

Is Discography Necessary?

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Disclosure

- Consulting/Research
 - MDT, Stryker, Nevro, Vertos, Vertiflex, Stimwave, APEX

Thanks to

- Rick Derby
- Charles Aprill
- Tim Maus
- Zack McCormick
- Nik Bogduk

History

Prediscography: Myelography with iophendylate (Pantopaque). (CT came along in the early 1970's)

- **Disc and epidural space remained opaque to imaging inspection.**

Lindblom 1947: introduced radio dense material into the disc, a morphologic imaging test.

Cloward, Buziad 1952: Technique, indications for lumbar discography in the US.

Fernstrom 1960: Back/leg pain may occur in the absence of nerve compression.

History

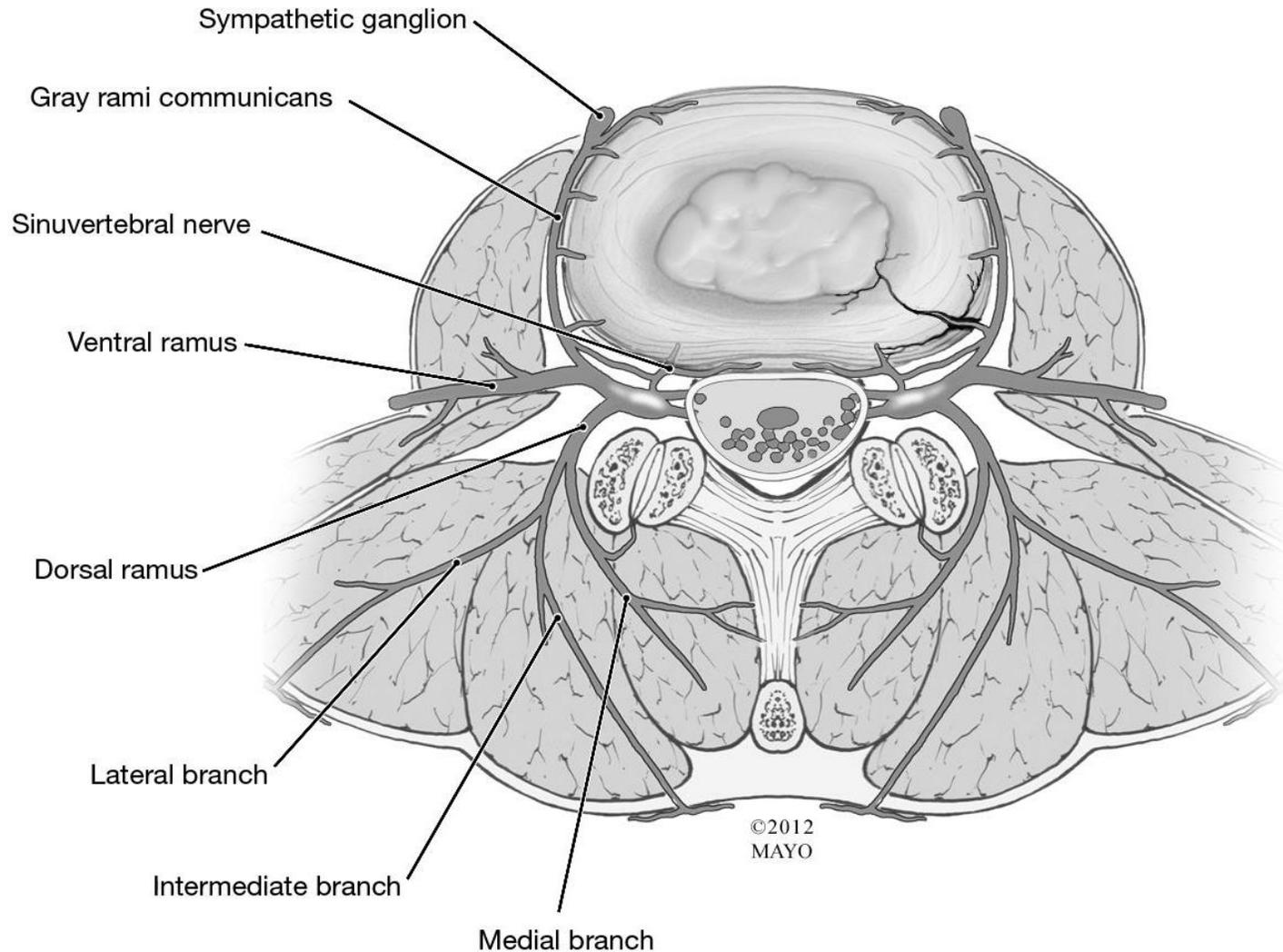
Massie & Stevens 1967: Pain provocation, not morphologic abnormality, may be important in diagnosis.

Pain provocation implies disc innervation, long controversial, until:

Yoshizawa 1980: Identified simple & complex nerve endings in the annulus fibrosis.

Bogduk 1981: Defined the presently understood pathways of afferent signaling from the disc.

Discovertebral Complex: Innervation



- Disc:** outer 1/3
annulus
- Sinuvetebral nerve
 - Grey rami
 - Sympathetic plexus
 - Neo-innervation

The Journal of Bone & Joint Surgery

Holt EP., Jr. The question of lumbar discography. J Bone Joint Surg Am. 1968;50(4):720–6.

In a population of prison inmates a 37% false positive rate was found



The Journal of Bone & Joint Surgery

Lumbar Discography in Normal Subjects: A Controlled, Prospective Study 1990

Walsh TR, Weinstein JN, Spratt KF,
Lehmann TR, Aprill C, Sayre H.

No False Positives
0%





Spine

The ability of pressure-controlled discography to predict surgical and nonsurgical outcomes 1999

Derby R, Howard MW, Grant JM,
Lettice JJ, Van Peteghem PK, Ryan DP.

Derby et al Study

Introduced use of manometric control to improve specificity of disc stimulation.

- **Chemically sensitized disc:** concordant pain at < 15 PSI above opening pressure (a.o.)
- **Mechanically sensitized disc:** concordant pain at 15- 50 PSI a.o.

Discography

- Discography has remained in use although it has had challenges along the way.

Does It Have Value & Is It Safe?

