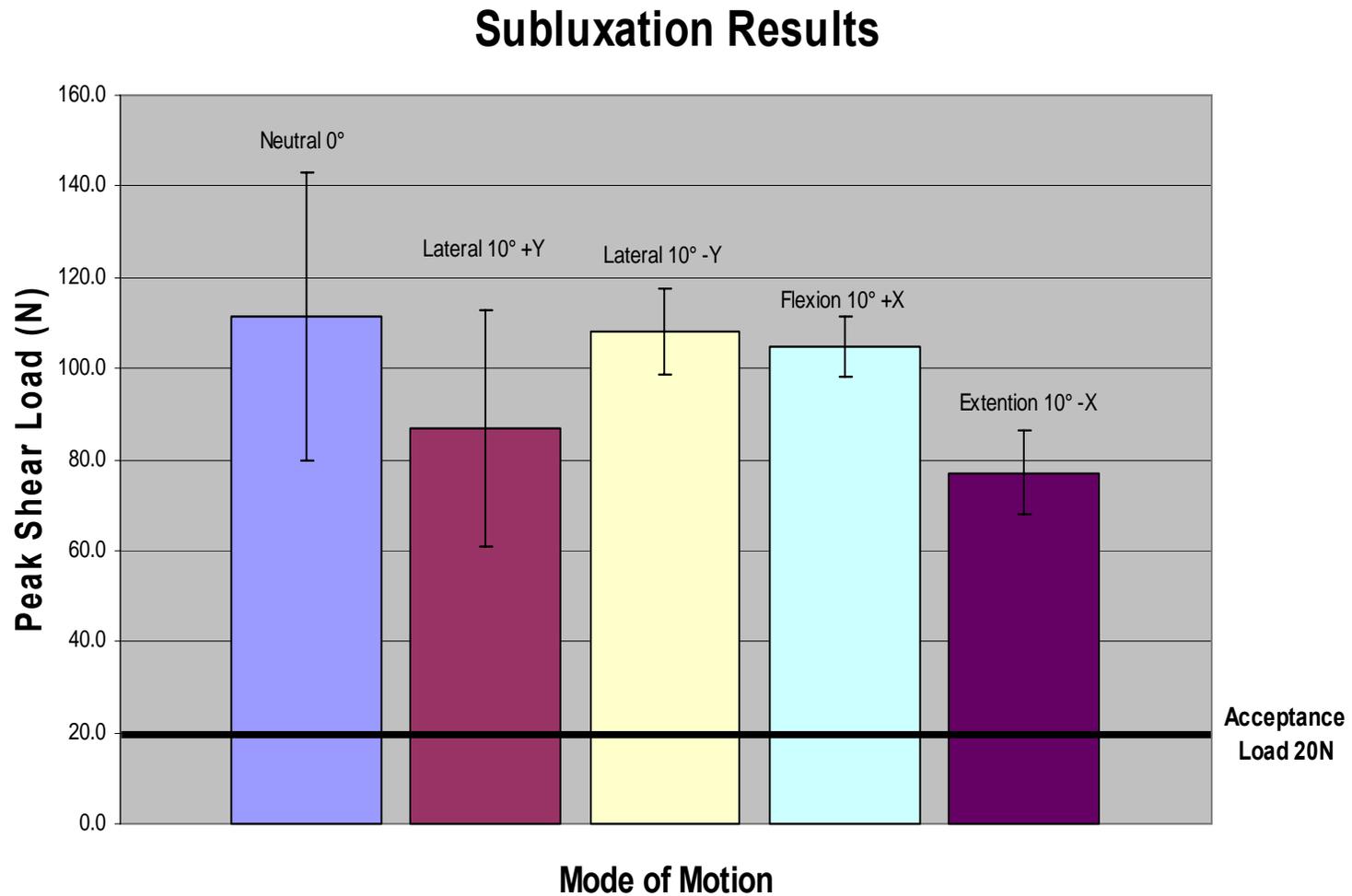
Axial Push Out and Pull Out Testing



Subluxation Testing



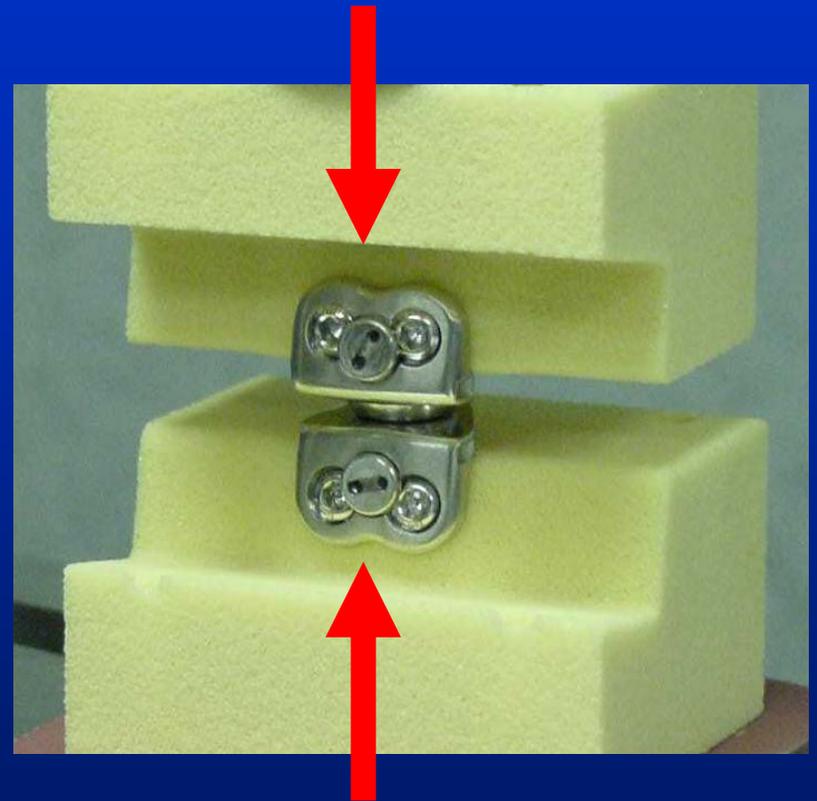
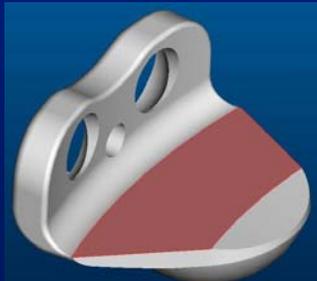
Subluxation Results



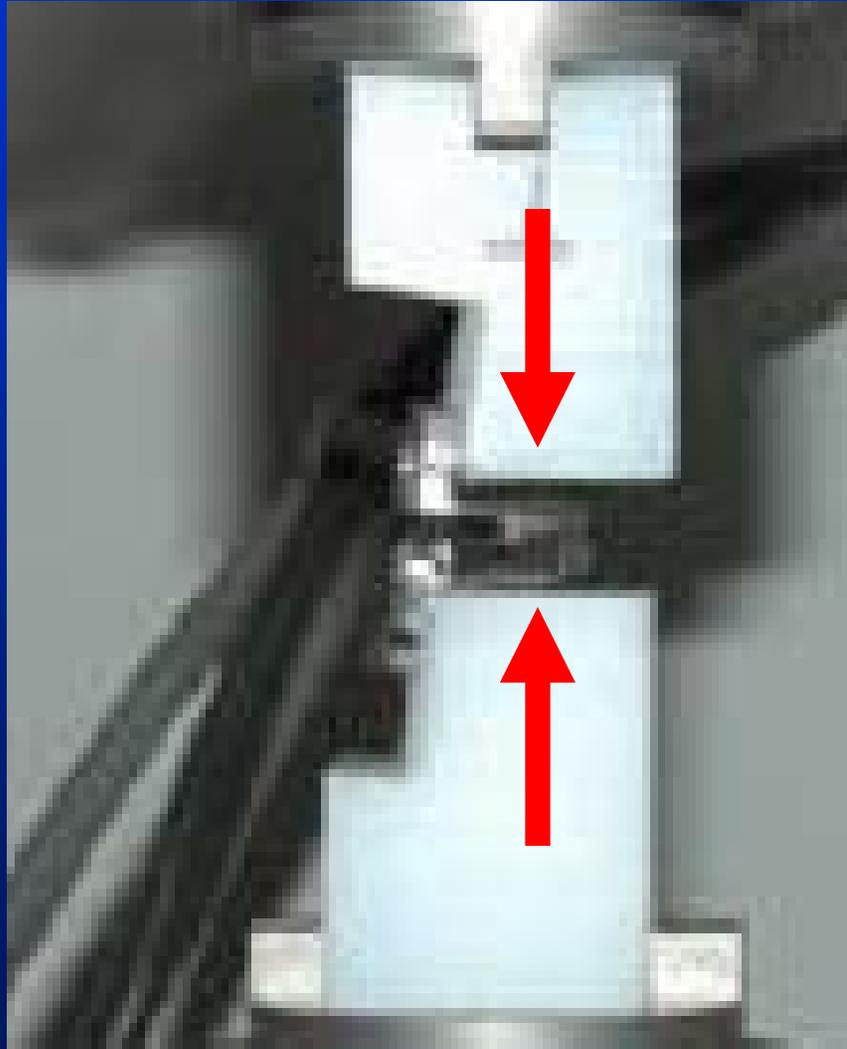
Subsidence Testing

- Results
 - 718N±62 (ultimate strength)
 - 550N±20 (yield strength)
- Design
 - 12mm footprint

PRESTIGE Area	Cornerstone Area
109mm ²	61mm ²

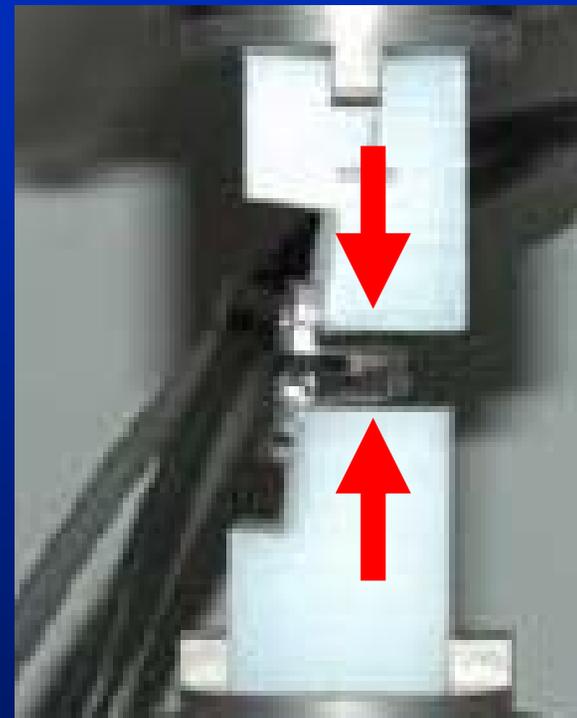


Compression Testing



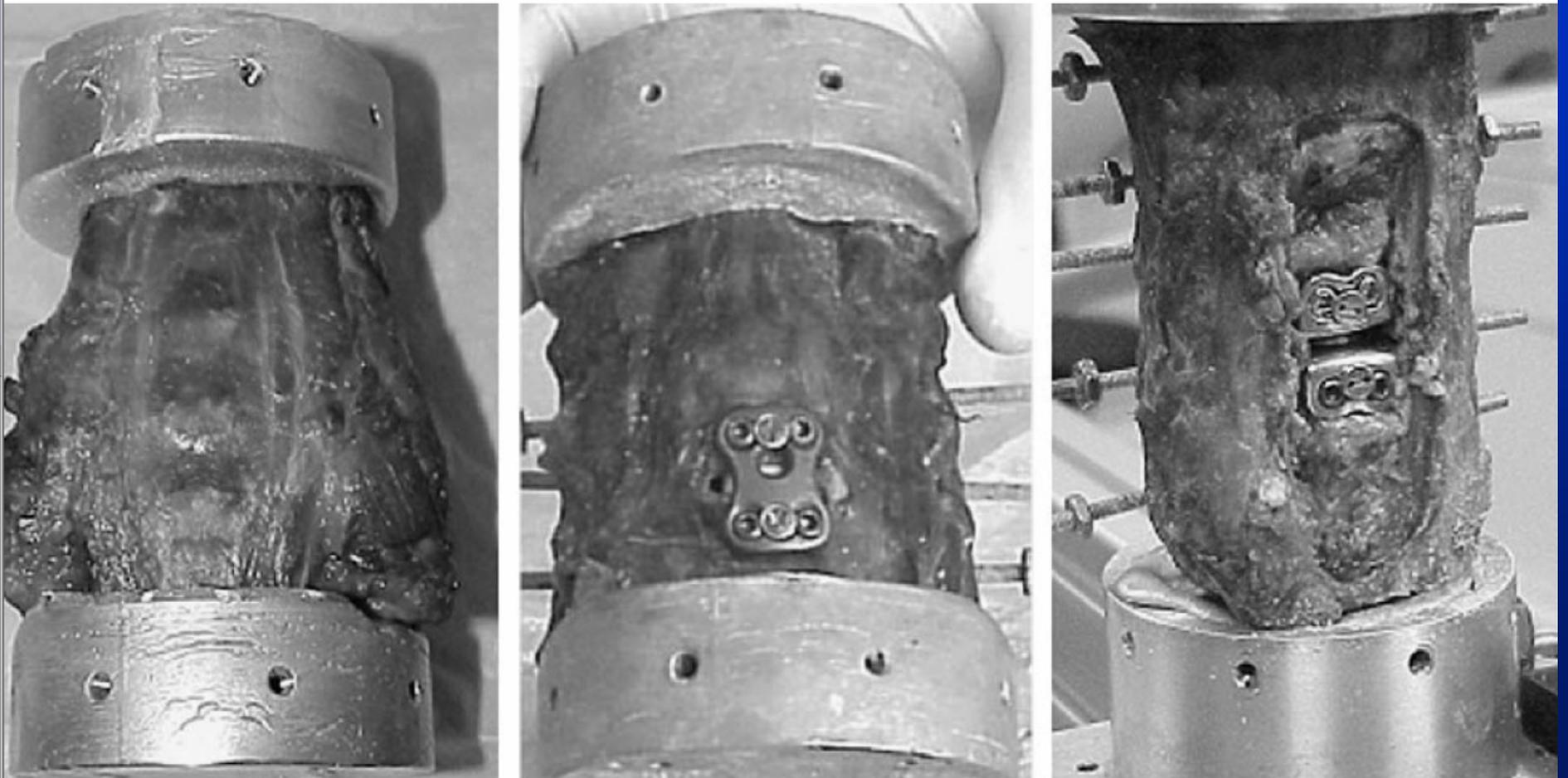
Compressive Fatigue Testing

- Acceptance Criteria $> 225\text{N}$ to 10 Mc
- Results
 - Met runout
- Design
 - $6 \times 16\text{mm}$
- Parameters
 - UHMWPE
block w/ 1mm gap



