

BRYAN[®] Cervical Disc

Orthopaedic and Rehabilitation Devices
Advisory Panel Presentation
July 17, 2007

Kathryn H. Simpson, PhD
Manager, Clinical/Regulatory Affairs
Medtronic Spinal and Biologics

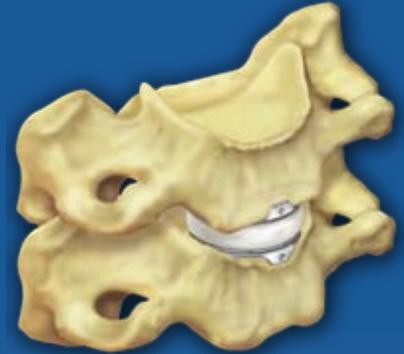
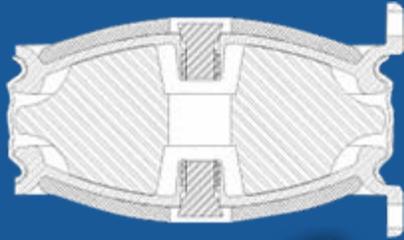


BRYAN[®] Cervical Disc



BRYAN® Cervical Disc

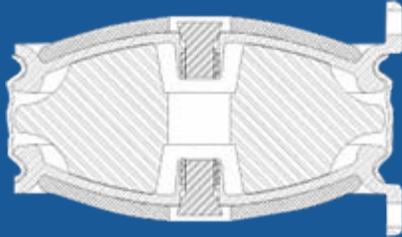
Historical Review



- Invented by Vincent Bryan, MD
 - Neurosurgeon from Seattle, Washington
- Began design in 1992
 - 1992-2000 – concept, design, testing
 - 2000-2002 – European clinical trial
 - 2002 – European market launch
- Implanted worldwide:
 - January 2000 to present ~15,000 devices implanted



Spinal Dynamics to Medtronic





BRYAN[®] Cervical Disc

IDE G00123

- Prospective, randomized, controlled, multi-center clinical trial
- 463 patients
- 30 investigational centers



BRYAN[®] Cervical Disc IDE G00123

- Cervical degenerative disc disease
- Single-level
- BRYAN[®] Cervical Disc vs. ACDF



BRYAN[®] Cervical Disc PMA P060023



BRYAN[®] Cervical Disc FDA Panel Presentations

- Design / Preclinical Testing: Stephen White
- IDE Clinical Trial Results: Rick Sasso, MD
- Case Presentations: Stephen Papadopoulos, MD
- Post-Approval Study: Hallett Mathews, MD
- Conclusion: Kathryn Simpson, PhD



Additional Resources

- Harry Genant, MD
- Donald Berry, PhD
- Paul Anderson, MD
- John Nemunaitis, MD
- Richard Fessler, MD, PhD
- John Heller, MD
- Jeffrey Toth, PhD
- Steven Kurtz, PhD
- Robert Ward
- Jim Anderson, MD, PhD
- Bailey Lipscomb, PhD
- Janice Hogan, JD
- Medtronic Staff

BRYAN[®] Cervical Disc

Stephen White

Vice President of Research and Development
Medtronic Spinal and Biologics



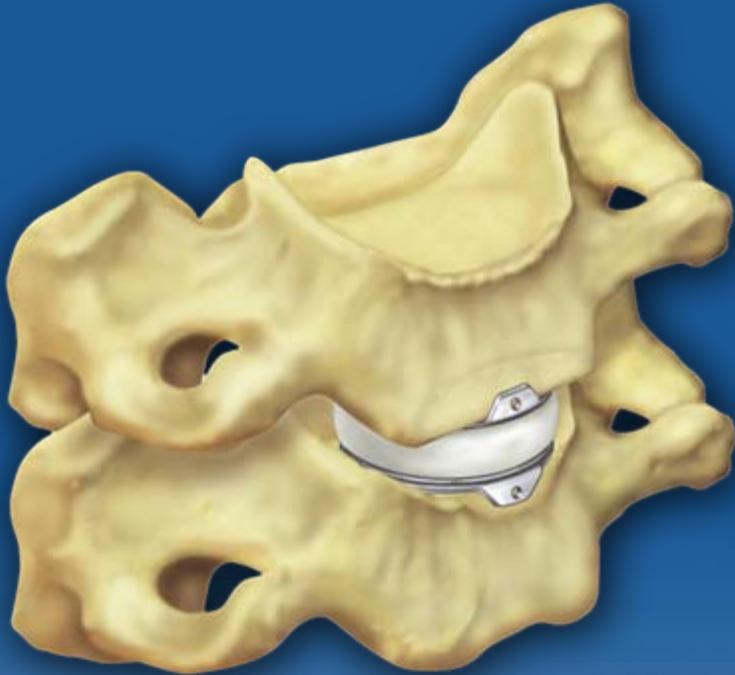


BRYAN® Cervical Disc

1. Review Design Intent
2. Review Materials
3. Review Testing



BRYAN® Cervical Disc





BRYAN[®] Cervical Disc

- Titanium Alloy Shells
- Polyurethane Nucleus
- Polyurethane Sheath





BRYAN[®] Cervical Disc

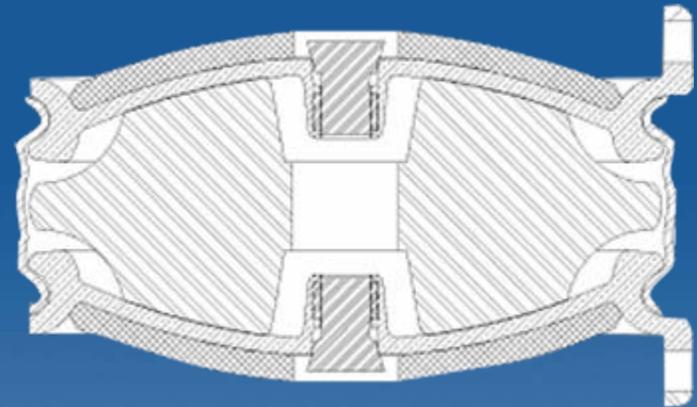




BRYAN[®] Cervical Disc

Polyurethane Nucleus

- Up to 2 mm of physiologic A/P translation
- Low wear
- Compliant characteristics – “more disc-like”





BRYAN[®] Cervical Disc

Polyurethane Sheath

- Facilitate 1-piece implant insertion
- Retain saline lubricant initially
- Prevent acute soft tissue ingrowth into articulation area



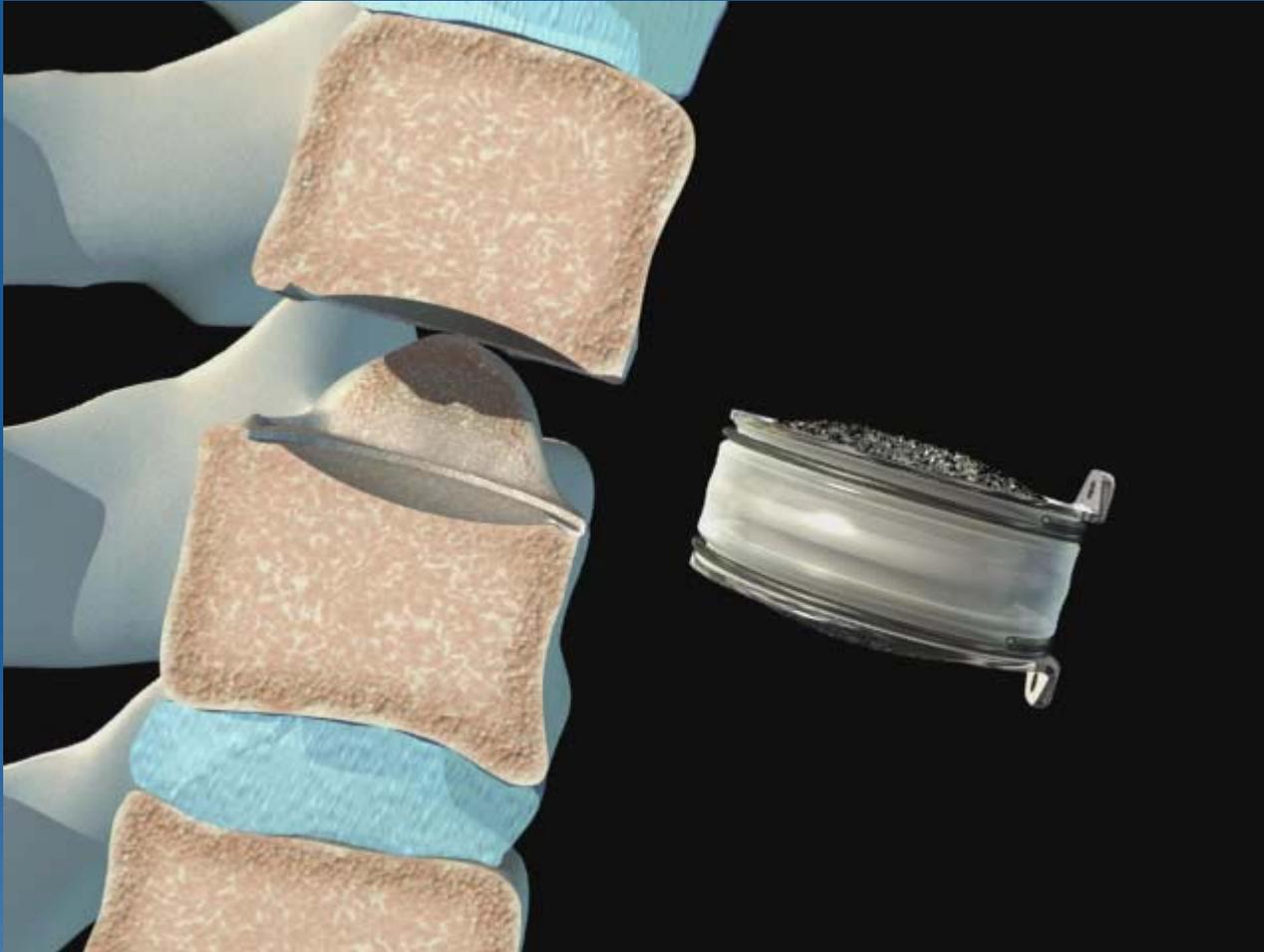


BRYAN[®] Cervical Disc





BRYAN[®] Cervical Disc





BRYAN® Cervical Disc

1. Review Design Intent
2. Review Materials
3. Review Testing



BRYAN[®] Cervical Disc Materials - Titanium

- ASTM F67 - porous coating
- ASTM F136 - shell





BRYAN® Cervical Disc

Polycarbonate Polyurethane Nucleus

- Silicone-modified end group
- Lubricious
- Compliant
- Low wear





Materials - Polyurethane

- Prosthetic spinal implants
- Specialty balloon and probe catheters
- Porous tissue scaffolds
- Intra-aortic balloons
- Cardiac-assist devices
- Vascular grafts and stents





BRYAN[®] Cervical Disc

Material Selection

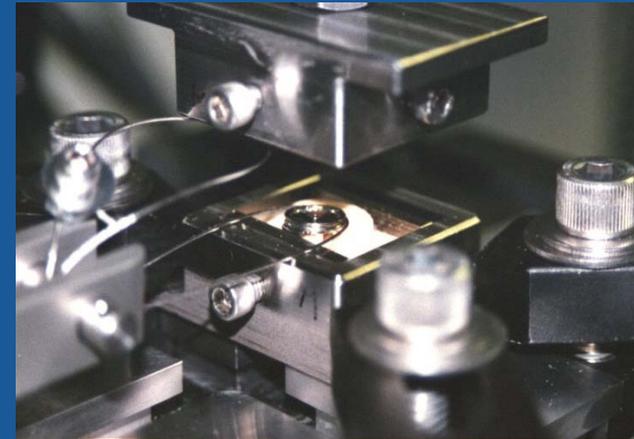
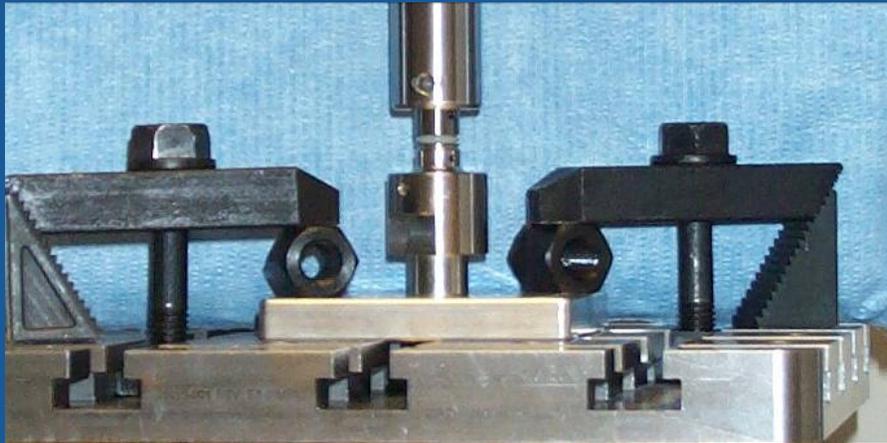
- Polyurethane
 - Compliant
 - More like the natural disc
 - Low wear
 - Biocompatible
 - Proven in cardiovascular, neurological, and other spinal products
- Titanium
 - Long history of safe use in orthopedic implants
 - Less distortion on CT and MRI
 - Proven biocompatibility with bone



BRYAN® Cervical Disc

1. Review Design Intent
2. Review Materials
3. Review Testing

BRYAN[®] Cervical Disc Testing





Testing Summary

- **Mechanical Performance: Shell**
 - Shell fatigue
 - Coating shear
 - Coating abrasion
 - Coating friction torque
- **Mechanical Performance: Nucleus**
 - Static compression
 - Compression fatigue
 - Creep
 - Nucleus fatigue
 - Durability
- **Mechanical Performance: Sheath**
 - Tensile
- **Implant Stability**
 - Antepulsion / retropulsion
 - Cadaver shear
 - RSA analysis
- **Biocompatibility Testing**
- **Animal Studies**
 - Chimpanzee study
 - Goat study
 - Rabbit study
- **Retrieval Analyses**



Physiologic Loading Cervical Spine

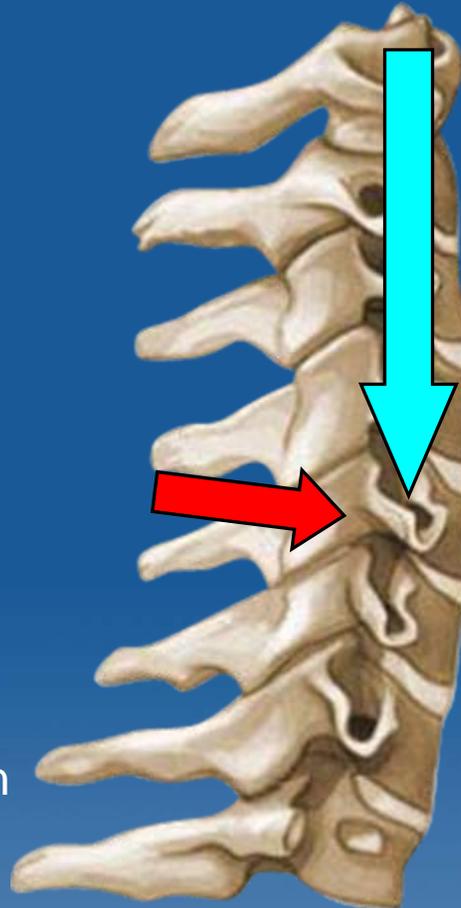
Compressive load

130 N *

- Wear/durability tests
- Shell compression fatigue
- Creep test
- Shell stability test

1164 N **

- Largest physiologic compressive load on cervical spine in fully extended position
- Nucleus static compression



Shear load

135 N **

- Maximum shear during anterior/posterior exertions
- Static and fatigue testing of shell post

* Snijders *et al.*, *J Biomechanics*, 1991

** Moroney *et al.*, *J Orthop Res*, 1988



Testing Summary

- **Mechanical Performance: Shell**

- Shell fatigue
- Coating shear
- Coating abrasion
- Coating friction torque

- **Mechanical Performance: Nucleus**

- Static compression
- Compression fatigue
- Creep
- Nucleus fatigue
- Durability