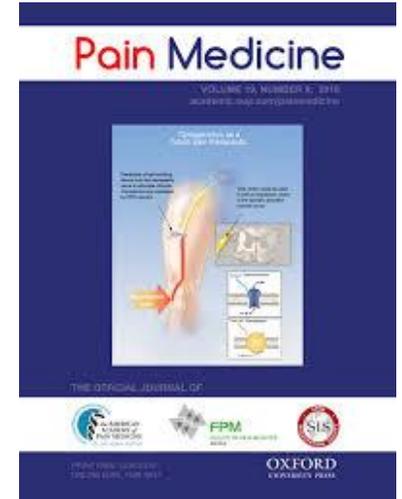
1. Value

- Diagnostic value
- Predictive value for surgical outcome

2. Safety

- Short-term
- Long-term

- Z McCormick and T Maus



[Diagnostic Value, Prognostic Value, and Safety of Provocation Discography](#)

[Zachary L McCormick, MD](#); [Fred DeFrancesch, MD](#); [Vivek Loomba, MD](#); [Maxim Moradian, MD](#); [Ramesh Bathina, MD](#) ...

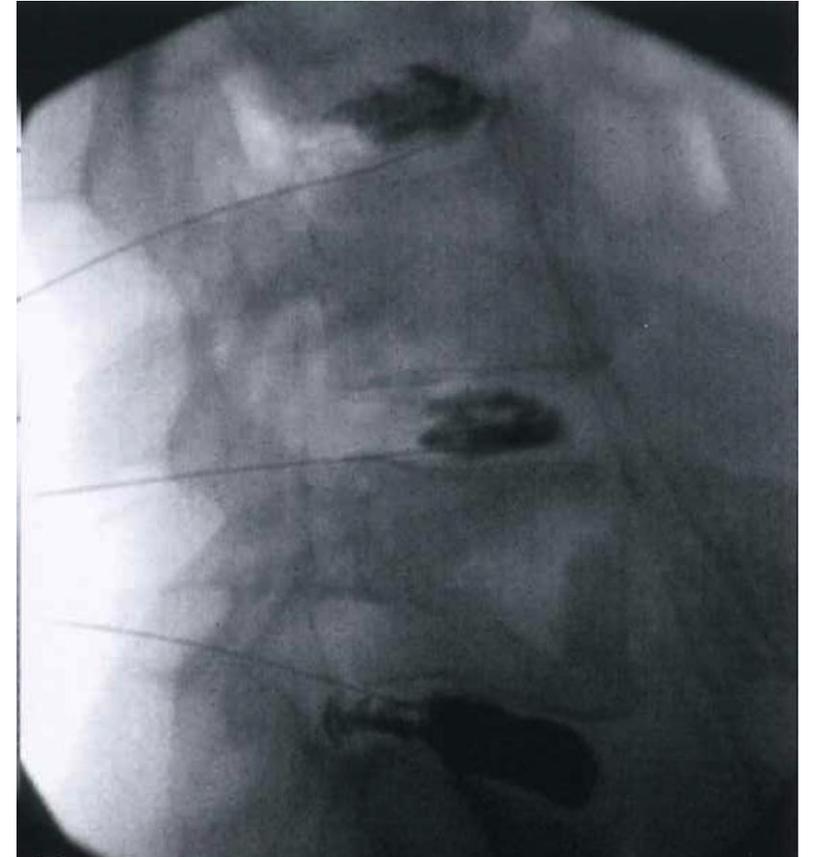
Provocation Discography

Rationale:

Determine whether a disc is or is not the cause of pain by pressurizing and injection of contrast to visualize internal architecture

Use:

Determine whether or not to provide treatment- and to which levels



Provocation Discography Diagnostic Value

Inherent Limitations: Criterion Standard for “true” discogenic pain?

- There is a specificity fault- no gold standard- can't send to pathology and find out whether it was painful
- Test results relies on subjective report.

Provocation Discography Diagnostic Value

Reasonable True Negative

- Asymptomatic volunteers, non-LBP patients → expose to discography
 - Presumed disease prevalence of 0%
 - False positive rate- has been shown to be very low

The FP rate correlates with diagnostic criteria

SIS/IASP Criteria:

1. Concordant pain response $>6/10$.
2. Volume limit 3 mL.
3. Pressurization ≤ 50 psi above opening pressure (AOP).
4. Adjacent disc(s) provide controls.
 - One control disc: painless response OR nonconcordant pain at >15 psi AOP.
 - Two adjacent control discs: painless response at both levels OR one painless disc AND one disc with nonconcordant pain at >15 psi AOP.

Diagnostic Value

The importance of using strict and accepted criteria

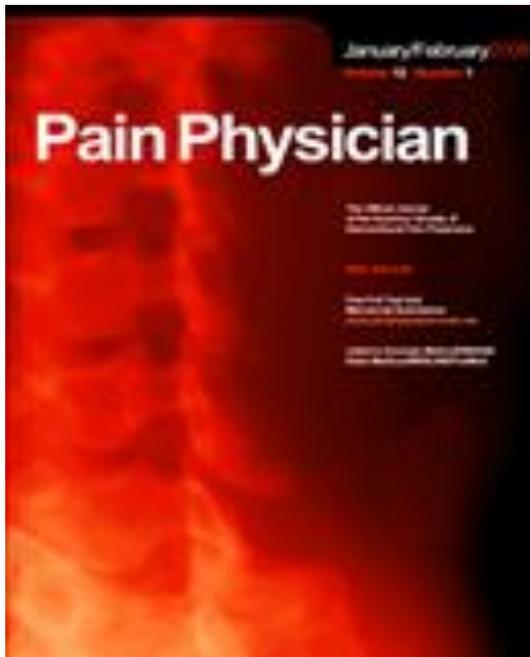
- Carragee reported a **29%** false positive rate per disc.
- Wolfer and Derby Meta-analysis **with application of SIS/IASP criteria** reported a **6%** false positive rate per disc.

Discography Validity Challenges

- Disc stimulation may reproduce symptoms from extra-spinal source
Carragee, Spine 1999
- False positives: 10% asym vol, 20% non-lumbar chronic pain, 75% somatization disorder. *Carragee, 2000*
- Painful disc injections in asymptomatic subjects are a poor predictor of future back pain. *Carragee, 2004*
- Psychosocial variables stronger predictors of future back pain disability in an at-risk population than MRI or discography. *Carragee, 2005*
- Low- pressure injection (< 22 PSI a.o.) were painful in 0% of subjects with no LPB, no chronic pain; 36% with no LBP, chronic pain; 25% with no LBP, prior discectomy; 28% minor benign back pain. *Carragee, 2006*

Pain Physician 2008

*Systematic review of lumbar
provocation discography in
asymptomatic subjects with a meta-
analysis of false positive rate*



Wolfer LR, Derby R, Lee JE, Lee SH

Wolfer et al Study

- 1. 11 studies , ISIS/ IASP criteria: 7/10 concordant pain, grade 3 tear, pressure < 50 psi a.o., normal control disc, 15 psi a.o. as low pressure positive**
- 1. Pooled data, false positives:**
 - 9.3% /patient; 6% /disc
- 2. Pooled data, no confounding factors, false positives:**
 - 3% /patient; 2.1% /disc
- 3. Pooled chronic pain patients, false positives:**
 - 5.6% /patient; 3.9% /disc

