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Establishing a Gold Standard for Noninvasive Identification of Painful Lumbar Discs: Prospective Comparison of Magnetic Resonance Spectroscopy vs Low-Pressure Provocation Discography

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ABSTRACT

Purpose: Verifying lumbar disc pain can present a clinical challenge. Low-pressure provocative discography (PD) has served as the gold standard, although it is invasive and often a challenge to interpret. We reported that magnetic resonance spectroscopy (MRS) biomarkers accurately predict PD results in lumbar discs and improved outcomes for patients with surgery at positive MRS levels versus nonsurgery. To further substantiate MRS for diagnosing painful discs, we report a prospective comparison of 2 MRS-derived measures: NOCISCORE (pain) and SI-SCORE (degeneration severity).

Methods: Lumbar MRS and software-based postprocessing (NOCISCAN-LS, Aclarion Inc.) was performed in 44 discs in 14 patients (prospective cohort [PC]). PC data were compared to prior data used to establish the NOCISCORE (training cohort [TC]). The NOCISCORE was converted to an ordinal value (high/intermediate/low; NOCI+/mild/–) and compared against painful (P) versus nonpainful (NP) control diagnosis (PD) for 19 discs where PD was performed in the PC (12 NP; 7 P). Sensitivity, specificity, and positive and negative predictive values were calculated. The SI-SCORE was compared against MRI Pfirrmann Grades for 465 discs in 126 patients (PC plus TC).

Results: For the PC, MRS (NOCI+/–) compared to PD (P/NP) with an accuracy of 87%, sensitivity of 100%, and specificity of 80%. The positive predictive value (PPV) in herniated discs, and negative predictive value (NPV) in non-herniated discs, were 100%. NOCISCOREs were significantly higher for PD+ versus PD– discs for PC and TC ($P < 0.05$), and the NOCISCORE distributions for PD+/– group were not statistically different between the PC and TC ($P > 0.05$). SI-SCORES differed between Pfirrmann Grades 1 and 2 (less degenerated) versus Grades 3 and 4 (more degenerated; $P < 0.05$), with a progressively decreasing trend with Pfirrmann Grades 1–5.

Conclusion: These current data provide prospective confirmation of the predictive value of disc MRS for distinguishing painful discs and for assessing the disc structural integrity.

Clinical Relevance: NOCISCAN is an adoptable, noninvasive, and objectively quantitative test to improve management of low back pain patients.

Level of Evidence: 2.

Lumbar Spine

Keywords: low back pain, magnetic resonance spectroscopy, pain biomarkers, lumbar disc surgery, discogenic, discogram, discography, diagnosis

INTRODUCTION

Chronic low back pain (cLBP) is a complex condition where a specific nociceptive cause is not identified in nearly all patients.[1] While it is tempting to attribute pain to age-related spinal degeneration as seen on traditional clinical imaging, many studies indicate that degeneration is not reliably associated with cLBP.[2] This underscores our limited understanding of causal relationships between risk factors and cLBP, which often becomes a reason for failed treatments. Clearly, interventions that manipulate features that are not risk factors, or risk factors that are not causal factors, are a waste of time and resources and may ultimately cause harm. This is particularly true for a commonly considered nociceptive source, the intervertebral disc. There is no widely accepted standard for discogenic pain, which makes the development of a validated tool to localize discogenic pain in individual patients imperative.

Comprehensive diagnostics that identify nociceptive sources in cLBP patients are needed to better align clinical practice with evidence.[1] Ideally, validated biomarkers

discriminate subsets of patients with shared characteristics and thereby optimize outcomes.[3] Additionally, objective biomarkers can be used for shared decision-making: to explain the treatment rationale to patients, to enhance the patient's understanding of the problem, and thus to enhance compliance during treatment. When patients are engaged, they are more satisfied with their elective spine care.[4]

To address the unmet need for a discogenic pain biomarker, we previously reported the first noninvasive, quantitative, and objective measure of lumbar disc pain based on single-voxel magnetic resonance spectroscopy (MRS).[5] This approach quantifies the chemical features of degenerating extracellular matrix[6] as well as metabolites of disc cell function related to pain, such as lactic acid[7] and propionic acid.[8] The clinical utility of MRS was established by validation against a reference diagnostic standard, low-pressure provocative discography (PD).[5]

The current study tests the performance generalizability of MRS vs PD in a new clinical validation dataset that was not part of the initial algorithmic development.

METHODS

Lumbar Disc MRS Study Design

A multicenter, observational, single-voxel MRS clinical study was conducted under institutional review board (IRB) approval and patient informed consent. The enrolled patients received magnetic resonance imaging (MRI) and PD as part of their standard care for discogenic low back pain (DLBP). Custom MRI acquisition protocols were conducted using the Siemens 3T Verio at a single center from November 2011 to May 2019. We previously reported an initial training cohort (TC) of patients who were used to develop the MRS acquisition and postprocessing techniques for optimal data quality and reliability and for training quantitative scoring algorithms for optimal correlation and diagnostic accuracy against standardized controls for diagnosing P/NP (PD±) and structural degeneration (Pfirrmann Grades).[5] For the current study, a subsequent prospective cohort (PC) of patients was used to further validate the accuracy of the previously trained algorithms against new cases.

