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

1. Review Design Intent
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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
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  – Rabbit study

• Retrieval Analyses
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
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

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  - 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
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
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
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
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

![Graph showing wear rate (mm³/MC) for different cervical discs and UHMWPE THR types.]

- BRYAN® Cervical Disc
- Highly X-Linked UHMWPE THR *
- Conventional UHMWPE THR **

* 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

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- **Implant Stability**
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  - 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
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• Biocompatibility Testing

• Animal Studies
  – Chimpanzee study
  – Goat study
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• 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
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.”

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- **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)
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  – 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

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
<table>
<thead>
<tr>
<th>Tissue</th>
<th>Baseline (n=1)</th>
<th>3 month (n=3)</th>
<th>6 month (n=3)</th>
<th>12 month (n=3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local tissues</td>
<td>no particles</td>
<td>no particles</td>
<td>2 part., 1 macro.</td>
<td>no particles</td>
</tr>
<tr>
<td>Spinal</td>
<td>no particles</td>
<td>no particles</td>
<td>2 part., no rxn</td>
<td>1 part., no rxn</td>
</tr>
<tr>
<td>Lymph nodes</td>
<td>no particles</td>
<td>N/A (thymus)</td>
<td>no particles</td>
<td>no particles</td>
</tr>
<tr>
<td>Liver</td>
<td>no particles</td>
<td>no particles</td>
<td>no particles</td>
<td>no particles</td>
</tr>
<tr>
<td>Spleen</td>
<td>no particles</td>
<td>no particles</td>
<td>no particles</td>
<td>no particles</td>
</tr>
</tbody>
</table>
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

![Graph showing particle size distribution with two categories: Rabbit Model - Nucleus and Wear Test Particles. The x-axis represents particle diameter in micrometers (μm) ranging from 0 to 20, while the y-axis represents number (%) ranging from 0% to 50%. The graph includes bars for different particle diameter ranges, with variations in height indicating the percentage of particles in each range.](Image)
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  - 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

<table>
<thead>
<tr>
<th></th>
<th>BRYAN® Disc</th>
<th>Fusion</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (yrs.)</td>
<td>44</td>
<td>45</td>
<td>0.723</td>
</tr>
<tr>
<td>Weight, mean (lbs.)</td>
<td>173</td>
<td>180</td>
<td>0.061</td>
</tr>
<tr>
<td>Height, mean (in.)</td>
<td>68</td>
<td>68</td>
<td>0.991</td>
</tr>
<tr>
<td>Sex (% male)</td>
<td>46</td>
<td>51</td>
<td>0.228</td>
</tr>
<tr>
<td>Worker’s Compensation (%)</td>
<td>6</td>
<td>5</td>
<td>0.687</td>
</tr>
<tr>
<td>Spinal Litigation (%)</td>
<td>2</td>
<td>3</td>
<td>1.000</td>
</tr>
</tbody>
</table>
## Surgery Data

<table>
<thead>
<tr>
<th></th>
<th>BRYAN® Disc</th>
<th>Fusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operative Time, mean (hrs.)</td>
<td>2.2</td>
<td>1.4</td>
</tr>
<tr>
<td>Blood Loss, mean (ml)</td>
<td>91.5</td>
<td>59.6</td>
</tr>
<tr>
<td>Hospital Stay, mean (days)</td>
<td>1.1</td>
<td>1.0</td>
</tr>
</tbody>
</table>
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

Statistically Superior (P_{sup} = 96.9\%)
Met and Surpassed Primary Objective
Safety Overview

- Neurological status
- Adverse events
- Second surgery procedures
Neurological Status Measurements

- Motor Function
- Sensory
- Reflexes
Neurological Success Rates

- **Success Rate (%)**
- **12 Months**
- **24 Months**
- **Statistically Non-inferior**
  - $P_{\text{noninf}} \sim 100\%$

**Graph Legend**
- **BRYAN® Disc**
- **Fusion**
Adverse Events
## Adverse Events

<table>
<thead>
<tr>
<th>Event</th>
<th>BRYAN® Disc</th>
<th>Fusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>At least 1 event (%)</td>
<td>83.5</td>
<td>78.7</td>
</tr>
<tr>
<td>WHO 3 or 4 (%)</td>
<td>26.4</td>
<td>24.9</td>
</tr>
<tr>
<td>Implant or implant/surgical procedure-associated (%)</td>
<td>2.9</td>
<td>5.4</td>
</tr>
</tbody>
</table>
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
<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>BRYAN® Cervical Disc</strong></td>
<td>2 (0.8%)</td>
</tr>
<tr>
<td><strong>Fusion</strong></td>
<td>0 (0.0%)</td>
</tr>
</tbody>
</table>
## Deaths

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Deaths</th>
<th>Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRYAN® Cervical Disc</td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td>Fusion</td>
<td>1</td>
<td>0.5%</td>
</tr>
</tbody>
</table>
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
## Secondary Interventions

### Number of Patients

<table>
<thead>
<tr>
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<th>Fusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Revisions</td>
<td>1 (0.4)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Removals</td>
<td>3 (1.2)</td>
<td>2 (0.9)</td>
</tr>
<tr>
<td>Supplemental Fixations</td>
<td>0 (0.0)</td>
<td>5 (2.3)</td>
</tr>
<tr>
<td>Re-operations</td>
<td>2 (0.8)</td>
<td>1 (0.5)</td>
</tr>
</tbody>
</table>
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

