Evidenced Based Outcomes for Lumbar Motion Preservation Devices

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Disclosures

- Consultant - Aesculap
- Royalties - Activ L

What is Evidence Based?

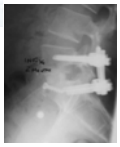
- Evidence based - denoting disciplines of health care that proceed empirically with regard to the patient and reject more traditional protocols.
- Empirical - by means of observation or experience rather than theory or pure logic.

Evidence

- Clinical outcomes
- Adjacent Level Degeneration/Reoperations
- Complications
- Cost/Value

Evidence Based Fusion Outcomes-FDA Studies

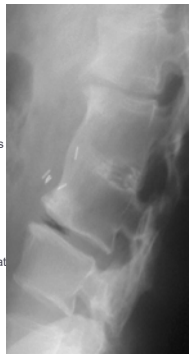


- Ray et al, Spine 1997
  - 96% fusion rate @ 2 yrs for Ray Cage
  - 65% good-to-excellent results
- Kuslich et al, Spine 2000
  - 95% fusion rate @ 4 yrs for BAK cage
  - 63% gainfully employed
- Boden et al, Spine 2000
  - 93% fusion rate @ 2 yrs for LT cage + InFUSE
  - 72% patient satisfaction
- Zigler et al, Spine 2007
  - 97% fusion rate @ 2 years 360 fusion control TDR IDE
  - 67% VAS Satisfaction @ 2 years

Radiographic success ≠ Clinical success

Adjacent Level Disease After Fusion



- Lehman et al. (Spine 1987)
  - > 30 yr f/u of 62 patients, uninstrumented fusions
  - X-ray signs of degen at adjacent segments in ~ 30%
- Rahm and Hall (J Spin Dis 1996)
  - 49 pts @ 5 yr f/u
  - 35% adjacent segment degeneration leads to worse clinical outcomes
- Etebar and Cahill (J Neurosurg 1999)
  - 4.5 yr f/u of 125 patients
  - 14 % adjacent segment disease
- Throckmorton et al. (Spine 2003)
  - > 2 yr f/u of 148 patients
  - 20% adjacent segment degeneration for fusions adjacent to degenerat discs
- Ghiselli et al. (JBJS July 2004)
  - 36% of pts >10 yrs after lumbar fusion required addt'l surg
  - 3x more likely after single level fusion, esp. L4-5

Total Disc Replacement (TDR): Clinical Goals

- Eliminate pain
- Restore disc height
- Restore/maintain range of motion
- Decelerate adjacent level degeneration
- Faster recovery
- Allow the body to restore spinal balance

A Paradigm Shift:
Reconstruction Versus Fusion

Lumbar Total Disc Replacement Developed as Alternative to Fusion

First Generation Unconstrained Core	Second Generation Constrained Core	Third Generation Controlled Mobile Core
• Clinical trials begin in 2000, launched 2004 • Unconstrained motion • Multiple step insertion • No longer on the US market (2011)	• 2nd generation launched 2006 • Constrained core – 3 degrees of freedom • Multiple step insertion • 2 endplate sizes	• 3rd generation launched 2015 • Controlled mobile core – 4 degrees of freedom • Single step insertion • 4 endplate sizes

What Have We Learned Over 18 Years of Use to Improve the Technology and Outcomes?

- More Natural Motion to Protect Adjacent Levels
- Minimize Component Migration/Dislocation
- Reduce Implant Height to Prevent Over-Distraction
- Maximize Endplate In-Growth and Long-Term Fixation
- Optimize Wear Properties

Prospective, Randomized, Controlled Multicenter FDA IDE Trials: 2-Year Data

A Prospective, Randomized, Multicenter Food and Drug Administration Investigational Device Exemptions Study of Lumbar Total Disc Replacement With the CHARITÉ™ Artificial Disc *Versus* Lumbar Fusion
Part I: Evaluation of Clinical Outcomes

Scott Blumenthal, MD,* Paul C. McAfee, MD,† Richard D. Guyer, MD,* Stephen H. Hochschuler, MD,* Fred H. Geisler, MD, PhD,‡ Richard T. Holt, MD,§ Rolando Garcia, Jr., MD, MPH,¶ John J. Regan,

SPINE 2005
Blumenthal et al
304 patients
TDR vs ALIF cages

Results of the Prospective, Randomized, Multicenter Food and Drug Administration Investigational Device Exemption Study of the ProDisc®-L Total Disc Replacement *Versus* Circumferential Fusion for the Treatment of 1-Level Degenerative Disc Disease