Chronic pain is not a confounding factor with strict criteria

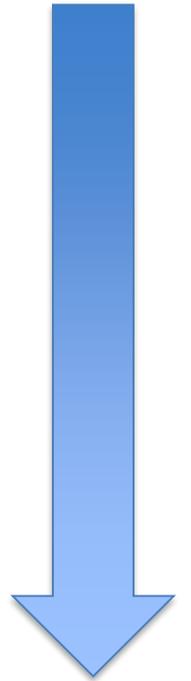
Wolfer et al Study

| Study | TP | FP | FN | TN | Specificity |
|------------------------------------|----|----|----|-----|----------------------|
| Walsh, 1990 Asympt subjects | 0 | 0 | 0 | 5 | 1.0 (0.48, 1.0) |
| Carragee, 1999 Iliac Crest Pain | 0 | 1 | 0 | 14 | 0.93 (0.68, 1.0) |
| Carragee, 2000 Asympt subjects | 0 | 3 | 0 | 31 | 0.91 (0.76, 0.98) |
| Carragee, 2000 Post-discectomy | 0 | 3 | 0 | 33 | 0.92 (0.78, 0.98) |
| Derby, 2005 Asympt subjects | 0 | 0 | 0 | 33 | 1.0 (0.89, 1.0) |
| Total | 0 | 7 | 0 | 116 | 0.94 (0.89, 0.98) |

Diagnostic Value In Population Groups

SIS/IASP criteria was applied to the populations groups

| <u>Population Group</u> | <u>False Positive Rate Per Disc</u> |
|--|-------------------------------------|
| Chronic mild to moderate LBP | 13% (95% CI 4-29%) |
| Prior lumbar discectomy | 9% (95% CI 0-19%) |
| No LBP, regional chronic pain (hx iliac crest bone bx) | 7% (95% CI 0-23%) |
| No LBP, non-regional chronic pain (cervical, non-spinal) | 4% (95% CI 0-12%) |
| Asymptomatic | 2% (95% CI 0-6%) |



Predictive Value

Does discography lead to improved clinical outcome?

Criterion Standard: Clinical success following spine surgery

Colhoun et al Study

- **Prospective cohort**
- **Lumbar Discography → Fusion**
- *Discography Technique/Criteria not specified*
- **“Success”**
 1. Complete or significant relief of symptoms
 2. Return to work/normal duties
 3. Discontinuation of analgesics

Results

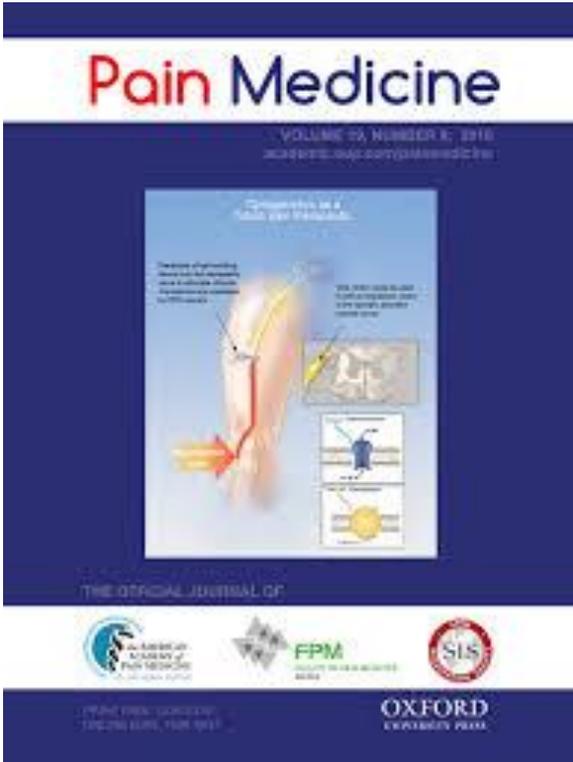
| | Positive Discography (n = 137) | Negative Discography (n=25) |
|-----------------------------|--------------------------------|-----------------------------|
| Success w/ fusion (n=135) | 122 | 13 |
| No Success w/ fusion (n=27) | 15 | 12 |

Positive response helpful for outcome prediction

Negative response NOT helpful

| | |
|---------------------|----------------------------|
| Sensitivity | 90% (95% CI 84-95%) |
| Specificity | 44% (95% CI 25-65%) |
| PPV | 89% (95% CI 85-92%) |
| NPV | 48% (95% CI 85-92%) |
| False Positive Rate | 11% (95% CI 6-17%) |
| False Negative Rate | 52% (95% CI 32-72%) |

*Success rate of fusion for chronic low back pain, DDD only = **50-63%***



PAIN MEDICINE

*Predictive value of provocative
lumbar disc stimulation 2008*

Cooper G, Kahn S, Lutz GE

Cooper et al Study

- Prospective cohort
- Lumbar Discography done using **SIS/IASP criteria**
- If disco was *positive*, patients had surgery- Discectomy and Fusion

We don't know the outcome of those with - discography
“Success:” Return to $\geq 50\%$ of daily activities

Results

| | Positive Discography (n = 52) | Negative Discography (n=?) |
|----------------------------|-------------------------------|----------------------------|
| Success w/ discectomy | 40 | ? |
| Lack Success w/ discectomy | 12 | ? |

No information about disco negative patients, due to none having surgery

| | |
|---------------------|---------------------|
| PPV | 77% (95% CI 63-88%) |
| False Positive Rate | 23% (95% CI 13-37%) |

Success rate of fusion for chronic low back pain, DDD only = 50-63%

- Discography has evidence of predictive validity but is it safe?

Past Reported Complications

- Bacterial discitis, meningitis, epidural abscess
- Spinal headache/cerebral spinal fluid leakage
- Retroperitoneal bleeding
- Intrathecal hemorrhage
- Arachnoiditis
- Allergic reaction
- Pulmonary embolism from nucleus pulposus material
- Seizure

Past Reported Complications

Only acute HNP and discitis have been reported in the last 15 years.

- Fluoroscopic guidance, improved disco technique + safety measures seem to have limited complications

Safety

- Long-term- does discography damage the disc?
 - Acceleration of disc degeneration?
 - Increased incidence of future disc herniation?