DLBP Patient and Lumbar Disc Population

Patient inclusion/exclusion criteria (Table 1) focused on patients receiving PD for suspected discogenic pain. Fourteen patients were enrolled, examined by MRS, and then received lumbar surgery (MRS data were not factored into treatment decisions). MRS was performed on 44 discs in the 14 patients (PC; vs the original 623 discs in 139 patients; TC group).

Disc levels for MRS were selected by physician preference, typically including discs receiving PD plus other non-PD levels (≥3 MRS levels recommended per patient). PD was performed using the physician's preferred techniques, with positive discogram (PD+) results requiring low-pressure provocation (<50 psi), ≥ Grade III annular tear, and a negative control disc (PD−).[9] PD was performed

Table 1. Inclusion/exclusion criteria for patients experiencing pain.

Inclusion Criteria

1. Male and nonpregnant female patients aged between 18 and 70 y.
2. Institutional review board–approved informed consent obtained.
3. Meet accepted criteria to be indicated for PD of the lumbar spine consistent with Practice Guidelines for Spinal Diagnostic and Treatment Procedures.[9]
4. Score ≥40% on the ODI.
5. VAS score for back pain ≥4 cm.
6. VAS score for leg pain:
   a. <4 cm OR
   b. <50% of VAS score for back pain
7. PD was performed >6 wk but <6 mo prior to scheduled MRS or PD will be conducted within 1 mo after MRS.

Exclusion Criteria

1. Has had prior lumbar back surgery or intradiscal treatments at the index lumbar disc levels (diagnostic provocative or anesthetic discography or epidural steroid injections, sacroiliac injections, or facet joint injections are not excluded).
2. Women who are currently pregnant (or believe they may be at risk of being or becoming pregnant), or are breastfeeding, during the study period when scans will be performed.
3. Diagnosis, based on radiographic evidence, of clinically relevant lumbar vertebral abnormalities (except modic end-plate changes, which are not excluded), including:
   - Spondylolisthesis with >2 mm of translation, or with pars fracture, at the involved level
   - Spondylolysis
   - Lumbar scoliosis with a Cobb angle >15°
   - Evidence of prior fracture or trauma to the L1, L2, L3, L4, or L5 levels in either compression or burst
   - Lumbar kyphosis
4. Radiological evidence of lumbar disc herniation comprising extrusion.
5. Prior PD showing evidence of Grade 5 annular tear with contrast leakage (eg, per radiographic evidence and/or inability to maintain or increase pressure with increased injection volume).
6. Motor strength deficit in lower extremities.
7. Chronic disease (other than degenerative disc disease), chronic pain (other than discogenic low back pain), or psychological dysfunction, which may, in the opinion of the principal investigator, compromise a patient's ability to comply with study procedures and/or may confound data.
8. Applicable exclusion criteria for standard lumbar MRI.

Abbreviations: MRI, magnetic resonance imaging; MRS, magnetic resonance spectroscopy; ODI, Oswestry Disability Index; PD, provocative discography; VAS, visual analog scale.

after MRS, except for 2 cases in the TC group where PD was performed at least 6 weeks prior to MRS. The NP group included the PD− discs. The P group included the PD+ discs plus other non-PD discs that were physician-diagnosed as painful (Dx+) based on other clinical criteria (eg, patient-reported symptoms, physical examination and neurological deficits, x-ray, MRI, myelogram, and diagnostic injections) in patients receiving PD at other levels.

Lumbar Disc MRS Protocol

The custom MRS protocol and postprocessing approaches for generating MRS-derived NOCISCOREs and NOCI+/mild/− classifications for discs were as previously published,[5] which include the following:

- Generating relative NOCISCORE Total (0–10 scale) and Normalized (0–1 scale) scores based on the different levels of degenerative pain biomarkers (alanine, lactate, and propionate) in each disc examined in a patient, and generating related high/low NOCI± classification ranges that were trained in the TC group to correspond with P/NP controls (and intermediate NOCI mild range reflecting degenerative pain biomarker levels that are below and above the respective thresholds for NOCI± classifications).
- Generating SI-SCORE (0–1 scale) values that are the disc's MRS-derived proteoglycan (PG) spectral value normalized to the highest calculated level for all discs examined in a patient.

Data Analysis

Statistical analyses for the trained MRS-based NOCISCORE correlations to P and NP data were initially performed with the TC group.[5] Subsequent to training, a paired Student *t* test was used for comparing NOCISCORE distributions between PD± control groups within each of the treatment groups (Group C and Group D) within the PC group and also for comparing SI-SCORE distributions between Pfirrmann Grades. Statistical comparisons of various patient baseline characteristics and diagnostic performance (eg, overall accuracy, sensitivity, and specificity) were performed, with success rate differences compared using a Pearson χ^2 test (JMP Pro, V16).