Jack Zigler, MD,* Rick Delamarter, MD,† Jeffrey M. Spivak, MD,‡‡‡ Raymond J. Linovitz, MD, FACS,§ Guy O. Danielson, III, MD,‖ Thomas T. Haider, MD,¶ Frank Cammisa, MD,# Jim Zucherman, MD,** Richard Balderston, MD,†† Scott Kitchel, MD,‡‡ Kevin Foley, MD,§§ Robert Watkins, MD,‖‖ David Bradford, MD,¶¶ James Yue, MD,## Hansen Yuan, MD,*** Harry Herkowitz, MD,††† Doug Geiger, MD,‡‡‡ John Bendo, MD,§§§ Timothy Peppers, MD,§ Barton Sachs, MD,* Federico Girardi, MD,# Michael Kropf, MD,† and Jeff Goldstein, MD§§§

SPINE 2007
Zigler et al
282 patients
ADR vs 360

Both found TDR at least as safe and effective as fusion, superior on some measures

Lumbar disc arthroplasty with Maverick disc versus stand-alone interbody fusion: a prospective, randomized, controlled, multicenter investigational device exemption trial.

Gornet MF, Burkus JK, Dryer RF, Peloza JH
Spine, 2011 Dec 1;36(25)

- 2:1 randomization
- 577 patients
  - 405 TDR with Maverick
  - 172 ALIF with LT cages and BMP
- The investigational group had statistically superior outcomes ($P < 0.05$) at all postoperative evaluations in:
  - ODI,
  - back pain
  - SF-36
  - Patient satisfaction.
  - Fewer implant or implant/surgical procedure-related adverse events ($P < 0.001$).
- Return-to-work intervals were reduced for investigational patients.
- In the investigational group, overall success **superiority** was found when compared to the control group as defined by the FDA IDE

Spine
RANDOMIZED TRIAL
OPEN
Lumbar Total Disc Replacement for Discogenic Low Back Pain: Two-year Outcomes of the activL Multicenter Randomized Controlled IDE Clinical Trial

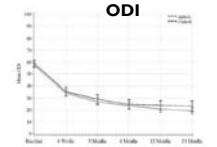
Rolando Garcia Jr., MD, MPH,* James I. Yue, MD,† Scott Blumenthal, MD,‡ Dean Coric, MD,§ Vikas V. Patel, MD,¶ Scott P. Leary, MD,‖ Dzung H. Dinh, MD,** Glenn R. Buttermann, MD,†† Hanel Deutsch, MD,‡‡ Federico Girardi, MD,§§ James Billys, MD,¶¶ and Larry E. Miller, PhD‖‖

- 324 patients
  - 218 randomized to ActivL
  - 106 randomized to control
- Overall treatment success with ActivL was superior (p=0.02)
- ActivL better in
  - Radiographic success p<0.01)
  - ODI success (p=0.08)

Garcia et al, Spine 2015

VAS Back Pain

ODI



Key Points

- A total of 324 patients with single-level lumbar degenerative disc disease unresponsive to at least 6 months of nonsurgical management were randomized to treatment with the activL (n = 218) or control (n = 106) total disc replacement.
- The primary composite treatment success endpoint was statistically superior with the activL implant versus controls at 2 years ($P = 0.02$).
- Radiographic success, defined as maintenance or improvement in range of motion at 2 years, was significantly higher in activL (59%) versus controls (43%).
- Device-related serious adverse events were less common in patients treated with activL versus controls (12% vs. 19%).

What Happened to Charite IDE Study Patients at 5-year Follow-up?

ELSEVIER

The Spine Journal 9 (2009) 374–386

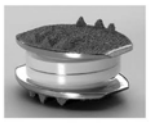
THE SPINE JOURNAL

Prospective, randomized, multicenter Food and Drug Administration investigational device exemption study of lumbar total disc replacement with the CHARITÉ artificial disc versus lumbar fusion: Five-year follow-up

Richard D. Guyer, MD[a,*], Paul C. McAfee, MD[b], Robert J. Banco, MD[c], Fabian D. Bitan, MD[d], Andrew Cappuccino, MD[e], Fred H. Geisler, MD PhD[f], Stephen H. Hochschuler, MD[a], Richard T. Holt, MD[g], Louis G. Jenis, MD[c], Mohamed E. Majd, MD[g], John J. Regan, MD[h], Scott G. Tromanhauser, MD[c], Douglas C. Wong, MD[i], Scott L. Blumenthal, MD[a]

CHARITÉ: 5-Year Follow-up

- 5-yr follow-up: 90 TDR vs. 43 ALIF
- ODI and VAS: no change between years 2-5
- ROM maintained in TDR group
- TDR had significantly greater RTW with fewer patients on long-term disability



Guyer et al, Spine J, 2009

What Happened to ProDisc-L IDE Study Patients at 5-year Follow-up?