2009 ISSLS Prize Winner: Does Discography Cause Accelerated Progression of Degeneration Changes in the Lumbar Disc

A Ten-Year Matched Cohort Study

Eugene J. Carragee, MD,* Angus S. Don, FRACS,* Eric L. Hurwitz, DC, PhD,†
Jason M. Cuellar, MD, PhD,‡ John Carrino, MD,§ and Richard Herzog, MD¶



Carragee & Cuellar et al Studies

Concluded that discography results in a higher rate of:

- lumbar disc degeneration
- lumbar disc herniation
- spine surgery
- repeat advanced imaging
- significant low back pain episodes
- work lost
- medical visits

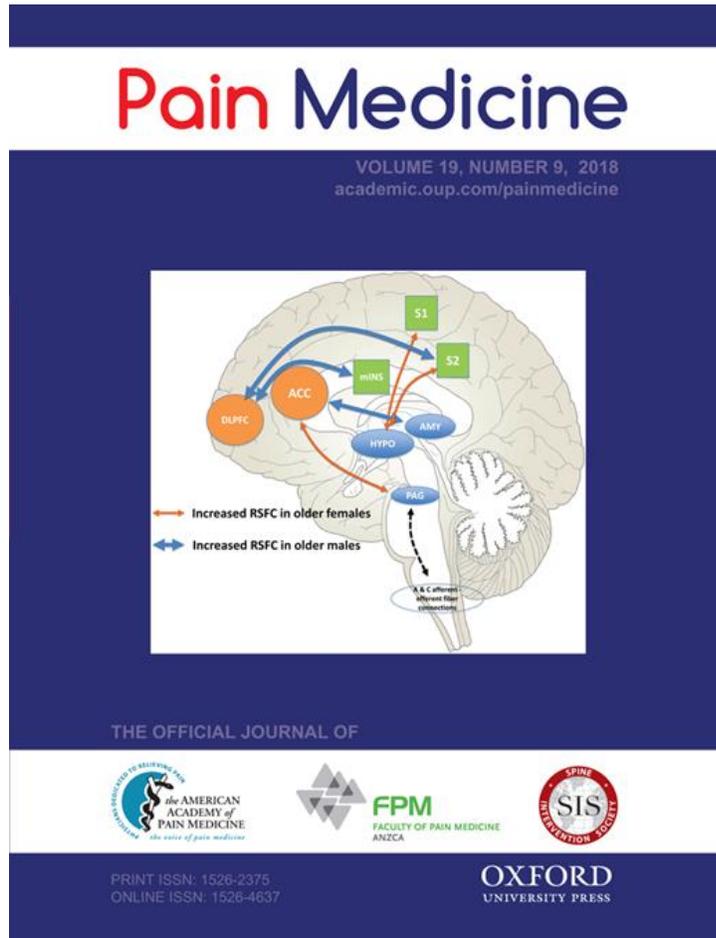
Carragee & Cuellar Limitations

- **Excluded actual back pain sufferers.**
 - None had LBP significant enough to warrant seeing a physician
 - Cannot generalize this study to a realistic discography population
- **Rate of Modic change in control group 11% -far less than 36% reported in general population.**
- **Loss to follow-up was reported as 30% in the 2009 data.**
 - Impairs ability to comment on true patient outcomes
- **Inappropriately high disc pressures were produced in the majority of subjects.**
 - Threshold of 100psi, 96% of subjects to 80psi or greater. Inconsistent with established standards.

PAIN MEDICINE

Low-pressure Lumbar Provocation Discography According to International Association for the Study of Pain/Spine Intervention Society Standards Does Not Cause Accelerated Progression of Disc Degeneration in Symptomatic Low Back Pain Patients; A 7 Year Matched Cohort Study.

McCormick ZL, Lehman V, Plastaras CT, Walega DR, Huddleston P, Moussallem C, Geske JR, Kennedy DJ, Maus TP, Carr C



Methodology

- Matched cohort study from Mayo Clinic.
- Consecutive patients with symptomatic LBP who underwent MRI, PD, and repeat MRI >7 years later, but no spinal fusion.
- Punctured discs matched (1:2-1:4 ratio) to corresponding discs in a control cohort by age, BMI, Pfirrmann score (+/-1), and presence of disc herniation.
- 66 discs exposed to PD, and 243 discs in the matched cohort

Results

No difference in:

- Advance in Pfirrmann score category in punctured discs (17%, 95% CI 9-28%) vs. matched cohort corresponding discs (26%, 95% CI 21-32%), $p=0.10$.

Results

*No difference**:

- T2-signal-intensity-to-CSF ratio
- Disc height
- New disc herniations
- HIZs
- Modic changes

*Punctured discs vs. matched cohort corresponding discs AND punctured versus non-punctured discs in disco cohort (p's>0.05)

Key Points

Value

- 1) *SIS/IASP Discography Criteria minimize false positives.*
- 2) *Inadequate study of predictive value for surgical outcome.*

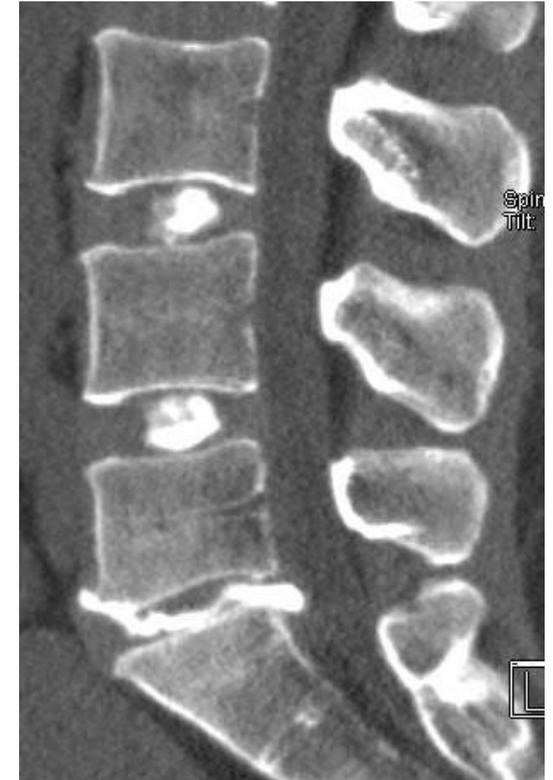
Safety

- 1) *Discitis – uncommon; take precautions.*
- 2) *Acute Disc Herniation- rare but possible.*
- 3) *Disc health not likely compromised by discography according to SIS/IASP standards.*

Can Imaging Provide Equivalent Utility to Disc Stimulation?