Cadaver Testing

DiAngelo et al



Biomechanical Testing of an Artificial Cervical Joint and an Anterior Cervical Plate

Denis J. DiAngelo, *James T. Roberston, †Newton H. Metcalf, Bobby J. McVay, and R. Champ Davis

*School of Biomedical Engineering and *Department of Neurosurgery, University of Tennessee Health Science Center, and †Medtronic Sofamor Danek, Memphis, Tennessee*

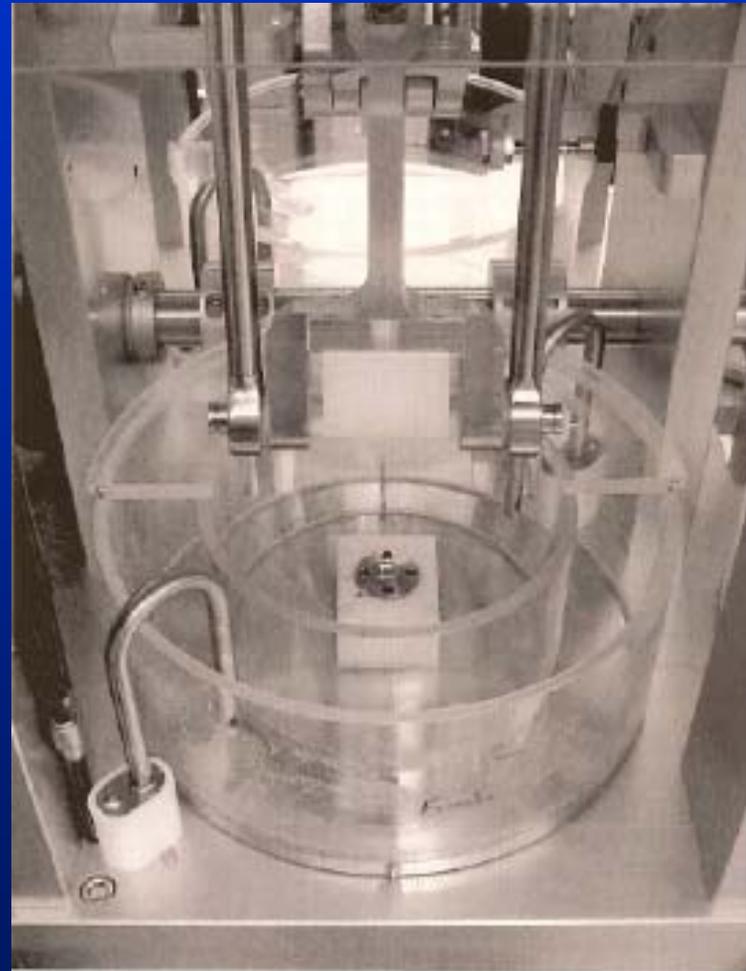
Summary: An in vitro biomechanical study was conducted to determine the effects of fusion and nonfusion anterior cervical instrumentation on cervical spine biomechanics in a multilevel human cadaveric model. Three spine conditions were studied: harvested, single-level artificial cervical joint, and single-level graft with anterior cervical plate. A

“did not alter the motion patterns at either the instrumented level or the adjacent segments compared with the harvested condition for all modes of testing.”

artificial joint spine conditions. The reduced motion was compensated for by an increase in motion at the adjacent segments. Use of an artificial cervical joint did not alter the motion patterns at either the instrumented level or the adjacent segments compared with the harvested condition for all modes of testing. **Key Words:** biomechanical testing, artificial cervical joint, anterior cervical plating, cervical spine, biomechanics

Wear Testing

- Volumetric Wear
 - F/E > LB/AR
 - $3.855 \pm 1.272 \text{ mm}^3$
 - LB/AR > F/E
 - $3.699 \pm 1.298 \text{ mm}^3$
- Parameters
 - 5 Mc LB/AR
 - 10 Mc F/E



Active Range of Motion Utilized in the Cervical Spine to Perform Daily Functional Tasks

*Susan E. Bennett, †Ronald J. Schenk, and ‡Edward D. Simmons

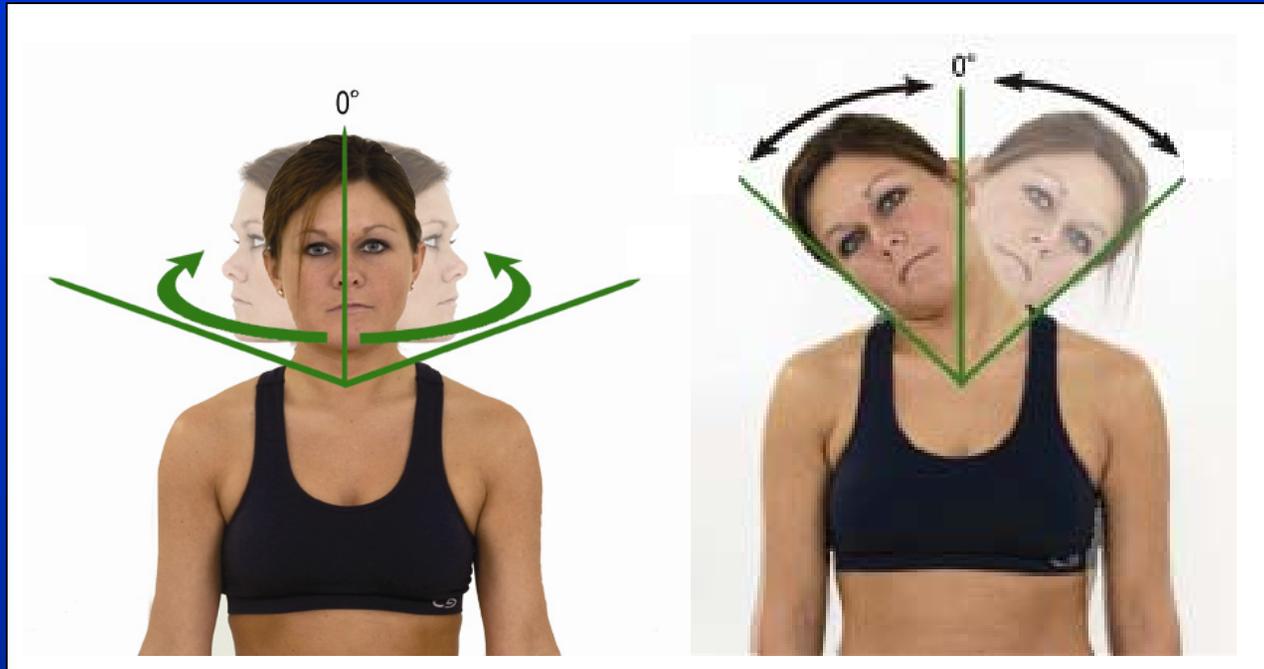
*Department of *Physical Therapy, and ‡Orthopaedic Surgery, State University of New York at Buffalo, and †D'Youville College, Buffalo, New York, U.S.A.*

Summary: This was a descriptive study to examine active range of motion required in the cervical spine during functional tasks of daily living. The objective of this study was to determine the mean active range of motion of the cervical spine required to perform 13 daily functional tasks. Previous research has examined the absolute ranges of cervical motion for women and men 20–60 years of age; however, no previous study has determined the amount and type of motion that is required for routine activities of daily living.

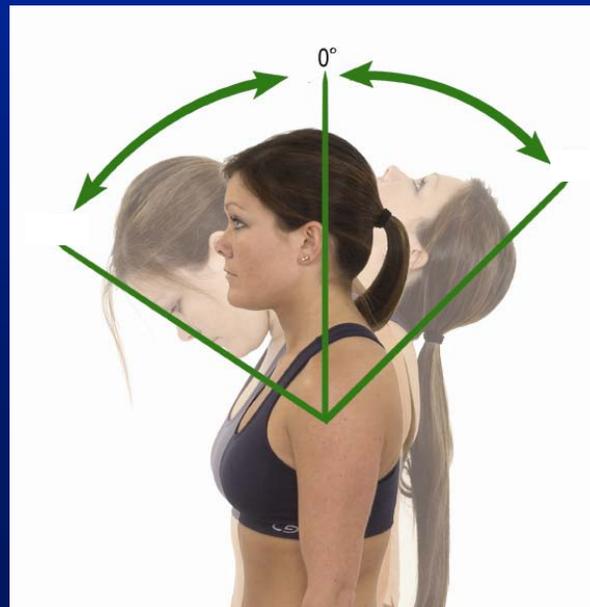
“...Tying shoes (flexion-extension 66.7°)...and crossing the street (rotation head left 31.7° and rotation head right 54.3°) requires the greatest full active range of motion of the cervical spine.”

cervical spine are important to enable functional activity. Four of the 13 daily tasks performed required 30–50% of active range of motion. Side bending was seen to be coupled with rotation in completion of tasks. This article provides a baseline of normal motion of the neck required for activities of daily living and can be used in the assessment of disease states and disability. **Key Words:** Cervical spine—Motion—Function.

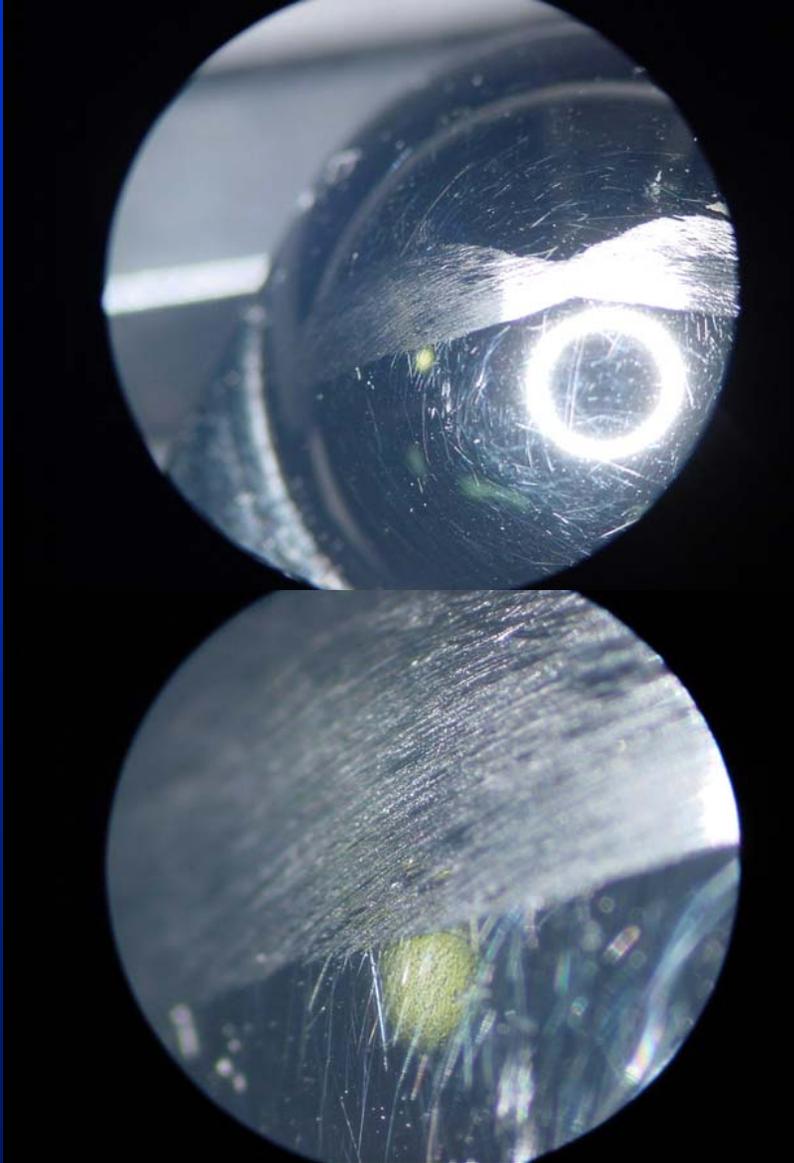
Coupled Axial Rotation with Lateral Bending