J Neurosurg Spine 17:493–501, 2012

Five-year results of the prospective, randomized, multicenter, Food and Drug Administration investigational device exemption study of the ProDisc-L total disc replacement versus circumferential arthrodesis for the treatment of single-level degenerative disc disease

Clinical article

JACK E. ZIGLER, M.D.,[1] AND RICK B. DELAMARTER, M.D.[2]

ProDisc-L: FDA IDE 5-yr Follow-up

- N = 236 patients (TDR and 360 fusion control)
- Overall follow-up rate - 81.8%
- Both groups improved significantly on VAS and ODI scores at 24 months with no significant changes between the 24- and 60-month follow-up
- At 60 months, successful radiographic ROM in 93.7% of TDR pts, mean 7.2°

Lumbar TDR vs. Multi-Disciplinary Rehab

ELSEVIER

The Spine Journal 17 (2017) 1480–1488

THE SPINE JOURNAL

Total disc replacement versus multidisciplinary rehabilitation in patients with chronic low back pain and degenerative discs: 8-year follow-up of a randomized controlled multicenter trial

Håvard Furunes, MD[a,b,c,*], Kjersti Storheim, PhD[b,c], Jens Ivar Brox, PhD[b,d], Lars Gunnar Johnsen, PhD[e,f], Jan Sture Skouen, PhD[g,h], Eric Franssen, MD[i], Tore K. Solberg, PhD[j,k,l], Leiv Sandvik, PhD[b], Christian Hellum, PhD[b,m]

- **8-year outcomes from RCT comparing lumbar artificial disc replacement to multidisciplinary rehabilitation demonstrated significant long-term improvement after both rehab and disc replacement, and statistically significant long-term results in favor of disc replacement compared with rehab in terms of functional improvement and pain relief**

ODI 2 Years After ActivL vs Other TDRs vs Fusion

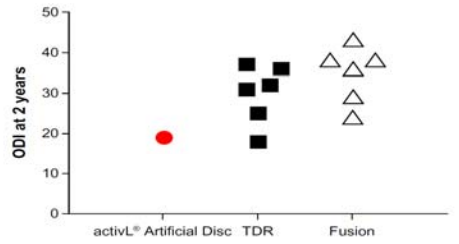


Figure 10 Comparison of 2-year Oswestry Disability Index (ODI) with activL® Artificial Disc versus randomized controlled trial outcomes of lumbar total disc replacement (TDR) or fusion.
Notes: Each marker represents outcomes from a single study. Data from studies.[31–34]

Level I(a) Data: 2-Year Meta-Analyses TDR vs Fusion

2010
2012
2013
2014
2014
2015

All meta-analyses reporting on disability, pain, and patient satisfaction demonstrate that TDR significantly improves these outcomes at 2 years in contrast to surgical fusion for the treatment of lumbar DDD

Published Meta-Analyses
Yajun et al., 2010
Jacobs et al., 2012
Wei et al., 2013
Rao et al., 2014
Noshchenko et al., 2014
Nie et al., 2015

Adjacent Segment Disease

SPINE Volume 33, Number 15, pp 1701–1707
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Lumbar Adjacent Segment Degeneration and Disease After Arthrodesis and Total Disc Arthroplasty

James S. Harrop, MD,* Jim A. Youssef, MD,† Mitch Maltenfort, PhD,* Peggy Vorwald, BS,†
Pascal Jabbour, MD,* Christopher M. Bono, MD,‡ Neil Goldfarb, BS,§
Alexander R. Vaccaro, MD,* and Alan S. Hilibrand*

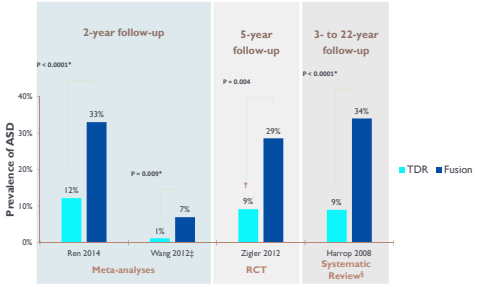
- **Reviewed 27 fusion and TDR studies**
- **314/926 fusion patients developed ASD (31%)**
- **31/313 TDR patients developed ASD (3%)**
- **p<0.0001**

