MRI-BASED GRADING SYSTEMS FOR ASSESSING LUMBAR DISC DEGENERATION

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CANDIDATE'S STATEMENT

This work has not previously been submitted for a degree or diploma in any university. To the best of my knowledge and belief, the thesis contains no material previously published or written by another person except where due reference is made in the thesis itself.

This work was completed with an amendment of an existing approval from the Human Research Ethics Committee (HREC), protocol number 52023580946889. The HREC letter of amendment, is provided in APPENDICES (Appendix 1)

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SUPERVISORS' STATEMENT

AS SUPERVISORS OF DEAN ESPOSITO, WE CERTIFY THAT WE CONSIDER THEIR THESIS "MRI-BASED GRADING SYSTEMS FOR ASSESSING LUMBAR DISC DEGENERATION" TO BE SUITABLE FOR EXAMINATION.

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PUBLICATIONS

Parts of the work presented in this thesis have been submitted to peer-reviewed journals.

Submitted papers

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ABSTRACT

Despite low back pain (LBP) being the leading cause of global disability, identifying a specific pain-generating structure remains difficult. Identifying pathoanatomic structures in LBP may help inform appropriate treatment, improve patient outcomes and reduce healthcare costs. Although structures like the intervertebral disc are thought to be pain producing, their clinical relevance in LBP remains uncertain. This may be partly due to the way changes to the intervertebral disc are measured on magnetic resonance imaging (MRI). The aim of this thesis is to identify and describe grading systems for lumbar disc degeneration (DD) and to assess whether different grading systems have stronger associations with clinical outcomes of LBP. **In Chapter 2** a scoping review was performed to identify and describe different grading systems for DD. A substantial number of grading systems were identified. There was also heterogeneity in the components used in the systems, and in the methods of synthesis across the studies. This variability likely hinders the ability to draw clear associations with LBP. **In Chapter 3** a secondary analysis was performed that assessed the predictive validity of five different grading systems of DD to predict a recurrence of LBP, including new normalised measures. The normalised measures were used as they showed preliminary evidence in a previous study of being more valid than existing systems. No differences in predictive value were identified between the systems; however, the magnitude and direction of effect was influenced by the components used, normalisation and the way the grading system was summarised for analysis. Future research should explore how to standardise which grading systems are used to measure DD and the way grading systems are summarised for analysis as this likely influences the measured association. Normalised measures must be further tested in bigger cohorts to determine if they are more valid when measuring LBP outcomes.

CHAPTER 1. INTRODUCTION

1.1 OVERVIEW OF LOW BACK PAIN

1.1.1 DEFINITION OF LOW BACK PAIN

Low back pain (LBP) is defined as pain and discomfort located below the costal margin and above the inferior gluteal folds, with or without the presence of leg pain [1-3]. Traditionally, symptoms of LBP have been classified as either acute (pain lasting 6 weeks or less), subacute (pain between 6 to 12 weeks) or chronic (pain greater than 12 weeks) [1-3]. There is however, increasing evidence highlighting that LBP often fluctuates or is recurring over time [4-6]. Thus, the traditional classification of LBP symptomatology based on symptom duration has been challenged in some of the more recent LBP models [7]. Low back pain is now commonly considered as a life-long diagnosis (similar to asthma or gastro-oesophageal reflux disease) which is managed per episode, over time [8].

1.1.2 PREVALENCE OF LOW BACK PAIN

Low back pain is the leading cause of global disability [9]. The lifetime prevalence of LBP is estimated to fall within a range of 38-80%, with point prevalence estimates ranging from 12-33% [9]. Higher prevalence rates have been identified in females, and in individuals in the 5^{th} to 7^{th} decades of life [10]. The prevalence of LBP seems to be higher in countries with a high gross domestic profit, with limited research suggesting any significant differences in the prevalence between rural and urban areas [10].

1.1.3 ECONOMIC BURDEN OF LOW BACK PAIN

The total costs of LBP are substantial [3]. The financial burden of LBP is estimated to be more than AUD$4.8 billion per year in Australia [11]. Comparatively, the annual expenditure in the United States of America exceeds USD$100 billion for the management of patients with LBP [12]. A large proportion of these costs are indirect, namely, the costs associated with decreased productivity in the workplace and/or household resulting from LBP disability [13]. A systematic review of studies investigating the cost of LBP [14] identified a ratio of approximately six to one of indirect to direct costs. Indirect costs, whilst inherently hard to measure, are forecasted to increase to AUD$21.8 billion by 2030 [15]. Low back pain is associated with significant costs and therefore requires affirmative action to reduce its economic burden.