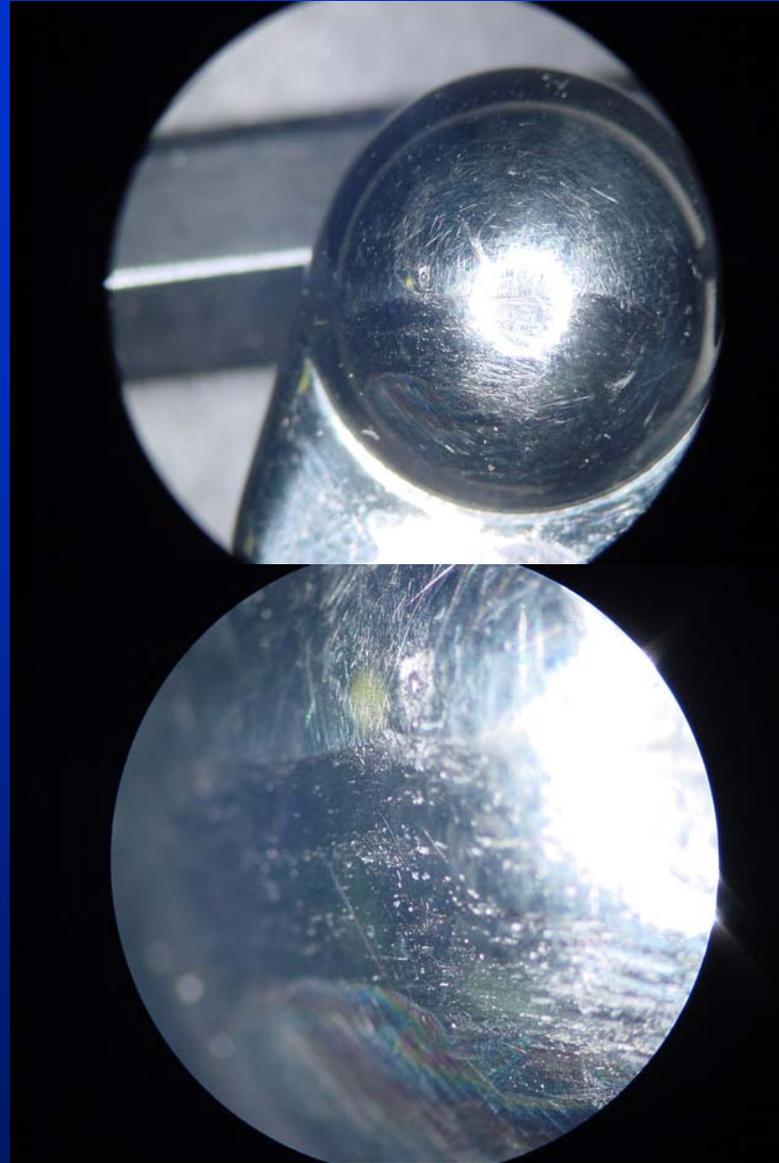
Flexion / Extension



Wear Comparisons



311,000 cycle in-vitro

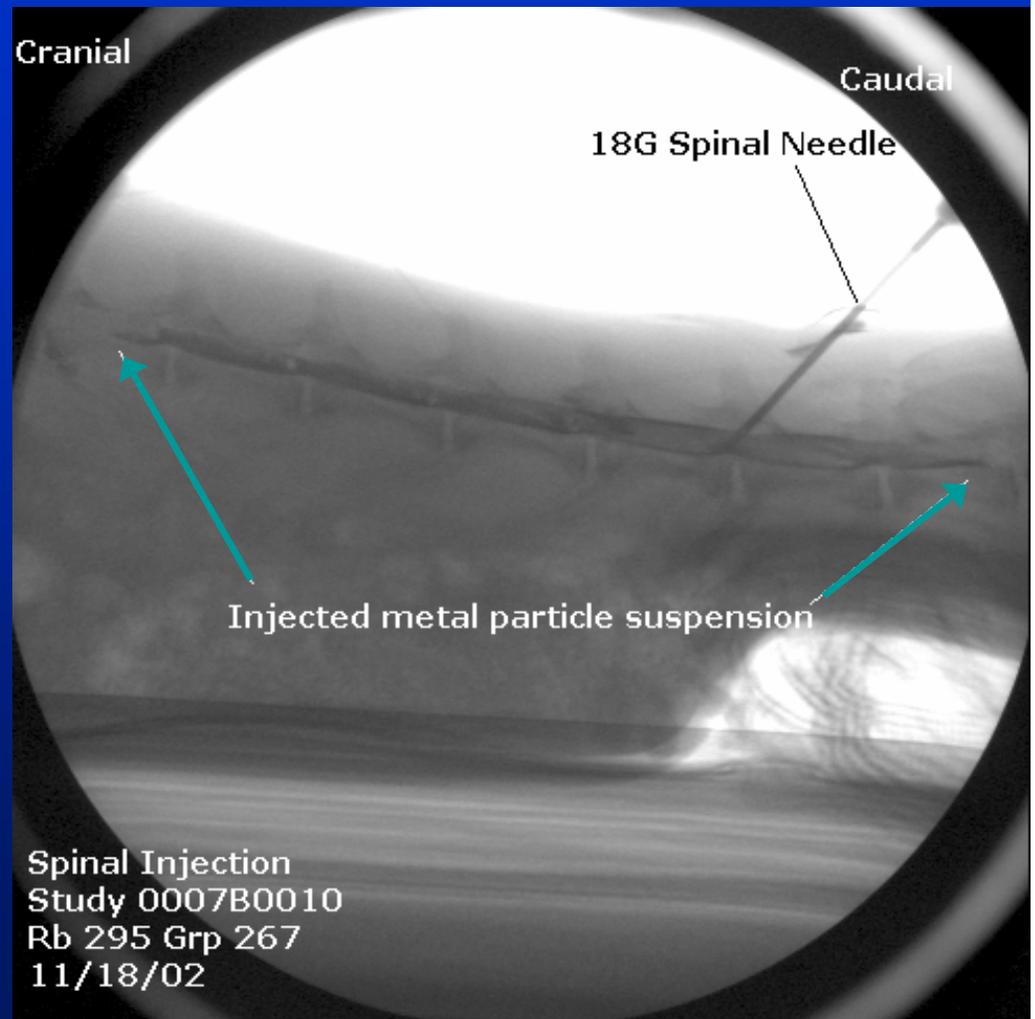


3.25 years in-vivo

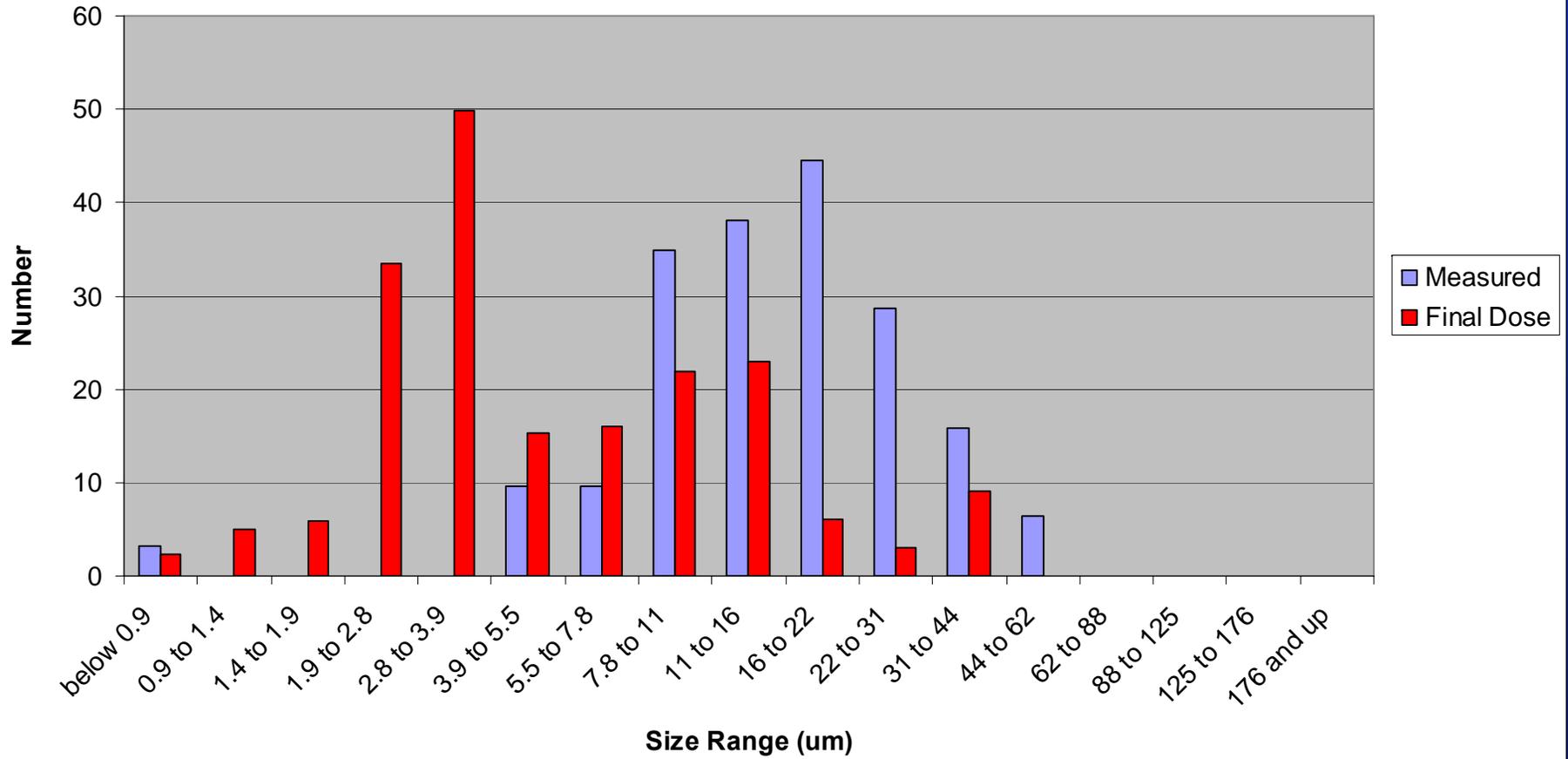
Biocompatibility

Rabbit study

- Bolus Injection (20 & 60 million cycles)
- Sacrifice at 3 & 6 months
- No dose related changes observed
- ISO10993



Particle Histogram



Testing Summary

- Mechanical (Benchtop)
 - Static
 - Dynamic
- Cadaver
- Wear
- Animal

**PRESTIGE® Cervical Disc
IDE Clinical Results
G010188**

**J. Kenneth Burkus, M.D.
Columbus, Georgia**

Important Findings

- Primary study objective met
- Statistical superiority was shown for the primary outcome variable
- Vertebral motion was maintained

Clinical Trial Results

Clinical Trial Design

- Prospective, randomized controlled design
- Investigational Treatment - PRESTIGE[®] Cervical Disc
- Control Treatment - Plated fusion with structural allograft interbody spacer

Study Objectives

- Primary Objective
Non-inferiority in Overall Success
- Secondary Objectives

Study Entrance Criteria

Inclusion

- Single level cervical degenerative disc
- C3-C4 to C6-C7
- No prior surgery at treated level
- ≥ 18 years of age
- NDI ≥ 30
- Neck pain ≥ 20
- Not pregnant
- Willing to comply with protocol

Exclusion

- Other disease at treated level
- Instability
 - translation $> 3.5\text{mm}$
 - angulation $> 20^\circ$
- Severe pathology of facet joints
- Osteopenia, osteomalacia, osteoporosis
- Spinal metastases
- Infection
- Diabetes
- Metal allergy to stainless steel or titanium

Patient Evaluation

- Preoperatively
- Surgery/Discharge
- Postoperatively:
 - 6 Weeks, 3 Months, 6 Months,
 - 12 Months, 24 Months

Patient Population

- Patients
 - 276 received PRESTIGE[®] device
 - 265 received fusion
- 32 Investigational Centers

Demographic Information

	PRESTIGE®	Fusion
Age (yrs.)	43	44
Weight (lbs.)	182	185
Height (in.)	67	68
Sex (% male)	46	46
Worker's Compensation (%)	12	13
Spinal Litigation (%)	11	12

Surgery Data

	PRESTIGE[®]	Fusion
Operative Time (hrs.)	1.6	1.4
Blood Loss (ml)	60	58
Hospital Stay (days)	1.1	1.0

Study Results Based
on 24-Month Data

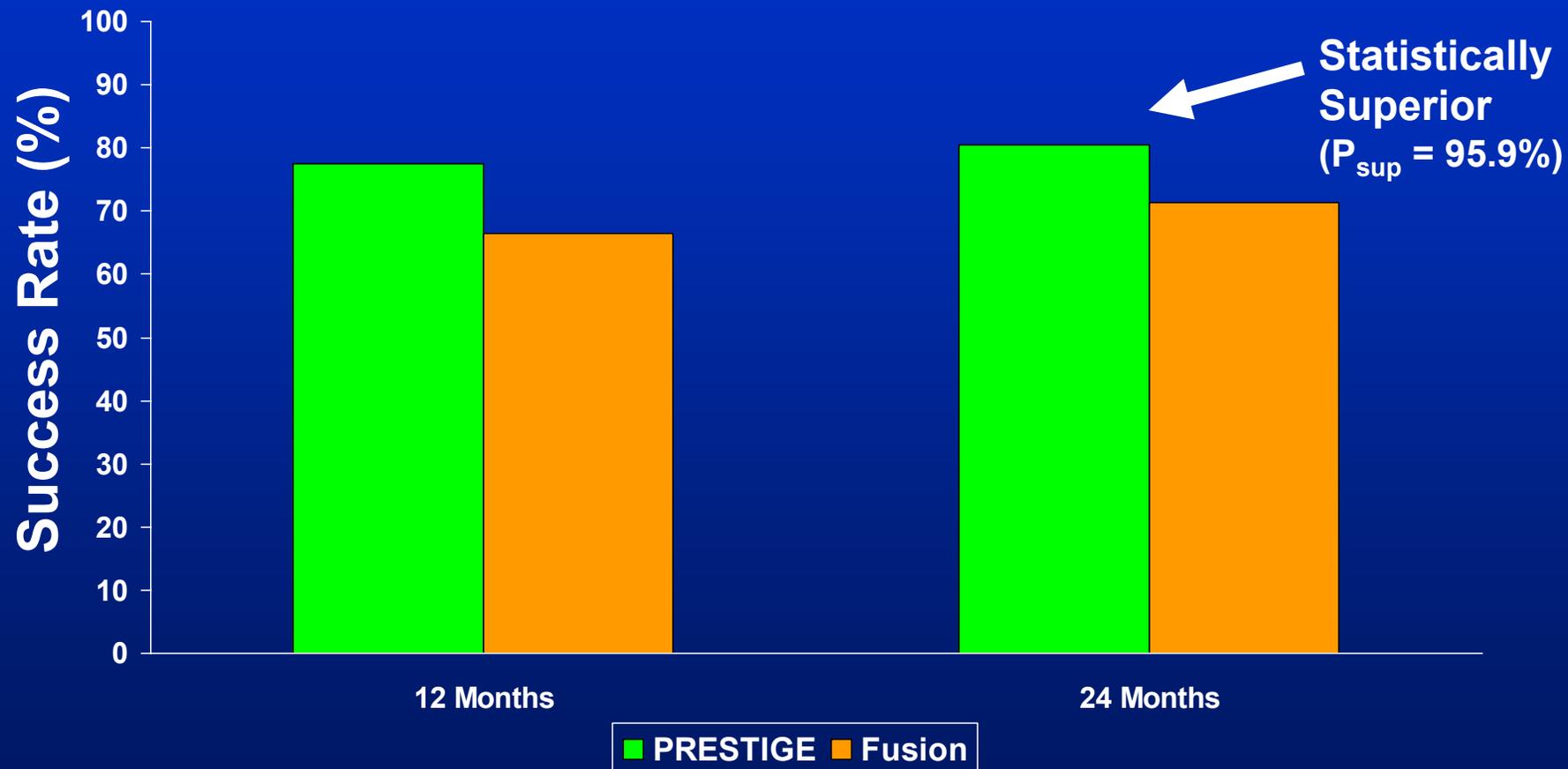
Interim Analysis

(All available data also analyzed)