Association between MRS results and surgical success was evaluated using ODI improvement relative to correspondence between the treated level and the MRS-based classifications for the patient's discs, with at least a 15-point ODI improvement considered "ODI Success."[10]

RESULTS

Prospective MRS-Derived NOCISCOREs vs PD± Controls

Of the 44 discs evaluated in the PC group, 4 (9%) were excluded from analysis due to technical MRS signal quality issues. Of the remaining 40 PC discs, 21 (53%) were non-PD discs that were neither P nor NP controls, and 19 were PD discs (PD+ or PD−).

The distribution of various patient characteristics in the PC group was comparable with the TC group (Table 2). The NOCISCORE Total and Normalized distributions were significantly higher ($P < 0.05$) for P controls (including both PD+ and Dx+ and also when only considering PD+) vs NP controls for both the PC and TC groups but were not significantly different between cohorts for either the PD+ or PD− control groups (Figure 1, Tables 3 and 4).

Successfully generated NOCISCOREs resulted in 79% (15/19) NOCI± and 21% (4/19) NOCI mild classifications for PC discs, as compared with 84% (173/207) NOCI± and 16% (34/207) NOCI mild classifications in the TC group. Diagnostic accuracy for the NOCI± classifications vs the P/NP controls was (PC % [n/N] vs TC % [n/N], *P*): total accuracy = 87% (13/15) vs 85% (147/173), $P = 0.9$; sensitivity = 100% (5/5) vs 81% (63/78), $P = 0.3$; and specificity = 80% (8/10) vs 88% (84/95), $P = 0.5$. The positive predictive value (PPV) for NOCI+ was 100% (8/8) for nonherniated discs, and the negative predictive value for NOCI− was 100% for herniated discs (4/4; Table 5). Only 2/15 of the NOCI± classified discs did not prospectively match P/NP controls. This was in 2 patients who each did not have a PD+ control disc but had 2 PD− control discs that corresponded with

Table 2. Baseline characteristics of training and prospective patient cohorts.

Characteristic	Patient Cohorts		
	Training (*n* = 139)	Prospective (*n* = 14)	*P*[a]
Age, y, mean (range)	41.4 (20–65)	34.5 (24–47)	0.009
Women, *n* (%)	43 (31)	2 (14)	0.19
Race/ethnic group, *n* (%)			0.57
Non-Hispanic	137 (99)	14 (100)	
White	122 (88)	13 (93)	
Black	15 (11)	1 (7)	
Body mass index, mean ± SD	30.0 ± 6.2	31.5 ± 5.3	0.32
Smoker, *n* (%)	49 (35)	1 (7)	0.04
Workers' compensation, *n* (%)	120 (86)	10 (71)	0.13
Oswestry Disability Index score, mean ± SD	56.5 ± 11.3	54.7 ± 14.1	0.65

[a]Determined using *t* test.