1.1.4 PROGNOSIS/NATURAL COURSE OF LOW BACK PAIN

The natural course of LBP is extremely variable lasting anywhere between a few days to several years [2, 16-17]. A systematic review of studies investigating the prognosis of acute LBP identified that most episodes improve within six weeks, and are fully resolved by the twelfth week [5]. Alternatively, chronic LBP has less favourable outcomes compared to acute LBP [17]. A large inception cohort study investigating the course of LBP identified that nearly a third of patients did not recover from a presenting episode within 12 months [18].

Through the study of LBP trajectories, we now know that some patients will recover quickly from an episode of LBP, some will have persistent pain and some will experience a reaggravation and recurrence of their symptoms [4, 5]. The reported yearly rate of recurrence varies between 25-82% and is dependent on the definitions of remission and recurrence [19, 20]. A Delphi study was conducted in 2011 to determine a consensus definition of a recurrence of LBP [21]. The agreed definition was "a return of LBP lasting at least 24 hours with a pain intensity of 3 or more on a 0-10 numeric pain rating scale" [21]. More recently some of the same authors have questioned if this threshold for recurrence is sufficient, arguing that a modified definition that also requires that the recurrence is, at the very least, accompanied by moderate impact on daily activities [22].

1.1.5 Prognostic factors for the development of persistent or recurrent low back pain

Having an understanding of prognostic factors is essential when formulating a management plan for patients with LBP. A systematic review of prognostic factors for chronic LBP found that social and psychological factors, such as anxiety and stress, were most commonly associated with the persistence of LBP [23, 24]. Other factors that contributed to an increased risk of persistent LBP included back pain severity, associated leg pain, pain and disability duration, older age and lower socioeconomic status [25, 26]. Whilst these prognostic factors are thought to be related, no single factor has been shown to be strongly predictive of LBP [27-29]. Studies have investigated predictors of recurrence, identifying two or more previous episodes to be the strongest known predictor of a recurrent episode of LBP [21, 22]. It is not currently known whether any other factors are predictive of recurrence.

Most of the current research has investigated external prognostic factors (e.g., psychosocial factors) with conflicting evidence on whether morphological changes within the spine have an influence on LBP prognosis [30]. While morphological changes on magnetic resonance imaging (e.g., changes to the disc) are seen in symptomatic individuals, they are also seen in asymptomatic populations as well [30-33]. Therefore, the significance of morphological structures as prognostic factors may be important; however, accurately determining which structural changes are responsible for pain-generation in LBP remains challenging.

1.1.6 Diagnostic triage of low back pain

Low back pain is commonly triaged into three categories: LBP due to serious spinal pathology, LBP with associated nerve root involvement or non-specific LBP [34, 35]. Most LBP (90-95%) is classified as nonspecific LBP, as a specific cause is unable to be identified [35]. In the remaining 5-10% of patients, the LBP can be attributed to an underlying cause such as lumbar nerve root involvement or in a minority of cases, serious pathology (e.g., fracture or neoplasm) [2, 25, 36]. There are a number of anatomical structures within the spine that could conceivably contribute to LBP presentations; however, many of these structures cannot be accurately and/or reliably visualised with modern imaging modalities. One

structure commonly identified as a source of LBP is the intervertebral disc (IVD) [32, 37]. Although nerve endings found in the outer third of the disc are thought to be pain producing, their relationship to LBP remains poorly understood [38-40]. Further, sensitisation processes that may occur within the disc when neural structures project into the disc may also increase the potential for pain production [40].

1.2 THE INTERVERTEBRAL DISC AND DISC DEGENERATION ON MAGNETIC RESONANCE IMAGING

1.2.1 THE INTERVERTEBRAL DISC

The intervertebral disc is a cartilaginous structure interposed between the vertebral bodies [41, 42]. Its function is to provide mobility to the anterior vertebral column [41]. The disc complex is made up of two separate structures: a central nucleus pulposus and an outer annulus fibrosis [41-43]. The gelatinous nucleus is made of chondrocytes, while the circumferential annulus consists of collagenous rings of lamellae [41, 42]. Collagen fibres from the annulus extend into the adjacent structures, including the rim of the vertebral body, surrounding ligaments and the hyaline cartilage of the endplates [41, 42].