Imaging Correlates of IDD

- **Imaging parameters**
 - Loss of disc space height
 - Loss of nuclear T2 signal
 - Disc contour alteration (herniation)
 - Endplate (Modic) changes
 - High Intensity Zone (HIZ), inflammatory fissure
- **Specificity fault:** high prevalence in asymptomatic subjects
- **Analysis in patients suspected of discogenic pain**

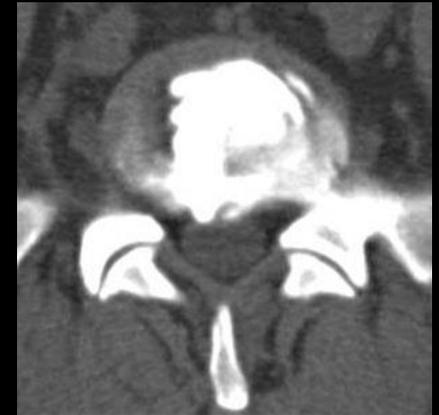
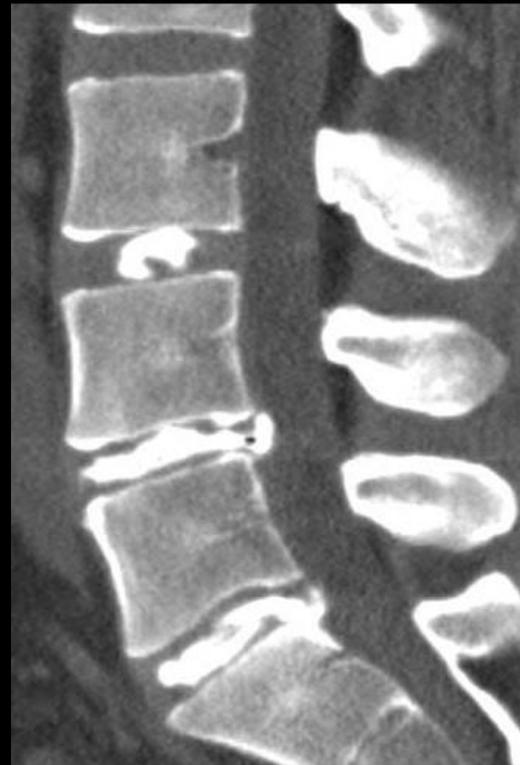


Severe Disc Space Narrowing, Marked T2 Signal Loss Strongly Correlate with Positive Provocation Discography



L5S1 disc space narrowing
L45 nuclear signal loss
Concordant pain at L45 and L5S1 on
discography

Disc Contour Abnormality: Bulge > Protrusion > Extrusion Predict Positive Provocation Discography



Disc bulge at L45 , mild disc height loss, Gr IV
HIZ + focal protrusion L5S1, Gr IV
Discogenic pain L45 & L5S1

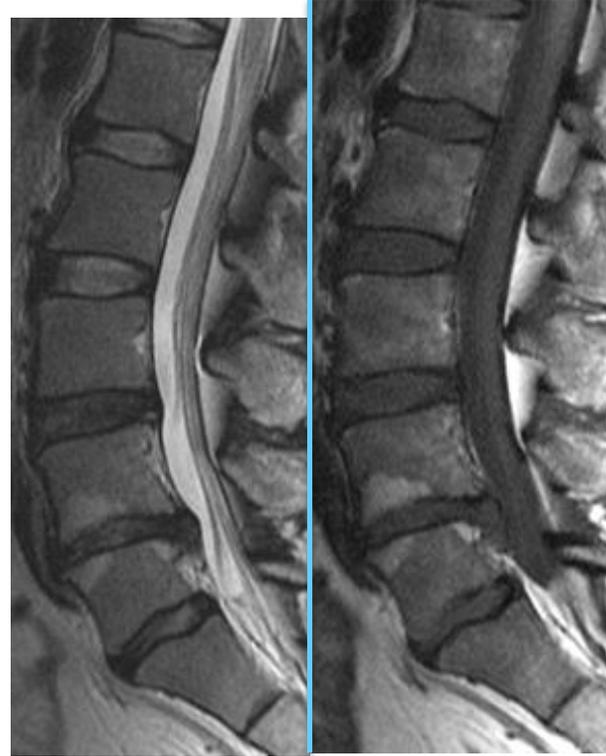
End Plate Inflammatory Change

- **Modic Changes:** endplate signal change
 - **Modic I:** Vascularized granulation tissue
 - **Modic II:** Fatty infiltration
 - **Modic III:** Sclerotic change
- **Modic I > II represent an inflammatory state:** increased levels of TNF α reactive cells, & cellular products.

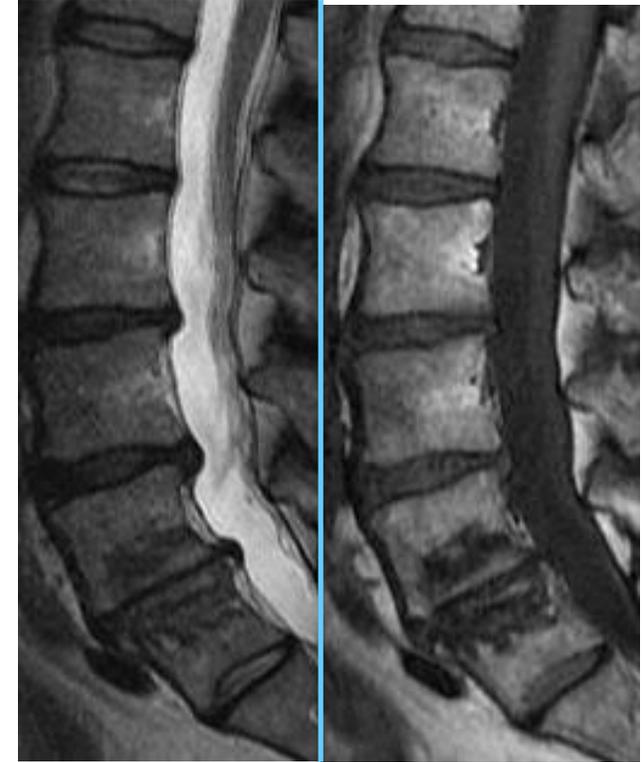
Endplate Inflammatory Change Modic Classification