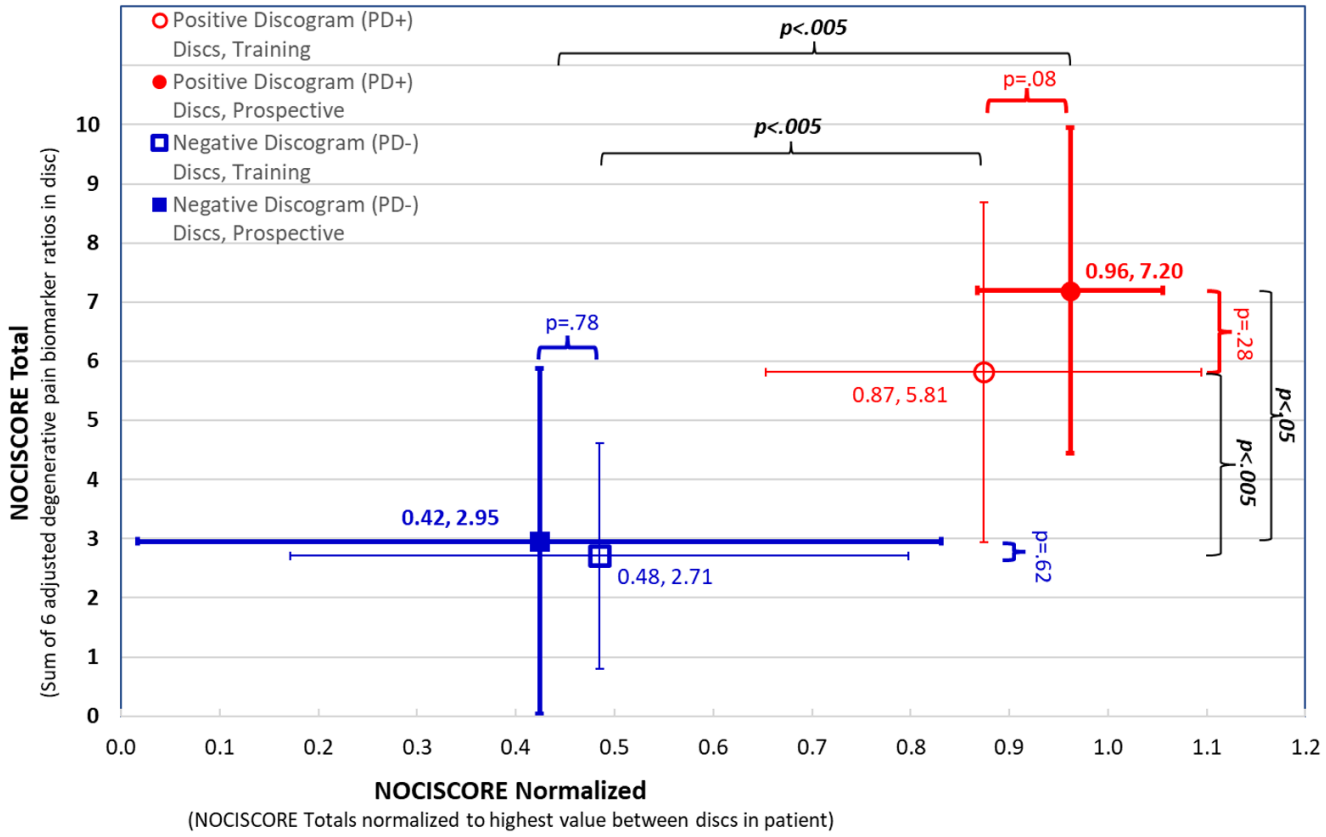

Figure 1. Distributions (mean ± SD) of NOCISCORE Total and Normalized values for PD+ and PD– controls. PD, provocative discography

Table 3. Distribution of NOCISCORE Total and Normalized values for different P/NP control groups in the prospective patient cohort.

		NOCISCORE Total			NOCISCORE Normalized		
P/NP Discs	***n***	**Mean**	**SD**	***p* (P vs NP)**	**Mean**	**SD**	***p* (P vs NP)**
P (PD+ & Dx+)	7	7.6	2.7	<0.005	0.97	0.09	<0.005
P (PD+ only)	6	7.2	2.7	<0.05	0.96	0.09	<0.005
NP (PD-)	12	3.0	2.9		0.42	0.41	

Abbreviations: NP, nonpainful; P, painful; PD, provocative discography.

Table 4. Distribution of NOCISCORE Total and Normalized values for different P/NP disc control groups and between training and prospective cohorts.

			NOCISCORE Total		NOCISCORE Normalized	
P/NP Disc Controls	**Population**	***n***	**Mean**	**SD**	**Mean**	**SD**
P (PD+ & Dx+)	(a) Training	98	5.8	2.9	0.87	0.23
	(b) Prospective	7	7.6	2.7	0.97	0.09
	p value (a) vs (b)		0.14		<0.05	
P (PD+ only)	(a) Training	85	5.8	2.9	0.87	0.22
	(b) Prospective	6	7.2	2.7	0.96	0.09
	p value (a) vs (b)		0.28		0.08	
NP (PD-)	(a) Training	109	2.7	1.9	0.48	0.31
	(b) Prospective	12	3.0	2.9	0.42	0.41
	p value (a) vs (b)		0.78		0.62	

Abbreviations: NP, nonpainful; P, painful; PD, provocative discography.

Table 5. Diagnostic accuracy metrics of magnetic resonance spectroscopy-based NOCISCORE results vs painful/nonpainful controls for prospective and training patient cohorts.

	Training						Prospective						All Patients					
	Overall		Non-Herniated		Herniated		Overall		Non-Herniated		Herniated		Overall		Non-Herniated		Herniated	
Accuracy Metrics	*%*	*n*	*%*	*n*	*%*	*n*	*%*	*n*	*%*	*n*	*%*	*n*	*%*	*n*	*%*	*n*	*%*	*n*
Sensitivity	81 %	63/78	83 %	10/12	80 %	53/66	100 %	5/5	100 %	1/1	100 %	4/4	82 %	68/83	85 %	11/13	81 %	57/70
Specificity	88 %	84/95	93 %	66/71	75 %	18/24	80 %	8/10	80 %	8/10	n/a	0/0	88 %	92/105	91 %	74/81	75 %	18/24
PPV	85 %	63/74	67 %	10/15	90 %	53/59	71 %	5/7	33 %	1/3	100 %	4/4	84 %	68/81	61 %	11/18	90 %	57/63
NPV	85 %	84/99	97 %	66/68	58 %	18/31	100 %	8/8	100 %	8/8	n/a	0/0	86 %	92/107	97 %	74/76	58 %	18/31
Overall Accuracy	85 %	147/173	92 %	76/83	79 %	71/90	87 %	13/15	82 %	9/11	100 %	4/4	85 %	160/188	90 %	85/94	80 %	75/94
NOCI+/–	84 %	173/207	87 %	83/95	80 %	90/112	79 %	15/19	73 %	11/15	100 %	4/4	83 %	188/226	85 %	94/110	81 %	94/116
NOCImild	16 %	34/207	13 %	12/95	20 %	22/112	21 %	4/19	27 %	4/15	0 %	0/4	17 %	38/226	15 %	16/110	19 %	22/116

Abbreviations: NA, not applicable; NPV, negative predictive value; PPV, positive predictive value.