A disc consists mostly of water, proteoglycans and a network of type II collagen fibres [43]. The hydrophilic nature of the proteoglycans allows for the IVD to act as a shock absorber, counteracting the compressive loads sustained by the spine [44]. Small numbers of both blood vessels and nerves are present in a disc, situated in the very outer portion of the annulus [41]. The remainder of the disc is aneural and avascular [45]. As the degenerative process of the disc begins, the health of the disc slowly deteriorates [41].

Degenerative findings are also commonly reported to progress as a part of ageing, regardless of LBP. This therefore implies that some degenerative findings found on MRI may not indicate pathology, but normal ageing. Other changes that occur to the disc that may not be related to pathology is the normal dynamic variations the disc experiences throughout the day (e.g., diurnal variation) [41, 45].

1.2.2 DISC DEGENERATION AND LOW BACK PAIN

Disc degeneration (DD) is described as a pathophysiological change to the structural elements of the disc (annulus fibrosis, nucleus pulposus and endplates) through trauma, genetics or normal ageing [41, 46]. The dehydration of the nucleus and subsequent disorganisation of the lamellae lead to a change in the distinctiveness between the boundaries of the annulus and nucleus [41, 47]. These changes eventually cause fissuring to occur [41, 43, 47]. Changes to the biochemical properties in the IVD cause a reduction in the height of the disc, usually towards the later stages of the degenerative process [48]. The pathophysiological changes that occur to the IVD during DD are similar to the changes seen in normal IVD ageing [49, 50]. For example, the extent of DD is strongly associated with a person's age, regardless of whether that individual suffers from LBP [51]. However, DD is more common in individuals with LBP than without [32, 52]. This suggests that a proportion of the pain experienced by LBP sufferers could be attributed to DD, not just the normal ageing process.

The role of the IVD in LBP is controversial. Current prevalence estimates of the IVD as a source of pain are estimated to be roughly 39% [30]. A better understanding of the role of the IVD in the development of LBP (as a risk factor or a pain producing structure) may assist in developing targeted prevention strategies for those at higher risks of recurrence. Despite the lack of evidence for candidate aetiological factors, a drastic increase in the use of imaging modalities (such as magnetic resonance imaging) in patients with LBP has been identified [53].

1.2.3 The diagnostic value of magnetic resonance imaging findings for low back pain

Magnetic resonance imaging (MRI) is one of the more frequently used imaging modalities for identifying changes to the IVD [54]. Degenerative disc changes that are reported on MRI are often considered to be nociceptive, and are commonly identified in patients with LBP [32, 55]. However, DD is also found in asymptomatic populations as well [31, 33]. A systematic review of the imaging features of spinal degeneration in asymptomatic populations [51] identified that DD was highly prevalent among asymptomatic individuals, and found in nearly 90% of individuals over 60 years of age. Comparatively, a systematic review investigating DD in adults with LBP found that DD was more prevalent in adults under 50 years of age compared to asymptomatic controls [32]. The inconsistent findings of these reviews reiterate the need for more specific investigation in this area. One potential explanation for the variability seen between studies may be differences in the grading systems used to measure changes to the IVD on MRI.

1.3 Grading systems for disc degeneration

1.3.1 Overview of grading systems for disc degeneration

Grading systems for DD are designed to quantify and categorise changes to the IVD on MRI. Given that DD may contribute to the development of LBP or may influence LBP recovery, valid and reliable grading systems are important to accurately measure the degree of DD. Grading systems that have a high sensitivity to change are also necessary to accurately assess conditions like DD, as progression is usually gradual over time. Grading systems that do not possess these qualities likely draw inaccurate conclusions when used to make associations with LBP. It is unclear which grading systems have been assessed for different measurement properties such as reliability, validity and sensitivity to change.

As mentioned previously, it is unclear which grading systems have been assessed for different measurement properties. The most important measurement properties when assessing grading systems include discriminative validity (the ability to distinguish between clinical and normal groups), predictive validity (the ability of a measure to predict a future event), reliability (the ability for a rater/s to repeatedly record the same result) and sensitivity to change (the responsiveness of the grading system to measure change over time) [56]. In this thesis, validity was defined as grading systems that were used to draw associations between different variables (such as other degeneration findings) or LBP, whether grading systems were compared to other systems, and how well grading systems predicted future episodes of LBP.