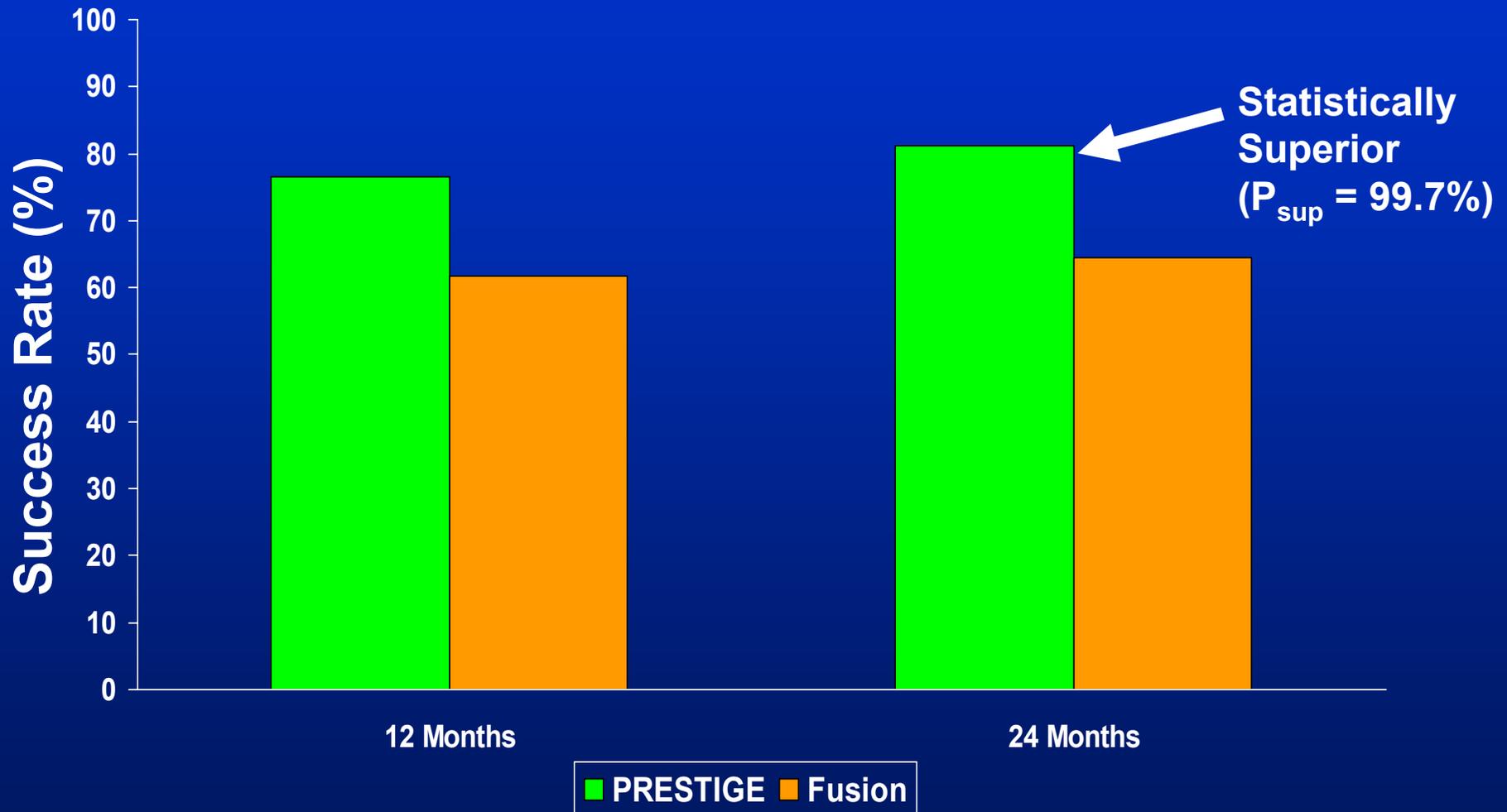
Overall Success

- ≥ 15 point improvement in NDI score
- Neurological maintenance or improvement
- No serious adverse event possibly associated to the device
- No second surgery failure
- Functional spinal unit height success

Overall Success



Overall Success (with Functional Spinal Unit Height)



Met and Surpassed
Primary Objective

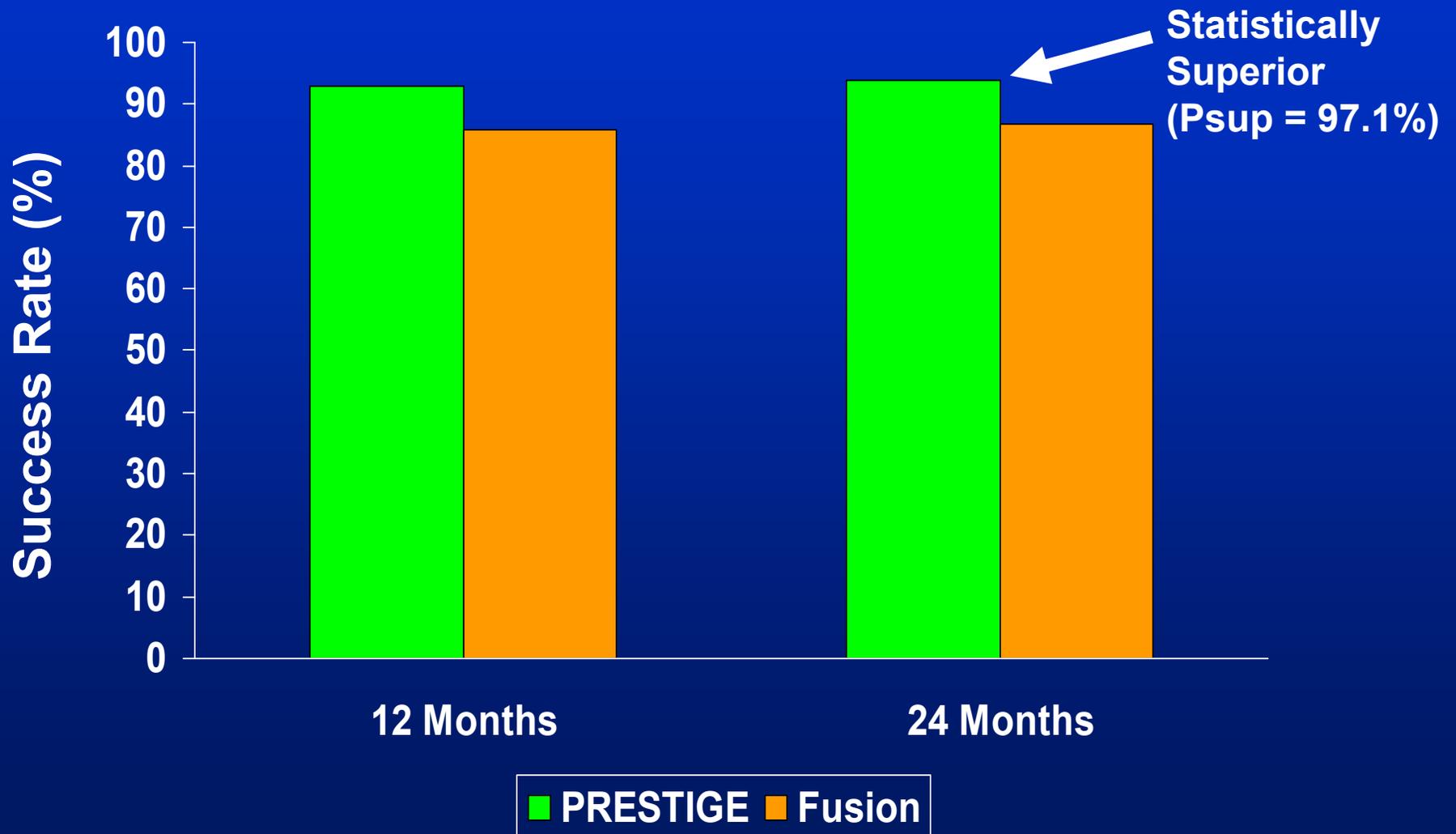
Safety Overview

- Neurological status
- Adverse events
- Second surgery procedures

Neurological Status Measurements

- Motor Function
- Sensory
- Reflexes

Neurological Success Rates



Adverse Events

Adverse Events

	PRESTIGE[®]	Fusion
At least 1 event (%)	81.9	80.0
WHO - 3 or 4 (%)	27.9	29.8
Possibly Related to Device (%)	3.3	9.8

Comparison of Adverse Events
in PRESTIGE[®] Device and Fusion
Treatment Groups

Differences Noted In

- Lower in PRESTIGE[®] device group
 - Non-unions
 - Pending non-unions
 - Spinal events
- Lower in fusion group
 - Urogenital

Deaths

PRESTIGE[®] Cervical Disc	0 (0.0%)
Fusion	3 (1.1%)

Cancer

PRESTIGE[®] Cervical Disc

- Basal cell carcinoma
- Thyroid
- Colon
- Breast
- Non-Hodgkins
lymphoma

Fusion

- Squamous cell
- Brain tumor

Cancer (cont.)

- No statistical difference between treatment groups
- No statistical differences in a matched population from NCI database

Adverse Events

- Typical for patient population
- Not unanticipated

Second Surgery Procedures

Classifications

- Revisions – Adjust implant position
- Removals – Remove implant
(elective and non-elective)
- Supplemental Fixations – Provide additional stabilization
- Reoperations – Procedures at treated level that are not revisions, removals, or supplemental fixations
- Other – Procedures not at treated level

Second Surgery “Failures”

- Revisions - Failure
- Removals (non-elective) - Failure
- Supplemental Fixations - Failure

Second Surgeries

Number of Patients

	PRESTIGE®	Fusion	Statistically Superior
Revisions	0 (0.0)	5 (1.9)	√
Removals <i>Non-elective/elective</i>	5 (1.8) <i>5/0</i>	9 (3.4) <i>7/2</i>	
Supplemental Fixations	0 (0.0)	8 (3.0)	√
Reoperations	4 (1.4)	2 (0.8)	
Other	58 (21.0)	44 (16.6)	

Second Surgeries Adjacent Levels

	Patients	Procedures
PRESTIGE[®] Cervical Disc	3	3
Fusion	9	11

Safety Summary

- PRESTIGE[®] Cervical Disc patients as compared to fusion:
 - Statistically higher neurological success rate
 - Similar adverse event rate
 - Statistically lower revision and supplemental fixation rates. Lower removal rate. Fewer adjacent level procedures.

