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Observational Report

Accuracy of MRI for Diagnosis of Discogenic Pain

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Background: Previous studies have compared MRI parameters to the results from discography. However, none have evaluated the overall diagnostic performance of MRI, taking into account that many MRI characteristics may be correlated.

Objective: Determine the accuracy of MRI for diagnosis of discogenic pain, taking into consideration the interdependence of MRI parameters.

Study Design: An observational report.

Setting: Sample of 143 patients, 92 male and 51 female in a spinal pain speciality center. Discography classification and scorings for MRI parameters were collected as outcome measures.

Methods: MRI and discography data were collected from patients with chronic low back pain. Five MRI characteristics were defined: high intensity zone, nuclear signal, disc height, disc contour, and bone marrow intensity change. On discography, each disc was classified as either positive or negative. The accuracy of MRI was evaluated using receiver operating characteristic curves.

Results: MRI parameters are correlated with each other and with discography findings, and these correlations affect the accuracy of MRI. Overall, nuclear signal alone is as accurate as any of the other MRI parameters, or combination of parameters, in the diagnosis of discogenic pain. While there is no difference in overall accuracy between nuclear signal and the other MRI parameters, these parameters do influence test performance when there is a moderate loss of nuclear signal . Moderate loss of nuclear signal and disc bulge has the best combination of sensitivity (79.8%) and specificity (79.3%). Adding moderate loss of disc height improves specificity (82.0%) slightly, and decreases sensitivity (73.6%) slightly, while incorporating high intensity zone grade II further improves specificity (92.6%) and decreases sensitivity (54.7%). High intensity zone grade I and bone marrow intensity change have minimal influence, even when there is moderate loss of nuclear signal.

Conclusions: MRI parameters are correlated with each other and with discography findings, influencing the diagnostic performance of MRI. Combining MRI parameters improves the diagnostic performance of MRI, but only in the presence of moderate loss of nuclear signal. When there is either normal nuclear signal or severe loss of nuclear signal the other MRI parameters have no influence on test performance. The practical implication for physicians that use discography is that the most important single MRI parameter to consider is nuclear signal. If nuclear signal is normal the disc is very likely to be negative on discography, while if there is severe loss of nuclear signal it is very likely to be positive. Discography will be most useful in discs with moderate loss of nuclear signal, particularly if there are no other MRI abnormalities present.

Key words: Discography, MRI, ROC curve, chronic back pain, neural signal, disc contour, high intensity zone

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The accuracy of a diagnostic test is its ability to make a correct diagnosis. Defining the accuracy of diagnostic tests requires a reference standard that test results can be compared against. In the case of diagnostic tests for discogenic low back pain, discography is commonly considered the reference standard (1-5). The rationale for discography is that disc pathology can lead to nociceptor activation, causing pain, and sensitization, causing tenderness (6). Disc tenderness, in turn, is manifested as pain on discography.

The weakness of discography as a reference standard is that studies on subjects without low back pain have shown that there are multiple other potential causes for a sensitive disc, including iliac crest donor site pain, chronic cervical pain, somatization disorders, mild low back pain, and a history of lumbar discectomy (7-9). While the utility of discography has been questioned (10), recent systematic reviews have concluded that there is strong evidence that it can identify the subset of patients with chronic discogenic pain (11,12).

MRI is highly accurate in detecting morphologic abnormalities of the disc, including degeneration (13-20), bulges and herniations (21-23), and annular tears (24-26). Despite this, its usefulness as a diagnostic test for patients with chronic low back pain (CLBP) is questionable (27), principally because of the high incidence of disc abnormalities on MRI scans of asymptomatic individuals. These abnormalities are present in roughly a third of adults below the age of 40 and virtually all individuals age 60 through 80 (28-30).

A number of studies have compared the results of MRI to provocation discography (22,31-38). A case in point is the study by Aprill and Bogduk (37), who concluded that a high intensity zone was "pathognomic for discogenic pain." While Aprill and Bogduk's conclusion has been challenged (39), if it was true, it would obviate the need for discography in a disc with a high intensity zone. However, all previous studies comparing MRI and discography share a common weakness; namely, treating MRI parameters as independent findings. Doing so does not take into account that MRI provides information about several characteristics of a disc, many of which are related to each other (40). These relationships, in turn, could affect the accuracy of discography.

The purpose of this study was to determine the accuracy of MRI for diagnosis of discogenic pain, taking into consideration the interdependence of MRI parameters.

Methods

Participants

The study was conducted at a spinal pain specialty center. Data was collected from a consecutive series of patients with chronic low back pain referred for provocation discography who met the following inclusion criteria: primary complaint of low back pain of at least 6 months duration, no neurologic deficits, no previous surgery, and an MRI scan obtained during the current episode of pain. Informed consent for discography obtained from all patients. As the study involved record review and data analysis only, with no risk to patient and no use of protected health information, it was exempt from IRB review.

MRI

All MRI scans were evaluated by an independent expert spinal radiologist (J.K.) who was blinded to the results from discography. All scans were obtained prior to entry into the study and were performed at a variety of outside institutions using a variety of imaging protocols. At a minimum T1 and T2 weighted sequences in both the axial and sagittal planes were available for review. After each patient had completed discography, their MRI scan was given to the spinal radiologist. After being evaluated by the radiologist it was returned to the patient or their referring physician, so that it could be used in their ongoing care.

Five MRI characteristics were defined: high intensity zone, nuclear signal, disc height, disc contour, and bone marrow intensity change.