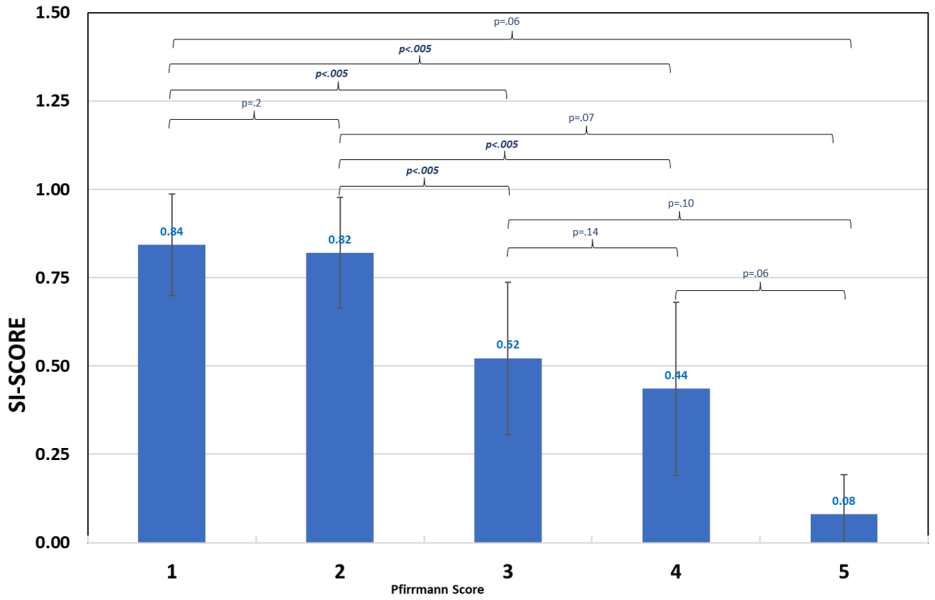

Figure 2. SI-SCORES vs Pfirrmann Grades for 465 discs in 112 patients.

one NOCI+ and one NOCI– result (neither received surgery).

Prospective MRS-Derived SI-SCORES vs Pfirrmann Grades (Both Cohorts Combined)

Unlike NOCISCOREs and NOCI+/mild/– classifications, SI-SCOREs are derived from a single region of the MRS spectrum. Therefore, SI-SCOREs did not require training to determine optimal weighting coefficients (as was necessary for the NOCISCOREs) and were evaluated prospectively in both TC and PC groups combined. SI-SCORES were significantly higher for each of Pfirrmann Grades 1 and 2 vs each of Pfirrmann Grades 3 and 4, with an overall trend for SI-SCORE reduction from each Pfirrmann Grade to the next (Table 6 and Figure 2).

DISCUSSION

The current data demonstrate that the previously reported, strong MRS/PD association is generalizable to discs in the PC group. NOCI± classifications in the PC group were similar to PD± control groups with 87% overall accuracy. NOCISCOREs were significantly higher for PD+ vs PD– controls in each of the PC and TC groups but did not significantly differ overall between the PC and TC groups for either of the PD+ and PD– control groups.

The prospective case series demonstrates that the MRS approach may be particularly useful for ruling out nonpainful discs from surgical intervention. Data from three subjects undergoing surgery during the evaluation period highlight the clinical utility of MRS, where an unsuccessful surgery (based on ODI criteria) left a non-NOCI– level untreated (L3/L4; Figure 3), while two clinical success were associated with treatment of single discs that were not NOCI– (Figures 3 and 4).It was particularly notable that the specificity and negative predictive value were both 100% (5/5 and 8/8, respectively). In addition, while only 4 herniated discs were included for the P/NP control comparison purposes in the PC group and all were only NOCI+; all 4 of them also accurately corresponded to PD+ controls for 100% PPV. The highest performance within the herniated disc population of the TC group was also a 90% (53/59) PPV. This may

Table 6. Distribution of magnetic resonance spectroscopy-derived SI-SCORES vs Pfirrmann Grades.

		SI-SCORE		*t* Test Between Pfirrmann Grades (*P*)			
Pfirrmann Grade	**No.**	**Mean**	**SD**	**vs 2**	**vs 3**	**vs 4**	**vs 5**
1	95	0.84	0.14	0.20	<0.005	<0.005	0.06
2	230	0.82	0.16	-	<0.005	<0.005	0.06
3	117	0.52	0.22	-	-	0.14	0.10
4	21	0.44	0.24	-	-	-	0.06
5	2	0.08	0.11	-	-	-	-