- **Mechanical Performance: Sheath**

- Tensile

- **Implant Stability**

- Antepulsion / retropulsion
- Cadaver shear
- RSA analysis

- **Biocompatibility Testing**

- **Animal Studies**

- Chimpanzee study
- Goat study
- Rabbit study

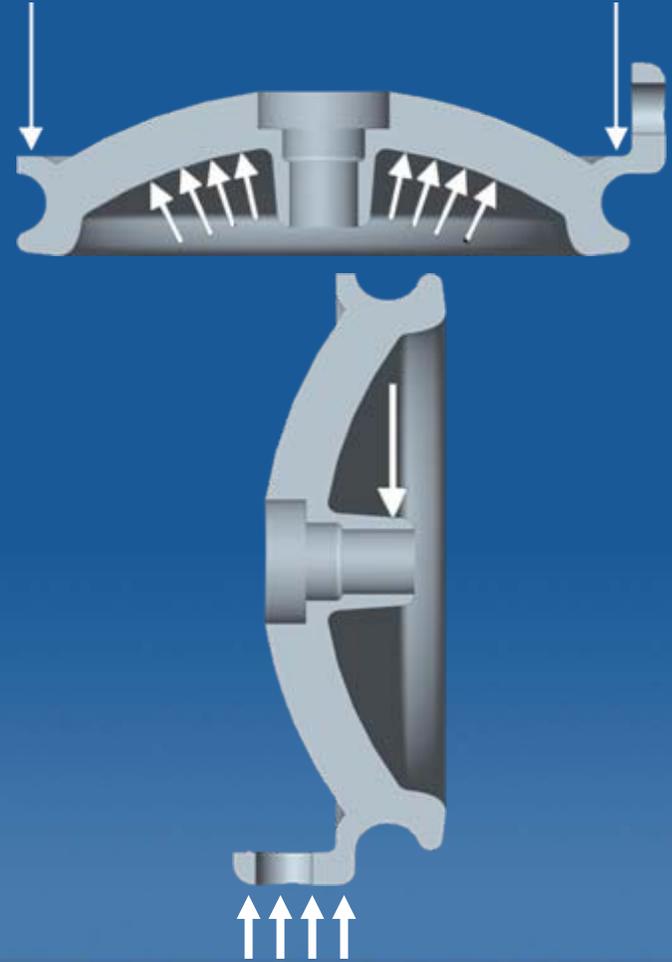
- **Retrieval Analyses**



BRYAN[®] Cervical Disc Fatigue Testing Summary

Shell Compression Fatigue

- Shell
 - 1000 N run-out load to 10 million cycles
 - 7.7 times higher than 130 N physiologic compression load reported in literature
- Shell Post
 - 300 N run-out load to 10 million cycles
 - 2.5 times higher than the 135 N physiologic shear forces reported in literature





Mechanical Performance: Shell

Porous Coating Testing

- ASTM Standards
 - F1160-98
 - F1044-95
 - F1147-99
 - F1978-99
- Static Tensile
- Static Shear
- Abrasion Testing



Mechanical Performance: Shell

Porous Coating Testing

- Shear Testing
 - Fatigue in pure shear per ASTM F1160
 - Static in pure shear per ASTM F1160 / F1044
- Tensile Testing
 - Static in pure tension per ASTM F1147
- Abrasion Testing
 - Abrasive wear measured per ASTM F1978 (Taber method)



Testing Summary

- **Mechanical Performance: Shell**

- Shell fatigue
- Coating shear
- Coating abrasion
- Coating friction torque

- **Mechanical Performance: Nucleus**

- Static compression
- Compression fatigue
- Creep
- Nucleus fatigue
- Durability

- **Mechanical Performance: Sheath**

- Tensile

- **Implant Stability**

- Antepulsion / retropulsion
- Cadaver shear
- RSA analysis

- **Biocompatibility Testing**

- **Animal Studies**

- Chimpanzee study
- Goat study
- Rabbit study

- **Retrieval Analyses**



Mechanical Performance: Nucleus

- Static Testing
- Creep Testing
- Compression
- Fatigue Testing
- Durability/Wear Testing





BRYAN[®] Cervical Disc Nucleus Testing Summary

Nucleus Static Compression

- All nuclei must support a compressive load of 1164 N without test mandrel contact
- 1164 N: Largest physiologic compressive load on the cervical spine in a fully extended position
- All tests exceeded 10,756 N

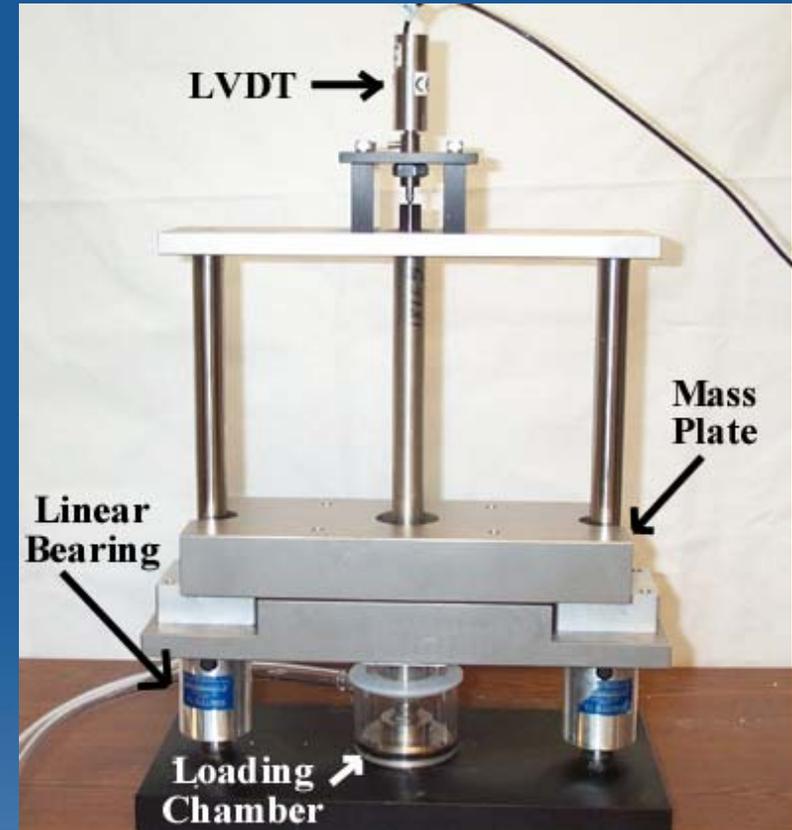




BRYAN[®] Cervical Disc Nucleus Testing Summary

Nucleus Creep

- Nuclei subjected to compressive load of 130 N for 700 hours
- Loads - 65, 130, 195, and 260 N
- Under 260 N load, nucleus compressed 0.4 mm





BRYAN[®] Cervical Disc Nucleus Testing Summary

Nucleus Compression Fatigue

- Cyclically loaded for 10,000,000 cycles at 285 N
- 12 times higher than 285 N worst-case compression load during flexion/extension reported in the literature
- 2 tests had 3500 N run-out load to 10,000,000 cycles





Wear/Durability Tests

Extensive Testing

- 30 durability wear specimens
- Over 365,000,000 combined cycles
- Up to 40,000,000 cycles
- Multiple frequencies
- Saline and bovine
- Loads at 130 N or 300 N



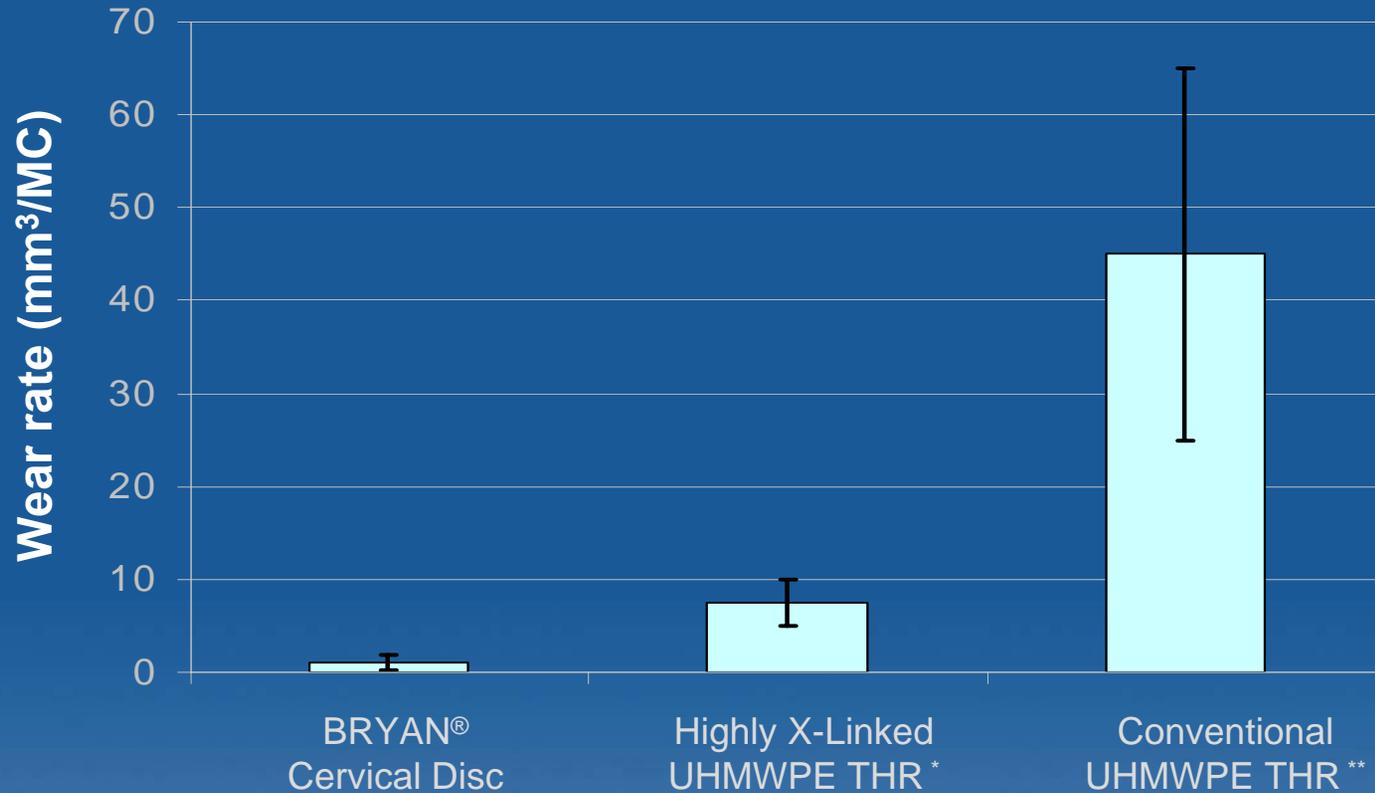
Wear/Durability Tests

- Wear Testing
 - Custom simulator at 130 N, 37° C, 4 Hz and 2 Hz
 - 10,000,000 cycles of combined flexion/extension to ± 4.9 degrees and axial rotation to ± 3.8 degrees
- Wear Rates
 - 0.96 +/- .84 mm³/MC at 4 Hz
 - 0.90 +/- .25 mm³/MC at 2 Hz





Wear/Durability Tests



* McKellop *et al.*, *JBJS*, 2000

** McKellop *et al.*, *J Orthop Res*, 1999



Wear/Durability Tests

Explant analysis shows:

- 100,000 to 200,000 simulator cycles = 1 year *in vivo* *
- 10M cycles of durability testing = *simulation* of 50 to 100 years clinical wear

* A comparison of simulator-tested and retrieved cervical disc prostheses.
Anderson PA, Rouleau JP, Toth JM, Riew KD. *J Neurosurg Spine* 2004; 2:202-10.



Testing Summary

- **Mechanical Performance: Shell**

- Shell fatigue
- Coating shear
- Coating abrasion
- Coating friction torque

- **Mechanical Performance: Nucleus**

- Static compression
- Compression fatigue
- Creep
- Nucleus fatigue
- Durability

- **Mechanical Performance: Sheath**

- Tensile

- **Implant Stability**

- Antepulsion / retropulsion
- Cadaver shear
- RSA analysis

- **Biocompatibility Testing**

- **Animal Studies**

- Chimpanzee study
- Goat study
- Rabbit study

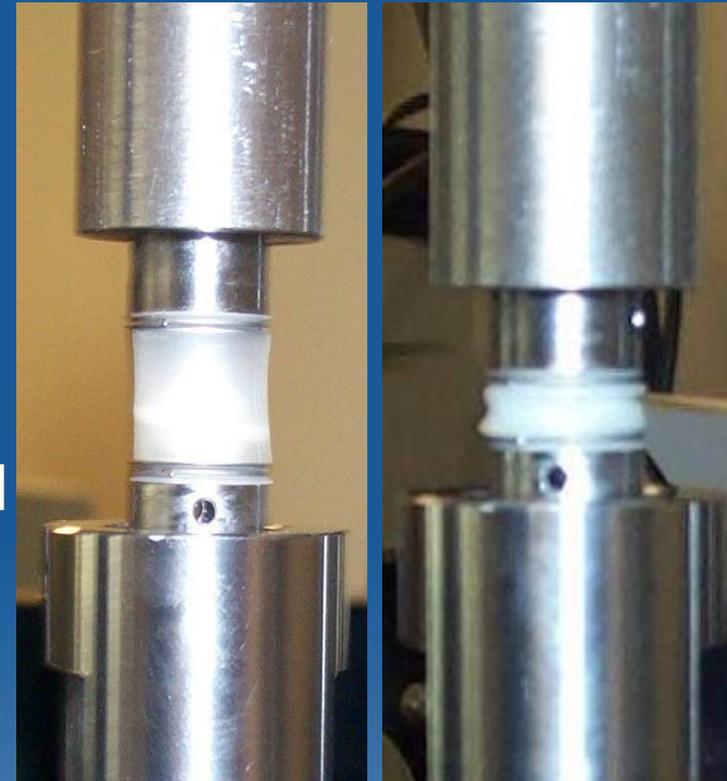
- **Retrieval Analyses**



Mechanical Performance: Sheath

Sheath Testing

- 10 test articles
- Axial displacement 2.1 mm
- 1 atmosphere pressure and checking for leakage
- All test articles were then subjected to 10 mm displacement in tensile direction to observe rupture characteristics of the sheath
- All test articles passed





Testing Summary

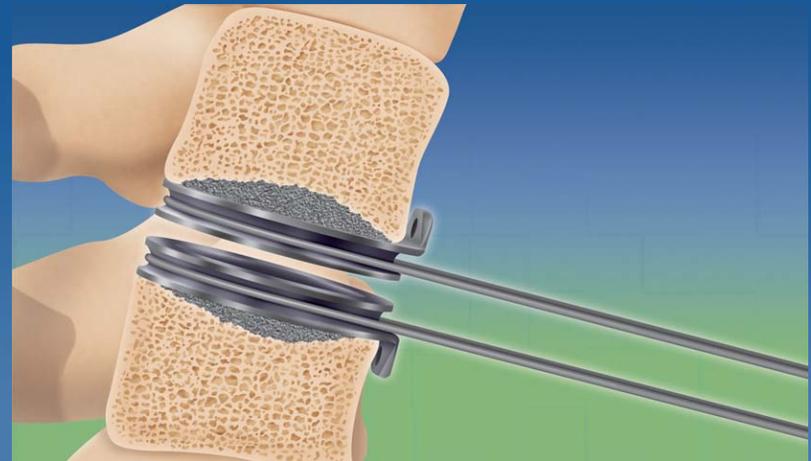
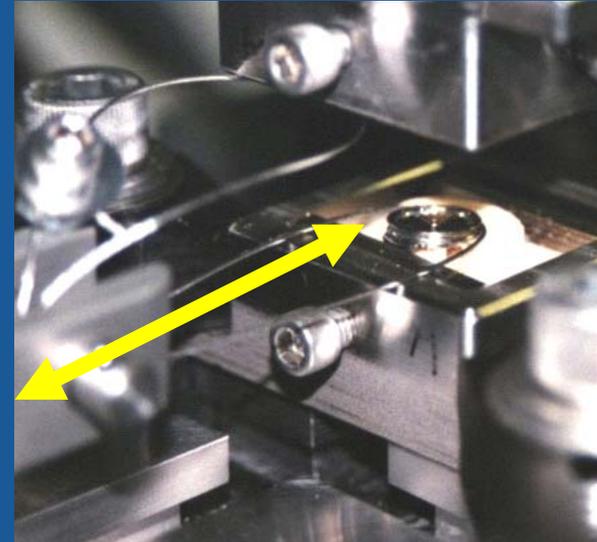
- **Mechanical Performance: Shell**
 - Shell Fatigue
 - Coating shear
 - Coating abrasion
 - Coating friction torque
- **Mechanical Performance: Nucleus**
 - Static compression
 - Compression fatigue
 - Creep
 - Nucleus fatigue
 - Durability
- **Mechanical Performance: Sheath**
 - Tensile
- **Implant Stability**
 - Antepulsion / retropulsion
 - Cadaver shear
 - RSA analysis
- **Biocompatibility Testing**
- **Animal Studies**
 - Chimpanzee study
 - Goat study
 - Rabbit study
- **Retrieval Analyses**