The criteria for a high intensity zone were a modification of the original criteria proposed by Aprill and Bogduk (37). As Aprill and Bogduk (37) did, we defined a high intensity zone as an area with a high intensity signal, brighter than nucleus pulposus, located in the substance of the posterior annulus fibrosus and surrounded by the low signal intensity (black) signal of the annulus fibrosus. However, we adopted the modification of Schellhas et al (34), who expanded the definition of high intensity zone to include those lesions that in addition to satisfying the original criteria of Aprill and Bogduk, had a thin horizontal line of T2 weighted high signal intensity either entirely within the posterior annulus or connecting the nucleus and high intensity zone. As proposed by Rankine et al (41), posterior, posterolateral, and lateral lesions were included. The signal brightness of each high intensity zone was classified as grade I — mildly hyperintense, grade II — moderately hy-

perintense, and grade III — markedly hyperintense. When a high intensity zone was evident in more than one cut, the one with the brightest signal was graded. Additionally, the type of tear represented by each high intensity zone was classified as either transverse, radial, or concentric using the criteria of Yu et al and Ito et al (36,42).

In accordance with a number of previous studies, nuclear signal was defined as a 3-level ordinal parameter (18,22,36,40,44). A pure white signal on T2 weighted images was defined as normal nuclear signal, while a homogenous black signal was defined as severe loss of nuclear signal. Signal loss that was intermediate between normal nuclear signal and severe signal loss was defined as moderate nuclear signal loss.

Disc height was classified as a 3-level ordinal parameter, according to the criteria of Ito, et al (36). Discs with either normal or less than 10% loss of expected height were considered normal. disc height loss between 10-50% was regarded as moderate narrowing, while loss of 50% of disc height or more was considered as severe narrowing.

Disc contour was treated as an ordinal parameter and defined according to the previously established criteria of Milette et al (43) and Brant-Zawadski et al (45) as normal, bulge, protrusion, and extrusion. A disc was classified as normal when no extension was visualized beyond the interspace. Bulge was defined as a circumferential, symmetrical disc extension beyond the interspace. Protrusion was identified as a focal or asymmetrical disc extension beyond the interspace into the canal with the base against the parent disc broader than any other diameter of the protrusion. Extrusion was defined as a focal disc extension beyond the interspace with the base against the parent disc either narrower than the diameter of the extruding material itself or without a connection to the parent disc.

Bone marrow intensity change was defined as a 3 level ordinal parameter using the criteria established by Modic (46). If the signal intensity from the bone marrow adjacent to the endplates was normal on both T1 and T2 weighted images, bone marrow intensity change was defined as absent. bone marrow intensity change Type I was defined as decreased signal intensity on T1 weighted images and increased signal on T2 weighted images. bone marrow intensity change Type II was defined as an increased signal on T1 weighted images and isointense or slightly hyperintense signal on T2 weighted images.

Discography

All discograms were performed by one of 2 experienced anesthesiologists. The discs selected for discography were at the discretion of the physician performing discography, who was not blinded to the MRI results. In general, all abnormal discs on MRI that were consistent with the patients' clinical findings (i.e., location of back pain, tenderness, and referred extremity pain) were injected. Additionally, at least one disc that was normal on MRI was injected to serve as an internal control. In most cases the selection process resulted in the injection of 3 – 4 of the lower levels in the lumbar spine.

Needles for discography were placed using a standard lateral approach (47) under light conscious sedation with meperidine and propofol. The level of sedation was closely monitored to ensure that all patients were awake, alert, and fully responsive prior to disc injection. After needle placement, each disc was injected with nonionic contrast medium using a syringe with an integrated pressure transducer connected to a pressure monitoring system (Merit Medical, Salt Lake City, Utah). Patients were blinded to the disc level that was being injected. Contrast was injected into the disc at a rate of approximately 0.1mL/sec, with fluoroscopic spot films at every 0.5 mL of injected volume or at any point where the patient complained of pain. If the patient experienced pain during disc injection he or she was asked to classify it as concordant (familiar location) or discordant (unfamiliar location) and to rate the intensity from 0 to 10 on a numerical pain scale. Among discs with concordant pain, no attempt was made to differentiate between similar and exact pain. If pain was provoked, but the patient could not determine whether it was concordant or discordant the disc was reinjected before the patient was asked to make their final determination. Contrast was injected to one of 3 endpoints; pain 6/10 or greater, 100 psi, or a plateau in the pressure volume curve (i.e., the disc could not be pressurized further due to epidural leak, venous uptake, or very high compliance). At the completion of disc injection, antero-posterior and lateral digital spot radiographs were obtained to assess disc morphology. As defined by Adams et al (48), discs with a cotton-ball or bilobed nucleus were considered normal. Any other appearance was classified as abnormal.

Four categories of pain response were defined; none, discordant, concordant with intensity greater than or equal to 6/10, and concordant with intensity less than 6/10.

Based on the pain response and morphology, discs were classified as either positive or negative. A disc was positive if it produced concordant pain with an intensity of greater than or equal to 6/10 and had abnormal morphology with a painless disc at an adjacent control level. All other discs were classified as negative. Discs from patients in whom no control disc could be identified were excluded from further analysis.

Data Analysis

The statistical association between MRI parameters and discography classification was evaluated with Spearman's rank correlation test and Pearson's Chi Square test. The sensitivity and specificity of the values of the individual MRI parameters were calculated using a positive disc on discography as the reference standard. Agreement between MRI parameters and discography was defined as the area under a receiver operating characteristic (ROC) curve. SPSS (Statistical Package for the Social Sciences, v11.5) software was used for data processing. Differences between areas under receiver operator characteristic curves for different parameters and/or their combinations were evaluated using nonparametric 95% confidence intervals. Confidence intervals (CI) were calculated assuming that discs from the same patient were correlated (49,50).