Adjacent Level Surgery in All Patients

- Adjacent level surgery:
  - 4.0%-14.0% of the Fusion patients
  - 1.9%-2.29% of the TDR patients

Zigler et al JNS 2012
Zigler et al Spine 2018
Harrop et al Spine 2008

5-Year Data: Lumbar TDR With Over 3-Fold Decrease in Adjacent Segment Disease (ASD) Compared to Fusion



* P-value is based on pooled results from meta-analytic analyses; † Rate of adjacent segment degeneration for TDR from 5-year follow-up reported in the Zigler 2012 RCT are similar to those reported in a 5-year prospective single-arm study of TDR (10.7%) (Aghayev et al., 2014). ‡ Examined adjacent segment pathology, a proposed umbrella term referring to the breadth of clinical and/or radiographical changes at adjacent motion segments that developed subsequent to a previous spinal intervention. § Included 27 prospective single-arm TDR and fusion studies.

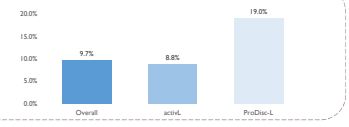
ent-level Degeneration After Lumbar Disc Replacement: Results of a Prospective Study v

Zigler JE, Blumenthal SL, Guyer RD, Ohnmeiss DD, Patel L
Spine, March, 2018

Maintenance of ROM has a protective effect on delaying the progression of ASD. As a result, the activL is less likely to result in progression of Adjacent Segment Disease (p=0.05).[1]

Maintenance of ROM has a protective effect on delaying the progression of ASD in DDD patients. The post-hoc analysis of ASD from the activL study demonstrated that for every degree of motion maintained, there was a lower incidence of ASD at 5-years

As a result, the activL is less likely to result in progression of Adjacent Segment Disease which may lead to reoperations and lower patient satisfaction (p=0.05)



5-Year Meta-Analysis Data

Comparison of Lumbar Total Disc Replacement with Surgical Spinal Fusion for the Treatment of Single-Level Degenerative Disc Disease: A Meta-analysis of 5-year Outcomes from Randomized Controlled Trials

Results of Meta-Analysis Provide Long-Term that Individual Studies Are Not Powered to Draw

- Meta-Analysis of Long-Term Randomized Controlled Trials considered Level 1(a) evidence
- Four outcomes selected based on what the studies had in common
- 3 of the 4 studies showed statistical favor to TDR at 5 years

Endpoint Evaluated	Outcomes Favor	p-Value
Disability (ODI)	TDR	0.05
Pain (VAS)	TDR	0.25
Reoperation	TDR	0.002
Patient Satisfaction	TDR	0.01

Pooling the Data Illustrates the Power of These RCTs

The long-term findings of this study showing improved clinical and safety benefits with TDR at 5 years have important implications for the clinical and economic burden associated with patients with symptomatic lumbar DDD

Studies	ODI	Back Pain	Reoperation	Patient Satisfaction
Guyer 2009	□		□□	□□
Gornet 2010	□□	□	□□	□□
Zigler 2012	□		□	□□
Skold 2013	□□	□	□□	□□
5-Year Meta-Analysis	□□	□	□□	□□

Legend: □□ = TDR significantly better than fusion on one or more outcomes. □ = TDR numerically better than fusion on one or more outcomes. Blank cells = No outcomes show TDR as numerically better than fusion.

Long-Term Data Demonstrate Similar or Lower Risk of Other Complications with Lumbar TDR vs Fusion

2 years

Meta-analysis	Complications	Reoperations
	TDR vs. Fusion: Odds Ratio (95% CI)	
Nie et al., 2015	0.50 (0.29, 0.84); P = 0.008	0.62 (0.36, 1.06); P = 0.08
Noshchenko 2014	0.60 (0.48, 0.75); P < 0.001	0.83 (0.58, 1.18); P = 0.302
Rao 2014	0.72 (0.45, 1.14); P = 0.16	0.83 (0.39, 1.77); P = 0.63
Ren 2014	---	0.15 (0.04, 0.61); P = 0.0008
Jacobs 2012	---	0.80 (0.51, 1.24); P = 0.31
Wei 2013	0.57 (0.38, 0.84); P = 0.31	0.91 (0.57, 1.46); P = 0.71