Prosthesis Stability

Mechanical Tests

- Pure shear device displacement under a variable compressive load to determine the force required to dislodge the prosthesis from a simulated bony cavity
- Antepulsion and retropulsion under 130 N axial load
 - Antepulsion force to dislodge was 270 N
 - Retropulsion force to dislodge was 429 N





Prosthesis Stability

- Cadaver spines, as harvested
- Flexion, extension, lateral bending
- No significant differences after implantation





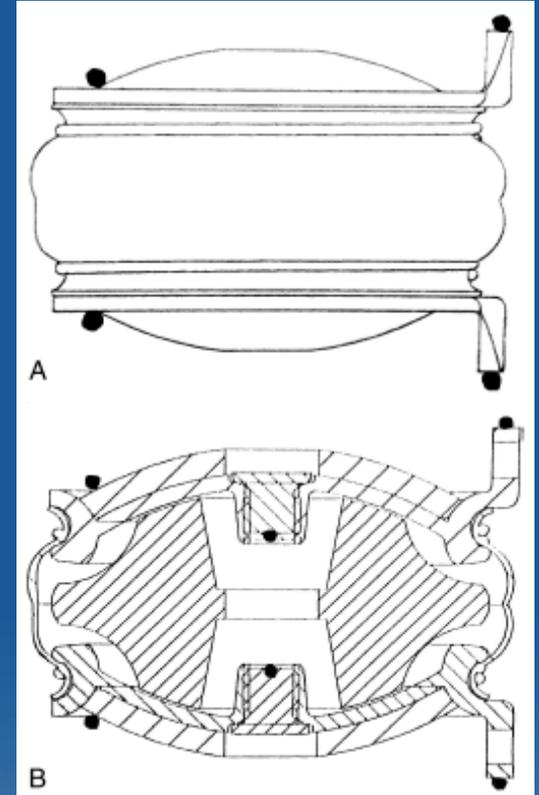
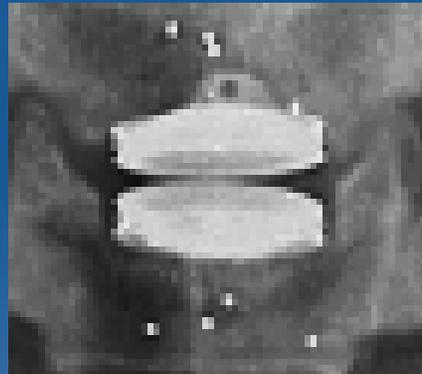
Prosthesis Stability

Radiostereometric Modified BRYAN® Cervical Disc Prosthesis

3-5 tantalum markers

Conclusions:

“The BRYAN® Cervical Disc prosthesis is securely fixed to the bone within 3–6 months in all patients.”*



* A Radiostereometric Analysis of the BRYAN® Cervical Disc Prosthesis. Bengt Lind, MD, PhD, Björn Zoëga, MD, PhD, and Paul A. Anderson, MD. *Spine* 32(8): 885-890, 2007.



Testing Summary

- **Mechanical Performance: Shell**
 - Shell fatigue
 - Coating shear
 - Coating abrasion
 - Coating friction torque
- **Mechanical Performance: Nucleus**
 - Static Compression
 - Compression fatigue
 - Creep
 - Nucleus fatigue
 - Durability
- **Mechanical Performance: Sheath**
 - Tensile
- **Implant Stability**
 - Antepulsion / retropulsion
 - Cadaver shear
 - RSA analysis
- **Biocompatibility Testing**
- **Animal Studies**
 - Chimpanzee study
 - Goat study
 - Rabbit study
- **Retrieval Analyses**



BRYAN® Cervical Disc Biocompatibility Testing

- Cytotoxicity ISO 10993-5
- Sensitization ISO 10993-10
- Intracutaneous Reactivity ISO 10993-10
- Acute Toxicity ISO 10993-11
- Pyrogenicity Tripartite (USP)
- Genotoxicity Tripartite (Ames, Chromosome Aberration, and Cell Transformation)
- Implantation Tripartite (USP)
- Chronic Toxicity Tripartite (USP)
- Two-year Carcinogenicity Tripartite (Rat)



Testing Summary

- **Mechanical Performance: Shell**

- Shell fatigue
- Coating shear
- Coating abrasion
- Coating friction torque

- **Mechanical Performance: Nucleus**

- Static compression
- Compression fatigue
- Creep
- Nucleus fatigue
- Durability

- **Mechanical Performance: Sheath**

- Tensile

- **Implant Stability**

- Antepulsion / retropulsion
- Cadaver shear
- RSA analysis

- **Biocompatibility Testing**

- **Animal Studies**

- Primate study
- Goat study
- Rabbit study

- **Retrieval Analyses**



Primate Study

- Animals tested to determine:
 - Feasibility of the device
 - Safety
 - Biocompatibility
- Animals followed for 3, 4, 6, and 6.5 months

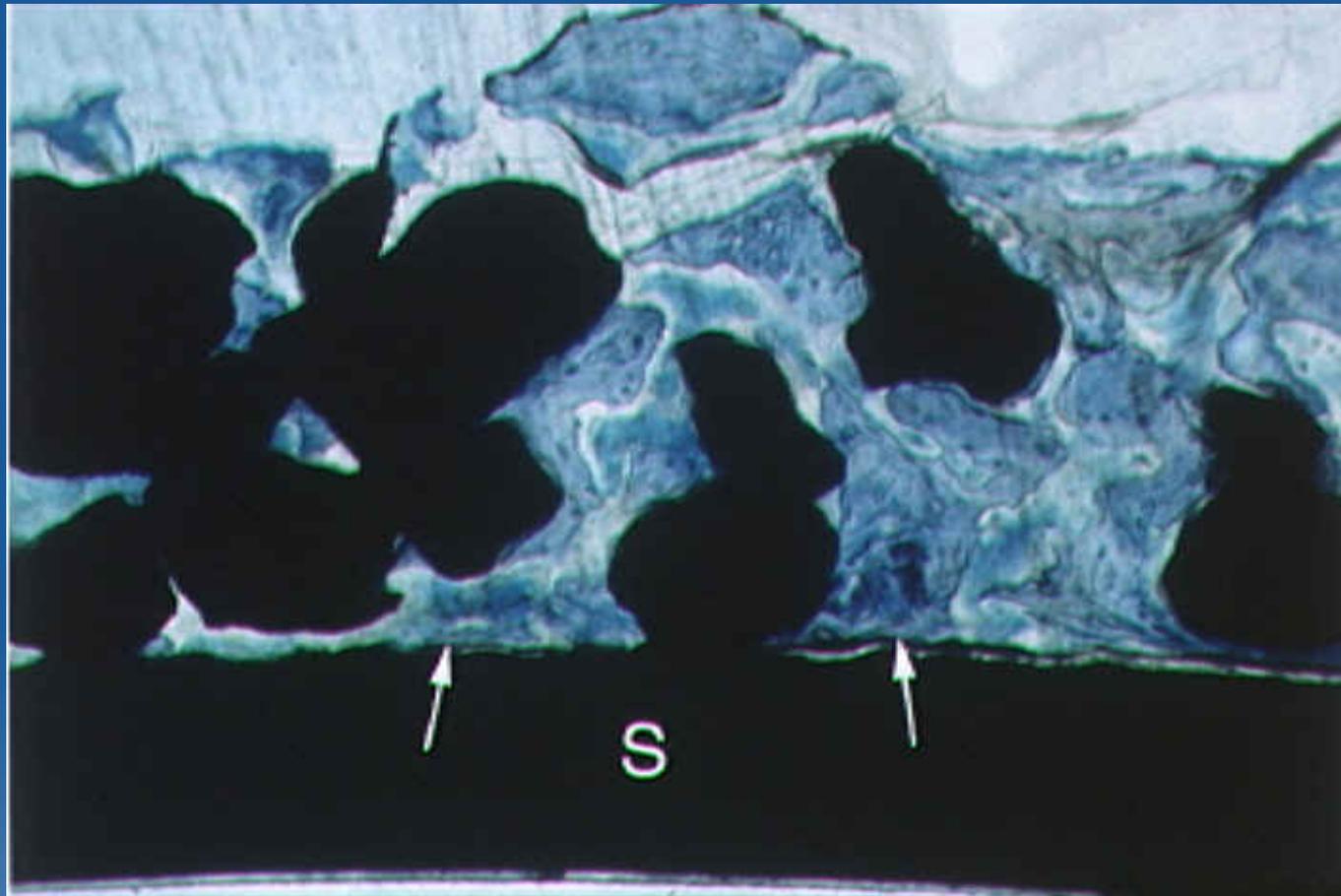


Primate Study

- Safety reaffirmed with all acceptance criteria
 - No behavioral, neurological, physical changes
 - No subluxation
 - No migration
 - No loosening
- All components in good condition with minimal particulates in tissues
- Range of motion equal to normal chimpanzee motion



Chimpanzee Bone Ingrowth



* Bone Ingrowth in Retrieved BRYAN® Cervical Disc Prosthesis. W.K. Jensen, P.A. Anderson, L. Nel and J.R. Rouleau, *Spine* 30(22): 2497-2502, 2005.



Goat Studies

- Ten animals followed for:
 - 0 months (n=1)
 - 3 months (n=3)
 - 6 months (n=3)
 - 12 months (n=3)
- Organs sampled at termination:
 - periprosthetic
 - local spinal cord
 - spleen, liver, lymph nodes
- Biologic response to wear particles assessed, if any





Goat Studies

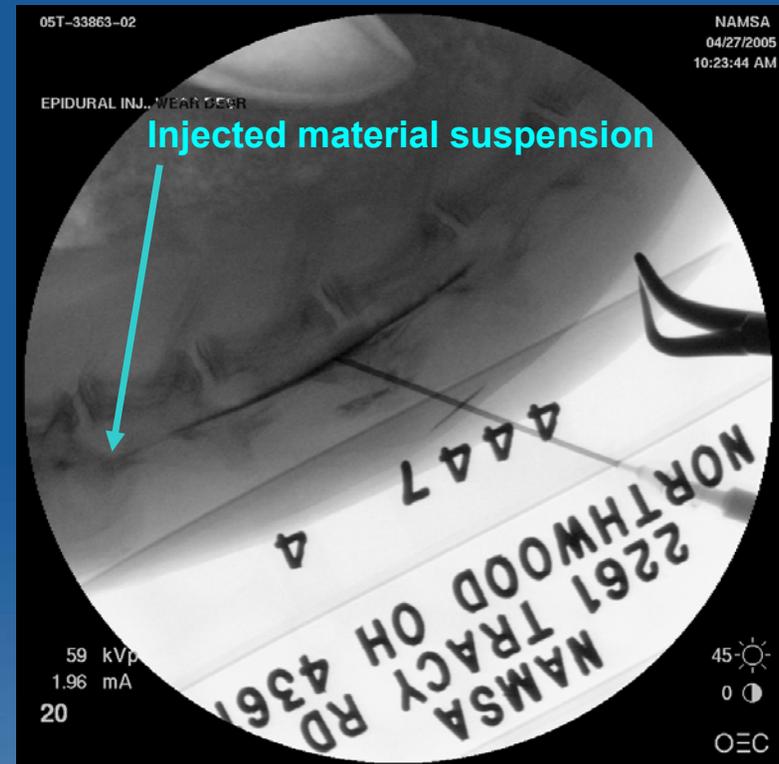
Tissue	Baseline (n=1)	3 month (n=3)	6 month (n=3)	12 month (n=3)
Local tissues	no particles	no particles	2 part., 1 macro.	no particles
Spinal	no particles	no particles	2 part., no rxn	1 part., no rxn
Lymph nodes	no particles	N/A (thymus)	no particles	no particles
Liver	no particles	no particles	no particles	no particles
Spleen	no particles	no particles	no particles	no particles



BRYAN[®] Cervical Disc Biocompatibility Testing

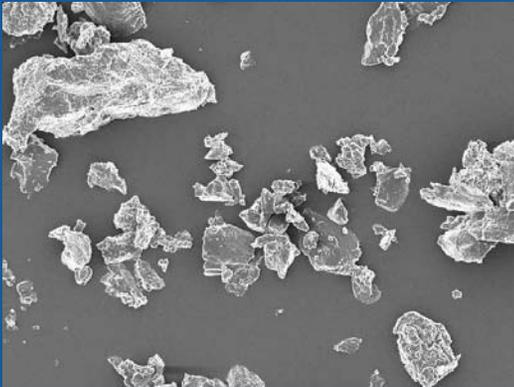
Rabbit Study

- Bolus injection:
Nucleus/sheath material
(20 & 60 million cycles)
- Sacrifice at 3 & 6 months

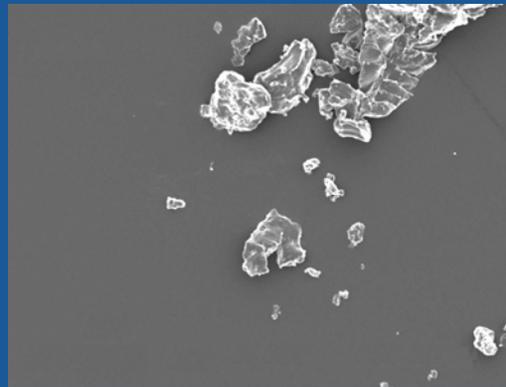




Particle Morphology



Sheath material in
the rabbit model



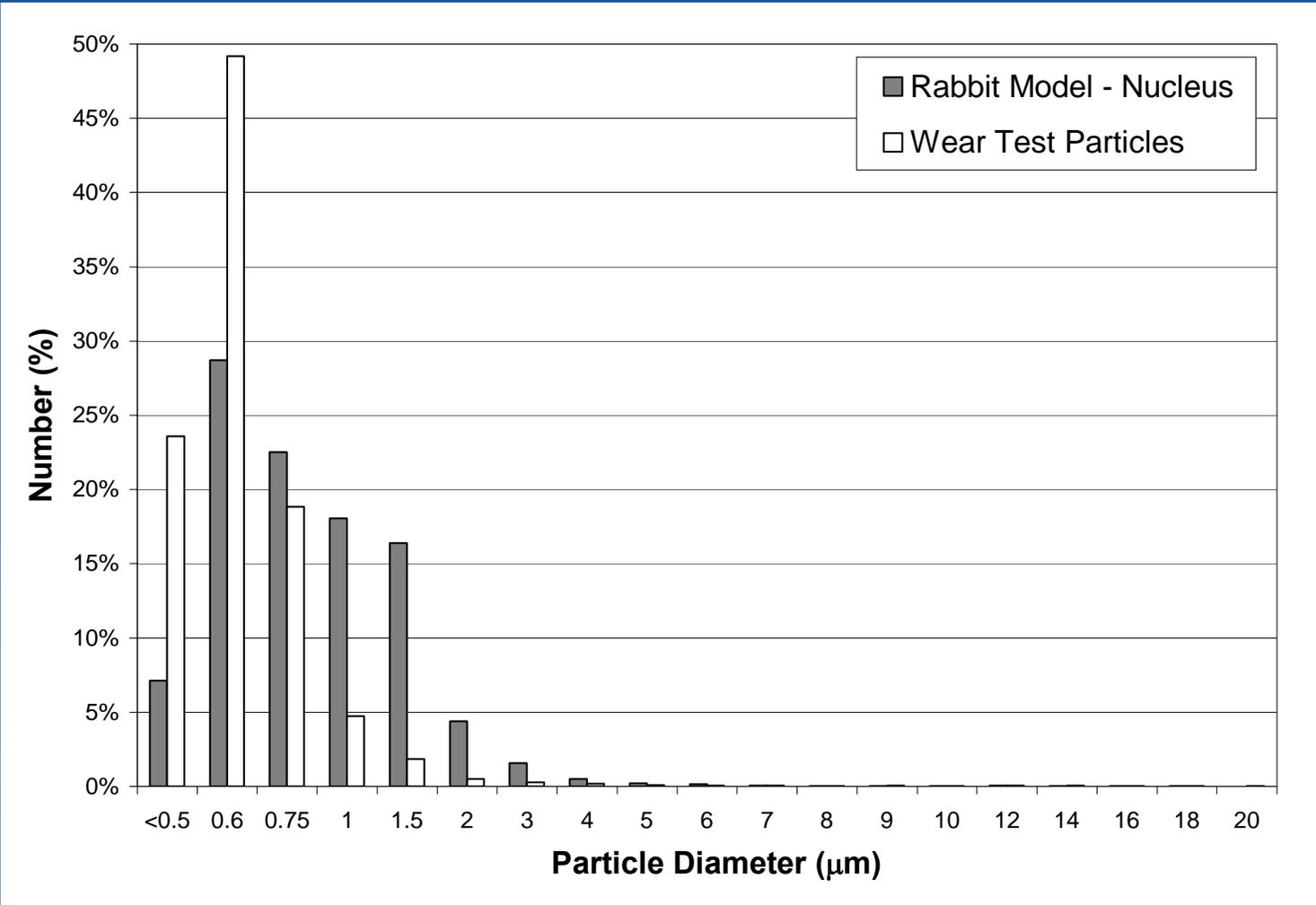
Nucleus material in
the rabbit model



Debris generated
in the wear test



Particle Size





Testing Summary

- **Mechanical Performance: Shell**

- Shell fatigue
- Coating shear
- Coating abrasion
- Coating friction torque

- **Mechanical Performance: Nucleus**

- Static compression
- Compression fatigue
- Creep
- Nucleus fatigue
- Durability