Results

Subject Data

The study included 143 patients, 92 male and 51 female. The ages of the patients varied from 21 to 71 years old, with a mean age of 42.6 years, 6 patients (4%) were 60 years or older. One hundred-thirty patients (91%) had at least one positive disc, and in 13 patients (9%) all discs were negative.

Data was collected on 460 discs, distributed as follows: T12/L1 (1); L1/L2 (8); L2/L3 (46); L3/L4 (133); L4/L5 (140); L5/S1 (132). Of these 460 discs 221 (48%) were classified as negative, and 239 (52%) as positive. The distribution of the positive discs was as follows: L1/L2, 1 (0.4%); L2/L3, 9 (3.8%); L3/L4, 37 (15.5%); L4/L5, 98 (41.0%); L5/S1, 94 (39.3%).

Correlation Between MRI Parameters

The interdependence of MRI parameters was evaluated by applying Spearman's rank correlation to the ordinal MRI parameters, and the chi-square test to the categorical parameters (tear type). The Spearman's rank correlation coefficients are presented in Table 1.

The strongest correlations were between nuclear signal, disc height, and disc contour. The correlations between high intensity zone, bone marrow intensity change, and the other parameters were relatively weak, with the exception of the correlation between high intensity zone and disc contour. Chi-square anal-

Table 1. *Spearman's rank correlation coefficients between MRI parameters.*

	Nuclear Signal	Disc Height	HIZ	BMIC	Disc Contour
Nuclear signal	1.000	**.776	**.408	**.308	**.627
Disc height	**.776	1.000	**.328	**.347	**.636
HIZ	**.408	**.328	1.000	*.109	**.518
BMIC	**.308	**.347	*.109	1.000	**.269
Disc contour	**.627	**.636	**.518	**.269	1.000

** Correlation is significant at the .01 level (2-tailed).
* Correlation is significant at the .05 level (2-tailed).

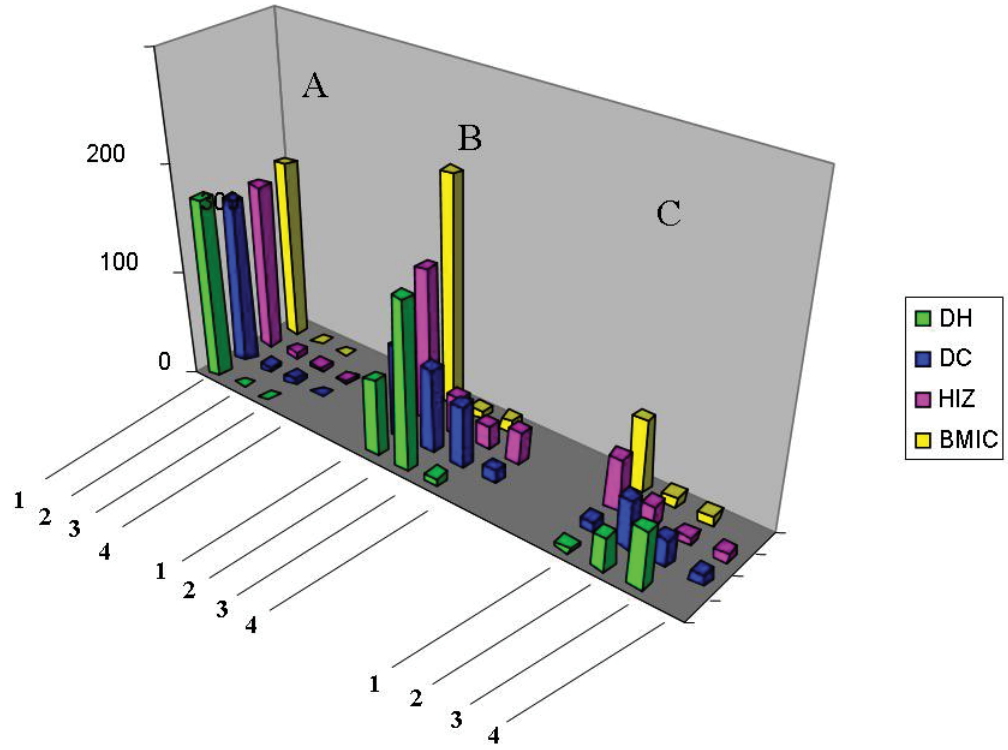

Fig. 1. Numbers of discs with different MRI characteristics for each value of nuclear signal. Group A corresponds to normal nuclear signal, Group B to moderate loss of nuclear signal, and Group C to severe loss of nuclear signal. Numbers 1–4 indicate the rank of the parameter: 1 represents normal for disc height and disc contour, absent for high intensity zone and bone marrow intensity change; 2 represents moderate narrowing for disc height, bulge for disc contour, grade I for high intensity zone, type I for bone marrow intensity change; 3 represents severe narrowing for disc height, protrusion for disc contour, grade II for high intensity zone, type II for bone marrow intensity change; 4 represents extrusion for disc contour, grade III for high intensity zone.

ysis demonstrated that the type of tear correlated to high intensity zone (p = 0.012) and to bone marrow intensity change (p = 0.014).

Figure 1 demonstrates the prevalence of abnormalities in the ordinal MRI parameters.

Among discs with normal nuclear signal only 9% of discs have other abnormalities, namely 4.6% with high intensity zone and 5.8% with abnormal contour, with none having narrowing or bone marrow intensity change. Discs with moderate loss of nuclear signal have a higher prevalence of other abnormalities — 39.5% with high intensity zone, 69.6% with narrowing (65.5% moderate, 3% severe), 63.2% with abnormal disc contour, and 8.2% with bone marrow intensity change. All discs with severe loss of nuclear signal have at least one other abnormal MRI parameters. Among discs with severe loss of nuclear signal there are 52.2% with high intensity zone, 95.5% with narrowing (60.9% with severe narrowing), 89.7% with abnormal contour and 23% with bone marrow intensity change.