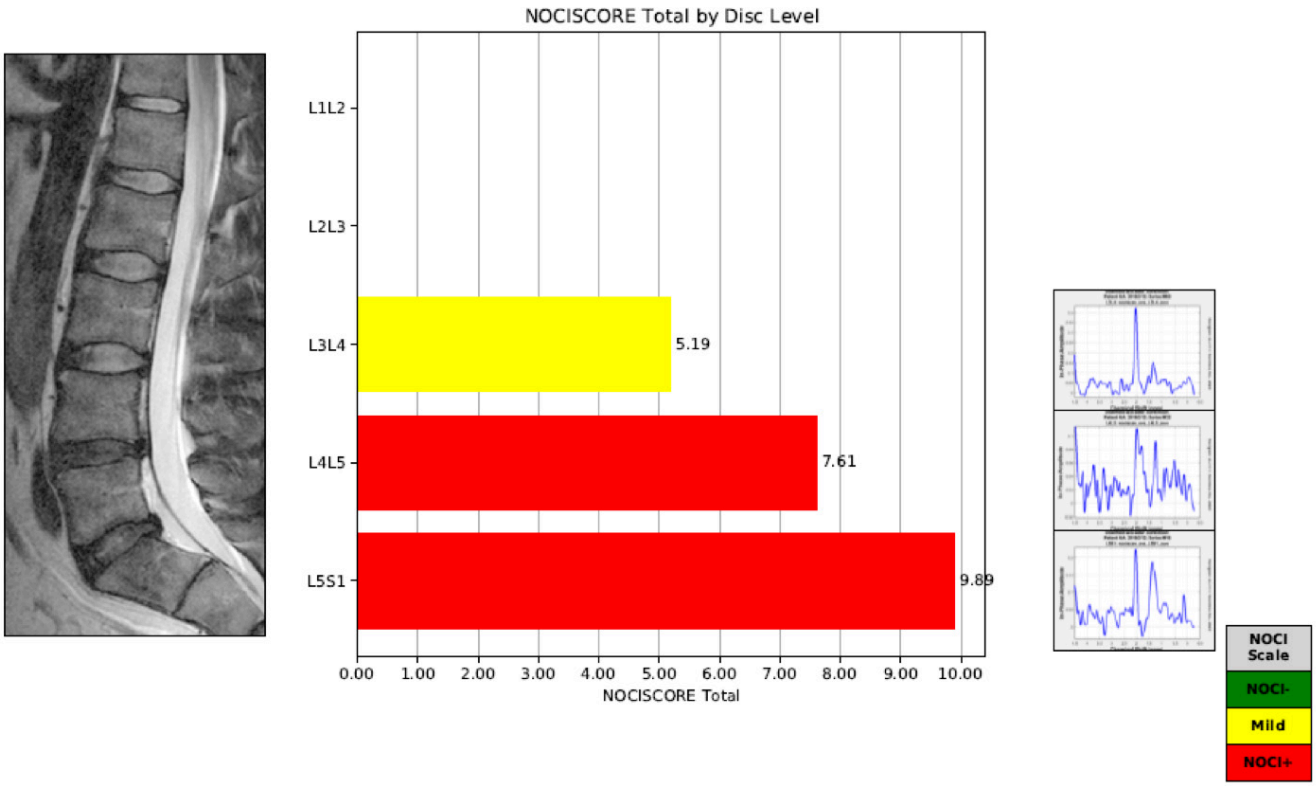

Figure 3. Prospective surgical patient example 1. Two-level total disc replacement surgery was performed at L5-S1 and L4-L5 disc levels that were both NOCI+ and PD+, with an adjacent L3-L4 disc left untreated that was PD- but with an MRS-derived NOCISCORE that was classified as NOCImild. Midsagittal lumbar magnetic resonance imaging (left), NOCISCORE Totals for each evaluated disc level (middle), postprocessed magnetic resonance spectroscopy spectra for each disc (right), and NOCI±/mild color legend (far right). At 6 months, Oswestry Disability Index was unchanged (52 versus 54) while the visual analog scale for back pain was increased compared with the preoperative baseline (6.4 versus 5.6)

suggest that, in the particular context of herniated discs, NOCI+ results may be especially reliable for identifying the presence of chemically mediated pain. In contrast, the lowest diagnostic performance across all comparison subgroups evaluated was the 58% negative predictive value for NOCI− corresponding to PD− controls in herniated discs. This may be explained by the increased potential for herniated discs to involve different sources of pain other than disc chemistry that is not tested via the MRS approach (no herniated discs were classified as NOCI− in the PC group). (Figures 3–5)

The current prospective data suggest a high reliability of NOCISCAN-LS for all diagnostic performance metrics vs PD controls, with perhaps the one exception of an apparently low negative predictive value for specifically ruling out herniated discs as nonpainful when other nonchemical sources of pain may be involved but are not tested by MRS (yet MRS may still propose utility for more specifically ruling out a chemical cause for pain).

The PG content of the nucleus pulposus is highly associated with disc degeneration.[11] Consequently, PG quantification by MRS as captured in the SI-SCORE can be a useful biomarker of disc degeneration status. As may be expected, we demonstrate that the SI-SCORE associates with an alternative method of rating disc degeneration, the Pfirrmann Grade.[12] The Pfirrmann Grade is a 5-level score often used clinically to classify the degenerative status of the disc and includes a subjective assessment of disc structure as seen on T2-weighted MRI. While the interobserver agreement of the Pfirrmann classification is considered good, the I to V Pfirrmann classification is an insensitive measure of disc quality that changes over time. Therefore, we expect that the SI-SCORE can be extremely valuable to track the longitudinal progression of degeneration in cLBP patients under clinical investigation. The ability to discriminate small changes in disc quality will naturally enhance the detection of treatment effects in clinical trials of novel therapies meant to improve disc health.