PRESTIGE[®] Cervical Disc

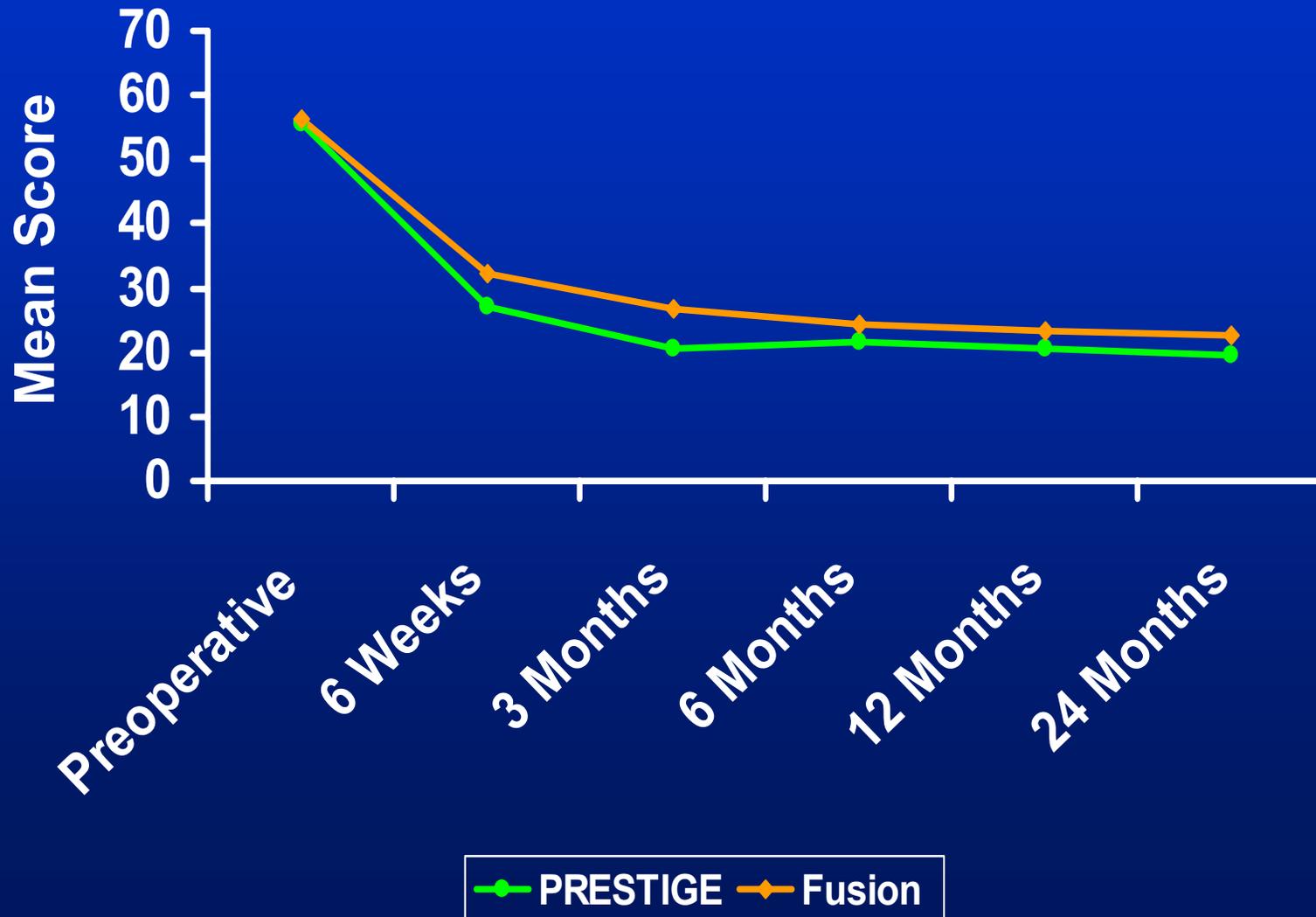
Safe for its intended use

Effectiveness Overview

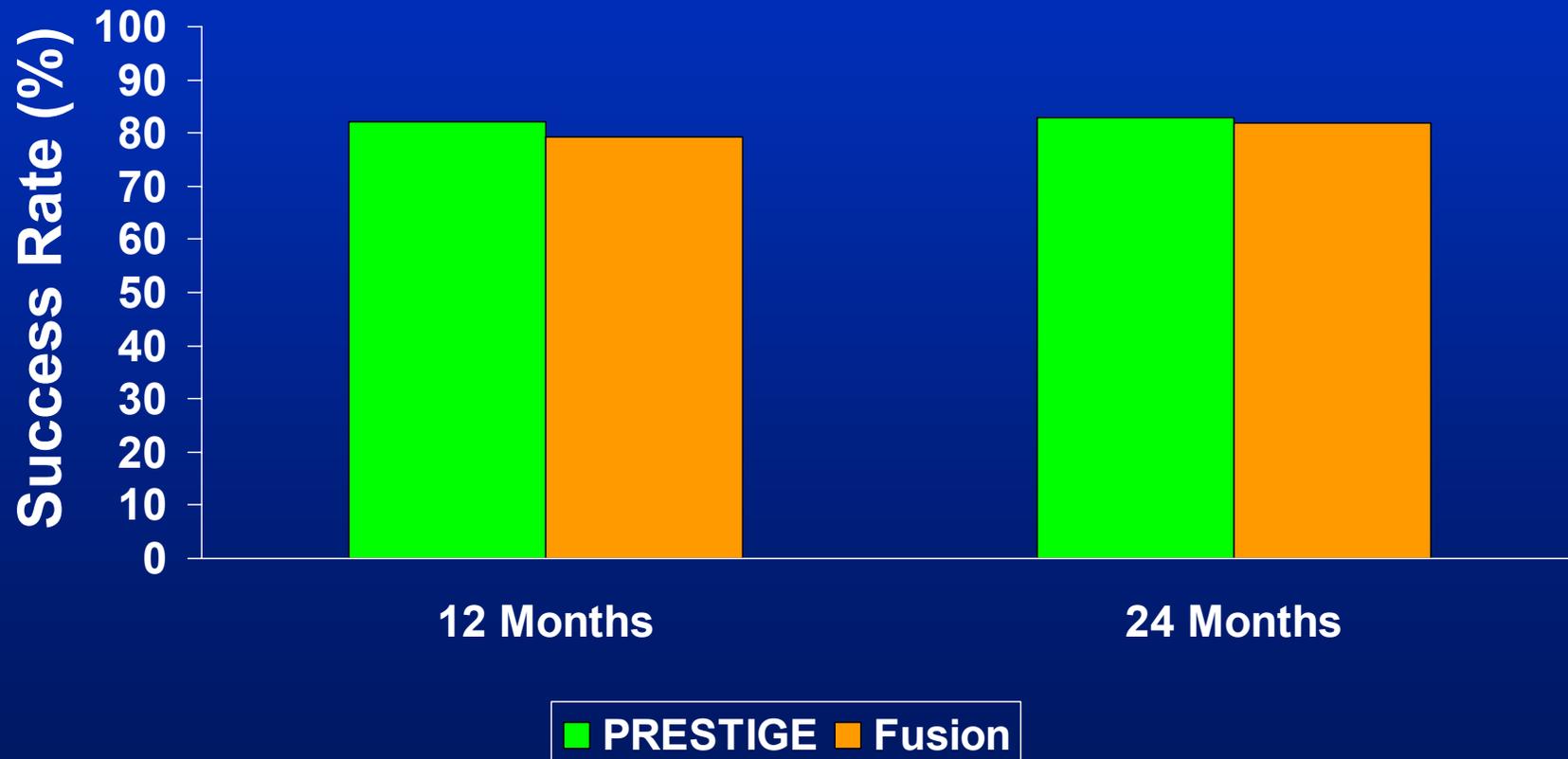
- PRESTIGE[®] Cervical Disc patients had:
 - Exceptional pain relief
 - Maintenance of motion

Neck Disability Index (NDI) Questionnaire

Mean Neck Disability Index Scores



Neck Disability Index Success 15 Point Improvement

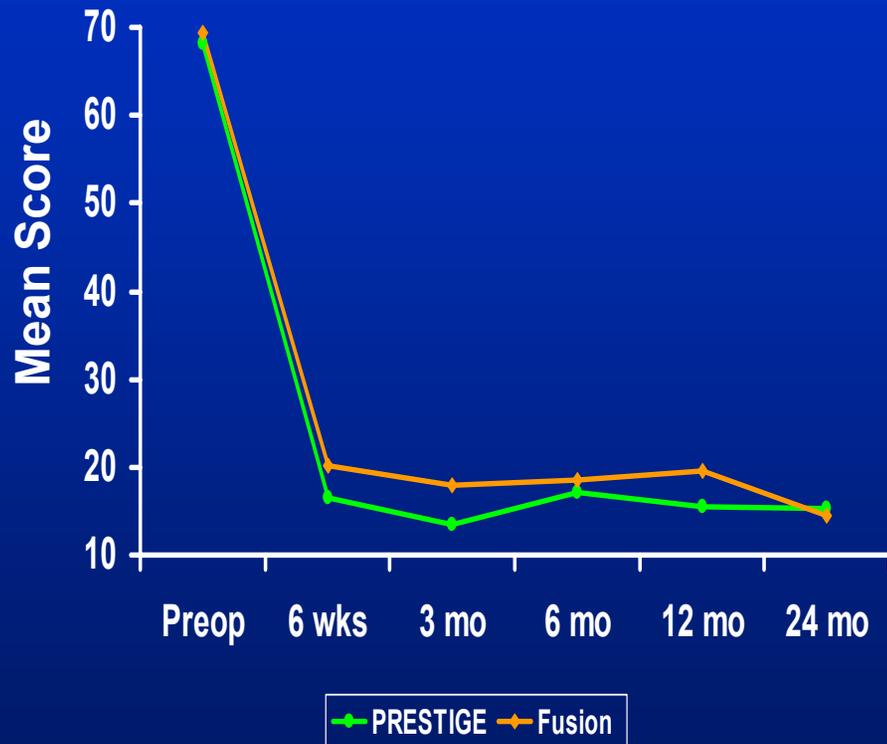


Secondary Effectiveness Endpoints

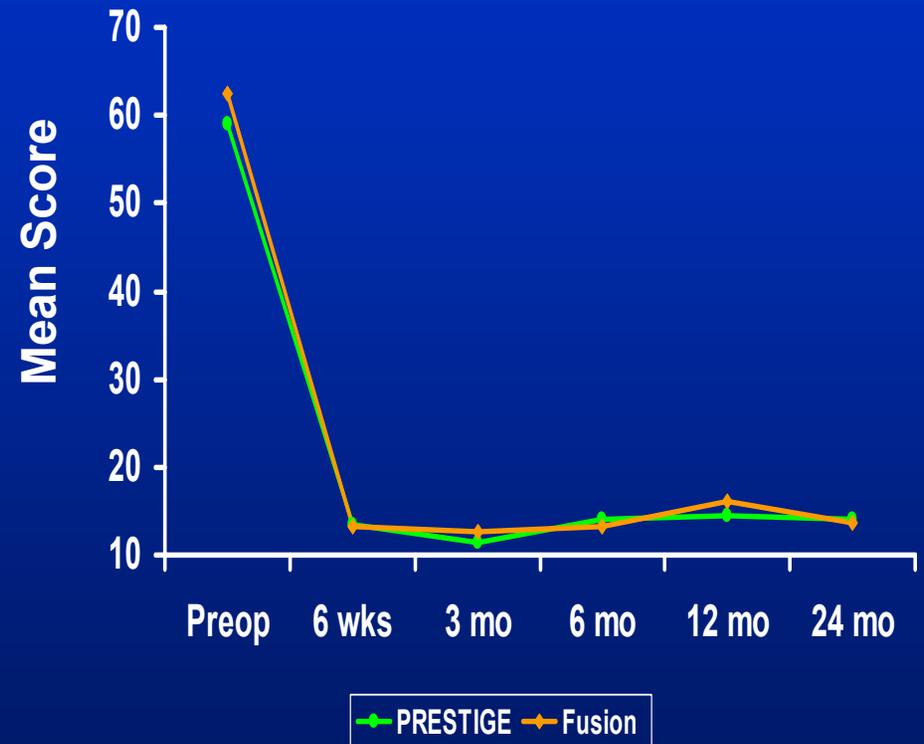
- Neck pain
- Arm pain
- Global perceived effect
- SF-36
- Gait analysis
- Foraminal compression