Correlation Between MRI Parameters and Discography Classification

Table 2 demonstrates the numbers of positive and negative discs for the different values of each MRI parameter.

Spearman's rank correlations established that there was a highly significant correlation between discography classification and the MRI ordinal parameters (p <0.0005). The parameter with the highest correlation with disc classification was nuclear signal (correlation coefficient = .598), followed by disc height (cc = .565), disc contour (cc = .531), high intensity zone (cc = .345), and bone marrow intensity change (cc = .206). The chi-square test demonstrated that there was no

Table 2. *Number of positive and negative discs for different values of each MRI parameter.*

MRI parameter		Discography classification		
		Negative	Positive	Total
Nuclear signal	Normal	148	25	173
	Moderate loss	64	156	220
	Severe loss	9	58	67
Disc height	Normal	180	65	245
	Moderate narrowing	36	131	167
	Severe narrowing	5	43	48
High intensity zones	Absent	197	133	330
	Grade I	14	44	58
	Grade II	5	25	30
	Grade III	5	37	42
Bone marrow intensity change	Absent	217	206	423
	Type I	2	15	17
	Type II	2	18	20
Disc contour	Normal	185	63	248
	Bulge	16	91	107
	Protrusion	15	69	84
	Extrusion	5	16	21
Tear type	No tear	197	133	330
	Transverse	14	73	87
	Radial	6	17	23
	Concentric	4	16	20
Total		221	239	460

statistical relationship between the tear type and discography classification (p= 0.54).

In order to determine if a combination of MRI parameters was better correlated with discography classification than the individual ones, we evaluated 2 combinations of parameters: one consisting of nuclear signal, disc contour, and disc height and the other of all 5 parameters. For each of the combinations the parameters were taken in order of the strength of correlation. For the combination of nuclear signal, disc height, and disc contour, each level of nuclear signal was classified to 3 levels of disc height and each level of disc height to 4 levels of disc contour. For the combination of 5 parameters each level of disc contour was classified to 4 levels of high intensity zone and each level of high intensity zone to 3 levels of bone marrow intensity change. Spearman's rank correlations for the 3 parameter combination (nuclear signal, disc height, disc contour) with discography classification were highly significant (p <0.0005), with a correlation coefficient = .662.

Receiver Operator Characteristic curves

A receiver operator characteristic curve can be used to compare a test with ordinal results (MRI findings) against a reference standard with a binary result (discography) which is classified as either positive or negative. The area under the curve is a measure of the overall performance of the test and can vary from 0.5 to 1.0 (51). A test with an area under the curve of 0.5 has no value, for random guessing will produce the same result (52). A test with an area under the curve of 1.0 is perfect, as it is completely associated with the reference standard.

In order to construct receiver operator characteristic curves, the sensitivity and specificity of individual and combinations of MRI parameters were calculated using the result from discography as the reference standard. The sensitivity and specificity for each of the individual MRI parameters is shown in Table 3.

Table 3 demonstrates that the presence of any MRI abnormality is associated with a specificity of at least 60%. Especially high specificities (90% or higher) are seen for severe loss of nuclear signal, severe narrow-

Table 3. Sensitivity and specificity for MRI parameters. The 95% confidence intervals (CI) expressed as lower, upper bounds.

	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)
Moderate loss of nuclear signal	89 (85.0, 93.0)	67 (58.2, 75.8)
Severe loss of nuclear signal	24 (17.3, 30.7)	96 (79.0, 100)
Moderate loss of disc height	73 (67.0, 79.0)	81 (69.2, 92.8)
Severe loss of disc height	18 (12.2, 23.8)	98 (80.3, 100)
HIZ Grade I	44 (37.5, 50.5)	89 (74.7, 100)
HIZ Grade II	26 (20.1, 31.9)	95 (78.4, 100)
HIZ Grade III	15 (9.7, 20.3)	98 (80.3, 100)
BMIC Type I	14 (9.4, 18.6)	98 (80.4, 100)
BMIC Type II	7 (3.4, 10.6)	99 (81.1, 100)
Bulge disc contour	74 (68.0, 80.0)	84 (71.2, 96.8)
Protrusion disc contour	35 (28.5, 41.5)	91 (75.8, 100)
Extrusion disc contour	7 (3.3, 10.7)	98 (80.4, 100)