These results demonstrate the added value of the MRS-based NOCISCOREs for diagnosis and treatment planning. The diagnostic accuracy vs PD suggests a noninvasive, safer, painless, more efficient,

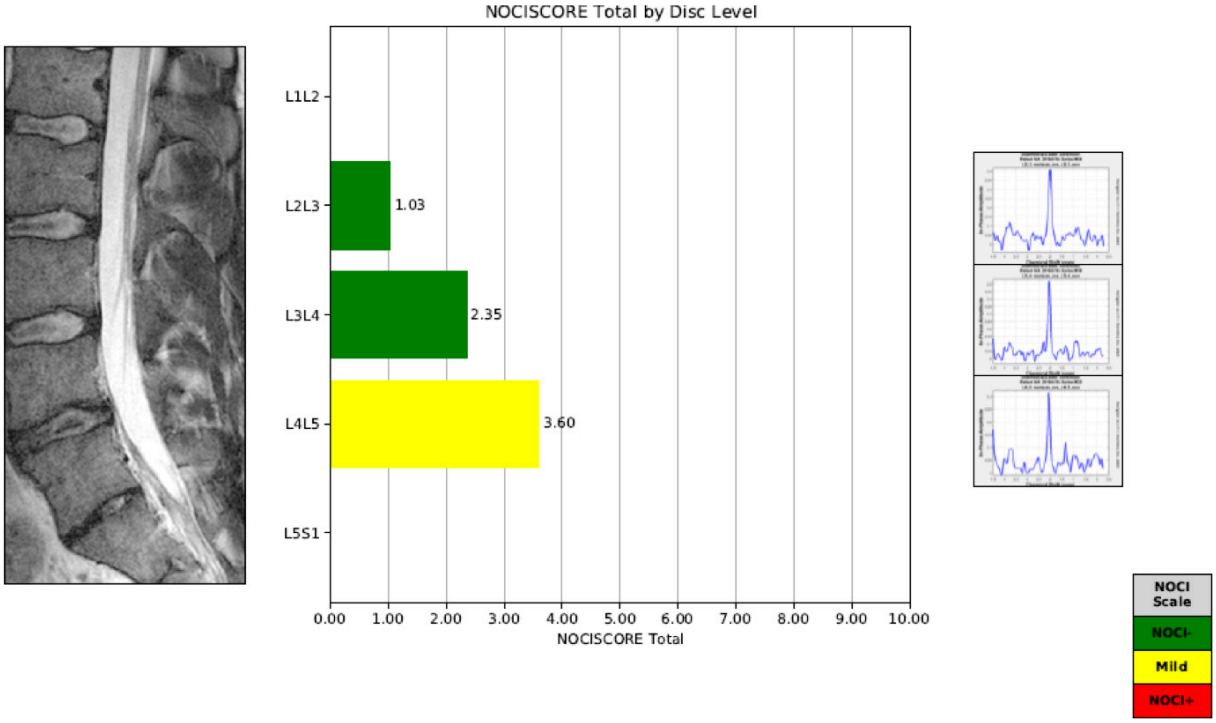

Figure 4. Prospective surgical patient example 2. One-level total disc replacement surgery was performed at the L4-L5 disc level above a sacralized L5-S1 disc and was PD+ and NOCImild (as the highest NOCISCORE disc in the patient, NOCISCORE Normalized = 1). Midsagittal lumbar magnetic resonance imaging (left), NOCISCORE Totals for each evaluated disc level (middle), postprocessed magnetic resonance spectroscopy spectra for each disc (right), and NOCI±/mild color legend (far right). Surgery for this patient was considered a success by Oswestry Disability Index and visual analog scale at 6 (28, 2.1), 12 (12, 0.9), and 24 (22, 6) months.