Modic I



Modic II

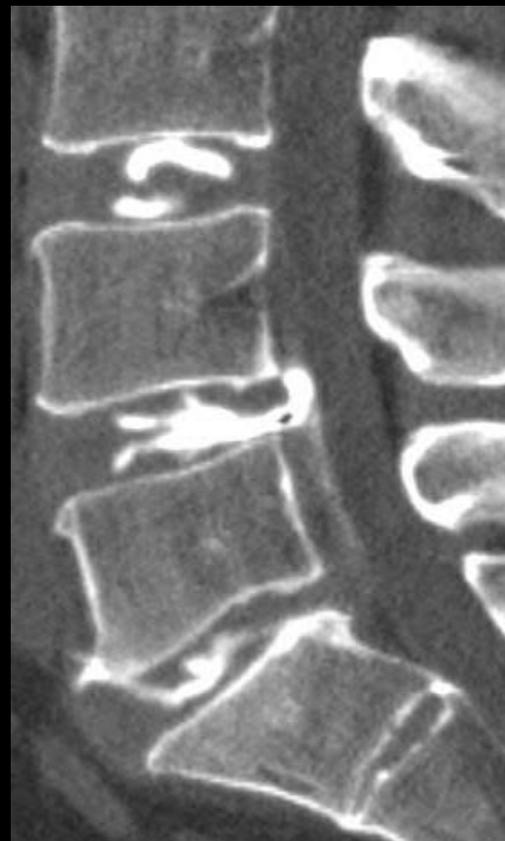


Modic III

Endplate (Modic) Change

| Author, Date | Discogram criteria | Modic type | Prevalence per disc | Sensitivity | Specificity | PPV | NPV | +LR (CI) | -LR (CI) |
|------------------|--------------------|---------------------------|--------------------------|-------------|-------------|------|-----|---------------------|-------------------|
| Braithwaite 1998 | Walsh | I + II | 25% imaged 15% tested | 24% | 96% | 91% | 47% | 6.0 (1.7-21.2) | 0.80 (0.7-0.9) |
| Ito 1998 | Walsh | I + II +III? | 9% | 23% | 94% | 56% | 80% | 4.0 (1.3-12.8) | 0.82 (0.7-1.0) |
| Weishaupt 2001 | IASP | I + II | 22% | 48% | 96% | 88% | 72% | 10.86 (3.5-34.1) | 0.55 (0.4-0.7) |
| | | I + II Mod + Severe | 16% | 38% | 100% | 100% | 69% | 52.1 (3.2-844) | 0.63 (0.5-0.8) |
| Kokkonen 2002 | Walsh | I + II | 36% | 38% | 65% | 38% | 65% | 1.1 (0.6-1.8) | 0.95 (0.7-1.3) |
| Lim 2005 | Walsh | I + II | 14% | 9% | 83% | 21% | 62% | 0.6 (0.2-1.7) | 1.1 (0.9-1.3) |
| Lei 2008 | IASP | I + II ? | 14% | 32% | 98% | 94% | 62% | 19.25 (2.7-140) | 0.69 (0.6-0.8) |
| O'Neill 2008 | IASP | I + II | 8% | 14% | 98% | 89% | 51% | 7.63 (2.8-21.2) | 0.88 (0.8-0.9) |
| Kang 2009 | IASP | I + II | 13% | 14% | 87% | 26% | 76% | 1.08 (0.5-2.6) | 0.99 (0.9-1.1) |

Modic Change



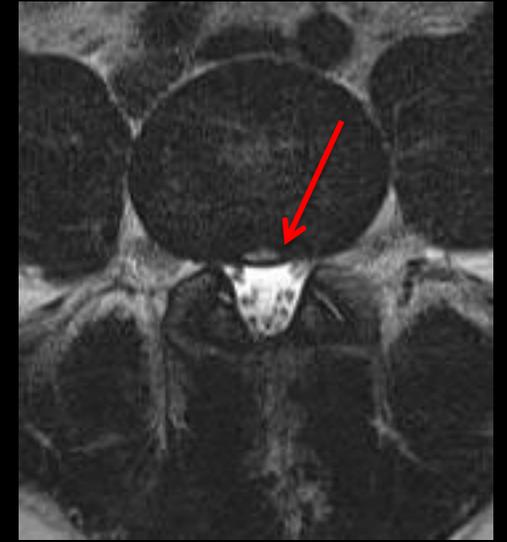
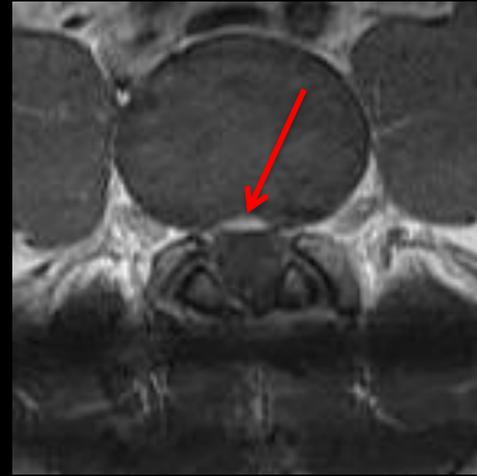
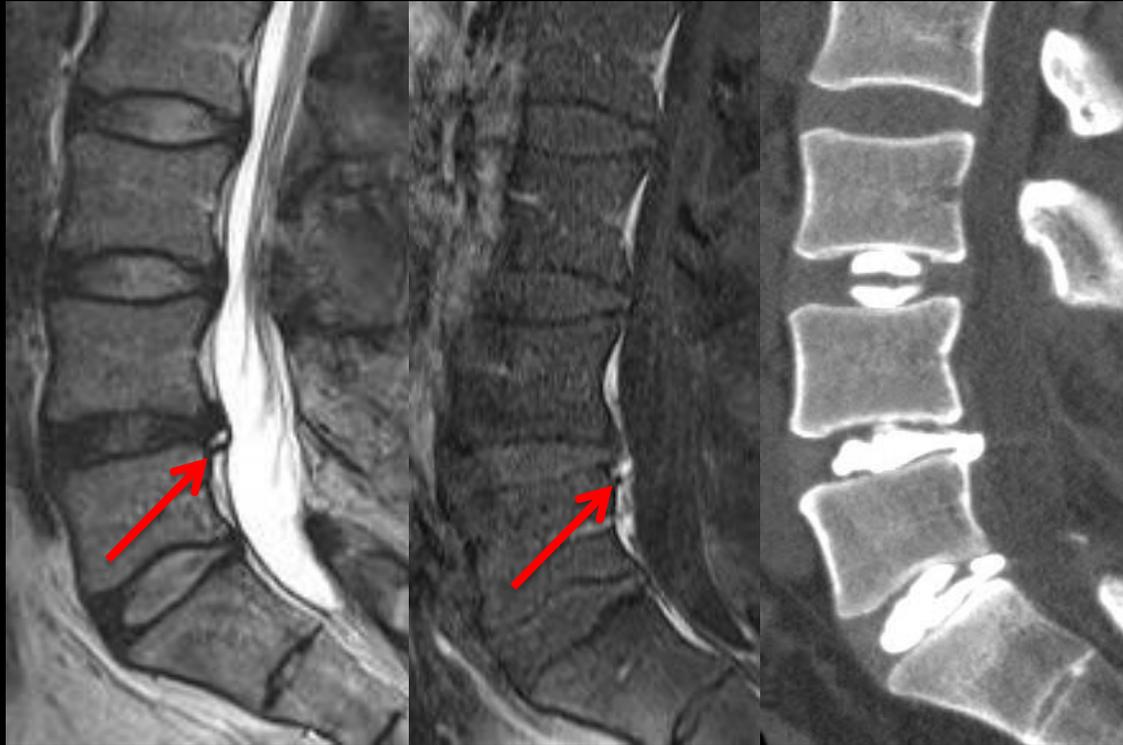
Modic Change of either Type I or II, involving $> 25\%$ of vertical height of a vertebral body very strongly correlates with positive provocation discography

Pooled data yields a +LR of 3.4. This translates into a 69% chance of a painful disc at disc stimulation.