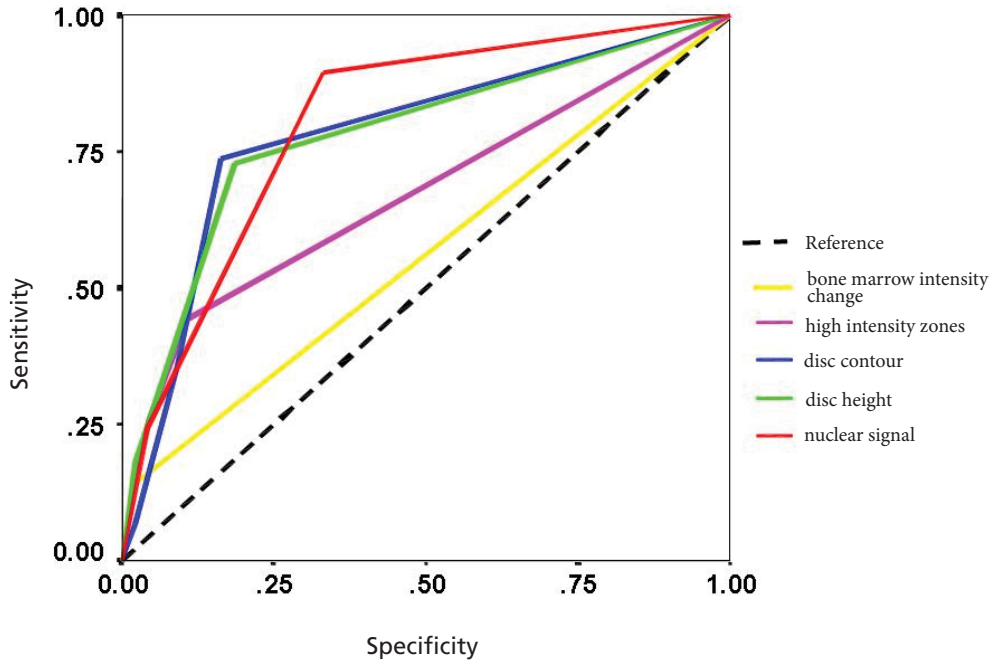

Fig. 2. *Receiver operating characteristics curves for individual MRI parameters.*

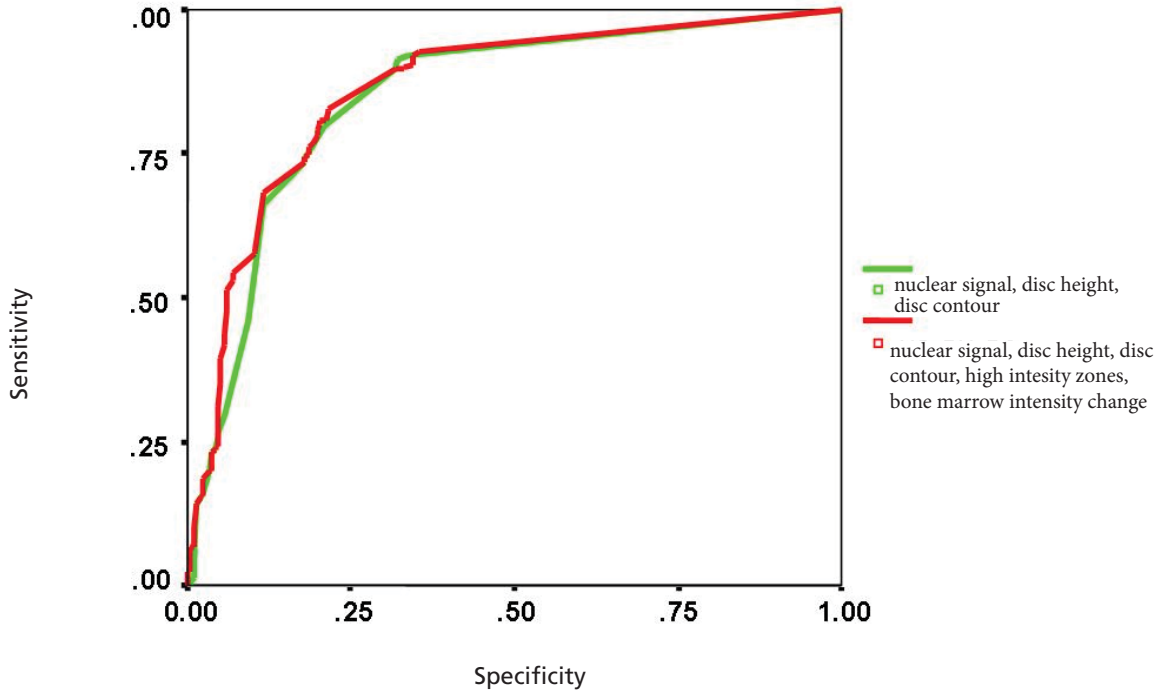

Fig. 3. *Receiver operating characteristics curves for combinations of MRI parameters.*

Table 4. *Area under the Receiver operating characteristics area under the curve for MRI parameters.*

MRI parameter	Area under the Curve	Standard Error	Significance (p)	95% Confidence Interval	
				Lower Bound	Upper Bound
Nuclear signal	0.809	0.021	> 0.0005	0.768	0.850
Disc height	0.784	0.022	> 0.0005	0.741	0.827
Disc contour	0.781	0.022	> 0.0005	0.737	0.825
High intensity zone	0.679	0.025	> 0.0005	0.631	0.728
Bone marrow intensity change	0.563	0.027	0.019	0.511	0.615
3 parameter combination (nuclear signal, disc height, disc contour)	0.851	0.019	> 0.0005	0.814	0.888
5 parameter combination (nuclear signal, disc height, disc contour, high intensity zone, bone marrow intensity change)	0.861	0.018	> 0.0005	0.826	0.896

Table 5. *P-values for differences in the area under the curves between MRI parameters. Significant differences are highlighted in bold italics.*

	5 parameter combination	3 parameter combination	Nuclear signal	Disc height	Disc contour	High intensity zone	BMIC
5 parameter combination (nuclear signal, disc height, disc contour, high intensity zone, bone marrow intensity change)	1	0.36	0.0805	0.024	0.019	< 0.0005	***< 0.0005***
3 parameter combination (nuclear signal, disc height, disc contour)	0.36	1	0.15	0.054	0.047	***< 0.0005***	***< 0.0005***
Nuclear signal	0.0805	0.15	1	0.272	0.248	***0.0019***	***< 0.0005***
Disc height	***0.024***	0.054	0.272	1	0.472	***0.011***	***< 0.0005***
Disc contour	***0.019***	***0.047***	0.248	0.472	1	***0.013***	***< 0.0005***
High intensity zone	***< 0.0005***	***< 0.0005***	***0.0019***	***0.011***	***0.013***	1	***0.011***
Bone marrow intensity zone	***< 0.0005***	***< 0.0005***	***< 0.0005***	***< 0.0005***	***< 0.0005***	***0.011***	1

ing, high intensity zone grade II or III, bone marrow intensity change, protrusion, and extrusion. Sensitivities are in general much lower, with the highest sensitivity being for moderate loss of nuclear signal at 89%.