- **Mechanical Performance: Sheath**

- Tensile

- **Implant Stability**

- Antepulsion / retropulsion
- Cadaver shear
- RSA analysis

- **Biocompatibility Testing**

- **Animal Studies**

- Chimpanzee study
- Goat study
- Rabbit study

- **Retrieval Analyses**



Retrieval Analysis

- Approximately 15,000 devices implanted worldwide
- Over 240 implanted for US IDE trial
 - 3 devices explanted
 - 2 due to residual pain
 - 1 secondary to trauma
 - 2 available for analysis
- Explant analysis has shown limited wear, consistent ingrowth, and excellent biomechanical stability

Summary



BRYAN® Cervical Disc IDE Clinical Results - G000123

Rick C. Sasso, MD
Indianapolis, Indiana





Hypothesis

Non-inferiority of primary outcome variable,
overall success



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 - BRYAN[®] Cervical Disc
- Control treatment - Plated fusion with structural allograft interbody spacer





Study Objectives

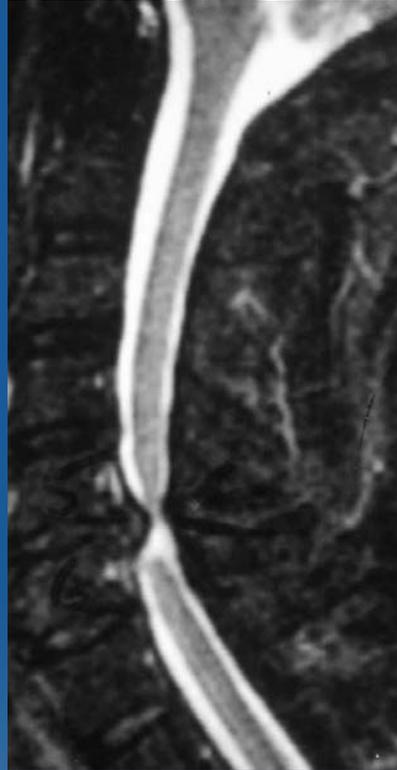
- Primary Objective:
 - Non-inferiority in Overall Success
- Secondary Objective
 - Superiority in Overall Success



Key Study Entrance Criteria

Inclusion

- Single level cervical degenerative disc
- C3-C4 to C6-C7
- 6 weeks conservative treatment
- ≥ 21 years of age
- NDI ≥ 30
- Willing to comply with protocol



Exclusion

- Significant cervical anatomical deformity
- Advanced degenerative changes (bridging osteophytes, loss of motion, disc collapse $>50\%$)
- Previous cervical spine surgery
- Metabolic bone disease
- Spinal metastases
- Infection
- Diabetes
- Allergy to titanium, polyurethane, or ethylene oxide residues
- BMI > 40
- Pregnant



Patient Evaluation

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



Patient Population

- Patients
 - 242 received BRYAN® Cervical Disc
 - 221 received fusion (ACDF)
- 30 investigational centers



Demographic Information

	BRYAN[®] Disc	Fusion	P-value
Age, mean (yrs.)	44	45	0.723
Weight, mean (lbs.)	173	180	0.061
Height, mean (in.)	68	68	0.991
Sex (% male)	46	51	0.228
Worker's Compensation (%)	6	5	0.687
Spinal Litigation (%)	2	3	1.000



Surgery Data

	BRYAN[®] Disc	Fusion
Operative Time, mean (hrs.)	2.2	1.4
Blood Loss, mean (ml)	91.5	59.6
Hospital Stay, mean (days)	1.1	1.0



Study Comparisons Focused on 24-Month Data

Interim Analysis

300 Patients at 24 Months

431 Patients at 12 Months

(All available data also presented)

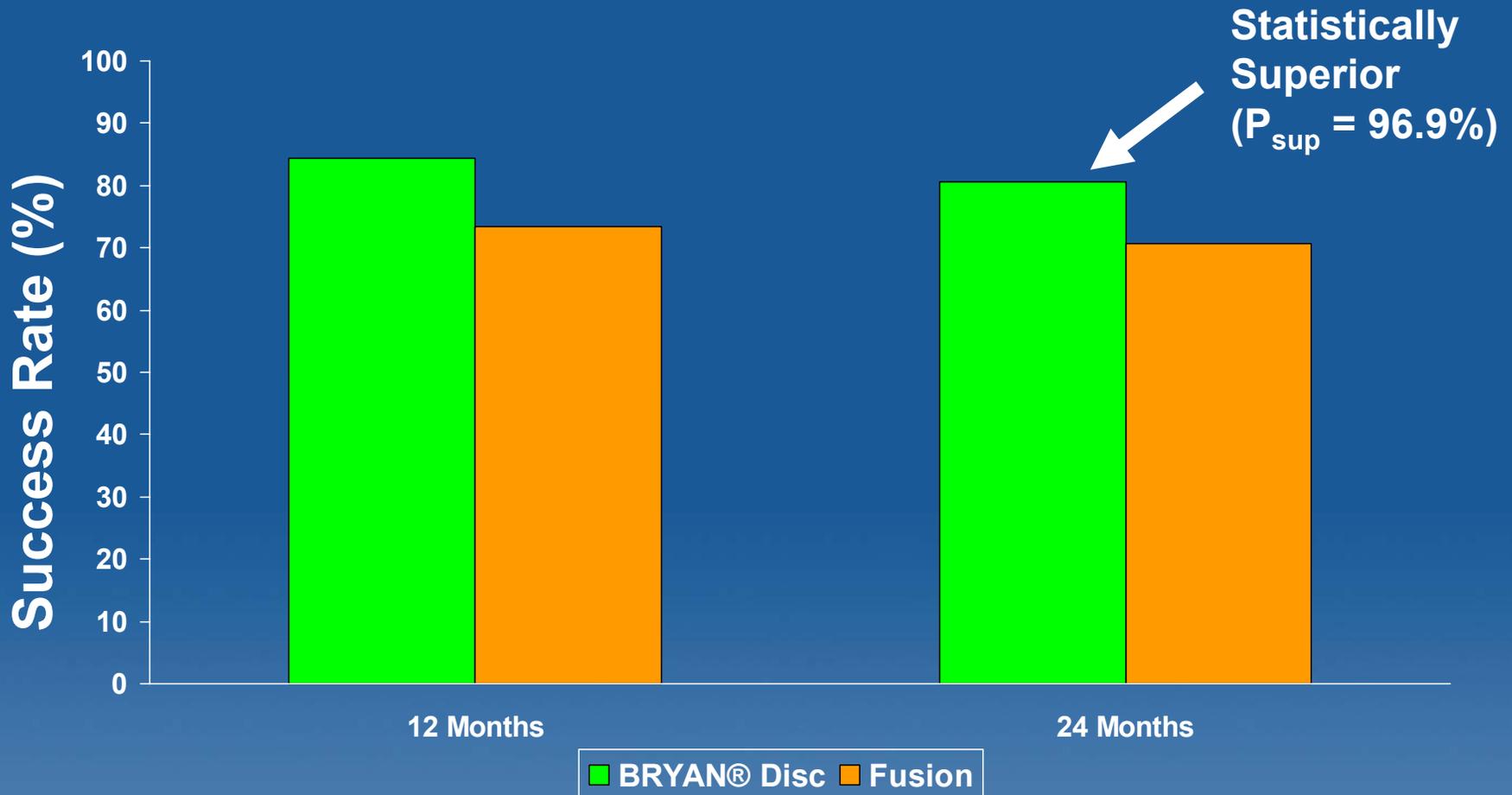


Overall Success

- ≥ 15 point improvement in NDI score
- Neurological maintenance or improvement
- No serious implant or implant/surgical procedure-associated adverse event
- No second surgery failure



Overall Success





Met and Surpassed Primary Objective



Safety Overview

- Neurological status
- Adverse events
- Second surgery procedures

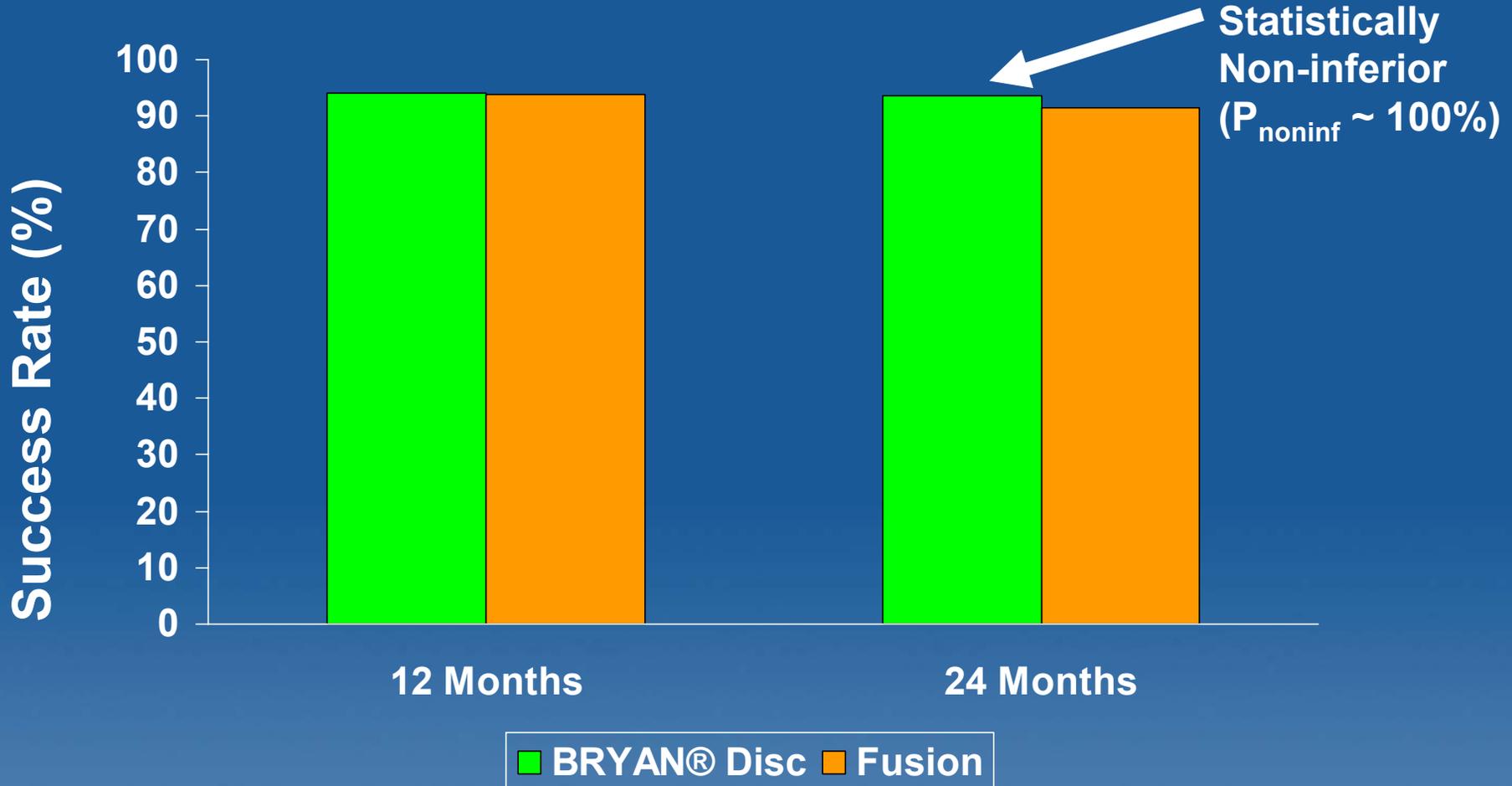


Neurological Status Measurements

- Motor Function
- Sensory
- Reflexes



Neurological Success Rates





Adverse Events



Adverse Events

	BRYAN® Disc	Fusion
At least 1 event (%)	83.5	78.7
WHO 3 or 4 (%)	26.4	24.9
Implant or implant/surgical procedure-associated (%)	2.9	5.4



Comparison of Adverse Events in BRYAN[®] Cervical Disc and Fusion Treatment Groups



Differences Noted

Lower in BRYAN[®] Cervical Disc group:

- Non-unions
- Pending non-unions



Cancer

BRYAN[®] Cervical Disc	2 (0.8%)
Fusion	0 (0.0%)



Deaths

BRYAN[®] Cervical Disc	0 (0.0%)
Fusion	1 (0.5%)



Adverse Events

- Typical for patient population
- Not unanticipated



Second Surgery Procedures



Classifications

- **Revisions** – Adjust implant position
- **Removals** – Remove implant
- **Supplemental Fixations** – Provide additional stabilization; includes bone growth stimulators
- **Reoperations** – Procedures at treated level that are not revisions, removals, or supplemental fixations
- **Other** – Procedures not at treated level

FAILURE



Secondary Interventions

Number of Patients

	BRYAN[®] Disc	Fusion
Revisions	1 (0.4)	0 (0.0)
Removals	3 (1.2)	2 (0.9)
Supplemental Fixations	0 (0.0)	5 (2.3)
Re-operations	2 (0.8)	1 (0.5)



Safety Summary

BRYAN[®] Cervical Disc patients as compared to fusion:

- Similar neurological success rate
- Similar adverse event rate
- Similar rate of secondary interventions



BRYAN[®] Cervical Disc

Safe for its intended use



Effectiveness Overview

BRYAN[®] Cervical Disc patients had:

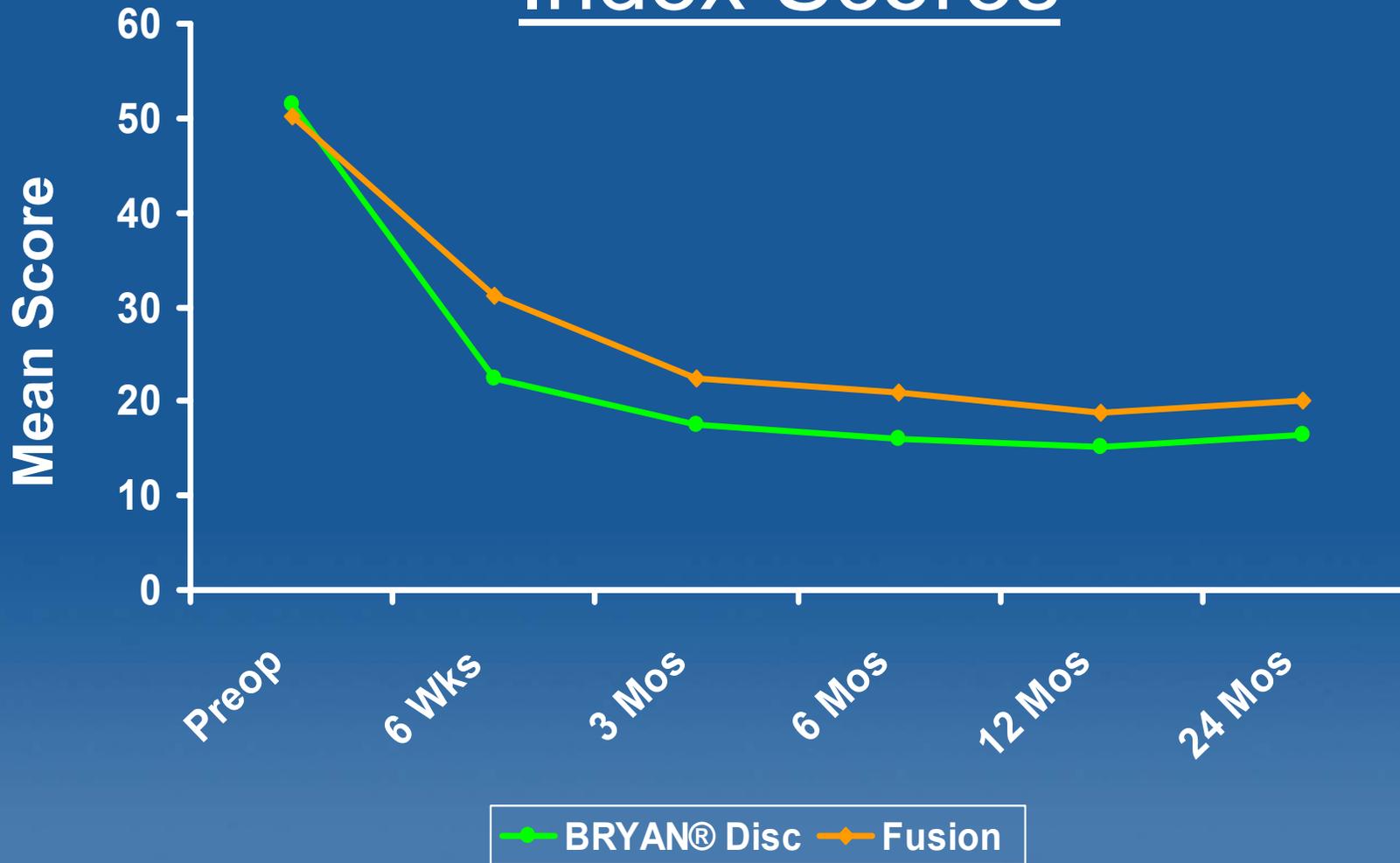
- Exceptional pain relief
- Maintenance of motion



Neck Disability Index (NDI) Questionnaire



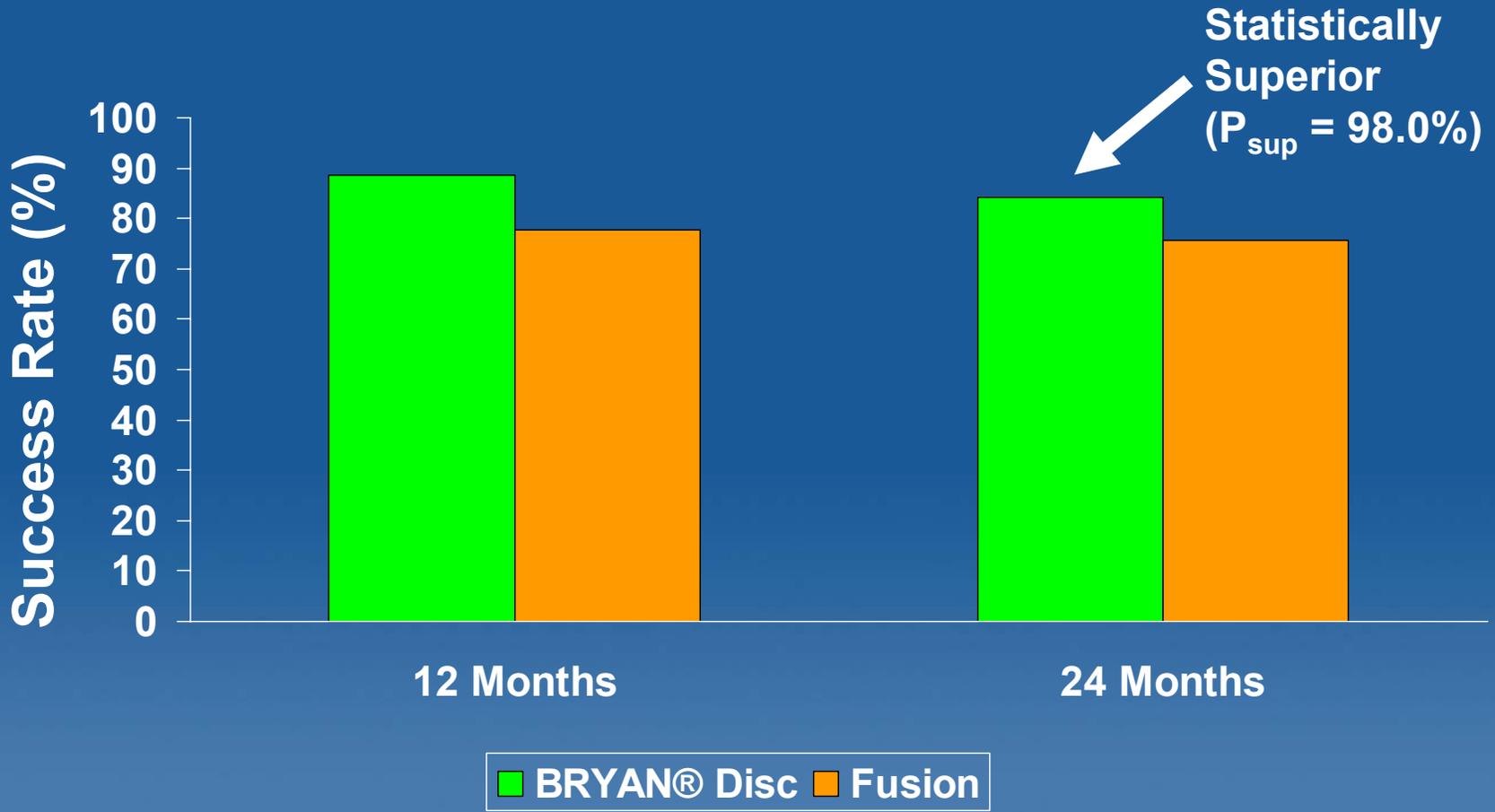
Mean Neck Disability Index Scores





Neck Disability Index Success

(Based on 15-Point Improvement)





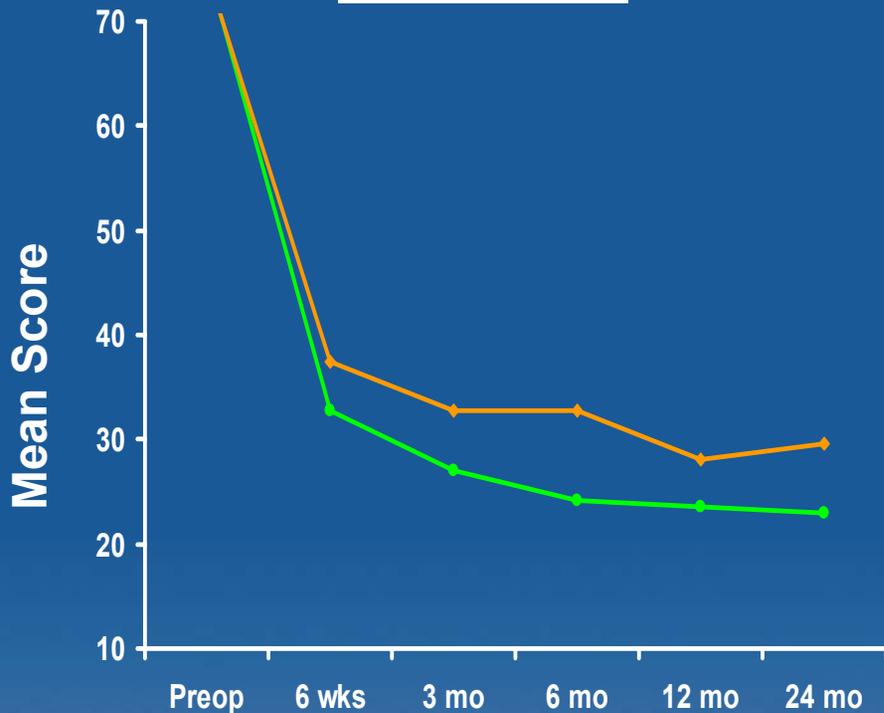
Secondary Effectiveness Endpoints

- Neck pain
- Arm pain
- Global perceived effect
- SF-36

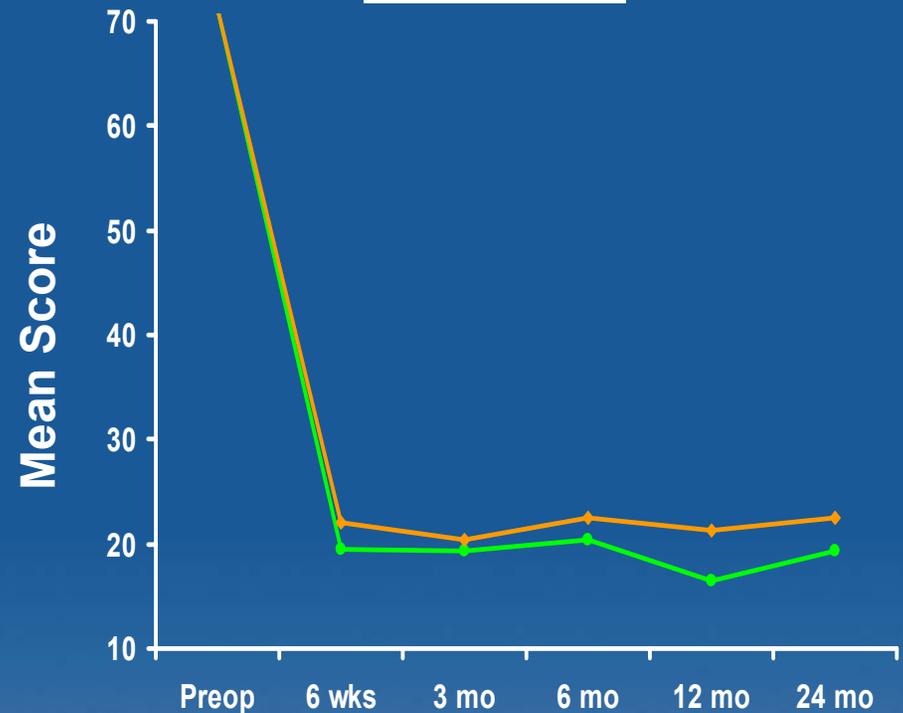


Mean Neck and Arm Pain Scores

Neck Pain



Arm Pain



■ BRYAN® Disc ◆ Fusion



Neck and Arm Pain Success

Neck Pain

Arm Pain

Statistically
Non-inferior
($P_{\text{noninf}} \sim 100\%$)



■ BRYAN® Disc ◆ Fusion



Patient Global Assessment

“Completely Recovered” or “Much Improved” Ratings

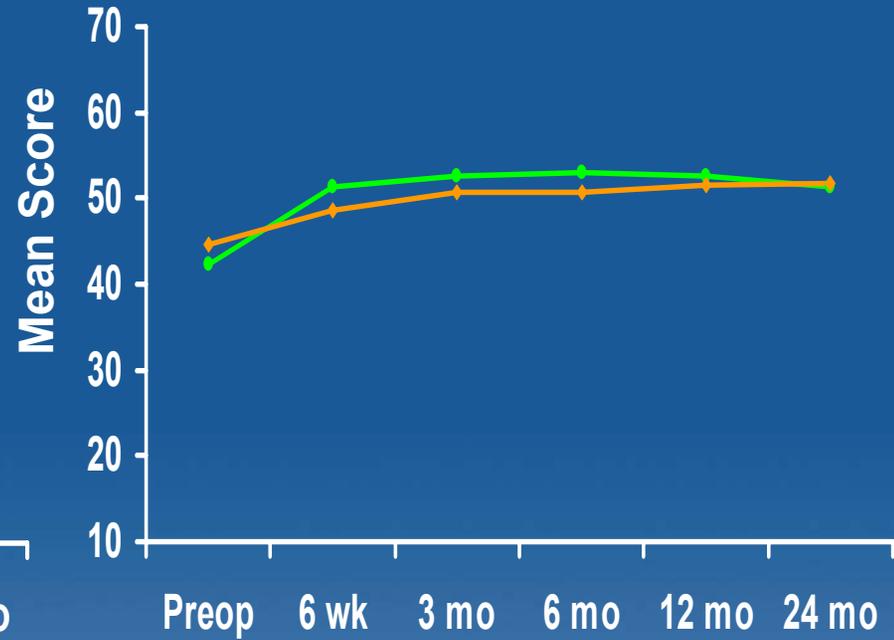
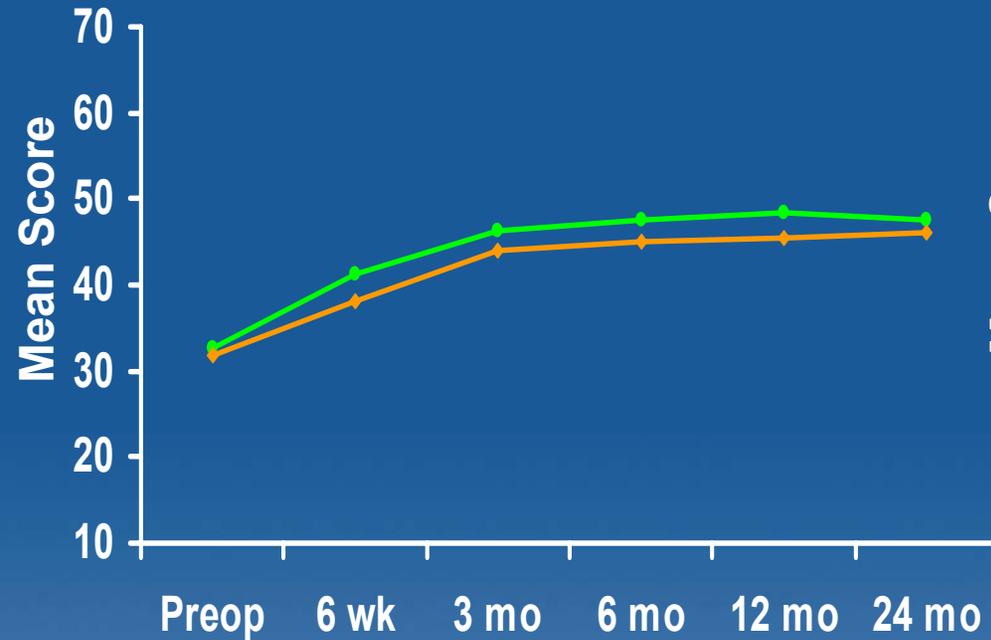




