

CAROLINA NEUROSURGERY & SPINE ASSOCIATES DOM CORIC, M.D.

## Castellvi Spine

### Are We Closer to Finding the True Lumbar Pain Generator?

Dom Coric, M.D.  
 Carolina Neurosurgery and Spine Associates  
 Chief, Department of Neurosurgery, CMC  
 Charlotte, NC  
 5/20/16

---

---

---

---

---

---

---

---

---

---

CAROLINA NEUROSURGERY & SPINE ASSOCIATES DOM CORIC, M.D.

## DISCLOSURE



- Spine Wave: Consultant/Stock/Royalties
- Spinal Kinetics: Stock
- Medtronic: Consultant
- Globus Medical: Consultant
- DiscGenics: Consultant/Stock
- Premia Spine: Consultant
- United HealthCare: Spine Advisory Board
- *All disc repair and nucleus procedures are investigational.*

---

---

---

---

---

---

---

---

---

---

CAROLINA NEUROSURGERY & SPINE ASSOCIATES DOM CORIC, M.D.

## Introduction

- The diagnosis and treatment of mechanical LBP remains challenging and controversial.
- A combination of relatively poor clinical results and judgement has significantly limited our ability to address lumbar DDD from a surgical perspective.
  - *Many payors limit or, increasingly, do not cover fusion and/or lumbar TDR procedures for lumbar DDD.*

---

---

---

---

---

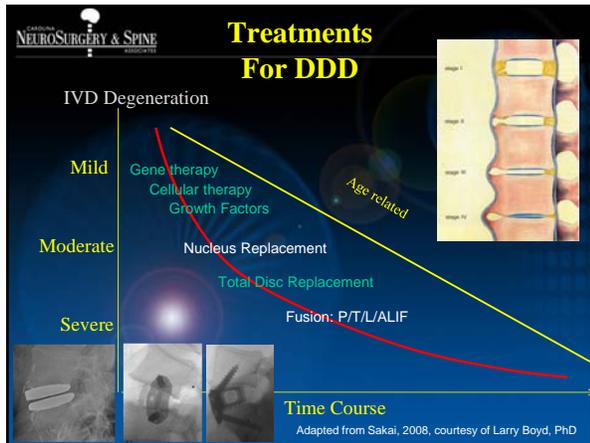
---

---

---

---

---




---

---

---

---

---

---

---

---

DOM CORIC, M.D.

## Introduction

- Surgical IDE results: Composite success results
  - Charite (57.1%) v BAK (46.5%): 2 year results
  - Charite (57.8%) v BAK (51.2%): 5 year results
  - Prodisc-L (53.4%) v Ant/Post Fusion (40.8%)
- *Payor conclusion: TDR is non-inferior to a 'gold standard' (i.e. surgical fusion) that is, in itself, largely ineffective.*

---

---

---

---

---

---

---

---

DOM CORIC, M.D.

## Introduction

- Investigational disc repair procedures:
  - Gene therapy
  - Growth factor therapy
  - Cell therapy
- Nucleus replacement procedures:
  - PDN, Dascor, Nucore, Nubac (only nucleus replacement device to reach pivotal trial – failed)
- *No FDA-approved devices/procedures.*

---

---

---

---

---

---

---

---

DOM CORIC, M.D.

## Introduction

- Based on clinical experience and intuition, many spine surgeons maintain that the disc is a pain generator.
- A subset of patients show dramatic and substained improvement following DDD surgery, but evidence-basis remains relatively weak.




---

---

---

---

---

---

---

---

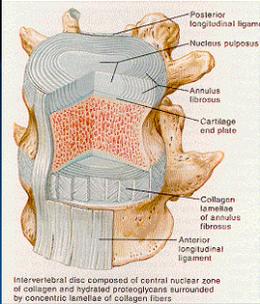
---

---

DOM CORIC, M.D.

## Intervertebral Disc (IVD)

- **ANNULUS FIBROSUS**
  - Heavily crosslinked, laminated collagen fibers
- **NUCLEUS PULPOSUS**
  - Remnant of notochord
  - Chondrocytic cells
- **ECM: Proteoglycans w/in Type II collagen scaffold:** keratan sulfate chondroitin
  - DDD: ↓ Proteoglycans
  - ↓ Type II / ↑ Type I, III collagen
- 70-90% water
  - DDD: ↓ H<sub>2</sub>O



Intervertebral disc composed of central nuclear zone of collagen and hydrated proteoglycans surrounded by concentric lamellae of collagen fibers.

---

---

---

---

---

---

---

---

---

---

## ECM

CC(=O)O[C@@H]1O[C@@H](OC(=O)C)[C@H](O)[C@@H](O)[C@H]1O

D-galactose

CC(=O)O[C@@H]1O[C@@H](OC(=O)C)[C@H](O)[C@@H](O)[C@H]1O

N-acetyl-D-glucosamine-6-sulfate

- Extracellular matrix primarily consists of:
  - (a) **Proteoglycans**
    - **Aggrecan** and **versican**; largest/most common
    - **Hydrophilic molecules**: protein stems surrounded by highly **neg-charged glycosaminoglycan (GAG)** side chains.
    - **Chondroitin-6-sulfate and keratin sulfate** :
      - » 2 most abundant GAG molecules, attract and hold pos-charged H<sub>2</sub>O molecules.
  - (b) **Type II collagen**: scaffold



Aggrecan

---

---

---

---

---

---

---

---

---

---

CAROLINA NEUROSURGERY & SPINE ASSOCIATES DOM CORIC, M.D.