The receiver operator characteristic curves for each of the 5 individual MRI parameters are shown in Fig. 2, and for 2 combinations in Fig. 3.

The area under each of the receiver operator characteristic curves is provided in Table 4, and the p-values for the differences between each area under the curve in Table 5.

The results from Table 5 can be summarized as follows. There is no statistical difference in the area under the curve between nuclear signal, disc height, and disc contour. The area under the curve of high intensity zone was significantly less than nuclear signal, disc height, or disc contour, and in turn was significantly greater than bone marrow intensity change. There was no significant difference in the area under the curve between the 2 combinations, nor was there a significant difference in the area under the curve between the 2 combinations and nuclear signal. The area under the curve of the 5 parameter combination was significantly greater than the area under the curve of disc height, disc contour, high intensity zone, and bone marrow intensity change individually. The area under the curve of the 3 parameter combination was significantly greater than the area under the curve of disc contour, high intensity zone, and bone marrow intensity change, while the difference between the area under the curve of the 3 parameter combination and disc height approached statistical significance with a *p*-value of 0.054.

One drawback of using the area under the curve as a measure of diagnostic performance is that it does not account for the fact that the receiver operator characteristic plot is a composite of different segments, and that there may be different diagnostic implications in different regions of the curve (53). Comparing plots in different segments may provide important diagnostic information that is not reflected in the area under the curve (53).

Figure 4 shows the receiver operator characteristic curves for nuclear signal and the 5 parameter combination, demonstrating that these 2 curves are nearly identical for normal nuclear signal and severe loss of nuclear signal, but diverge in the region of moderate loss of nuclear signal. The positive predictive value (PPV) of severe loss of nuclear signal is 87%; that is, 87% of discs with severe loss of nuclear signal will be positive on discography. The PPV of a moderate loss of nuclear signal falls to 71%. In the region of normal nuclear signal the negative predictive value — the probability that a disc with normal nuclear signal will be negative on discography — is 86%. In the region of moderate loss of nuclear signal

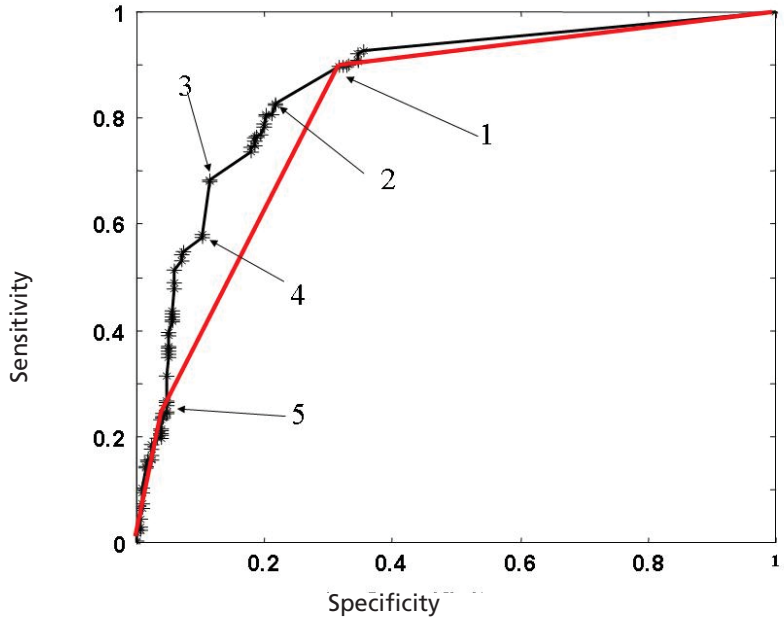

Fig. 4. *ROC curve for nuclear signal (red curve) and a combination of 5 MRI parameters (black curve). 1– moderate loss of nuclear signal, 2– moderate loss of nuclear signal and bulge, 3– moderate loss of nuclear signal and moderate loss of disc height, 4– moderate loss of nuclear signal and moderate loss of disc height and high intensity zone grade II, 5– severe loss of nuclear signal.*

there are several points that represent natural break points between one segment of the graph and the next. Using the upper right hand corner of the curve as the starting point (i.e. considering the curve from right to left), point 1 in Fig. 4 represents discs that have moderate loss of nuclear signal, but no other abnormalities. Point 2 represents discs that have moderate loss of nuclear signal and disc bulge, with other parameters being normal. This is the point closest to the upper left hand corner of the curve and therefore represents the test result with the best combination of sensitivity and specificity (sensitivity = 79.8%, specificity = 79.3%). Moving farther to the left of the curve at point 3, the first disc with moderate loss of disc height in addition to moderate loss of nuclear signal occurs. Adding moderate loss of disc height to moderate loss of nuclear signal improves specificity (82.0%) slightly and decreases sensitivity (73.6%) slightly. Point 4 represents discs with moderate loss of nuclear signal, moderate loss of disc height, and high intensity zone grade II. Combining moderate loss of disc height and moderate loss of nuclear signal with high intensity zone further improves specificity (92.6%) and decreases sensitivity (54.7%). Beginning at point 5 all discs has severe loss of nuclear signal.