Mean Score

Preop  6 Wks  3 Mos  6 Mos  12 Mos  24 Mos

BRYAN® Disc  Fusion

Medtronic
Neck Disability Index Success
(Based on 15-Point Improvement)

Success Rate (%)

12 Months
24 Months

Statistically Superior
($P_{sup} = 98.0\%$)

BRYAN® Disc
Fusion

Medtronic
Secondary Effectiveness Endpoints

- Neck pain
- Arm pain
- Global perceived effect
- SF-36
Mean Neck and Arm Pain Scores

Neck Pain

Arm Pain

Mean Score

Mean Score

Preop  6 wks  3 mo  6 mo  12 mo  24 mo

Preop  6 wks  3 mo  6 mo  12 mo  24 mo

BRYAN® Disc  Fusion

Medtronic
Neck and Arm Pain Success

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

Arm Pain:

BRYAN® Disc vs. Fusion

12 Months: Maintenance or Improvement (%)
- 100%
- 90%
- 80%
- 70%
- 60%
- 50%
- 40%
- 30%
- 20%
- 10%
- 0%

24 Months: Maintenance or Improvement (%)
- 100%
- 90%
- 80%
- 70%
- 60%
- 50%
- 40%
- 30%
- 20%
- 10%
- 0%
Patient Global Assessment
“Completely Recovered” or “Much Improved” Ratings

<table>
<thead>
<tr>
<th>Completely Recovered or Much Improved (%)</th>
<th>12 Months</th>
<th>24 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRYAN® Disc</td>
<td>95</td>
<td>92</td>
</tr>
<tr>
<td>Fusion</td>
<td>80</td>
<td>85</td>
</tr>
</tbody>
</table>

BRYAN® Disc 95% Completely Recovered or Much Improved at 12 Months, 92% at 24 Months. Fusion 80% Completely Recovered or Much Improved at 12 Months, 85% at 24 Months.
SF-36 Success

**PCS**

(P_{noninf} = 94.3%)

**MCS**

(P_{noninf} = 87.2%)

**Maintenance or Improvement (%)**

12 Months  |  24 Months

- **BRYAN® Disc**
- **Fusion**
Radiographic Measurements
Functional Spinal Unit Height Success

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

Success Rate (%)

12 Months 24 Months

BRYAN® Disc Fusion
Flexion/Extension Motion Measurements

Mean Angular Motion (°)

Preop | 3 Mos | 6 Mos | 12 Mos | 24 Mos

BRYAN® Disc
Flexion / Extension Motion
Histogram – 24 Months

Degrees of Motion

Number of Patients

0 2 4 6 8 10 12 14 16 18 20
Adjacent Level Motion

Level Above

Treated Level

Level Below

Mean Angular Motion (°)

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

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<tr>
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</thead>
<tbody>
<tr>
<td>Satisfied with results of surgery</td>
<td>95.5%</td>
<td>92.9%</td>
</tr>
<tr>
<td>Helped as much as they thought they would be</td>
<td>89.8%</td>
<td>83.5%</td>
</tr>
<tr>
<td>Would have the surgery again for same condition</td>
<td>94.3%</td>
<td>90.7%</td>
</tr>
</tbody>
</table>
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

Days

% Patients

Mean Score

BRYAN® Disc

Fusion

Medtronic
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 X-Rays*

*5.5° C6-C7 motion
2-Year X-Rays
2-Year X-Rays
Neck Disability Index Scores

Preop 6 Wks 3 Mos 6 Mos 12 Mos 24 Mos
Neck and Arm Pain Scores

Neck Pain

Arm Pain
SF-36 PCS and MCS Scores

- PCS
- MCS
4-Year X-Rays
## Secondary Interventions

**Number of Patients**

<table>
<thead>
<tr>
<th></th>
<th>BRYAN® Disc</th>
<th>Fusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Revisions</td>
<td>1 (0.4)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Removals</td>
<td>3 (1.2)</td>
<td>2 (0.9)</td>
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<tr>
<td>Supplemental Fixations</td>
<td>0 (0.0)</td>
<td>5 (2.3)</td>
</tr>
<tr>
<td>Re-operations</td>
<td>2 (0.8)</td>
<td>1 (0.5)</td>
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</tbody>
</table>
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

C5-C6

C6-C7
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

[Images of MRI and 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
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

Statistically Superior
($P_{sup} = 96.9\%$)
FDA Questions to the Panel

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

<table>
<thead>
<tr>
<th>Dataset</th>
<th>Posterior Probability of Overall Success Superiority (%)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>1st 300 patients</td>
</tr>
<tr>
<td>Primary</td>
<td>96.9</td>
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<tr>
<td>Per-protocol</td>
<td>94.4</td>
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<tr>
<td>Intent-to-treat</td>
<td>97.6</td>
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# Overall Success at 24 Months

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>BRYAN Disc (%)</th>
<th>Fusion (%)</th>
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</thead>
<tbody>
<tr>
<td>NDI</td>
<td>84.3*</td>
<td>75.7</td>
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<tr>
<td>Neurological</td>
<td>93.7</td>
<td>91.4</td>
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<tr>
<td><strong>Overall Success</strong></td>
<td><strong>80.6</strong>*</td>
<td><strong>70.7</strong></td>
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</table>

* Statistical Superiority
BRYAN® Cervical Disc

Reasonable Assurance of Safety and Effectiveness
Thank You