The validity, or clinical relevance, of a grading system may also be influenced by the method of analysis or the synthesis of the grading system. For example, variations in thresholds used to describe the presence or absence of DD, the spinal levels assessed and summary measures for analysis or reporting (e.g., worst level, average of all levels or sum of all levels) may change the information provided by the grading system, and potentially the strength of association between DD and LBP. It would be useful to identify the different methods of analysis and synthesis of grading systems that are currently being used and whether standardised methods are required. A number of grading systems for DD exist which use either subjective or quantitative assessment of different IVD changes to measure the severity of degeneration. Within each subjective and quantitative system, different grading components are used to measure DD changes on MRI. The most common measures to assess DD are disc signal intensity (DSI) and disc height (DH) [57]. Subjective grading systems use visual assessments of DSI and DH, and are usually categorised ordinally. Alternatively, quantitative grading systems measure DSI and DH on a continuous scale of brightness and distance respectively [58, 59].

1.3.2 Subjective measurements of disc degeneration

Subjective MRI-based grading systems are commonly used to measure DD in the lumbar spine. A spectrum of different disc changes are used within these subjective systems [60, 61]. The most visible changes to the IVD include alterations to DSI, narrowing of the DH and loss of the distinction between the boundary of the annulus fibrosis and nucleus pulposus [60, 61].

Disc signal intensity on MRI is used to measure the water concentration within the disc [38, 59, 60, 61]. The assessment primarily relies on T2-weighted MRI sequences [62]. A grader, usually a radiologist, visually assesses DSI to determine the level of signal intensity [61, 63]. When visually assessing DSI several factors are considered by the radiologist as a reference standard, including the signal intensity of the surrounding structures like the cerebro-spinal fluid (CSF). A lower DSI is indicative of a more dehydrated disc and therefore more severe degeneration [61, 63].

Disc height is another morphological feature used to measure DD [59]. The DH is directly assessed in subjective measures, usually with consideration of the surrounding discs to determine the relative severity of the DH loss [60, 61, 63, 64]. As DD progresses, the DH gradually reduces indicating more severe degeneration [48]. Disc height loss is more indicative of later stage DD [48].

The ability to visibly discern between the boundary of the nucleus and annulus of the IVD is also commonly used in subjective grading systems. The distinction refers to whether the nucleus and annulus are clearly visible and have distinct boundaries within the IVD [60, 61]. When grading for the distinction between the annulus and nucleus, subjective thresholds such as clear, unclear and lost may be used to visually describe the boundary [60, 61]. As the amount of DD increases, it becomes more difficult to distinguish between the two structures [60, 61].

The ability to visibly discern between the boundary of the nucleus and annulus of the IVD is also commonly used in subjective grading systems. The distinction refers to whether the nucleus and annulus are clearly visible and have distinct boundaries within the IVD [60, 61]. When grading for the distinction between the annulus and nucleus, subjective thresholds such as clear, unclear and lost may be used to visually describe the boundary [60, 61]. As the amount of DD increases, it becomes more difficult to distinguish between the two structures [60, 61]. Subjective grading systems are useful when grading for DD as they are able to assess for a number of different degenerative changes to the disc. When using a multitude of grading components, the system can encapsulate all of the different changes to the IVD throughout the degenerative process. Common subjective grading systems that use DSI, DH and the distinctiveness between the annulus and the nucleus are the Pfirrmann and modified Pfirrmann classifications [60, 61]. These standardised systems subjectively categorise DD on a scale from I (no degeneration) to V (severe degeneration) for the Pfirrmann, and 1 (no degeneration) to 8 (severe degeneration) for the modified Pfirrmann [60, 61]. The Pfirrmann and modified Pfirrmann systems are widely used [56, 65]. The systems are described in Table 1.1 and Table 1.2.

Table 1.1 The Pfirrmann system for disc degeneration [61].

Grade	Distinction of nucleus and annulus	Signal intensity	Height of intervertebral disc
I	Clear	Hyperintense, isointense to cerebrospinal fluid	Normal
II	Clear	Hyperintense, isointense to cerebrospinal fluid	Normal
III	Unclear	Intermediate	Normal to slightly decreased
IV	Lost	Intermediate to hypointense	Normal to moderately decreased
V	Lost	Hypointense	Collapsed disc space

Table 1.2 The modified Pfirrmann system for disc degeneration [60].