High Intensity Zone (HIZ)

| Author, date | Discogram criteria | HIZ criteria | Prevalence per disc | Sensitivity | Specificity | PPV | NPV | +LR (CI) | -LR (CI) |
|----------------------------|------------------------------|--|---------------------|-------------|-------------|------|-----|--------------------|---------------------|
| Aprill, Bogduk 1992 | <i>IASP Exact pain</i> | Aprill | 34% * | 82% | 89% | 78% | 91% | 7.3 (3.9-13.7) | 0.21 (0.1-0.4) |
| | <i>Exact or similar pain</i> | Aprill | | 63% | 97% | 95% | 72% | 18.4 (4.6-72.7) | 0.38 (0.3-0.5) |
| Schellhas 1996 | <i>IASP</i> | Schellhas# | 60% * | 97% | 83% | 87% | 97% | 5.7 (3.5-9.3) | 0.03 (0.01-0.11) |
| Ricketson 1996 | <i>Walsh</i> | Aprill | 9% | 12% | 92% | 57% | 54% | 1.5 (0.4-5.6) | 0.96 (0.8-1.1) |
| Saifuddin 1998 | <i>Walsh</i> | Aprill | 18% | 27% | 94% | 89% | 47% | 4.8 (1.7-14.2) | 0.77 (0.7-0.9) |
| Ito 1998 | <i>Walsh</i> | Aprill | 20% | 52% | 89% | 60% | 87% | 4.8 (2.3-10.2) | 0.54 (0.4-0.8) |
| Smith 1998 | <i>Walsh</i> | Aprill | 13% | 27% | 90% | 40% | 80% | 2.6 (1.2-5.6) | 0.82 (0.7-1.0) |
| Carragee 2000 | <i>Walsh</i> | Carragee@ | 30% | 45% | 84% | 73% | 62% | 2.8 (1.5-5.5) | 0.7 (0.5-0.9) |
| Weishaupt 2001 | <i>IASP</i> | Aprill | 20% | 27% | 85% | 56% | 62% | 1.8 (0.8-3.7) | 0.86 (0.7-1.0) |
| Peng 2006 | <i>Walsh</i> | Aprill | 12% | NC | NC | 100% | NC | NC | NC |
| Lei 2008 | <i>Walsh</i> | Aprill | 19% | 25% | 87% | 62% | 57% | 1.8 (0.8-4.1) | 0.87 (0.7-1.1) |
| O'Neill 2008 | <i>IASP</i> | O'Neill^ 1+2+3 Intensity grades | 28% | 44% | 89% | 82% | 60% | 4.1 (2.7-6.1) | 0.62 (0.5-0.7) |
| | | 2+3 | 16% | 26% | 95% | 86% | 54% | 5.7 (3.0-10.9) | 0.78 (0.7-0.8) |
| | | 3 | 9% | 15% | 98% | 86% | 52% | 6.8 (2.7-17.1) | 0.87 (0.8-0.9) |
| Kang 2009 | <i>IASP</i> | Aprill | 26% | 57% | 84% | 53% | 86% | 3.46 (2.2-5.5) | 0.52 (0.4-0.7) |

High Intensity Zone (HIZ): Strongly predicts a painful disc



Pooled data: + LR \approx 4 If prevalence of IDD is 46%, LR of 4 provides 73% confidence of a painful disc at provocation discography

Painful Disc Chemical Signature

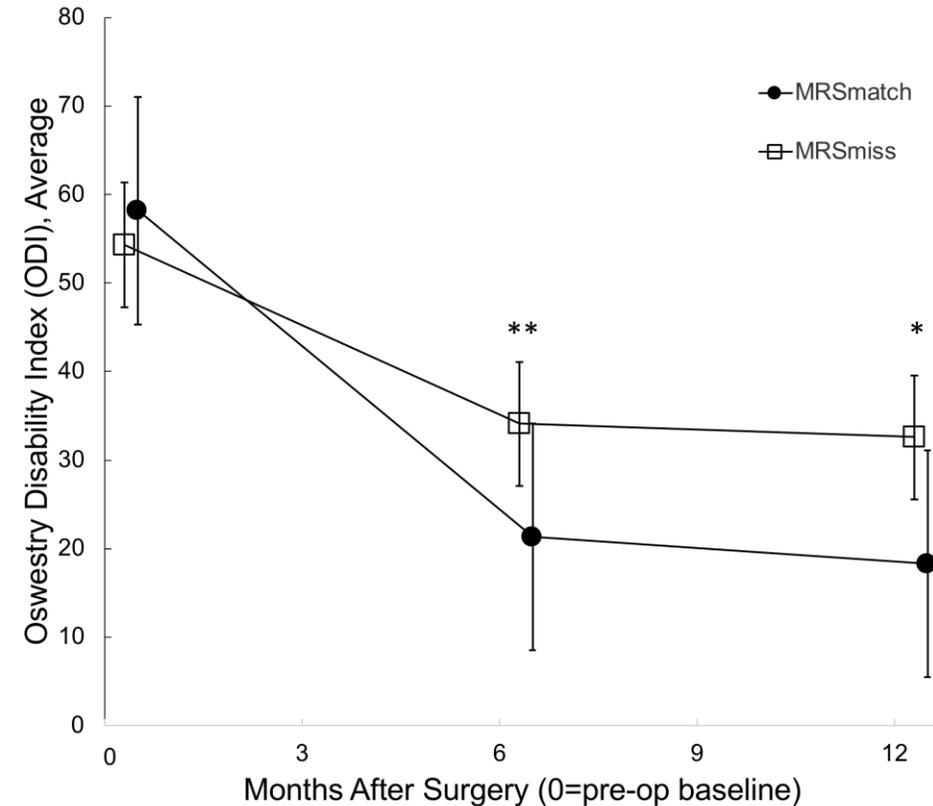
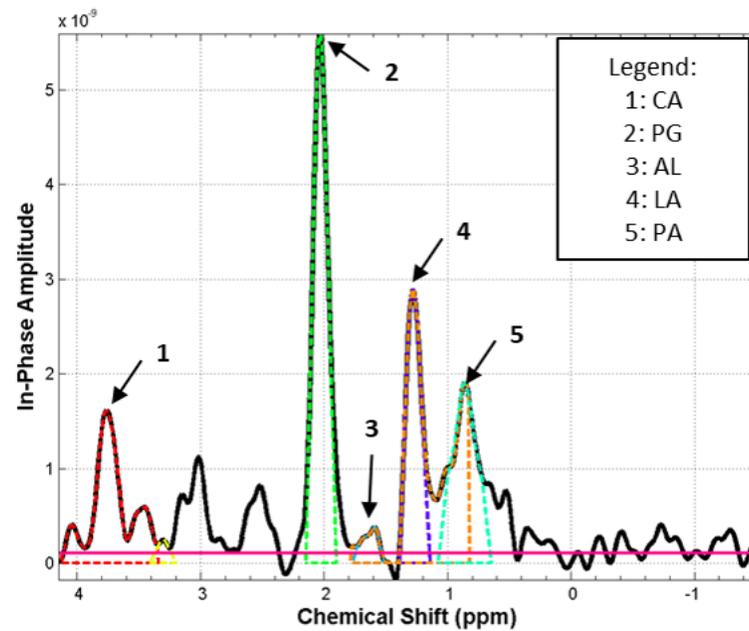
- The discs is avascular- disc cells live in a nutritionally challenged environment.
- Disc cells consume glucose and product lactate.
- Lactic acid lowers disc pH, accelerates degeneration, and is linked to back pain.
- Acid sensing ion channels (ASICs) are stimulated by ischemia
 - chest pain arising from myocardial infarction
 - bone pain secondary to cancer
 - **ASICs are expressed by disc cells**, increased with degeneration, **role in DLBP???**