Mean Neck and Arm Pain Scores

Neck Pain



Arm Pain

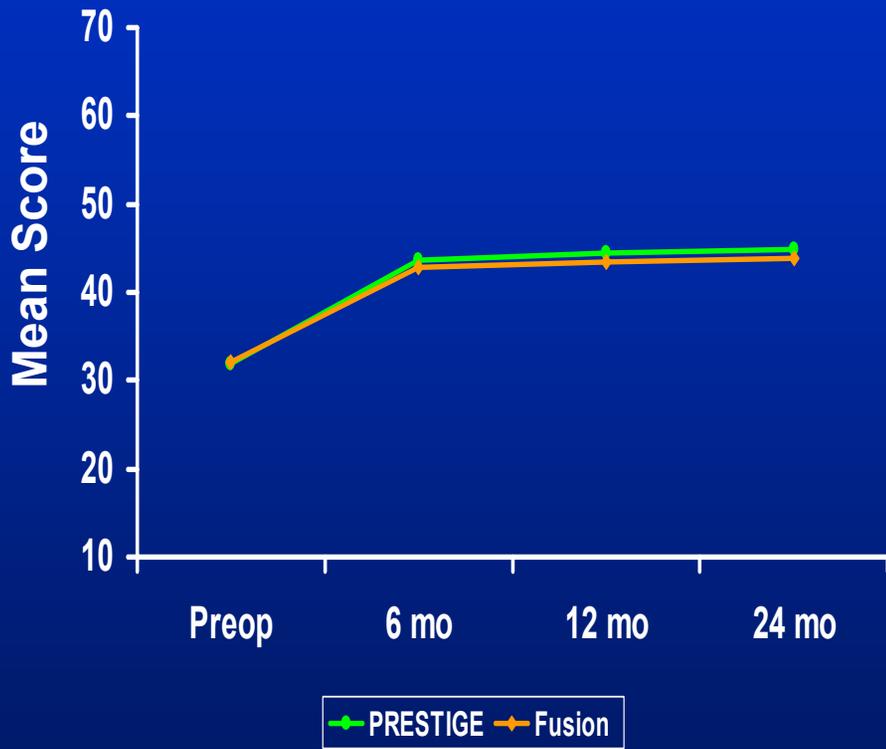


Global Perceived Effect Completely Recovered or Much Improved

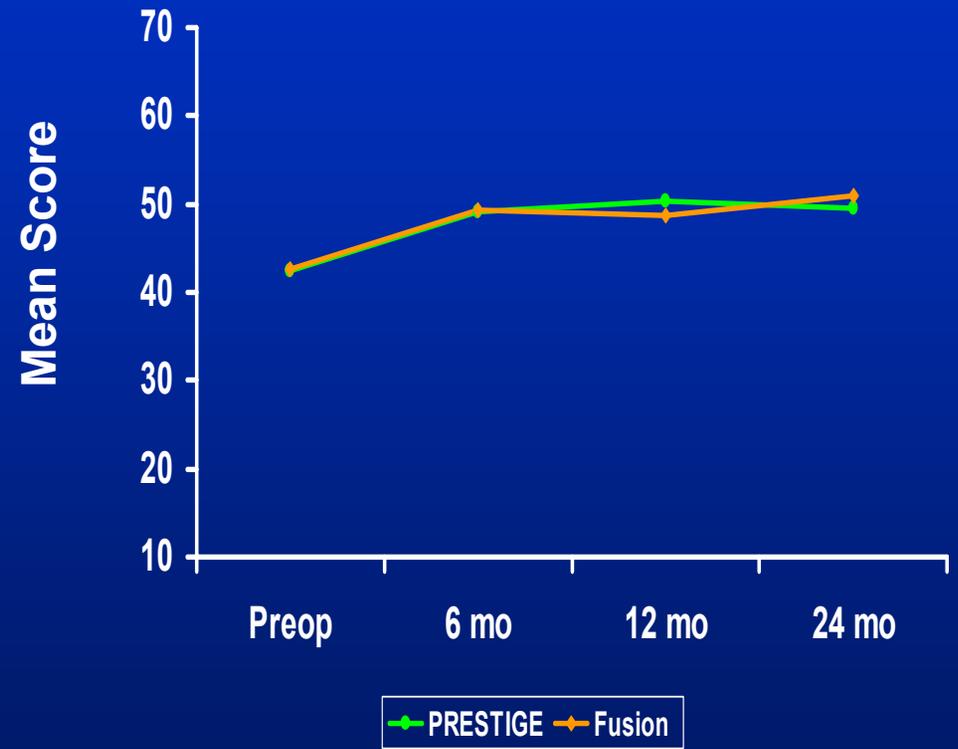


SF-36

PCS



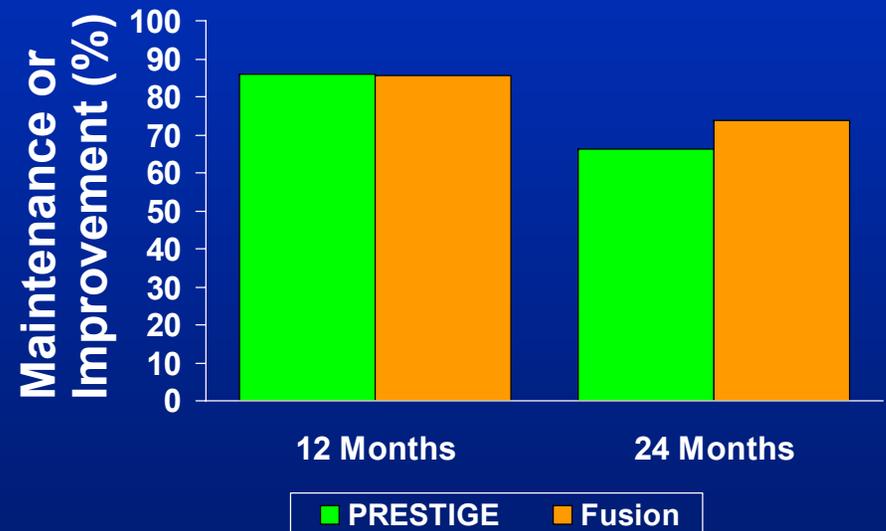
MCS



SF-36 Success

PCS

MCS



Gait Analysis

Foraminal Compression Test

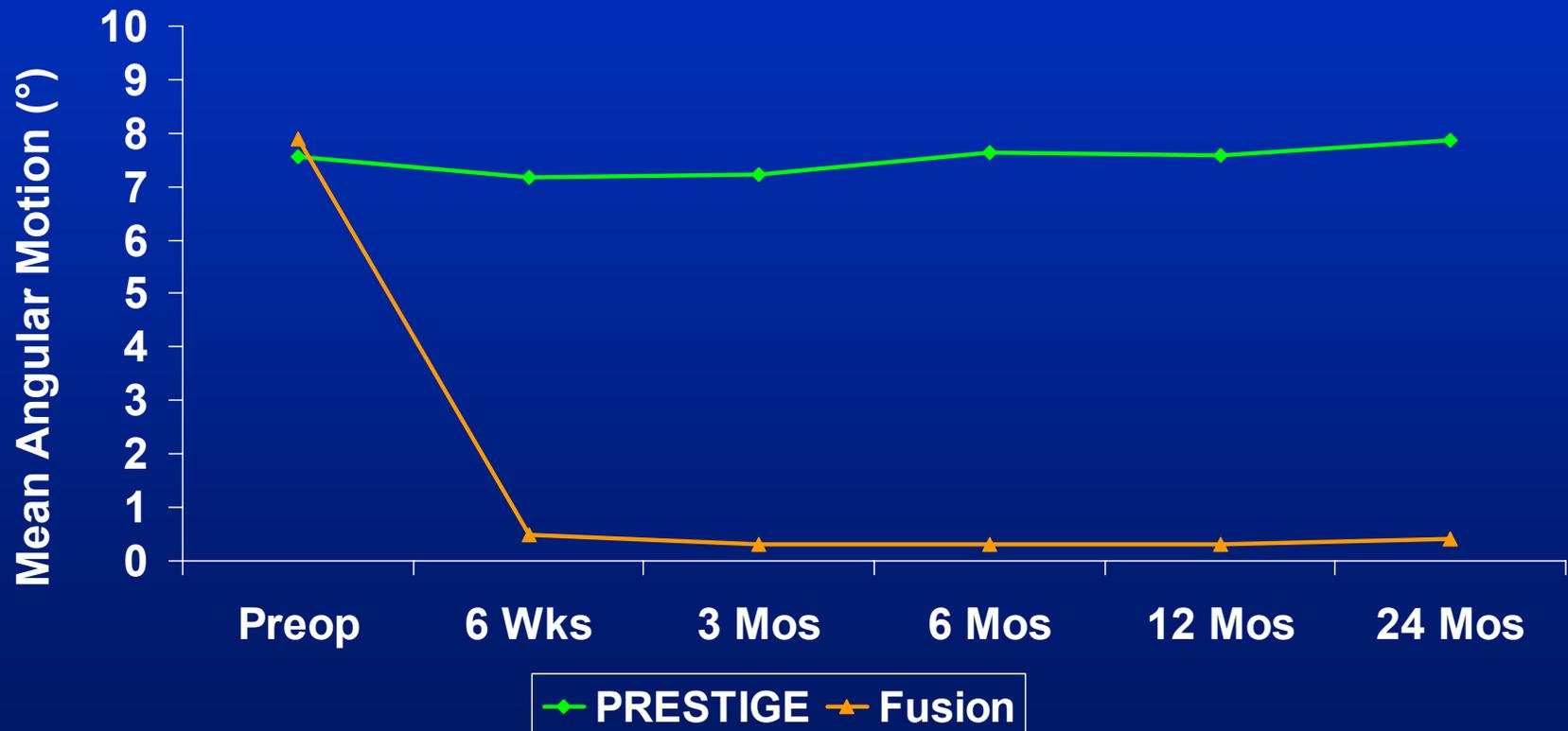
Radiographic Measurements



Functional Spinal Unit Height Success



Flexion / Extension Motion Measurements



Lateral Bending Measurements



Fusion Criteria

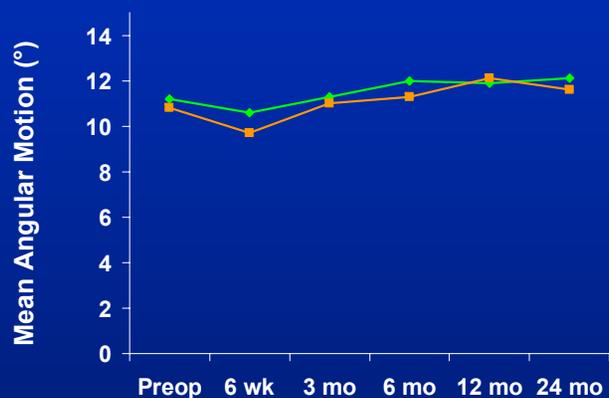
- Bridging bone
- Segmental stability
- Lucent line criteria

Fusion Success Rates

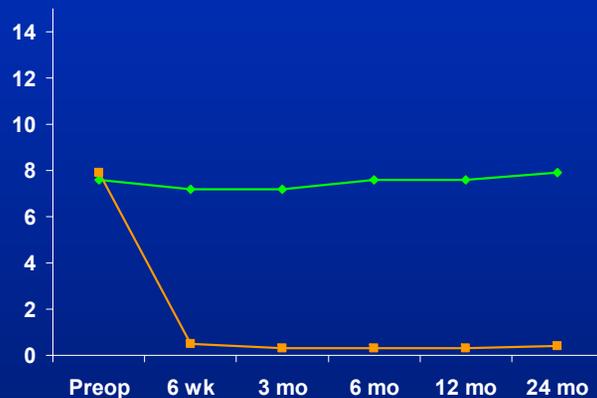


Adjacent Level Motion

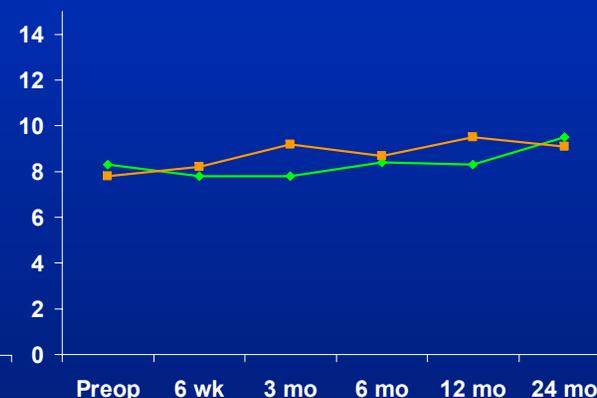
Level Above



Treated Level



Level Below



■ PRESTIGE ◆ Fusion

Patient Satisfaction – 24 Months

	PRESTIGE[®]	Fusion
Satisfied with results of surgery	89%	90%
Helped as much as they thought they would be	85%	85%
Would have the surgery again for same condition	87%	84%

Return to Work Median

PRESTIGE[®] Cervical Disc
Fusion

45 Days

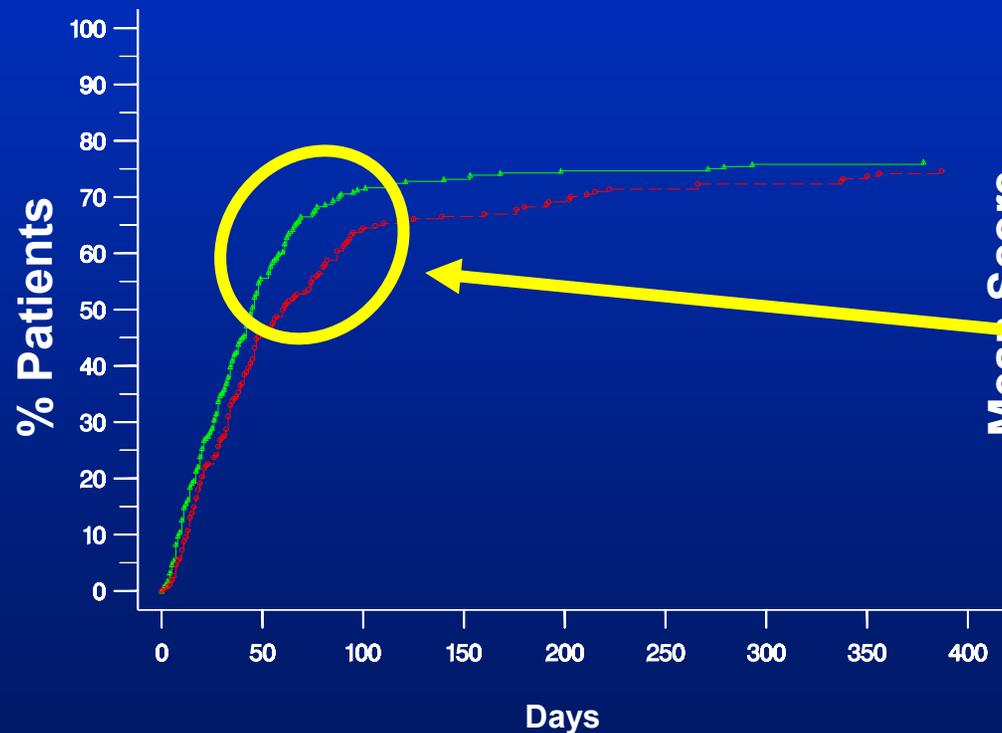
61 Days

16

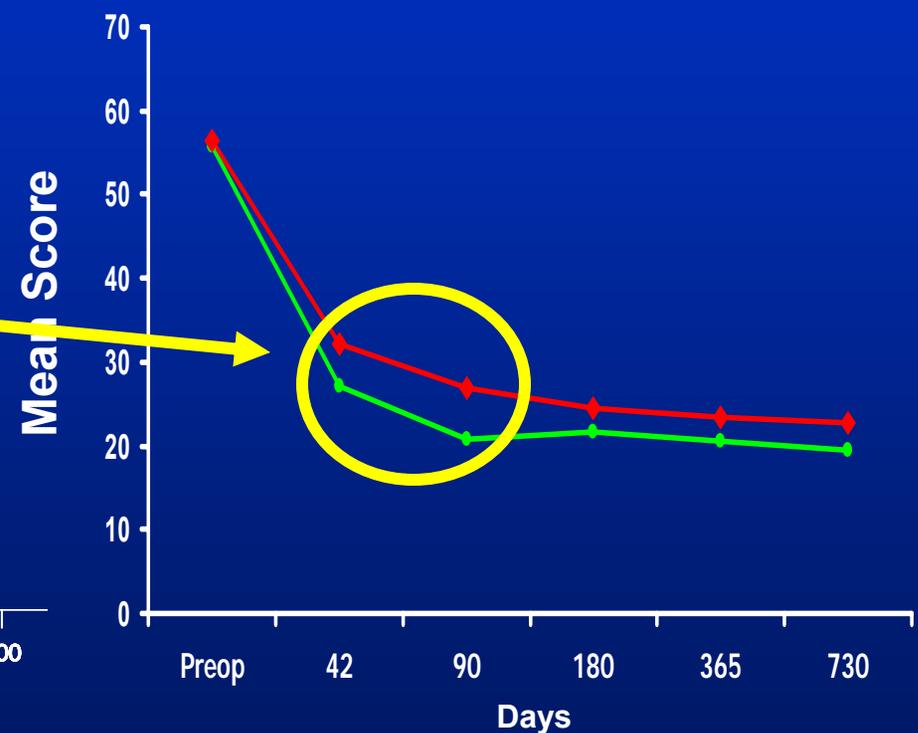
Days

Comparison of Return to Work and Pain

Return to Work



NDI Score



■ PRESTIGE ◆ Fusion

Conclusions from Clinical Trial

- Achieved Primary Objective - Overall Success Rate Statistically Non-inferior to Control
- Statistical Superiority to Control for Primary Outcome Variable
- Benefits – Pain and Neurological Symptom Relief With Maintenance of Motion

All Available Data

- All available data at 24 months
 - > 400 patients
- Same conclusions
 - PRESTIGE® Cervical Disc group statistically superior to fusion control
 - SF-36 MCS non-inferior