Discussion

Summary of Findings

Our results demonstrate that MRI parameters are correlated with each other and with discography findings, and that these correlations affect the accuracy of MRI.

Analysis of the areas under the receiver operator characteristic curves demonstrate that, overall, nuclear signal alone is as accurate as any of the other MRI parameters, or combination of parameters, in the diagnosis of discogenic pain (Table 5). While there is no difference in overall accuracy between nuclear signal and the other MRI parameters, these parameters do influence test performance when there is a moderate loss of nuclear signal, as demonstrated in Fig 4. Figure 4 shows that in the region of the curve with the highest sensitivity, nuclear signal is normal and the other

MRI parameters do not influence test performance. Similarly, in the region of the curve with the highest specificity there is severe loss of nuclear signal, and the other MRI parameters also do not influence test performance. However, the influence of the other parameters is apparent in the area of the curve corresponding to moderate loss of nuclear signal. Analysis of this section of the curve reveals that moderate loss of nuclear signal and disc bulge has the best combination of sensitivity (79.8%) and specificity (79.3%). Adding moderate loss of disc height improves specificity (82.0%) slightly, and decreases sensitivity (73.6%) slightly, while incorporating high intensity zone grade II further improves specificity (92.6%) and decreases sensitivity (54.7%). high intensity zone grade I and bone marrow intensity change have minimal influence, even in this part of the curve.

Explanation of Findings

The MRI parameters with the greatest correlations between each other were nuclear signal, disc height, and disc contour, all of which can be considered degenerative parameters. Disc degeneration is characterized by degradation of the extracellular matrix, with the most consistent change being loss of proteoglycan and water content (54). As proteoglycan and water content is lost, the T2 signal in the disc deteriorates (55). As a result, the biomechanical properties of the disc are altered, leading to morphologic changes such as bulges, herniations, and loss of disc height that are readily appreciated on MRI. The underlying process responsible for these morphologic changes, namely the loss of proteoglycan content, is the same. This is reflected in the strong correlations between nuclear signal, disc height, and disc contour; i.e., if one is abnormal there is a high probability that the others will be also. This suggests that these parameters represent different manifestations of the same characteristic- the loss of proteoglycan content. On the other hand, the correlations between high intensity zone and bone marrow intensity change and the other parameters, and between each other, were generally weak. This suggests that these parameters differ in some fundamental way from the degenerative parameters and that they result from factors other than loss of proteoglycan content. This would be consistent with existing theories regarding the etiology of these findings, as a high intensity zone has been hypothesized to represent nuclear material that has become trapped between the lamellae of the annulus and becomes inflamed (37), while bone marrow intensity change is believed to result from endplate inflammation (56).

All of the MRI parameters were correlated with discography to some degree, although the strongest correlations were with the degenerative parameters. The factors responsible for the correlations seen between MRI parameters and discography are unknown, although there are a number of possibilities. Nociceptive processes certainly may play a role. For example, as discs degenerate, nociceptive nerves grow in (57), noxious chemicals accumulate (58-62), and abnormal mechanical loading (63) occurs, all which could affect the sensitivity of the disc. In the case of high intensity zone and bone marrow intensity change there may be localized inflammation in the annulus or endplate. The fact that the strongest correlations with discography were with the degenerative parameters may be an indication that nociceptive processes accompanying degeneration play a greater role in discogenic pain than those related to either high intensity zone or bone marrow intensity change. However, it is also possible that the observed correlations have nothing to do with nociceptive processes. In particular, the structural characteristics of a disc may have an effect on the pain provoked by contrast injection (64) independent of any nociceptive processes. For example, in a highly disrupted disc there may be greater stimulation of the posterior annulus during discography. However, even in a highly disrupted disc there may not be adequate stimulation of the endplates to reproduce pain associated with bone marrow intensity change.

Comparison with Previous Studies

While no previous studies have examined the effect of the interdependence of MRI parameters on the results from discography, a number have defined the sensitivity and specificity of the same individual MRI parameters that we examined in this study. The results from those studies are summarized in Table 6, with those that are significantly different from ours bolded and italicized.

In order to provide a valid comparison between studies, we included in Table 6 only those studies that provided data enabling us to determine sensitivity and specificity using comparable criteria to those used in our study; namely, variables were defined as ordinal, the MRI parameter was considered the test and a positive discogram the disease, and a positive discogram was defined as concordant pain (incorporating

Table 6. *Previous studies on sensitivity and specificity of MRI for diagnosis of discogenic pain. Significant differences with results of present study are highlighted in bold italics.*