## IVD

- Degenerative Disc Disease
  - Loss of chondrocytic nucleus pulposus cells results in inability to produce and maintain normal ECM.
  - Annulus fibrosus
    - *Delamination*: annular tears.
  - Nucleus pulposus
    - *Cellular loss*: depletion of extracellular matrix, replacement with fibrocartilage.
    - *Dessication*: progressive loss of proteoglycans/H2O.

---

---

---

---

---

---

---

---

CAROLINA NEUROSURGERY & SPINE ASSOCIATES DOM CORIC, M.D.

## IVD

- DEGENERATIVE DISC DISEASE (DDD)
  - Progressive changes in disc composition and function *out of proportion those associated with normal aging.*
  - Calcification of cartilaginous endplate (sclerosis) limits blood/nutrient supply.
  - *Factors favor ECM destruction (catabolism) over production (anabolism).*



---

---

---

---

---

---

---

---

CAROLINA NEUROSURGERY & SPINE ASSOCIATES DOM CORIC, M.D.

## IVD

### DEGENERATIVE DISC DISEASE (DDD)

↓ Proteoglycans

↓ Hydration

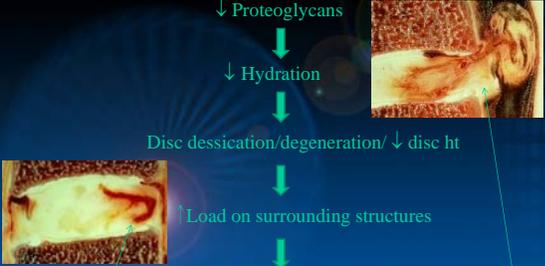
Disc dessication/degeneration/ ↓ disc ht

↓ Load on surrounding structures

Annular tears/disc dessication, loss of ht/Modic changes/HNP

**PAIN**

Photos courtesy of Prof Rauschning MD



---

---

---

---

---

---

---

---

CAROLINA NEUROSURGERY & SPINE ASSOCIATES DOM CORIC, M.D.

### Lumbar Pain Generator

- Altered biochemical composition
  - Loss of GAGs
  - Loss of water content
- Altered biomechanical properties
  - Loss of viscous behavior
  - Loss of compressive resistance
- Injury response
  - Elevated inflammatory cytokine expression

---

---

---

---

---

---

---

---

CAROLINA NEUROSURGERY & SPINE ASSOCIATES DOM CORIC, M.D.

### CASE STUDY

- EIW: Pt is a motivated, professional 40 yo F who presents with progressively severe mechanical LBP 4 years after L5-S1 microdiscectomy for RLE radiculopathy.
  - Sxs requiring routine narcotic usage, pt unable to continue work activities.
- PE: Nonfocal
- PSH: s/p hemilaminotomy/discectomy L5

---

---

---

---

---

---

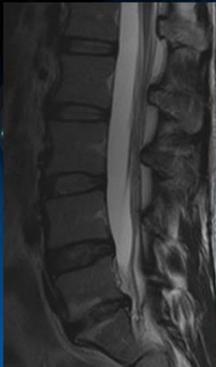
---

---

CAROLINA NEUROSURGERY & SPINE ASSOCIATES DOM CORIC, M.D.

### CASE STUDY

- MRI: severe spondylosis L5-S1 with loss disc ht and Modic changes, mild disc dessication L4-5 with 'minimal' bulge.
- Remainder of lumbar spine is unremarkable.



---

---

---

---

---

---

---

---

**CASE STUDY** DOM CORIC, M.D.

- Provocative discography
  - L5-S1: internal disc disruption, but no pain/press
  - L4-5: internal disc disruption, 9/10 concordance
  - L3-4: nl control



---

---

---

---

---

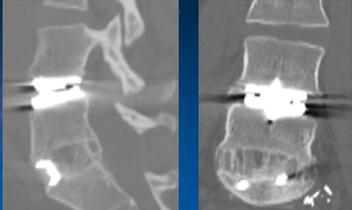
---

---

---

**CASE STUDY** DOM CORIC, M.D.

- EIW (con't):
  - Pt undergoes L4-5 TDR (Lg disc, 10mm core, 6 degrees lordosis) and L5-S1 ALIF hybrid (off-label).



---

---

---

---

---

---

---

---

**CASE STUDY** DOM CORIC, M.D.

- EIW (con't):
  - Off all narcotics and pain meds by 4 wks postop and back to work as a Secret Service agent without restrictions by 12 wks postop.
  - Pt now over 6 yrs postop continues full time employment, off all narcotics and muscle relaxers.



---

---

---

---

---

---

---

---

CAROLINA NEUROSURGERY & SPINE ASSOCIATES DOM CORIC, M.D.

## Conclusion

- Lumbar pain generator remains elusive.
- Potential lumbar pain generators include:
  - Disc: nucleus pulposus/annulus pulposus
  - Facet Joints
  - SI Joint
  - Musculoskeletal
  - Psychological overlay
    - *Powerful placebo effect, at least 2 separate IND studies with sustained saline injection success rate in the 40-50% range at two year follow-up.*

---

---

---

---

---

---

---

---

---

---

CAROLINA NEUROSURGERY & SPINE ASSOCIATES DOM CORIC, M.D.

## Conclusion

- Are we closer to finding the true lumbar pain generator?
  - No
  - Intuitively, we recognize the lumbar disc can be a pain generator, but not the only pain generator.
  - We are not good at diagnosing mechanical LBP and the relatively poor treatment results are a direct reflection of this diagnostic inadequacy.
  - Continued investigation into the diagnosis and treatment of this common and often debilitating diagnosis is warranted.

---

---

---

---

---

---

---

---

---

---

CAROLINA NEUROSURGERY & SPINE ASSOCIATES DOM CORIC, M.D.

# THANK YOU!

---

---

---

---

---

---

---

---

---

---