PRESTIGE® Cervical Disc

Reasonable Assurance

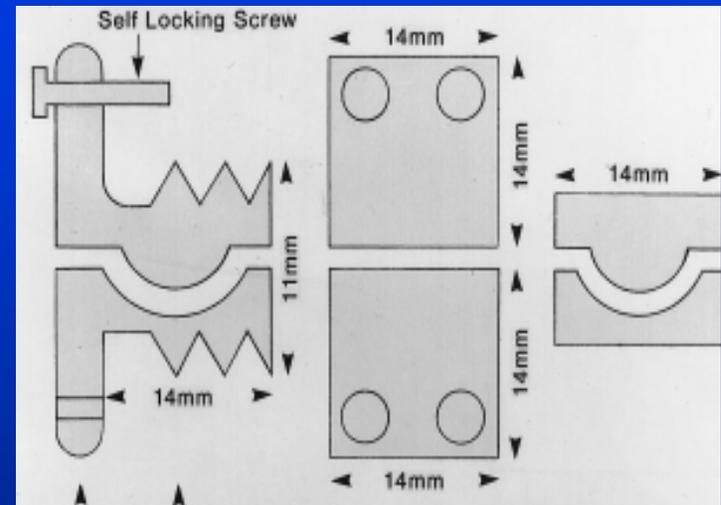
SAFETY AND EFFECTIVENESS

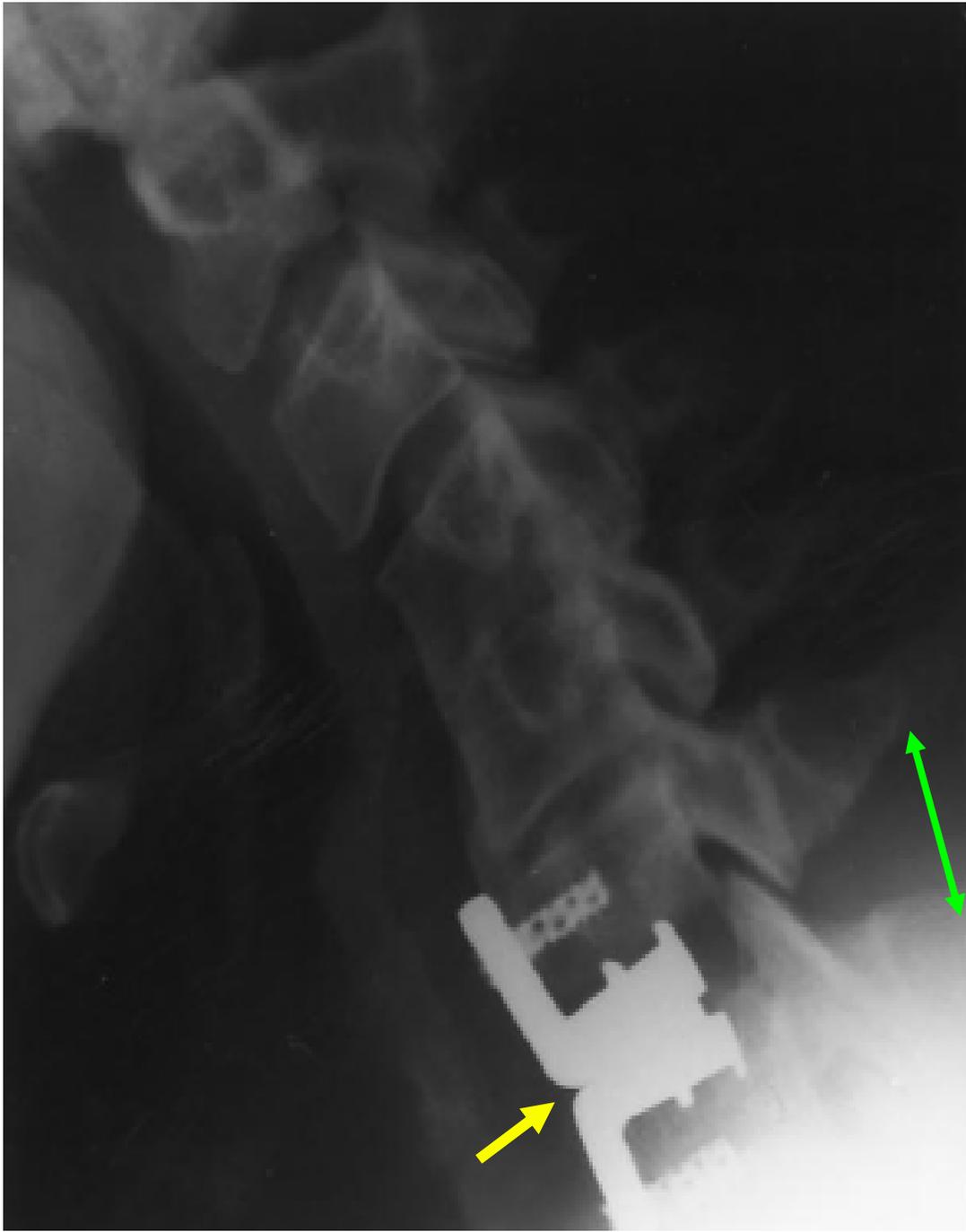
PRESTIGE® CERVICAL DISC

Vincent C. Traynelis, M.D.
Iowa City, Iowa

Cummins Disc

- Frenchay Hospital, Bristol, England
- 1989
- Stainless steel
- Ball and socket articulation
- Fixed with screws of varying design and materials
- Manufactured in hospital machine shop





Surgical experience with an implanted artificial cervical Joint

BRIAN H. CUMMINS, F.R.C.S., JAMES T. ROBERTSON, M.D., AND STEVEN S. GILL, F.R.C.S.

Department of Neurosurgery, Frenchay Hospital, Bristol, United Kingdom; and Department of Neurosurgery, University of Tennessee Health Science Center, Memphis, Tennessee

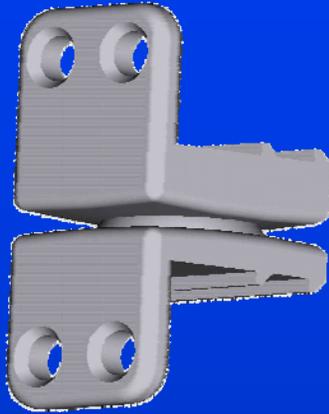
Object. To assess the effectiveness of Cummins' artificial cervical joint, the authors reviewed the cases of 20 patients in whom the joint had been placed.

Methods. A review of patients' medical records and reexamination of 18 patients were performed. The review of the surgical experience with the implantation of movable stainless-steel joints in 20 patients treated for cervical myelopathy (16 patients), cervical disc disease (4 patients), and severe pain (one patient) indicated that the procedure is safe and well tolerated. Cervical joint motion in most patients over an extended period of observation. To date, adjacent segmental symptomatic degenerative changes leading to further surgical treatment have been avoided. The joint has been placed in patients with advanced congenital and acquired cervical

fusion and has been determined to be stable, mobile, and biomechanically and biochemically compatible

shown no subsidence into adjacent bone. The design appears to be suitable for this joint replacement design.

KEY WORDS • cervical spine • degenerative disc disease • artificial vertebral joint



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- **Radiculopathy significantly improved**
- **Myelopathy improved or stabilized**

Cummins Case Study

- 60 year old male
- Radiculopathy and myelopathy
- C3/4 and C6/7 placement of
Cummins disc in 8/95



5 Years Post Surgery

Patient active, without significant pain

No complications related to cervical discs



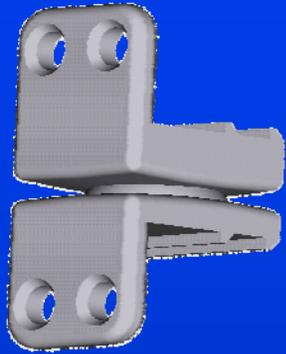
Case Study

- 52 year old female
- Congenital narrowing of cervical spine
- C3/4 and C5/6 previous ACDF
- Recurrence of myelopathic symptoms
- Anterior cervical decompression
Bristol-Cummins disc implanted at
C6/7 on 8/18/95

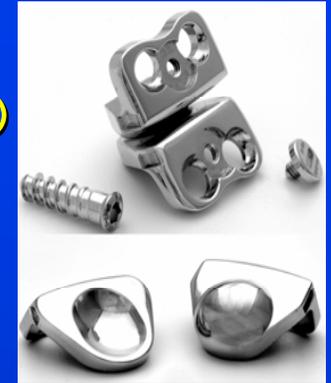
Cummins Disc

- Patient doing well clinically 11 years post op
- Myelopathic symptoms resolved
- Patient returned to active lifestyle
 - raised £4.5 million to support a hospice





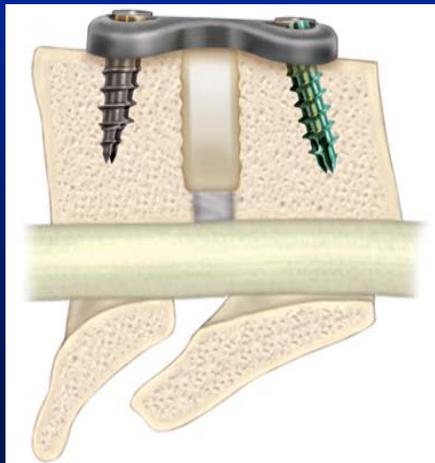
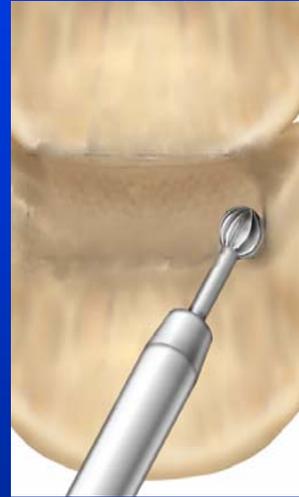
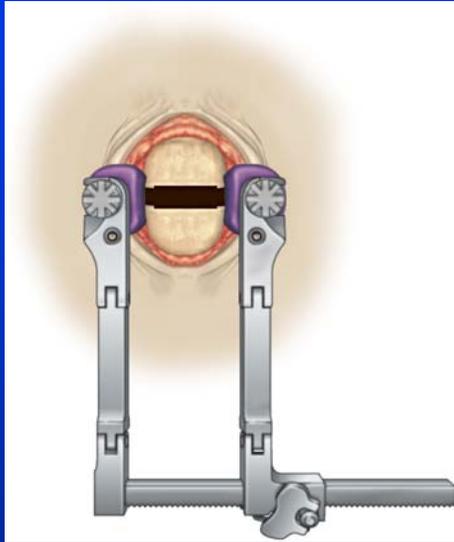
Cummins vs. PRESTIGE®



- Cummins “worst case scenario” of Prestige®
 - Stainless steel
 - Hospital foundry vs. precision manufacturing
 - Articulation
 - Ball/socket vs. ball/trough
 - Fixation
 - Multiple screw designs vs. uniform screw/lock mechanism
 - Size
 - One vs. many

- Over a decade after implantation patients doing well

Discectomy, Decompression & Endplate Preparation **ATLANTIS® Plate and PRESTIGE® Cervical Disc**



PRESTIGE[®] Study Patient

- Patient: 43 year old female
- Radiculopathy with herniated disc and osteophyte formation
- C6-C7 ACD with PRESTIGE[®] Cervical Disc-September 2003