5 to 10+ years

5-year RCTs

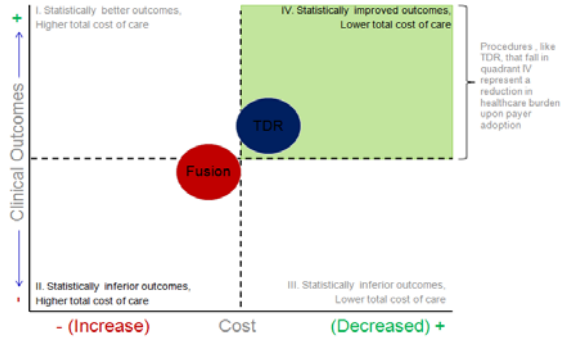
- Reoperation rates never higher with TDR[1,2,3,4]
  - 2.3% to 8% for TDR
  - 8.3% to 16.3% for fusion
- Significantly lower SAEs with TDR[2]
- Very low device migration / subsidence

Long-Term Observational

- Reoperation rates typically ≤7% for TDR[5-9]
- Not seeing studies with high rates of failed TDRs, catastrophic failures, deaths
- Reasonably low rates of overall complications
- Per FDA-required, real-world medical device reporting (MDR), explantation rate of 3rd Gen disc 0.006%

RCTs: [1] Guyer 2009; [2] Zigler 2012; [3] Skold 2013; [4] Gornet 2010. Observational: [5] Lemaire 2005; [6] Siepe 2006; [7] Katsimihas 2010; [8] Aghayev 2014; [9] Siepe 2014.

Value of Lumbar TDR to Health Plans



Summary: Long-Standing Perceptions vs. Current Reality of Lumbar TDR

Perception	Reality
▪ **Lumbar TDR lacks the scientific evidence from published, long-term studies to demonstrate safety and efficacy**	▪ Lumbar TDR is now the most rigorously studied spine procedure ▪ The newly published meta-analysis shows a statistically significant difference in the long-term outcomes for lumbar TDR versus fusion ▪ There are now five FDA IDE clinical trials published, three with a fusion control and two with a comparator lumbar disc control ▪ There is now 13 years of data on lumbar TDR, including multiple publications with 5-10 year follow-up and with 10 or more years of follow-up, both in the US and outside the US ▪ While some of the studies are based on non-inferior outcomes, many of the more recent studies and publications include superiority outcomes (studies have evolved with the technology)

Summary: Long-Standing Perceptions vs. Current Reality of Lumbar TDR

Perception	Reality
▪ **Lumbar TDR is associated with considerable complications**	▪ Lumbar TDR is now considered to be a safer procedure than lumbar fusion, based on controlled studies ▪ The design of the lumbar TDR devices has improved dramatically since their inception 17 years ago, leading to a substantial improvement in both the safety and the efficacy of the devices and of the procedure ▪ No implant is reported to have worn out from normal wear in >30 years outside the US or in 13+ years within the US

Summary: Long-Standing Perceptions vs. Current Reality of Lumbar TDR

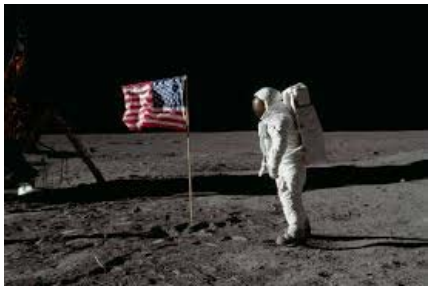
Perception	Reality
▪ **The impact of lumbar TDR on adjacent segments is unknown**	▪ Because lumbar TDR preserves motion, adjacent segments are significantly less likely to show signs of degeneration than with fusion ▪ Five-year controlled data demonstrate that lumbar TDR is associated with an over three-fold decrease in adjacent segment degeneration as compared to fusion

Summary: Long-Standing Perceptions vs. Current Reality of Lumbar TDR

Perception	Reality
▪ **The cost of lumbar TDR is higher than the cost of fusion**	▪ The cost of care with lumbar TDR is generally less than the cost of care with fusion ▪ Both the surgeon payment and the facility payment for lumbar TDR are LOWER than the payments for fusion ▪ Over the long-term, the cost of care has been proven to be lower as well due to a reduction in reoperations associated with both complications at the index level and with adjacent segment breakdown

Executive Summary from an Investigator, Researcher, and Daily Clinician

- We have identified the patients (by FDA inclusion and exclusion criteria) who will benefit from lumbar TDR
- We have followed and analyzed these patients better than for ANY OTHER orthopedic implant technology
- TDR **outcomes** better than fusion, long-term rehab
- TDR **complications** lower than fusion
- TDR **adjacent segment degeneration** less than fusion
- TDR **reoperation rates** lower than fusion
- TDR **direct and indirect costs** lower than fusion



Thank you!