Study	MRI parameter	Sensitivity (%), (95% CI)	Specificity (%), (95% CI)
Ito et al (33)	moderate loss nuclear signal	96, (87, 104)	***46, (35, 57)***
Ito et al (36)	severe loss nuclear signal	***70, (51, 88)***	88, (81, 96)
Ito et al (36)	moderate loss disc height	87, (73, 101)	***69, (59, 79)***
Ito et al (36)]	severe loss disc height	30, (12, 49)	97, (94, 101)
Ito et al (36)	HIZ	52, (32, 73)	90, (83, 96)
Ito et al (36)	BMIC	22, (5, 39)	95, (90, 100)
Simmons et al (33)	moderate loss nuclear signal	88, (83, 93)	63, (58, 69)
Horton and Daftari (22)	moderate loss nuclear signal	95, (85, 105)	***43, (27, 58)***
Horton and Daftari (22)	severe loss nuclear signal	37, (15, 59)	88, (77, 98)
Osti and Fraser (35)	moderate loss nuclear signal	***69, (55, 84)***	64, (53, 75)
Osti and Fraser (35)	severe loss nuclear signal	23, (10, 36)	92, (86, 98)
Aprill and Bogduk. (37)	HIZ	***63, (51, 76)***	97, (92, 101)
Saiffuddin et al (32)	HIZ	***27, (18, 36)***	95, (90, 101)
Ricketson et al (31)	HIZ	***11, (1, 21)***	93, (85, 101)
Smith et al (65)	HIZ	***23, (9, 37)***	90, (84, 95)
Braithwaite et al (67)	BMIC I	23, (14, 32)	97, (92, 100)
Braithwaite et al (67)	BMIC II	***18, (9, 26)***	97, (92, 100)
Kokkenon et al (69)	BMIC I	***40, (24, 56)***	***64, (52, 75)***
Kokkenon et al (69)	BMIC II	***22, (8, 35)***	***79, (69, 89)***
Weishaupt et al (73)	HIZ	56, (36, 77)	***62, (52, 72)***
Weishaupt et al (73)	BMIC I	***48, (34, 62)***	96, (91, 100)
Weishaupt et al (73)	BMIC II	***19, (8, 30)***	98, (96, 100)

both similar and exact pain) with abnormal morphology. While our criteria for a positive discogram also included the presence of a control level, many of the other studies did not (22,33,36,37,65,67). As can be appreciated from Table 6, for most parameters and most studies there is good agreement between our results and those of the previous study, with differences likely related to variability in sample populations, discography and MRI technique, and the criteria for MRI and discography parameters.

Limitations

This study has a number of limitations. Some of these relate to our sample population, which consisted of patients with chronic low back pain referred to a private practice for discography, in most circumstances because spinal fusion was being considered. This has several implications. First, our findings do not necessarily apply to other study populations, such as individuals with chronic low back pain who would not ordinarily be considered for spinal fusion (e.g., too many suspected levels, high psychosocial risk). Second, the physician performing discography selected which discs to study based at least partially on the MRI results, introducing a potential bias (unfortunately, it is difficult to blind treating physicians in a clinical practice). The greatest source of bias is probably that the majority of discs with a normal nuclear signal intensity were injected as controls, as they were not considered to be likely sources of pain. There may be circumstances where a disc with a normal nuclear signal intensity is suspected of causing pain, and our conclusion regarding the likelihood of a disc with a normal nuclear signal being positive may not apply in that circumstance. A third limitation related to our sample population is that the subjects had their MRIs done on a diverse group of scanners, before presenting to our practice. Therefore, we had no control over the imaging protocols used, nor did we have any control over the time interval between the scan and discography. This is typical for practices of our nature, and in that sense may be a strength, as our results may be generalized to other practices that rely on MRI scans obtained from multiple outside facilities. It is possible that if a standard imaging protocol was used on all patients different results would ensue.

Another limitation is the single radiology observer. Observer variability has previously been evaluated for interpretation of nuclear signal (37,43,68), disc contour (43), disc height (37,43), and bone marrow intensity change (37,69), with interobserver agreement being at least substantial for each of these, according to the criteria of Landis and Koch (70). Interobserver agreement for high intensity zone has ranged from fair-to-good (65) to almost perfect (38). The grading system that we used to classify the brightness of the high intensity zone has not previously been reported, and further studies are needed to determine its associated observer variability.

Finally, in considering the receiver operator characteristic curve analysis that we have presented, the limitations of discography as a reference standard for discogenic pain need to be addressed. All reference standards have limitations (71), and discography is no exception. One limitation is that there is no consensus on what constitutes a positive discogram. Some of the unresolved issues are the pain threshold that should be used to be classified as a positive discogram and the pressure cut-offs that should be used. However, the principle limitation of discography is that it is not necessary for a disc to be pathologic for it to hurt on discography. This limitation has been demonstrated in studies on subjects without LBP. If such subjects are healthy, pain on discography is unusual. Studies using contemporary methodology show a false positive rate of 0% (72) to 10% (7). However, experimental studies have also demonstrated that there are conditions, such as chronic pain syndromes and psychologic distress, that can lead to considerably higher false positive rates in subjects without low back pain (7,8). The presumed mechanism for pain provocation in the presence of these conditions is abnormal processing of noxious stimuli (10). Incorporating a control level into the criteria for a positive discogram, as we did, is a commonly employed method for decreasing false positive discography resulting from abnormal pain processing (32,35,38,73). Nonetheless, given the inherent limitations of discography, it is important to emphasize that a more valid reference standard is needed to better define the accuracy of MRI.

Conclusion

In conclusion, our results demonstrate that MRI parameters are correlated with each other and with discography findings, influencing the diagnostic performance of MRI. The MRI parameters with the greatest correlations between each other were the degenerative parameters nuclear signal, disc height, and disc contour. The correlations between high intensity zone and bone marrow intensity change

and the other parameters, and between each other, were generally weak which is consistent with existing theories regarding the etiology of those findings. Receiver operator characteristic curve analysis, using discography as a reference standard, reveals the effect of the interdependence of MRI parameters on the accuracy of MRI. This analysis shows that combining MRI parameters improves the diagnostic performance of MRI, but only in the presence of moderate loss of nuclear signal — when there is either normal nuclear signal or severe loss of nuclear signal, the other MRI parameters have no influence on test performance. The practical implication for physicians that use discography is that the most important single MRI parameter to consider is nuclear signal — if it is normal the disc is unlikely to be positive on discography, while if there is severe loss of nuclear signal it is likely to be positive. The most useful information from discography will be provided in discs with moderate loss of signal intensity, particularly if there are no other MRI abnormalities present.

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