Grade	Signal From nucleus and inner fibres of annulus	Distinction between inner and outer fibres of annulus at posterior aspect of disc	Height of disc
1	Uniformly hyperintense, equal to CSF	Distinct	Normal
2	Hyperintense (>presacral fat and <CSF) ± Hypointense intranuclear cleft	Distinct	Normal
3	Hyperintense though < presacral fat	Distinct	Normal
4	Mildly hyperintense (slightly>outer fibres of annulus)	Indistinct	Normal
5	Hypointense (= outer fibres of annulus)	Indistinct	Normal
6	Hypointense	Indistinct	<30% reduction in disc height
7	Hypointense	Indistinct	30%-60% reduction in disc height
8	Hypointense	Indistinct	>60% reduction in disc height

1.3.3 LIMITATIONS OF SUBJECTIVE GRADING OF DISC DEGENERATION

Subjective grading systems have limitations, primarily due to their insufficient discriminatory capacity and lack of sensitivity to change. The obvious limitation of subjectively designed systems is the inability to measure the continuous nature of DD on an ordinal scale [66]. There are no objective criteria to precisely distinguish the distance or difference between each category of degeneration, and therefore no grading system can reliably determine exactly which grade a disc should be categorised within [66].

Subjective systems are also limited by poor inter-rater reliability [63, 67]. As the systems require a radiologist to report DD findings, factors such as the radiologists' experience can also bias the grading process [64]. For example, the intra-rater reliability of subjective reports of MRI findings of the lumbar spine were found to be moderate (κ = 0.50-0.74 and κ = 0.69-0.80) compared to the reports of inter-rater reliability which were significantly worse (κ = 0.43-0.66, κ = 0.57-0.67, and κ = 0.24) [67-69]. To combat this, more standardised systems like the Pfirrmann classification are used to assist radiologists in minimising the amount of disagreement between different graders.

While subjective systems like the Pfirrmann are more reliable, they are limited by poor sensitivity to change [60, 61]. Namely, the Pfirrmann classification was shown to be non-discriminatory when assessing DD at higher grades in older populations [60, 61]. Additional grades were added to the classification, resulting in the creation of the modified Pfirrmann system, to discriminate between more severe degenerative changes in the later stages of DD [60, 61, 70]. While the modified Pfirrmann classification has higher sensitivity to change, the additional grades further reduce inter-rater reliability [60, 61, 66]. For example, the inter-rater reliability of the modified Pfirrmann was found to be (κ = 0.65-0.67) compared to the Pfirrmann (κ = 0.74-0.81) [60, 61, 68]. A balance exists between the complexity of the system, and its ease of applicability. Thus, the challenge of subjective grading systems is balancing the complexity of the system with its reliability and efficiency.

1.3.4 QUANTITATIVE MEASUREMENTS OF DISC DEGENERATION

Unlike subjective measurements of DD, quantitative grading systems represent a more reliable measure of DD, as they can be used to measure changes to the IVD more objectively [58, 71-73]. This is achieved by using measurements of DSI and DH directly from the MRI image [58, 70, 74]. The reliability of measuring DSI and DH quantitatively is considered to be excellent for both intra- and inter-rater reliability (ICC = 0.95-0.99 and ICC = 0.85-0.99) [75-78].

Disc signal intensity is quantitatively assessed using a pixel-based analysis method, whereby a region of interest (ROI) is drawn around the nucleus pulposus and annulus fibrosis, allowing for the measurement of DSI within a particular region of the disc [59]. Different DICOM-viewing programs employ measuring tools which automatically measure the water concentration of the disc within the ROI. The minimum,

maximum and mean signal intensity measurements are recorded which provide a quantitative assessment of disc brightness [58, 74].

Disc height is geometrically measured on MRI to produce a quantitative measure of changes to the disc morphology. Software tools are used to measure the height of the disc using a multitude of different methods [44, 59, 74]. Common methods of calculating the DH include directly measuring the anterior, middle and posterior height between adjacent vertebrae and calculating the average, or using a measurement of the midsagittal disc area and dividing it by the diameter [60, 79, 80].