SF-36

PCS

MCS



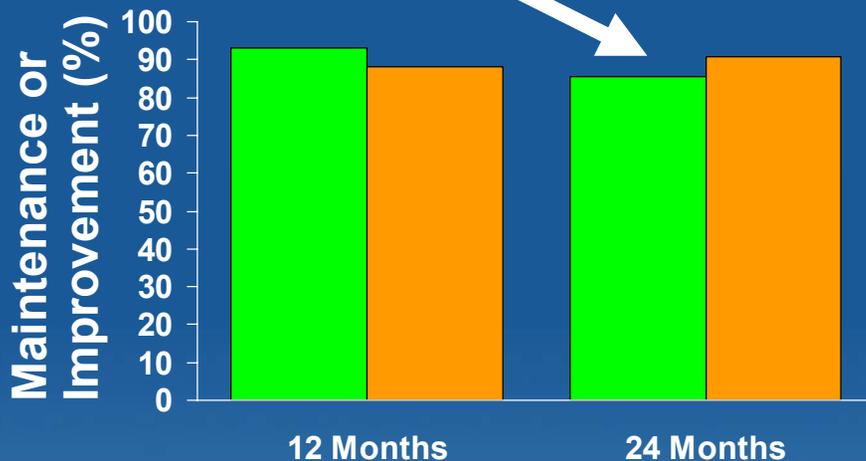
■ BRYAN® Disc ◆ Fusion



SF-36 Success

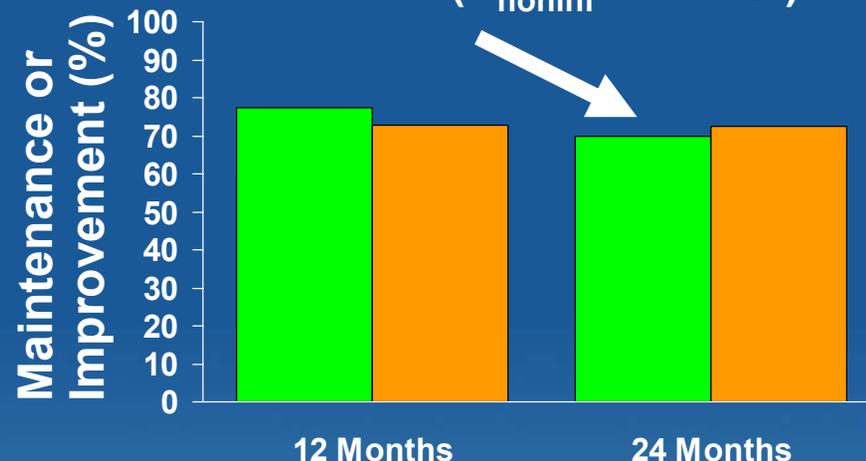
PCS

($P_{\text{noninf}} = 94.3\%$)



MCS

($P_{\text{noninf}} = 87.2\%$)





Radiographic Measurements





Functional Spinal Unit Height Success



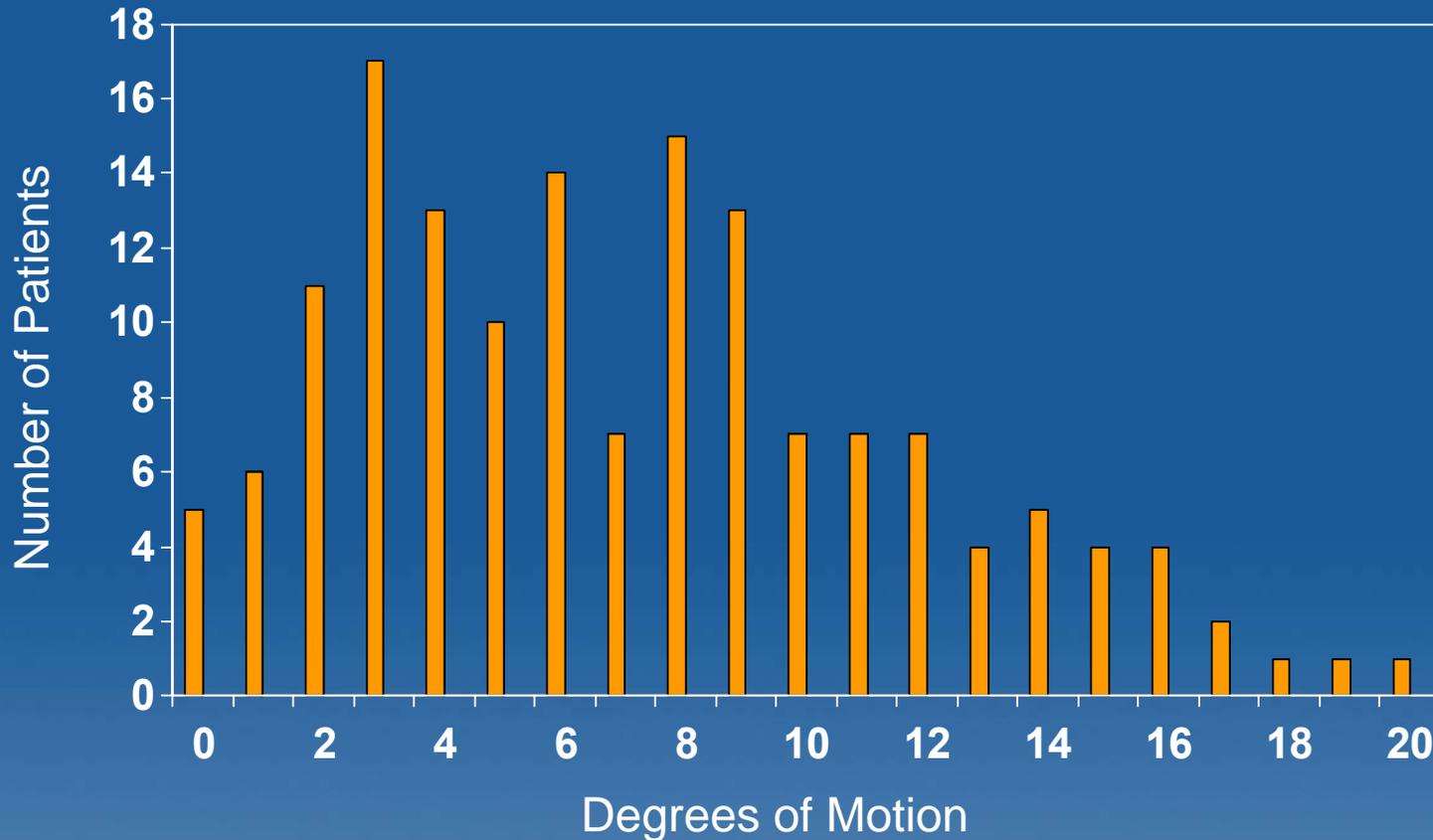


Flexion/Extension Motion Measurements





Flexion / Extension Motion Histogram – 24 Months





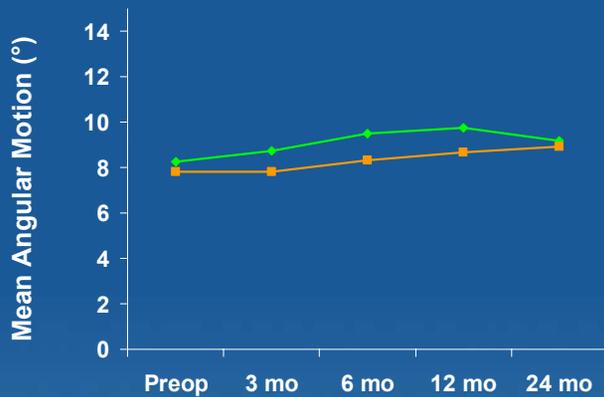
Lateral Bending Measurements



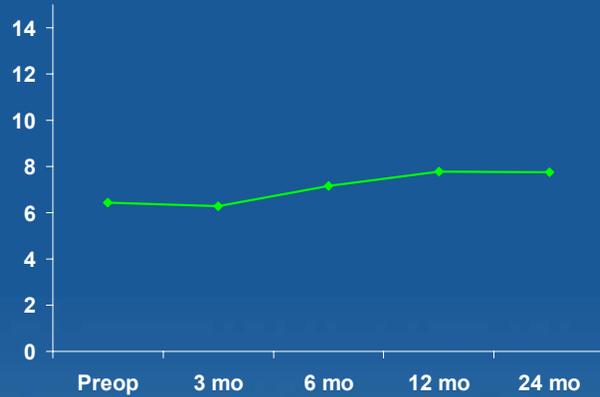


Adjacent Level Motion

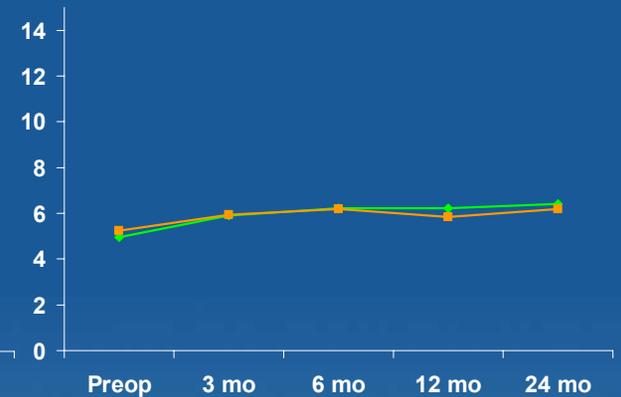
Level Above



Treated Level



Level Below



■ BRYAN® Disc ◆ Fusion



Fusion

- Criteria
 - Bridging bone
 - Segmental stability
 - Lucent line criteria
- 93% success at 24 months



Patient Satisfaction – 24 Months

“Definitely True” or “Mostly True” Ratings

	BRYAN® Disc	Fusion
Satisfied with results of surgery	95.5%	92.9%
Helped as much as they thought they would be	89.8%	83.5%
Would have the surgery again for same condition	94.3%	90.7%



Return to Work Median

BRYAN[®] Cervical Disc
Fusion

48 Days

61 Days

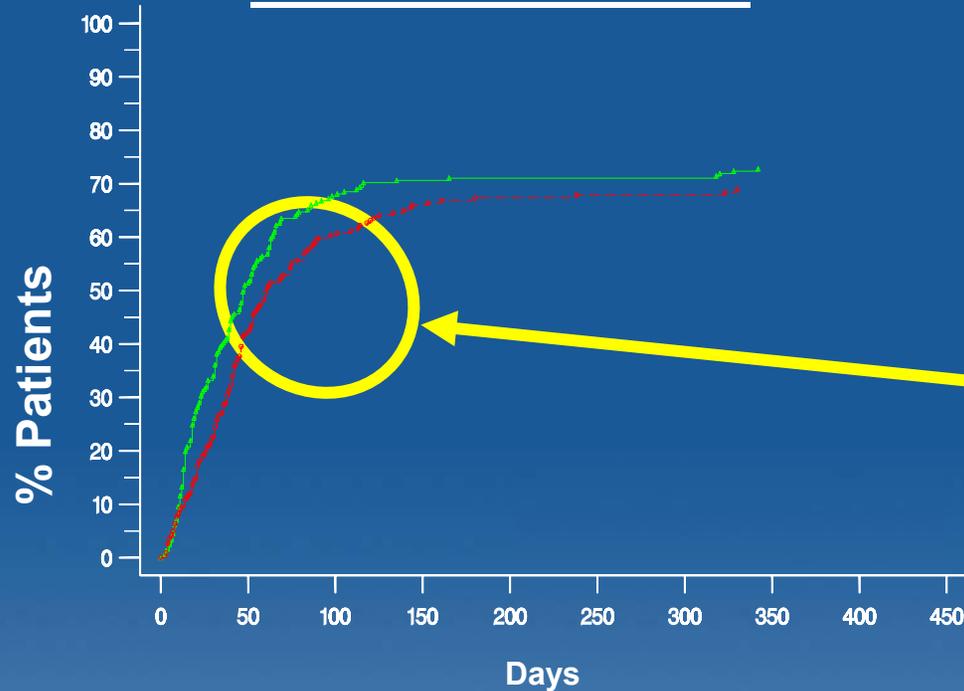
13
Days



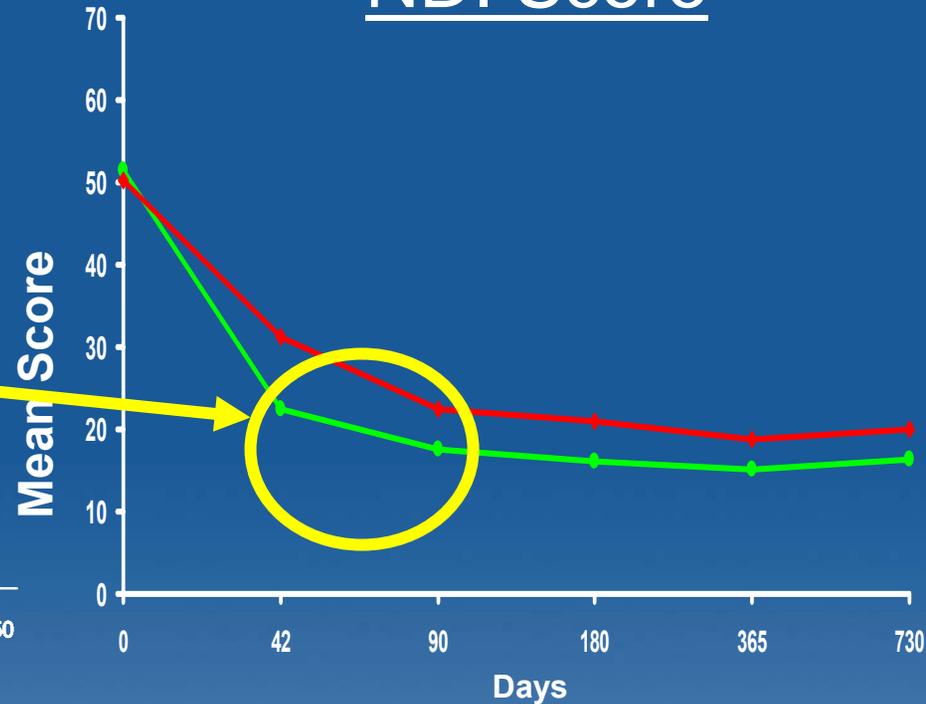


Comparison of Return to Work and Pain

Return to Work



NDI Score



■ BRYAN® Disc ◆ Fusion



All Available Data

- All available data at 24 months
 - 383 patients at 24 months; 431 patients at 12 months
 - ~ 82% of enrolled patients
- Same conclusions
 - BRYAN[®] Cervical Disc group statistically superior to fusion control for overall success and NDI
 - Arm pain success superior
 - SF-36 PCS and MCS non-inferior



Conclusions from Clinical Trial

- Achieved primary objective – overall success rate statistically non-inferior to control
- Statistical superiority to control – primary outcome variable
- Benefits – pain and neurological symptom relief with maintenance of motion



BRYAN[®] Cervical Disc

SAFE AND EFFECTIVE

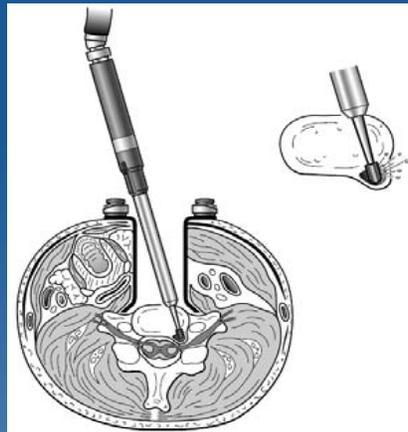
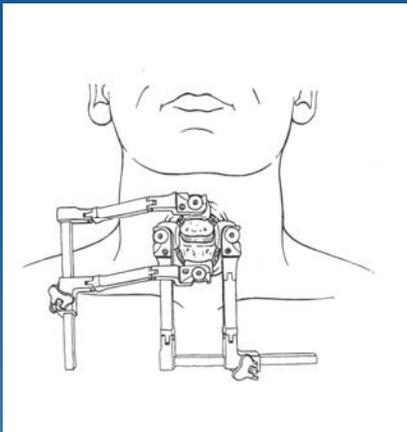
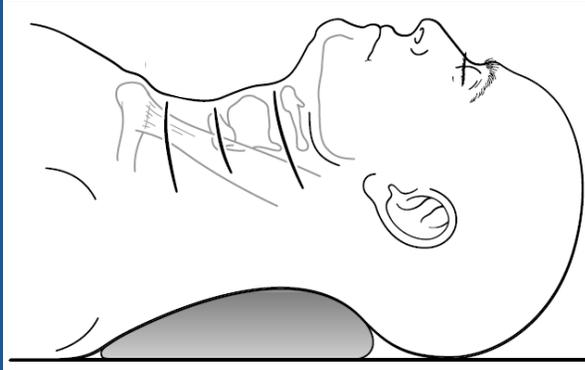
BRYAN® Cervical Disc Case Studies