Magnetic Resonance Spectroscopy (MRS)

- Magnetic resonance spectroscopy (MRS) can be used to characterize in vivo metabolic features within tissue.
- Using ex vivo MRS, Keshari and colleagues demonstrated that lactate (LA) and proteoglycan (PG), provide spectroscopically quantifiable biomarkers for discogenic pain. Spine 2008 33(3):312–317
- Recent advances in MRS protocols have now enabled in vivo biomarker quantification within patients.

Biomarkers Studied with MRS

- **Carbohydrate/collagen (CA) and PG** are markers of structural integrity expected to decrease with disc degeneration
- **Alanine (AL), LA, and propionate (PA)** are acidic pain markers expected to increase with discogenic pain
- **Gornet, M.G., Peacock, J., Claude, J., Lotz, J. et al. Eur Spine J (2019) 28: 674. <https://doi.org/10.1007/s00586-018-05873-3>**



Gornet MG, Peacock J, Claude J, Schranck FW, Copay AG, Eastlack RK, Benz R, Olshen A, Lotz JC (2018) Magnetic Resonance Spectroscopy (MRS) can identify painful lumbar discs and may facilitate improved clinical outcomes of lumbar surgeries for discogenic pain. *Eur Spine J*;

Key points

1. Non-invasive, Single-voxel Magnetic Resonance Spectroscopy (MRS) can accurately distinguish painful from non-painful lumbar intervertebral discs in chronic low back pain (CLBP) patients.
2. Analysis of 206 lumbar discs from 139 CLBP patients reflected 85 % Total Accuracy, 82 % Sensitivity, and 88 % Specificity overall as compared to a gold-standard provocation discography.
3. For the subset of CLBP patients with non-herniated discs, MRS demonstrated 93 % total accuracy with 91 % sensitivity and 93 % specificity.
4. MRS forecasted outcomes for CLBP patients. Six (n=73) to 12-month (n=62) surgical success (>15 points on ODI) rates were very high (>90 percent) for patients treated at MRS+ discs, versus low (near 50 %) for treated MRS- discs.

Take Home Messages

1. MRS data correlate with discogenic pain status as characterized by the reference standard provocation discography.
2. MRS may support improved surgical outcomes for chronic low back pain patients.
3. Non-invasive MRS is a potentially valuable approach to clarifying pain mechanisms and designing targeted CLBP therapies that are customized to the patient.

The Disc

- Suffers inevitable non-painful age-related change, often inappropriately called “degeneration”
- Internal Disc Disruption (IDD) is a distinct disease process causal of discogenic pain
- Disc stimulation or provocation discography is the reference standard for IDD

UTILITY

Negative predictive value

| Disc Stimulation Negative | Avoid Operation |
|------------------------------------|-----------------|
| Disc Stimulation Indeterminate | Avoid Operation |
| Disc Stimulation 3 Levels Positive | ?????? |

Disc stimulation is a barrier to excessive surgery

When negative,

disc stimulation prevents unnecessary surgery, including IDET, cold RF, methylene blue, etc

DISC STIMULATION

Does it have utility? YES

Does it alter management? YES

DISC STIMULATION

Disc stimulation

Negative

Prevent surgery

Positive

Closure/Guide Treatment Planning

Prevent further investigations

Avoid inappropriate interventions

Discogenic Pain: Imaging Correlates

Population: clinically suspected discogenic pain

1. Severe loss of nuclear signal/loss of disc height strongly predicts a painful disc
2. Normal nuclear signal excludes a painful disc

Discogenic Pain: Imaging Correlates

Intermediate nuclear signal:

1. High intensity zone – infrequent - strongly predicts painful disc
2. HIZ + disc protrusion very strongly predicts painful disc
3. Marrow endplate change, I or II, involving $> 25\%$ of vertebral body – infrequent- very strongly predicts a painful disc

Discogenic Pain: Imaging Correlates

Is this adequate for therapeutic decisions?

The answer is dependent on what therapeutic interventions are available:

- *what is the evidence of efficacy?*
- *what is the safety profile?*

The Disc

- Imaging can suggest a likely diagnosis of IDD, confirmed by discography

References

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The Disc As A Pain Generator

Self Assessment

1. Is loss of T2 signal in the disc nucleus a specific indicator of a painful disc? **No**
1. How is the diagnosis of Internal Disc Derangement (IDD) achieved? **Disc Stimulation**
1. How does disc stimulation manifest negative predictive value? **Prevent unnecessary surgery / interventions**
1. How does disc stimulation manifest diagnostic utility when positive? **Closure**