1.3.5 Limitations of quantitative grading of disc degeneration

Although quantitative grading systems improve upon some of the limitations of subjective grading systems, they also present limitations when measuring DD. The main limitation of quantitative grading systems is that they fail to account for inter-patient variability. Inter-patient variations in DSI and DH arise from both intrinsic and extrinsic factors, which may impact the clinical value of DSI and DH measurements when drawing comparisons between patients. For example, variability in DSI may be caused by inhomogeneities within the magnetic field or the MRI protocol (extrinsic factors) which change the signal intensity, despite the water concentration within the disc being the same as another individual [58, 80]. When quantitatively measuring DH, factors such as different heights between individuals (intrinsic factors) may account for different disc heights. For example, on average, individuals with a greater standing height also have a greater DH. The relative change in an individual's DH who has a shorter standing height may be due to intrinsic factors, rather than due to degeneration.

Grading systems for DD can also be impacted upon by other intrinsic factors including age [81]. Changes that occur during DD are not dissimilar to changes seen with normal ageing. Thus, a similar DSI measure in a 35 year-old may indicate more severe DD compared to the same change in a 70 year-old, where some level of DD would normally be expected. A range of other different intrinsic factors may also be important when measuring changes to the IVD quantitatively. If quantitative measures of DSI and DH lack the ability to consider different factors when measuring the degenerative process, these measures may not adequately measure DD in a way that is clinically relevant. Therefore, quantitative measurements of DSI and DH may be limited by added noise (extrinsic and intrinsic factors) which may limit the clinical relevance of the measures.

1.3.5 Normalised quantitative measures

Normalised quantitative measures (Z-scores) are used to overcome some of the limitations of using quantitative systems by drawing comparisons between quantitative measurements and different individuals. The use of a normalised quantitative measure in clinical contexts allows practitioners to make meaningful comparisons by accounting for specific factors that may be related to the condition being

measured. Using osteoporosis as an example, bone density scores are normalised so that they can be compared across patients with different intrinsic characteristics (e.g., sex and age) [82]. The Z-score is used to age-match individuals of the same sex for a more meaningful score [82]. The T-score is used to rate the relative risk of osteoporotic fracture in sex-matched bone density scores [82]. The scores are therefore easy to understand and clinically relevant for both the clinician and patient.

1.3.6 Current normalisation of intrinsic and extrinsic factors of disc degeneration

Normalisation formulas have been used for certain intrinsic and extrinsic factors of DD to facilitate more consistency when comparing between individuals using quantitative grading systems. Different extrinsic factors are sometimes normalised when quantitatively grading DD on MRI. For example, formulas are used to adjust for imaging variability between different MRI procedures (e.g., adjusting DSI for CSF signal intensity) [74, 83]. Due to the high-water content of CSF, and its consistency throughout the course of life, it is commonly used to adjust DSI to account for variability in the magnetic field or MRI protocol. Similarly, in patients with different standing heights, some grading systems have used a DH index measure to adjust the image for differences in the individual's standing height to account for the variability between different patients [60, 83].

A very limited number of studies have identified factors that are associated with raw quantitative measurements of DSI and DH. Within the current literature, age is one of the more common intrinsic factors used to make comparisons with DSI. A strong association has been pre-determined when comparing age to DSI, but variability is seen in studies measuring the association between age and DH. Other intrinsic factors that show significant associations with DSI and DH include disc level and BMI, while sex tends to only show a relationship with DH.

While some grading systems have used normalisation formulas to adjust for certain intrinsic (standing height) and extrinsic factors (imaging variability), no grading systems have systematically adjusted DSI and DH for additional factors such as age, vertebral height and vertebral level. In a study by King *et al* [81], a normalisation process was developed to normalise DSI and DH for a range of intrinsic factors in the quantitative assessment of DD. It was found that normalised quantitative measures markedly changed where an individual is placed within the degeneration distribution, indicating that normalised measure are clearly different and may be more relevant clinically [81]. Consequently, if the measured severity of DD is impacted by the normalisation process, subsequent assessment of the association between DD and LBP may change. Determining whether normalised quantitative grading systems are more valid may result in a more relevant assessment of associations with LBP.

Chapter 3 will address this issue by assessing the predictive validity of normalised measures compared to other common subjective and quantitative grading systems for DD to determine whether normalised measures are more predictive of LBP.

1.4 THESIS RATIONALE

The underlying cause of LBP is still unknown, despite the overwhelming clinical, epidemiological and socioeconomic burden of the condition. Disc degeneration has been identified as a potential factor in LBP; however, its role is still unclear due to varying results in studies investigating associations with LBP outcomes. Some of the ambiguity in our understanding of the association between LBP outcomes and DD may be explained by the different grading systems that are used to measure DD on MRI and the variability in the way in which they are analysed. If the most common grading systems, their methods of analysis and their measurement properties could be identified and described, this may determine if there is a need to standardise grading systems for measuring DD in the lumbar spine.