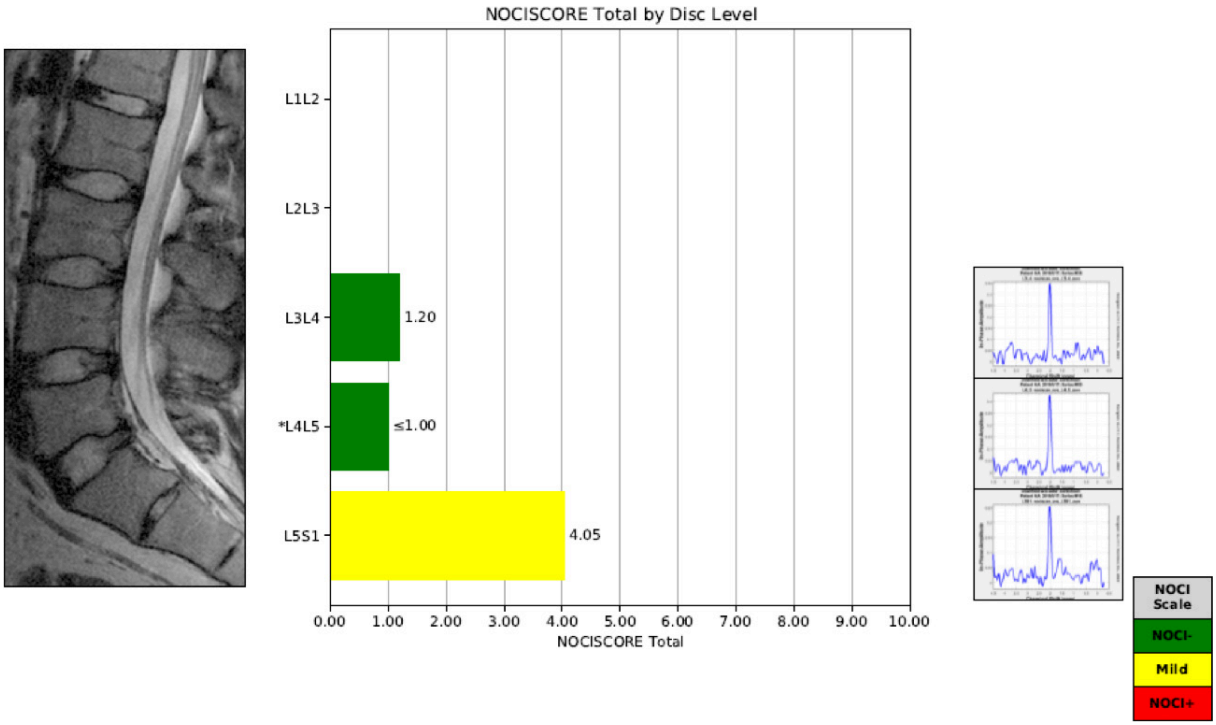

Figure 5. Prospective surgical patient example 3. Midsagittal lumbar magnetic resonance imaging (left), NOCISCORE totals for each evaluated disc level (middle), postprocessed magnetic resonance spectroscopy spectra for each disc (right), and NOCI±/mild color legend (far right).

and more widely adoptable alternative to invasive, potentially risky, and painful PD examination. The MRS diagnostic information provided by this approach may similarly improve the success of other interventions meant to treat discogenic pain. In particular, biological therapies to regenerate the disc or suppress inflammatory processes also require specificity for level selection during preoperative planning. Indeed, MRS may be even more critical in this case because biological-based therapies target discs early in the degenerative cascade where painful levels may only subtly differ from adjacent asymptomatic discs via routine clinical imaging. Furthermore, because biologically treated discs are not surgically removed or reinforced with implants, MRS can be used to track the activity of the therapy over time. Of note, because MRS has the potential to discriminate features of anaerobic bacterial activity[8] and because of the growing awareness of subclinical disc infection as an important discogenic pain mechanism,[13] MRS may be uniquely valuable to distinguish discs that should be treated using antibiotic vs regenerative therapies.

One limitation of this study is the small sample size of discs and respective patients evaluated in the PC group as a validation of the disc MRS approach as previously trained in the TC group for the study. However, despite the relatively small sample sizes, they were sufficient to demonstrate certain observations of statistical significance, such as in particular the significantly higher NOCISCOREs for PD+ vs PD− controls in the PC group (and nonsignificant differences of those NOCISCOREs between the PC and TC groups).

Another limitation of this study is that successful MRS execution may not be feasible on some spinal levels. As discs degenerate, they dehydrate and lose height, potentially degrading the quality of the MRS signal. Currently, MRS voxel heights are limited to a minimum of 3 mm, which may prevent successful data acquisition from severely degenerated discs. This aspect, however, does not meaningfully limit clinical utility in most situations since MRS information is combined with other clinical data when making treatment choices. For example, traditional clinical examination and other radiographic features may indicate that severely degenerated discs are indicative of fusion surgery. Alternatively, severely degenerated discs are not suited for biological therapies and may be excluded using routine clinical imaging. The unique value that MRS provides is that it reduces ambiguity when making treatment decisions for discs that are not severely degenerated and where routine clinical imaging provides insufficient actionable information.

Despite these limitations, we prospectively show that MRS-derived NOCISCAN-LS data that distinguish PD+ from PD− discs have the potential to significantly improve surgical outcomes. These data motivate the use of MRS as a valuable new approach to help doctors, in combination with other available clinical information, better diagnose and evaluate treatment options toward more successful outcomes.

Future studies are being planned to further evaluate the NOCISCAN-LS disc MRS approach prospectively in more patients and to investigate additional disc MRS applications in the cervical and thoracic spines and develop algorithms that optimally combine MRS with other clinical data that capture the multidimensional aspects of pain within individual DLBP patients. We also anticipate future use of this MRS tool for other purposes, such as screening for infection, tracking the success of biological therapies meant for disc repair, and studying biochemical mechanisms of action for such new therapies.

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