Stephen Papadopoulos, M.D.
Barrow Neurological Institute
Phoenix, Arizona

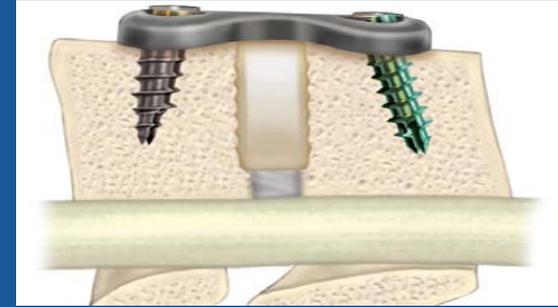




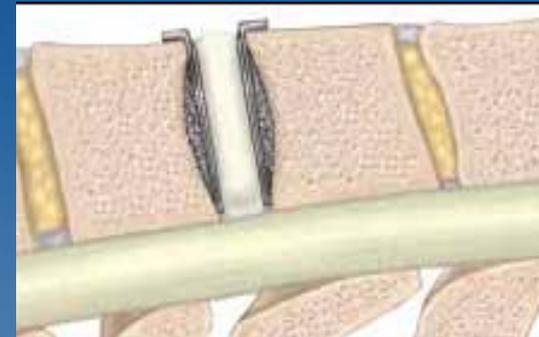
Surgical Technique Comparison



ATLANTIS® Plate

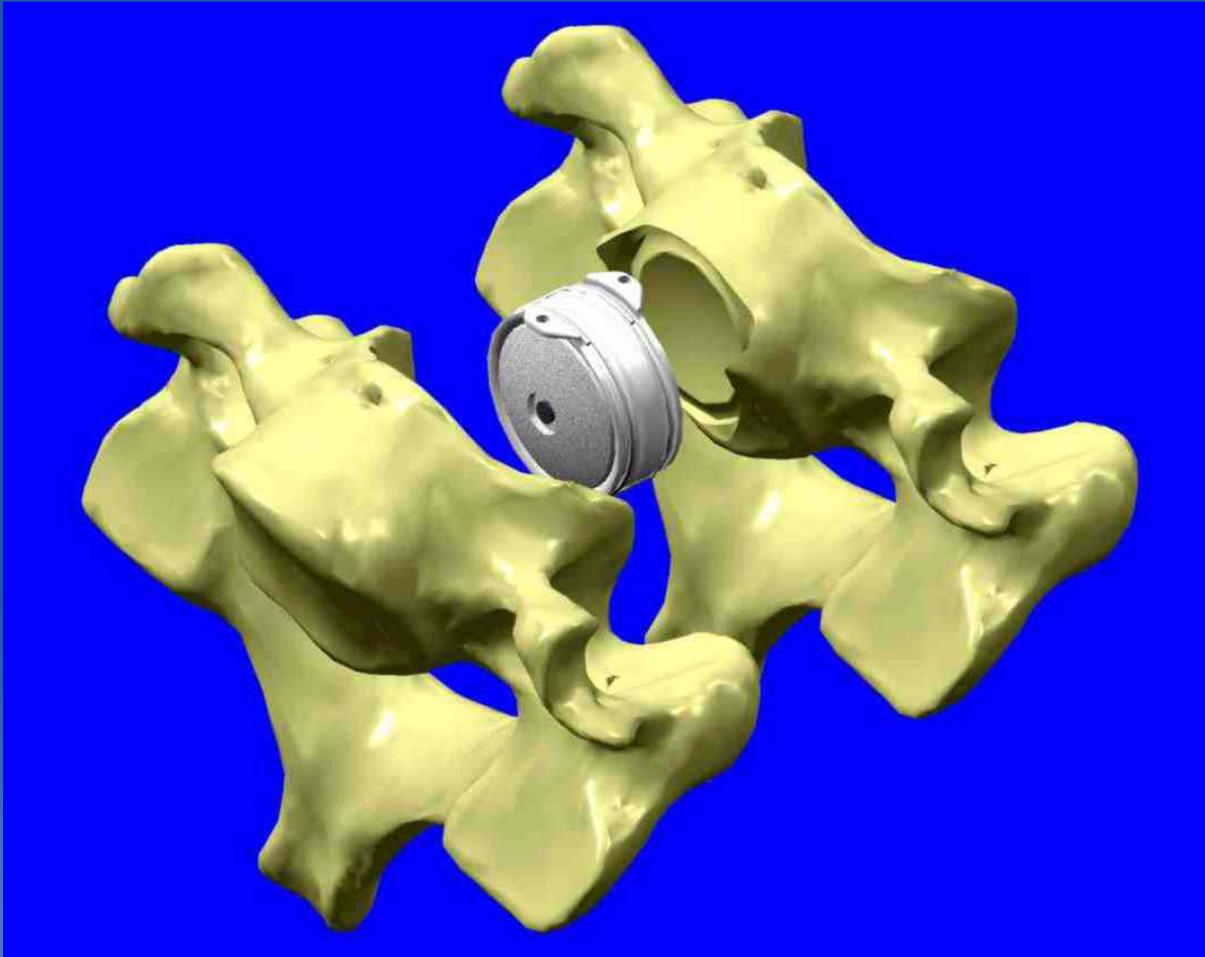


BRYAN® Disc





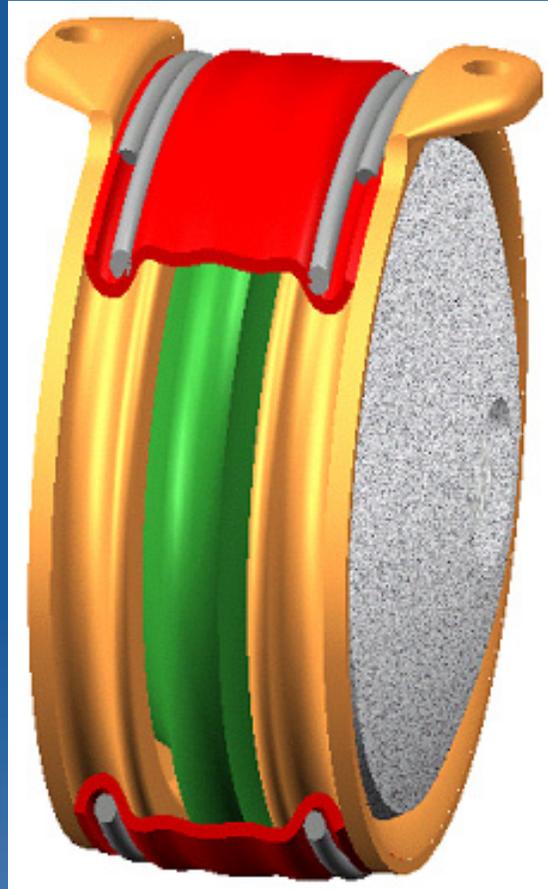
Precision Endplate Preparation





BRYAN[®] Cervical Disc Prosthesis

- Nucleus
- Shell with Rigid Wings
- Porous Coating on Shell Dome
- Sheath (shown cut away)
- Retaining Wires (shown cut away)



Note: Colors shown are not actual implant colors. Rather, they have been selected to illustrate the various prosthesis components. The wire/sheath/shell interface is fixed and is identical for all designs. The bone/shell interface is also present for all designs.



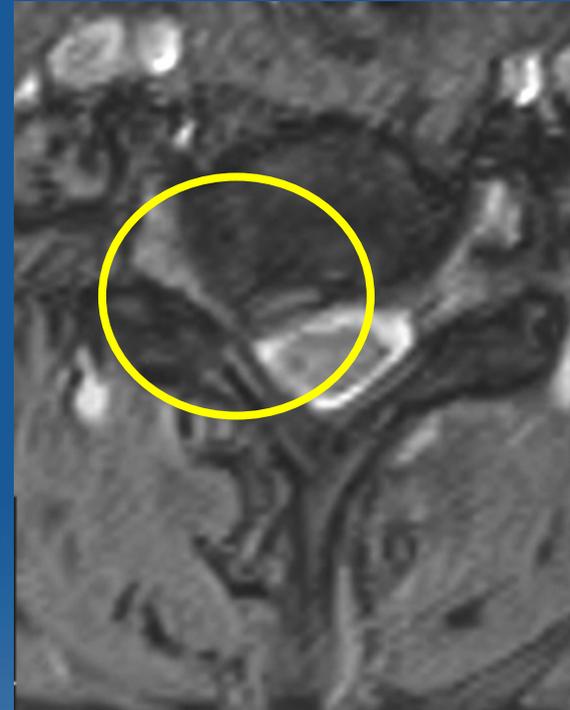
BRYAN[®] Disc IDE Study

Case Report #1

- Patient: 45-year-old female
- Occupation: Veterinary technician
- Diagnosis: Radiculopathy with herniated disc and osteophyte formation
- Treatment: C6-C7 ACD w/ BRYAN[®] Disc - July 2003