The grading systems that are currently used to grade DD suffer from fundamental limitations which may impact their clinical relevance when measuring associations with LBP outcomes. Grading systems that are reliable, but also clinically relevant (valid) are essential for clinicians that treat patients with LBP. How well a grading system predicts LBP, identifies favourable responses to treatment and distinguishes between patients with and without LBP are all clinically relevant outcomes. Testing whether different grading systems have stronger associations with LBP outcomes may assist in better understanding the role DD has in LBP.

1.5 THESIS AIMS

This thesis aims to identify and describe MRI-based grading systems for lumbar DD and assess whether normalised quantitative systems have stronger associations with clinical outcomes of LBP compared to common subjective and quantitative grading systems.

Specifically, the thesis aims to

i. Perform a scoping review of the current literature to describe different MRI-based grading systems for DD in the lumbar spine and report whether measurement properties such as reliability, validity and sensitivity to change have been assessed and reported.
ii. Perform a secondary analysis to assess the predictive validity of five MRI-based grading systems of DD in the lumbar spine in predicting a recurrent episode of LBP in a cohort of participants who recently recovered from an episode of acute low LBP.

1.6 REFERENCES

1. Burton AK, Balagué F, Cardon G, Eriksen HR, Henrotin Y, Lahad A, et al. Chapter 2. European Guidelines for Prevention in Low Back Pain : November 2004. *European Spine Journal*. 2006;15 Suppl 2(S2):S136-s168.

2. Hoy D, Brooks P, Blyth F, Buchbinder R. The Epidemiology of Low Back Pain. *Best Practice & Research. Clinical Rheumatology*. 2010;24(6):769-781.

3. Knezevic NN, Candido KD, Vlaeyen JWS, Van Zundert J, Cohen SP. Low Back Pain. *The Lancet (British Edition)*. 2021;398(10294):78-92.

4. Coste J, Delecoeuillerie G, De Lara AC, Leparc JM, Paolaggi JB. Clinical Course and Prognostic Factors in Acute Low Back Pain: An Inception Cohort Study in Primary Care Practice. *BMJ*. 1994;308(6928):577-580.

5. Da C Menezes Costa L, Maher CG, Hancock MJ, Mcauley JH, Herbert RD, Costa LOP. The Prognosis of Acute and Persistent Low-Back Pain: A Meta-Analysis. *Canadian Medical Association Journal*. 2012;184(11):E613-E624.

6. Hancock MJPB, Maher CMPF, Petocz PP, Lin C, Steffens DP, Luque-Suarez AP, et al. Risk Factors for a Recurrence of Low Back Pain. *The Spine Journal*. 2015;15(11):2360-2368.

7. Aspinall SL, Jacques A, Leboeuf-Yde C, Etherington SJ, Walker BF. Pressure Pain Threshold and Temporal Summation in Adults with Episodic and Persistent Low Back Pain Trajectories: A Secondary Analysis at Baseline and after Lumbar Manipulation or Sham. *Chiropractic & Manual Therapies*. 2020;28(1):36-36.

8. Axen I, Leboeuf-Yde C. Trajectories of Low Back Pain. *Best Practice & Research. Clinical Rheumatology*. 2013;27(5):601-612.

9. Walker BF. The Prevalence of Low Back Pain: A Systematic Review of the Literature from 1966 to 1998. *Journal of Spinal Disorders*. 2000;13(3):205-217.

10. Hoy D, Bain C, Williams G, March L, Brooks P, Blyth F, et al. A Systematic Review of the Global Prevalence of Low Back Pain. *Arthritis and Rheumatism*. 2012;64(6):2028-2037.

11. Schofield DJP, Shrestha RNP, Percival RBA, Passey M, Callander EJBA, Kelly SJP. The Personal and National Costs of Early Retirement Because of Spinal Disorders: Impacts on Income, Taxes, and Government Support Payments. *The Spine Journal*. 2012;12(12):1111-1118.

12. Katz JN. Lumbar Disc Disorders and Low-Back Pain: Socioeconomic Factors and Consequences. *Journal of Bone and Joint Surgery. American Volume*. 2006;88(Suppl 2):21-24.