Preop MRI



Preop X-Rays



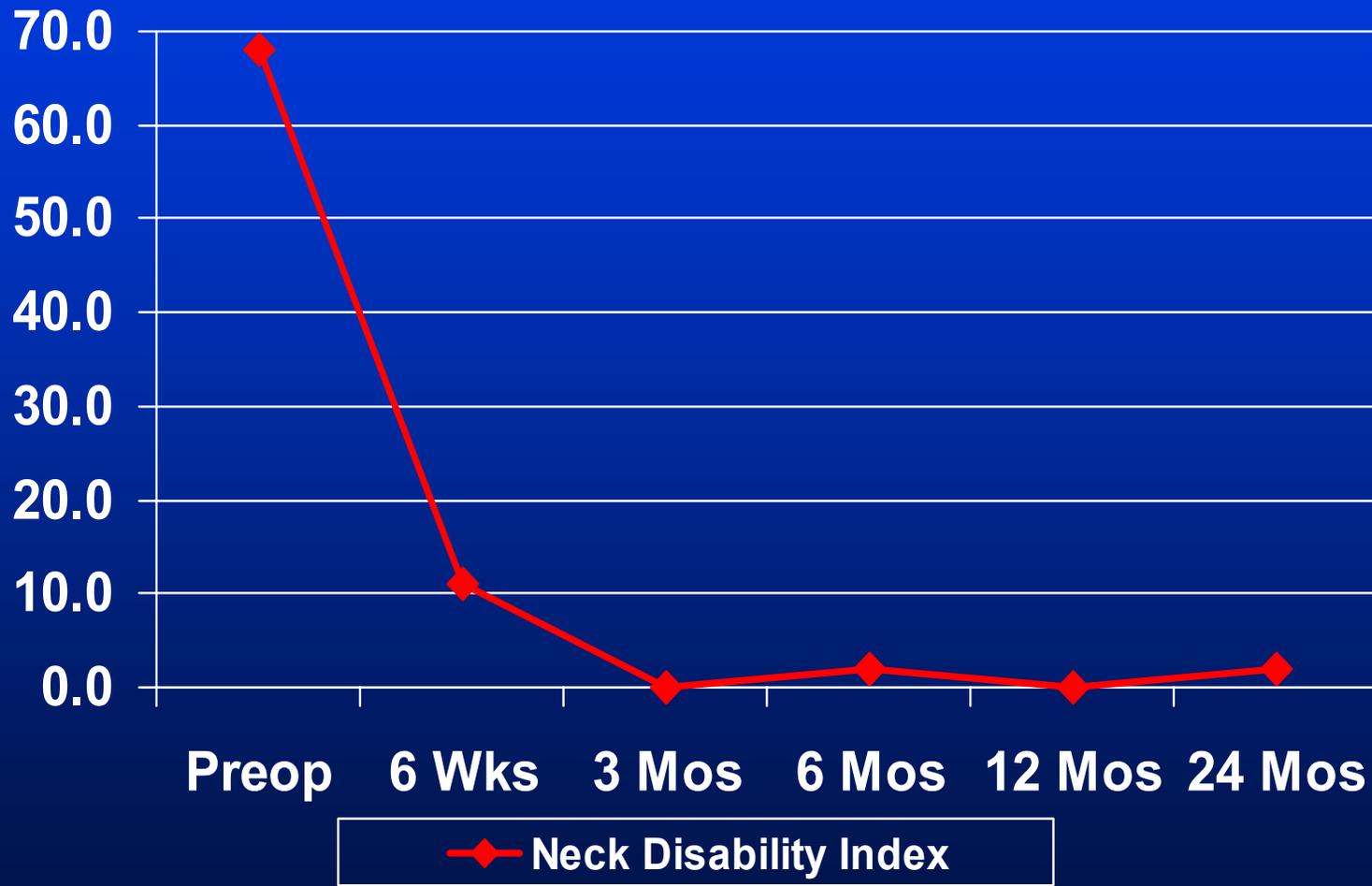
Preop X-Rays



Surgical Information

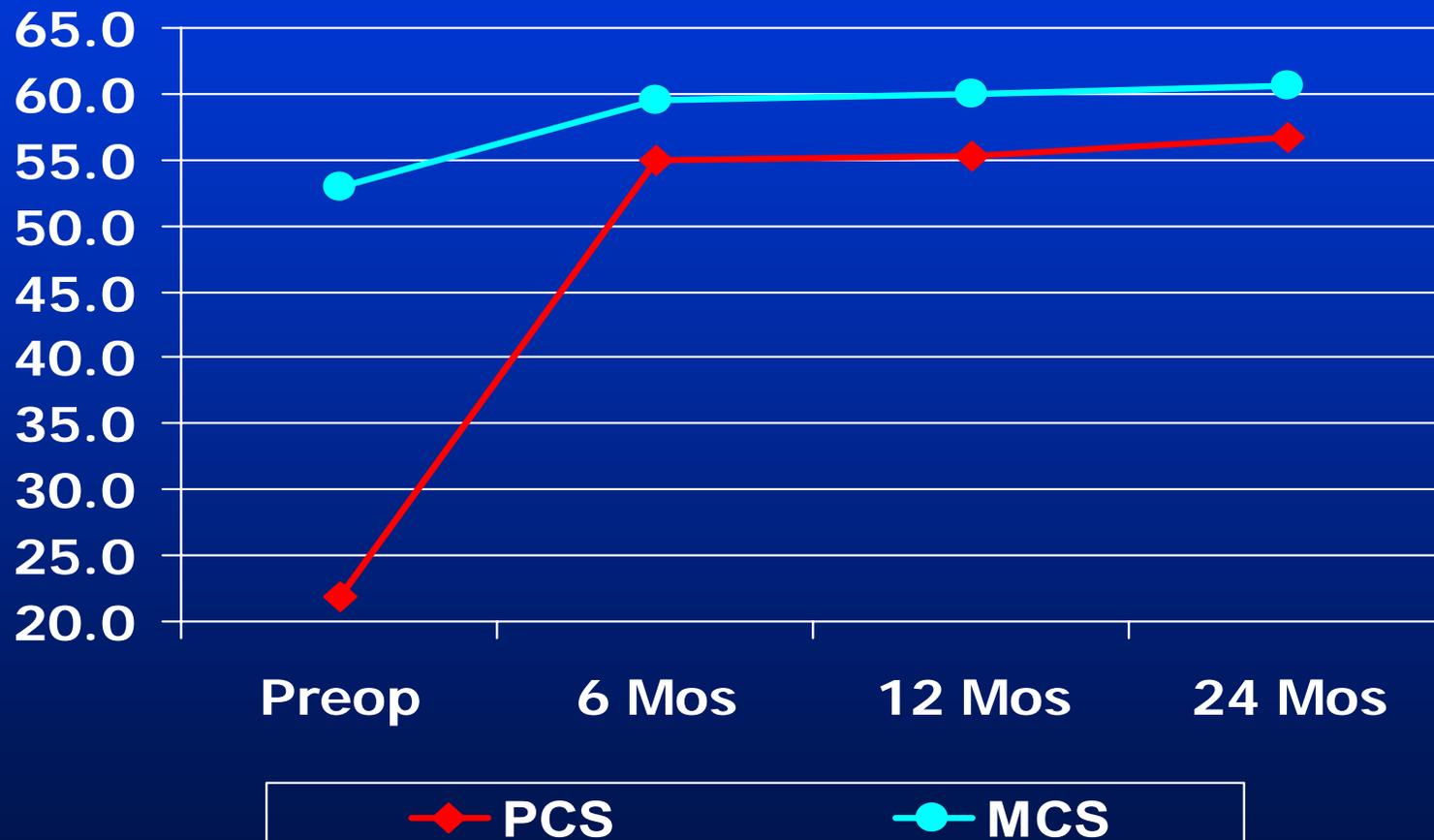
- Operation time 3.1
hours
- Blood loss 50 ml
- Hospital stay ≤ 23
hours
- Postop bracing none

Neck Disability Index

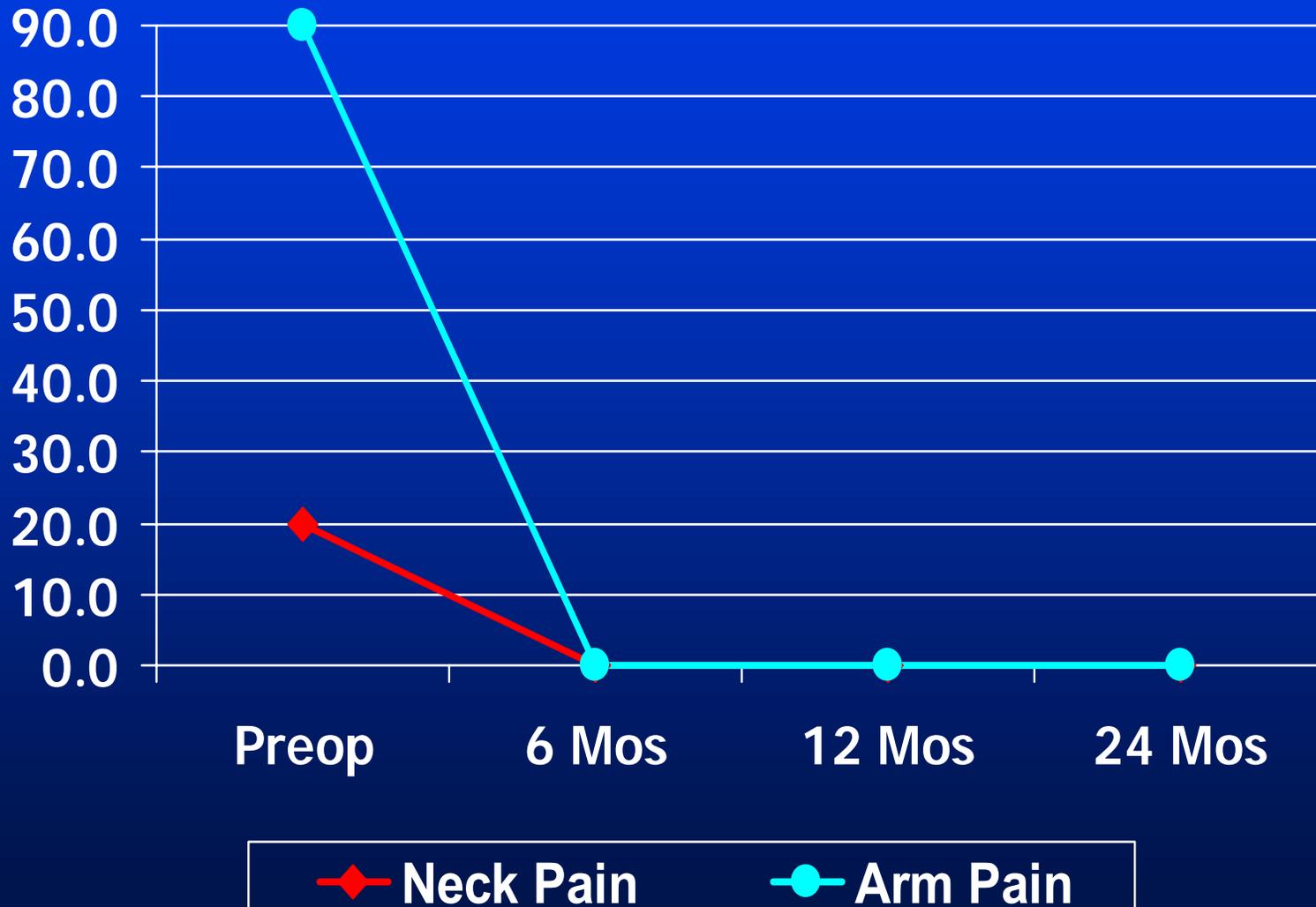


SF-36 PCS and MCS Results

Mean Scores



Neck and Arm Pain



12 months X-rays



24 month X-rays



Adverse Events

- Sinus infection @ 12 months

PRESTIGE[®] Cervical Disc Explant Case Study

- Patient: 41 year old male
- C6-C7 disc herniation and radiculopathy



12 Month X-Rays



PRESTIGE[®] Cervical Disc Explant Case Study

- Bilateral arm pain, increasing neck pain and aching in both shoulders
- Imaging studies demonstrated a herniated disc at C5-C6
- C5-C6 ACDF was performed
- Two months later the PRESTIGE[®] Cervical Disc was removed and an ACDF was performed at C6-C7.
- At the 24 month visit, the patient was still symptomatic and he was referred to a pain specialist.

PRESTIGE[®] Cervical Disc Explant Case Study

- **Removal of device**
- **Evaluation of technical aspects of arthrodesis revision surgery**
- **Examination of device after one year of implantation**

Explant Surgery Summary

- Routine anterior cervical exposure
- Remove lock screws and bone screws
- Disengage implant
- Prepare endplates in the standard fashion for bone graft and fusion
- Implant appropriate size graft and plate

Explant Analysis

- Inferior (concave) and superior (convex) surfaces of the artificial disc maintained a highly polished appearance.
- Stereomicroscopic examination at magnifications up to 60X revealed only a slight wear track on the articular surface.
 - Similar pattern, less severe than seen in bench testing.



24 Month X-Rays



PRESTIGE[®] Cervical Disc

- Long term results of a similar device are very favorable
- Prospective randomized trial demonstrates excellent outcomes
- PRESTIGE[®] is easily revisable
- PRESTIGE[®] *in vivo* wear is minimal

PRESTIGE® Cervical Disc
Concluding Remarks

Bailey Lipscomb, Ph.D.
Medtronic

**Have Demonstrated a
Reasonable Assurance of
Safety and Effectiveness**

FDA Questions to Panel

- **Adequacy of preclinical testing**

FDA Questions to Panel

- **Adequacy of preclinical testing**
- **Device design modification**

FDA Questions to Panel

- Adequacy of preclinical testing
- Device design modification
- Sample size
 - Interim analysis

FDA Questions to Panel

- Adequacy of preclinical testing
- Device design modification
- Sample size
 - Interim analysis
 - Disc height (FSU)

FDA Questions to Panel

- Adequacy of preclinical testing
- Device design modification
- Sample size
- Incidence of cancer

FDA Questions to Panel

- Adequacy of preclinical testing
- Device design modification
- Sample size
- Incidence of cancer
- Range of motion in labeling

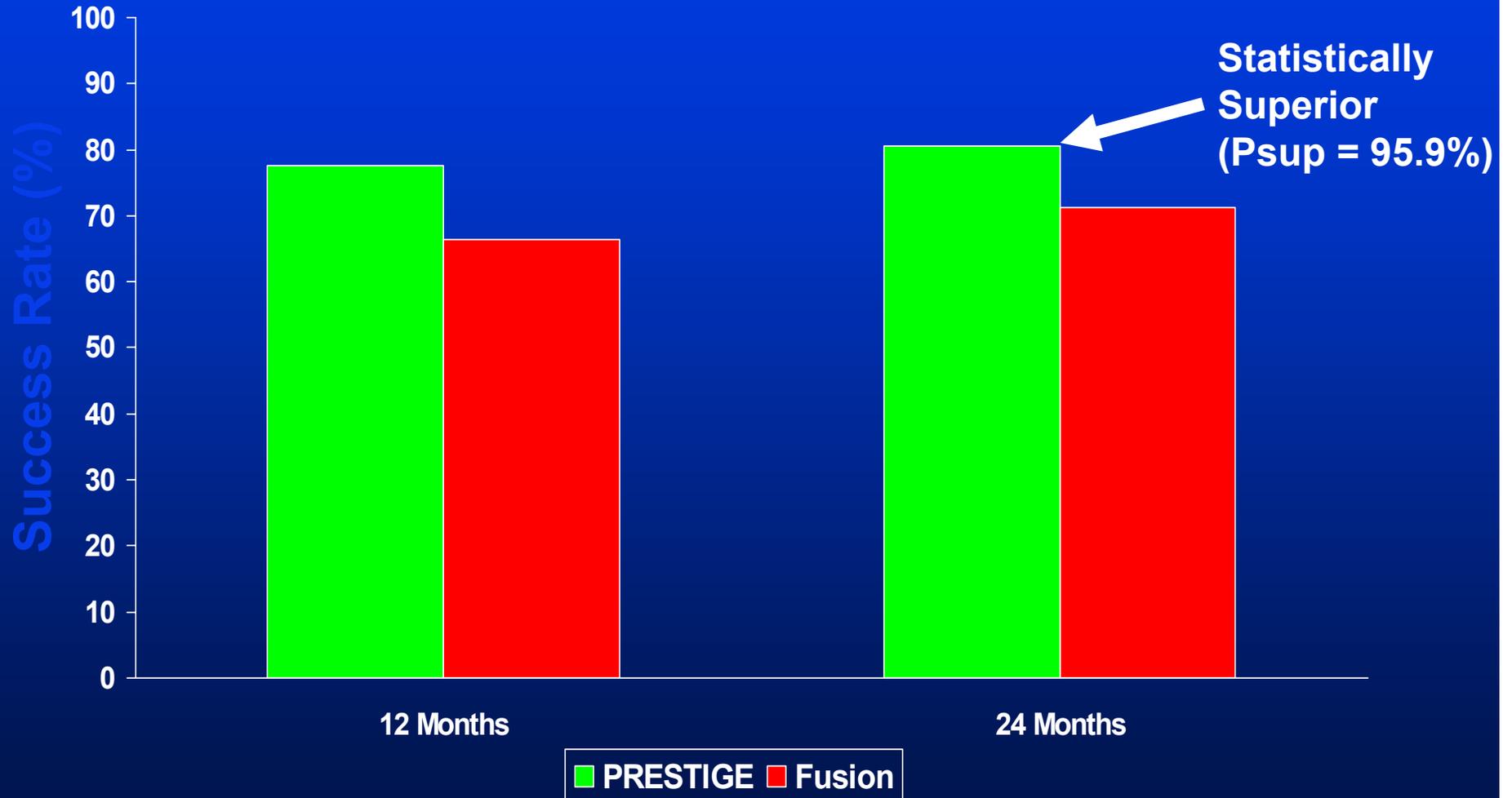
FDA Questions to Panel

- Adequacy of preclinical testing
- Device design modification
- Sample size
- Incidence of cancer
- Range of motion in labeling
- Bayesian analyses in labeling

FDA Questions to Panel

- Adequacy of preclinical testing
- Device design modification
- Sample size
- Incidence of cancer
- Range of motion in labeling
- Bayesian analyses in labeling
- Safe and effective

Overall Success



FDA Questions to Panel

- Adequacy of preclinical testing
- Device design modification
- Sample size
- Incidence of cancer
- Range of motion in labeling
- Bayesian analyses in labeling
- Safe and effective

PRESTIGE® Cervical Disc

Reasonable Assurance

SAFETY AND EFFECTIVENESS

Thank You