Preop MRI





Preop X-Rays*



*5.5° C6-C7 motion



2-Year X-Rays



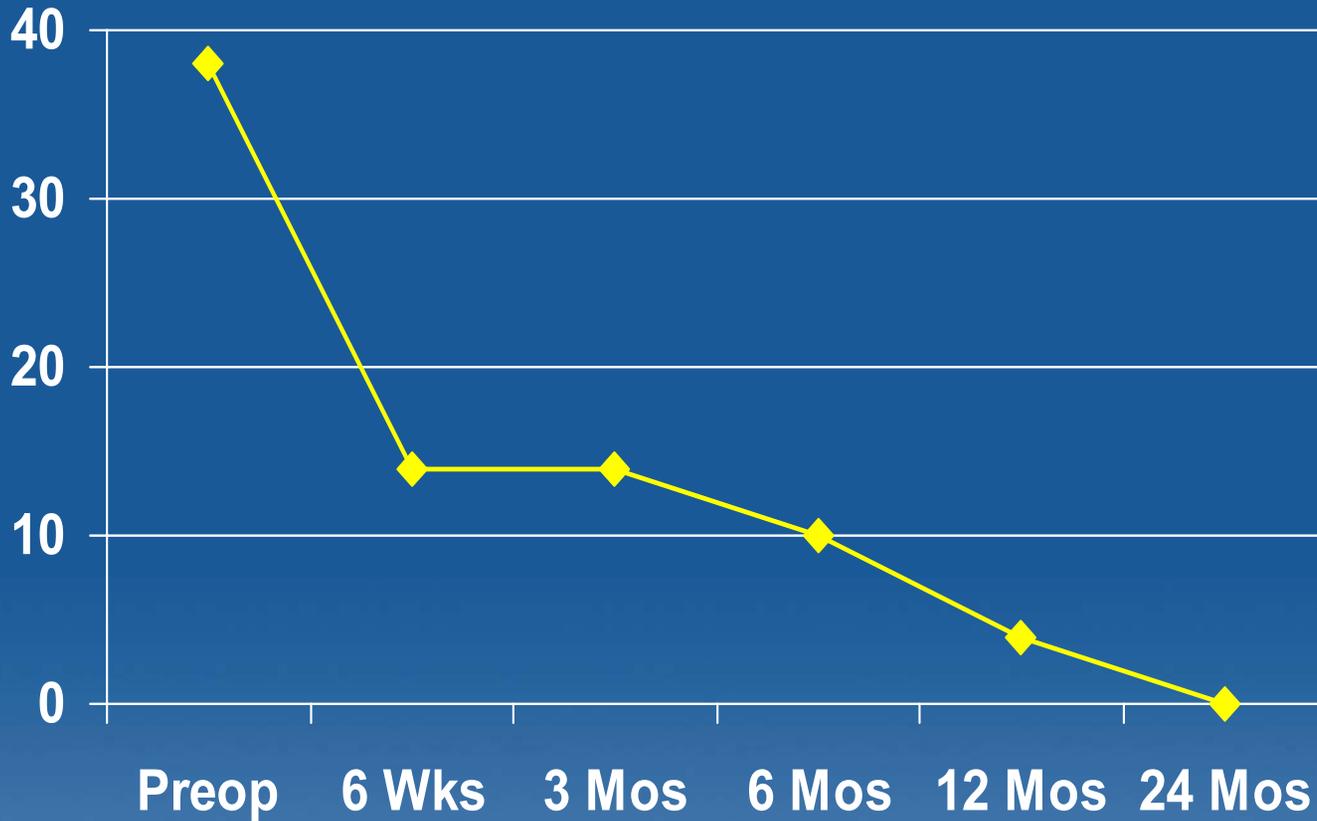


2-Year X-Rays



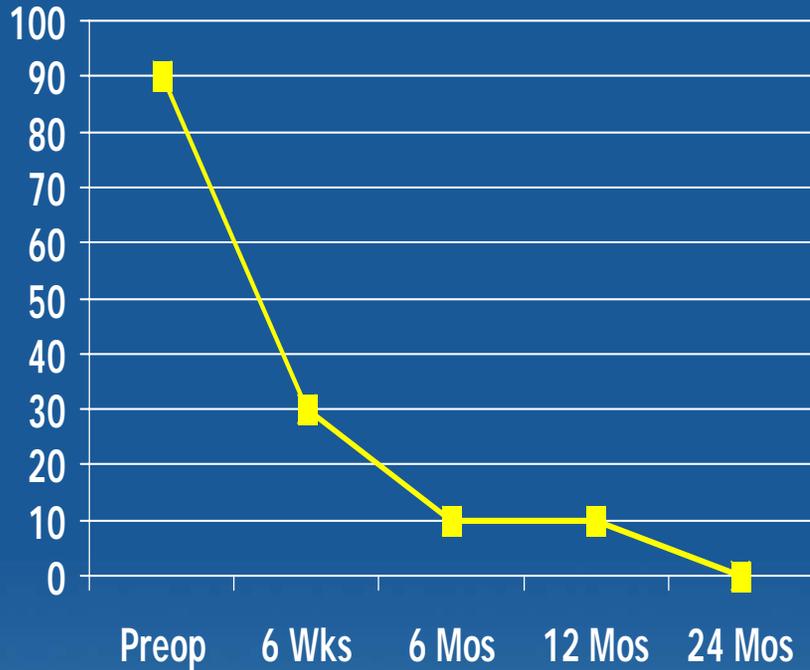


Neck Disability Index Scores

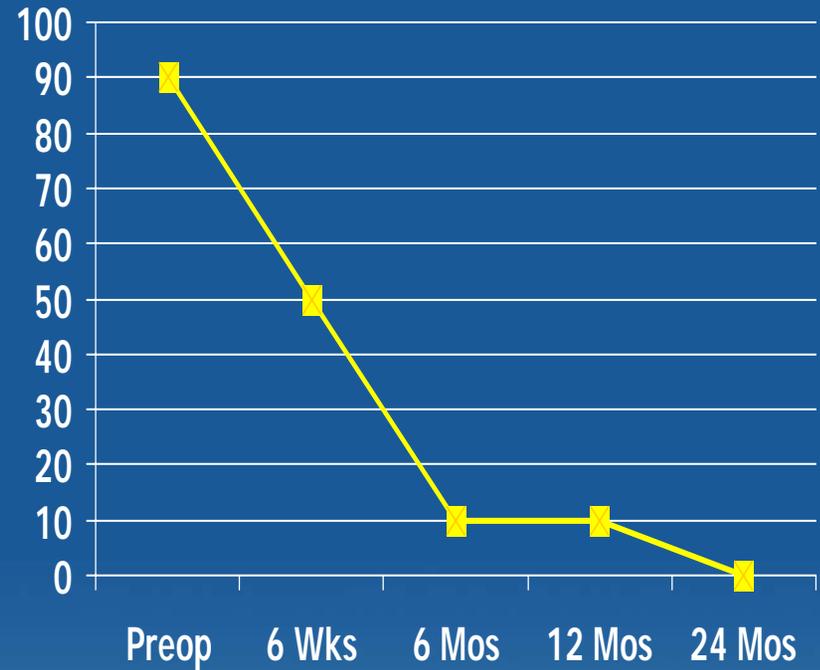




Neck and Arm Pain Scores



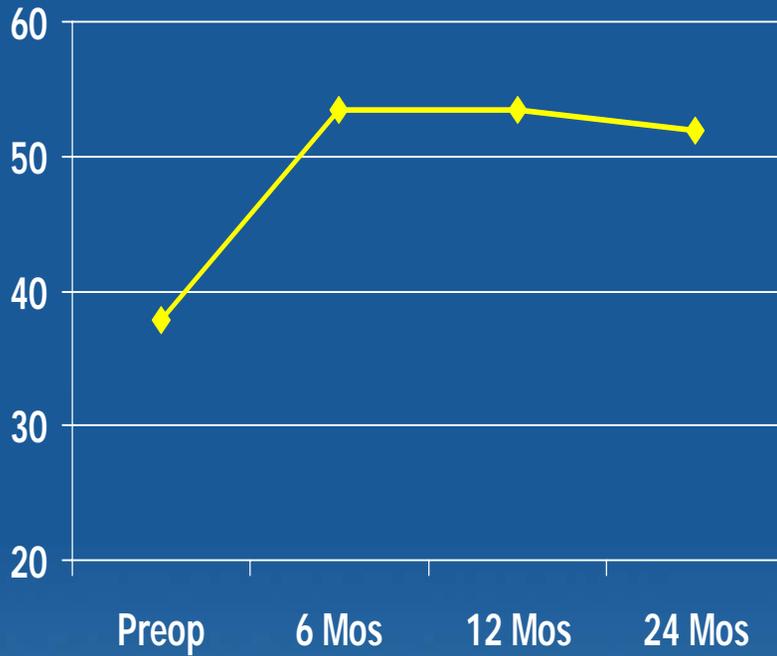
■ Neck Pain



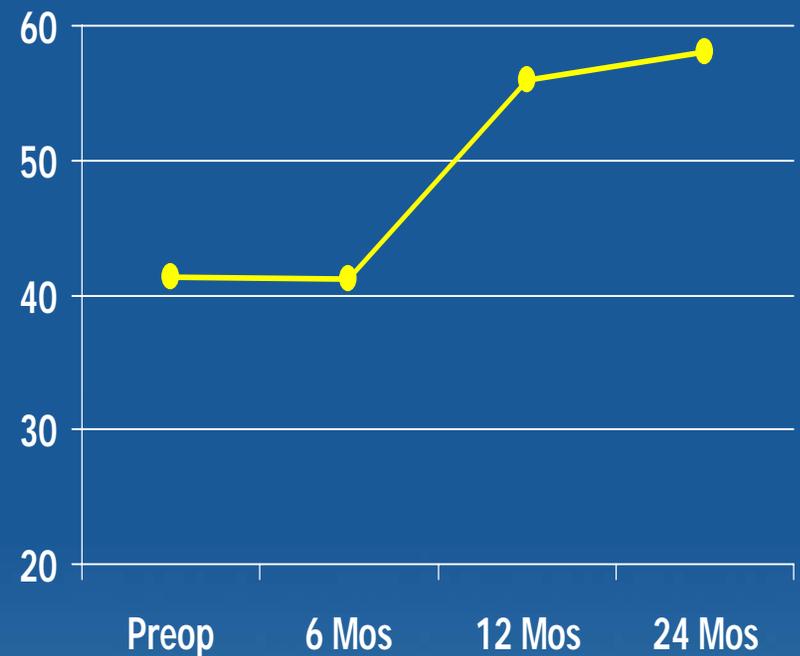
■ Arm Pain



SF-36 PCS and MCS Scores



◆ PCS



● MCS



4-Year X-Rays





4-Year X-Rays





Secondary Interventions

Number of Patients

	BRYAN® Disc	Fusion
Revisions	1 (0.4)	0 (0.0)
Removals	3 (1.2)	2 (0.9)
Supplemental Fixations	0 (0.0)	5 (2.3)
Re-operations	2 (0.8)	1 (0.5)



BRYAN[®] Disc IDE Study

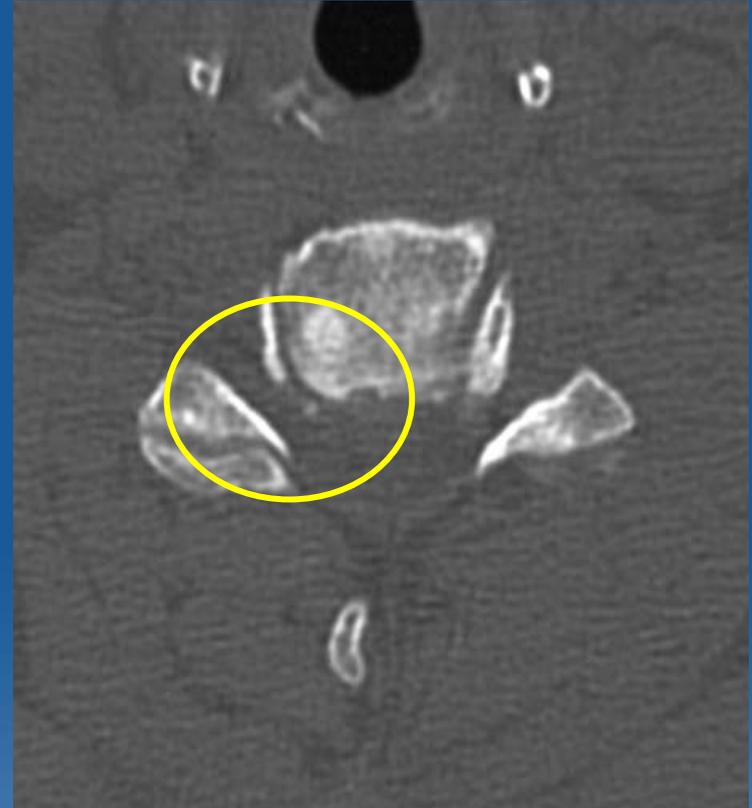
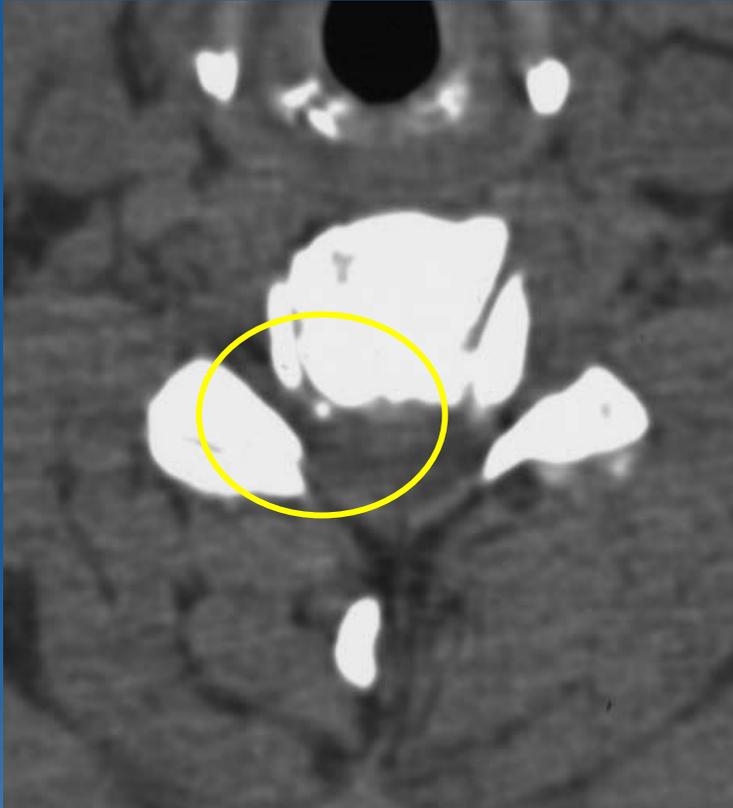
Case Report #2

- Patient: 40-year-old female
- Occupation: Secretary
- Diagnosis: Radiculopathy with herniated disc and osteophyte formation
- Treatment: C5-C6 ACD w/ BRYAN[®] Disc - May 2003



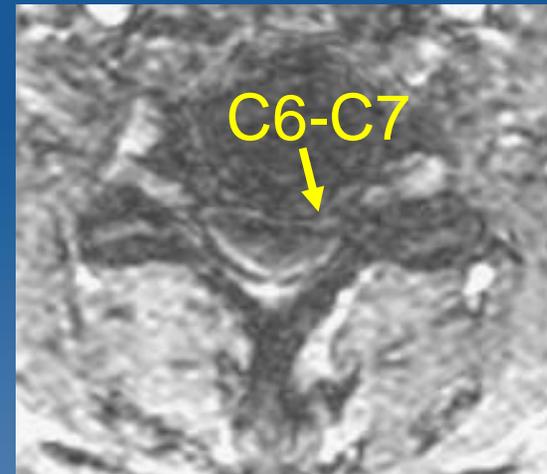
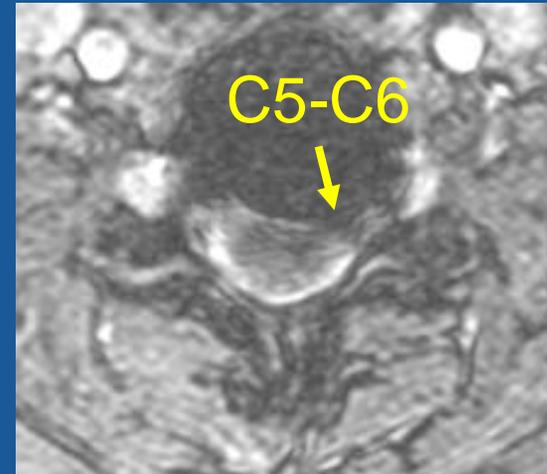


Preop CT Scan





Postoperative MRI





BRYAN[®] Disc Explant Procedure

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



BRYAN® Disc Explant Analysis

Nucleus, shells, and sheath condition:

- Highly polished appearance of articulating surfaces of shells
- Nucleus and sheath well-preserved



* Note: Nucleus stored in formalin



BRYAN[®] Disc European Study

Case Report #3

- Surgeon: Jan Goffin, MD, PhD, Leuven, Belgium
- Patient: 41-year-old female
- Occupation: Janitor
- Diagnosis: Radiculopathy with herniated disc and osteophyte formation
- Treatment: C5-C6 ACD w/ BRYAN[®] Disc – Jan. 2000



Preop Images

MRI



X-Ray





6-Year X-Rays





6-Year Range of Motion



BRYAN[®] Cervical Disc Proposed Post-Approval Study

Hallett Mathews, MD
Vice President, Medical Affairs
Medtronic Spinal and Biologics





Patient Evaluations & Sample Size

- Evaluation timepoints
 - 4 years
 - 5 years
 - 7 years
- Minimum of 200 patients
 - 100 each from control & investigational
 - Includes pivotal and continued access



Endpoints

Same as IDE study

- Overall success
 - NDI improvement
 - Neurological status maintenance or improvement
 - No adverse event classified as serious and implant- or implant/surgical procedure-associated
 - No secondary procedure classified as failure
- Other endpoints



Analysis

- Similar to IDE
- Non-inferiority of BRYAN[®] Cervical Disc group to control at 7 years



Reporting

- 6-month intervals for first 2 years after approval
- Annually thereafter



Questions Raised by FDA

- Motion measurements at treated and adjacent levels, adjacent-level disease



Questions Raised by FDA

- Motion measurements at treated and adjacent levels, adjacent-level disease
- Heterotopic ossification, kyphosis



Questions Raised by FDA

- Motion measurements at treated and adjacent levels, adjacent-level disease
- Heterotopic ossification, kyphosis
- Recruitment of new patients

BRYAN[®] Cervical Disc Concluding Remarks

Kathryn H. Simpson, PhD
Medtronic Spinal and Biologics





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



FDA Questions to the Panel

- Adequacy of preclinical testing



FDA Questions to the Panel

- Adequacy of preclinical testing
- Motion measurements



FDA Questions to the Panel

- Adequacy of preclinical testing
- Motion measurements
- Adequacy of labeling

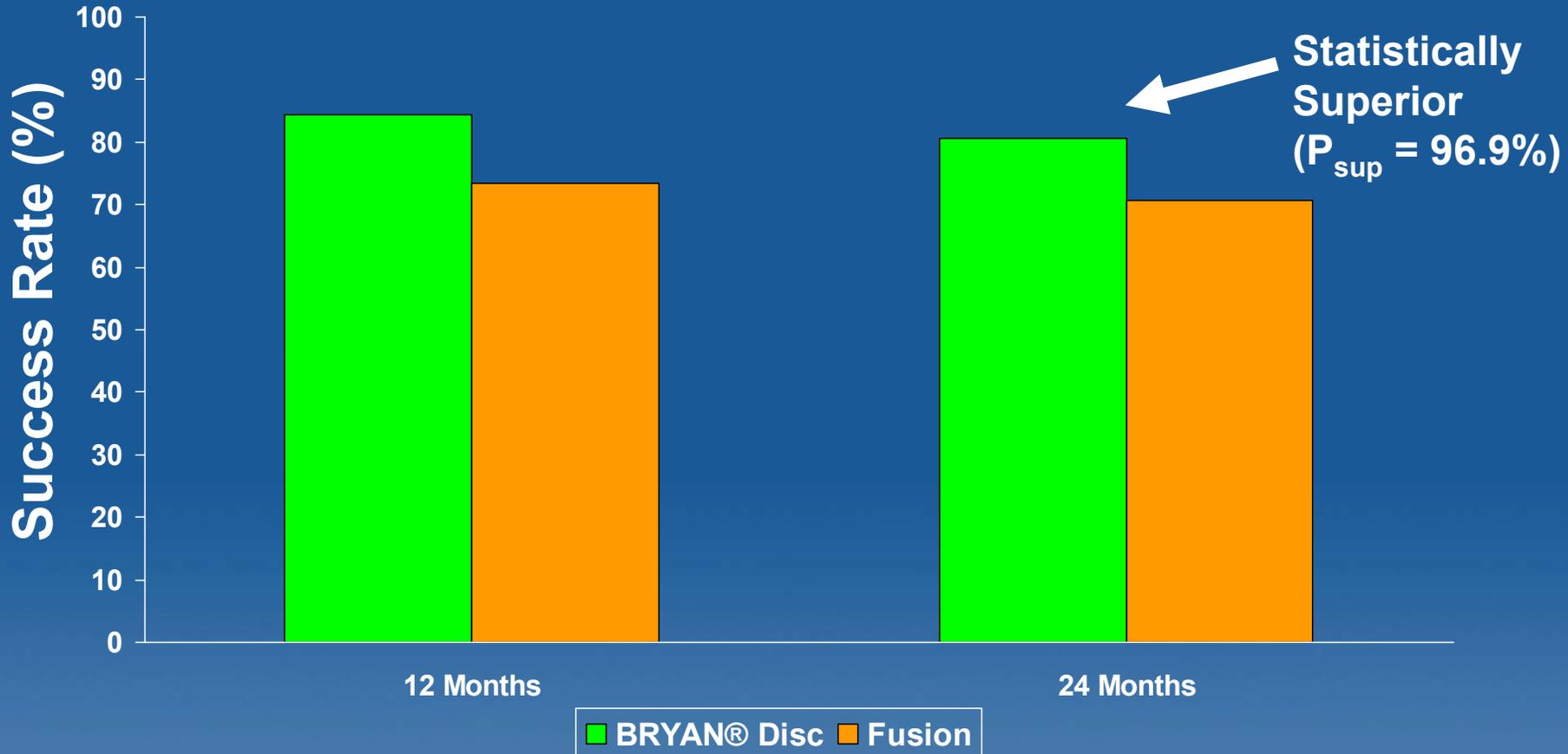


FDA Questions to the Panel

- Adequacy of preclinical testing
- Motion measurements
- Adequacy of labeling
- Safety
- Effectiveness



Overall Success





FDA Questions to the Panel

- Adequacy of preclinical testing
- Motion measurements
- Adequacy of labeling
- Safety
- Effectiveness
- Superiority claims



Comparison of Analyses

Dataset	Posterior Probability of Overall Success Superiority (%)	
	1st 300 patients	All available data
Primary	96.9	98.7
Per-protocol	94.4	96.0
Intent-to-treat	97.6	97.7



Overall Success at 24 Months

Endpoint	BRYAN Disc (%)	Fusion (%)
NDI	84.3*	75.7
Neurological	93.7	91.4
Overall Success	80.6*	70.7

* Statistical Superiority



BRYAN[®] Cervical Disc

**Reasonable Assurance of
Safety and Effectiveness**



Thank You