13. Kigozi J, Konstantinou K, Ogollah R, Dunn K, Martyn L, Jowett S. Factors Associated with Costs and Health Outcomes in Patients with Back and Leg Pain in Primary Care: A Prospective Cohort Analysis. *BMC Health Services Research*. 2019;19(1):406-406.

14. Dagenais S, Caro JMD, Haldeman S. A Systematic Review of Low Back Pain Cost of Illness Studies in the United States and Internationally. *The Spine Journal*. 2008;8(1):8-20.

15. Schofield D, Cunich MM, Shrestha RN, Tanton R, Veerman L, Kelly SJ, et al. The Indirect Costs of Back Problems (Dorsopathies) in Australians Aged 45 to 64 Years from 2015 to 2030: Results from a Microsimulation Model, Health & Wealth Model 2030. *Pain (Amsterdam)*. 2016;157(12):2816-2825.

16. Pengel LHM, Herbert RD, Maher CG, Refshauge KM. Acute Low Back Pain: Systematic Review of Its Prognosis. *BMJ*. 2003;327(7410):323-325.

17. Heuch I, Foss IS. Acute Low Back Usually Resolves Quickly but Persistent Low Back Pain Often Persists. *Journal of Physiotherapy*. 2013;59(2):127-127.

18. Henschke N, Maher CG, Refshauge KM, Herbert RD, Cumming RG, Bleasel J, et al. Prognosis in Patients with Recent Onset Low Back Pain in Australian Primary Care: Inception Cohort Study. *BMJ*. 2008;337(7662):154-157.

19. Stanton TR, Henschke N, Maher CG, Refshauge KM, Latimer J, Mcauley JH. After an Episode of Acute Low Back Pain, Recurrence Is Unpredictable and Not as Common as Previously Thought. *Spine*. 2008;33(26):2923-2928.

20. Wasiak R, Pransky G, Verma S, Webster B. Recurrence of Low Back Pain: Definition-Sensitivity Analysis Using Administrative Data. *Spine*. 2003;28(19):2283-2291.

21. Stanton TR, Latimer J, Maher CG, Hancock MJ. A Modified Delphi Approach to Standardize Low Back Pain Recurrence Terminology. *European Spine Journal*. 2011;20(5):744-752.

22. Da Silva T, Mills K, Brown BT, Herbert RD, Maher CG, Hancock MJ. Risk of Recurrence of Low Back Pain: A Systematic Review. *The Journal of Orthopaedic and Sports Physical Therapy*. 2017;47(5):305-313.

23. Pincus T, Burton AK, Vogel S, Field AP. A Systematic Review of Psychological Factors as Predictors of Chronicity/Disability in Prospective Cohorts of Low Back Pain. *Spine*. 2002;27(5):E109-E120.

24. Linton SJ. Occupational Psychological Factors Increase the Risk for Back Pain: A Systematic Review. *Journal of Occupational Rehabilitation*. 2001;11(1):53-66.

25. Hartvigsen J, Hancock MJ, Kongsted A, Louw Q, Ferreira ML, Genevay S, et al. What Low Back Pain Is and Why We Need to Pay Attention. *The Lancet (British Edition)*. 2018;391(10137):2356-2367.

26. Chou R, Qaseem A, Snow V, Casey D, Cross JJT, Shekelle P, et al. Diagnosis and Treatment of Low Back Pain: A Joint Clinical Practice Guideline from the American College of Physicians and the American Pain Society. *Annals of Internal Medicine*. 2007;147(7):478-491.

27. Flynn T, Fritz J, Whitman J, Wainner R, Magel J, Rendeiro D, et al. A Clinical Prediction Rule for Classifying Patients with Low Back Pain Who Demonstrate Short-Term Improvement with Spinal Manipulation. *Spine*. 2002;27(24):2835-2843.

28. Hancock MJ, Maher CG, Latimer J, Herbert RD, Mcauley JH. Can Rate of Recovery Be Predicted in Patients with Acute Low Back Pain? Development of a Clinical Prediction Rule. *European Journal of Pain*. 2009;13(1):51-55.

29. Cruz EB, Canhao H, Fernandes R, Caeiro C, Branco JC, Rodrigues AM, et al. Prognostic Indicators for Poor Outcomes in Low Back Pain Patients Consulted in Primary Care. *PloS One*. 2020;15(3):e0229265-e0229265.

30. Hancock MJ, Maher CG, Latimer J, Spindler MF, Mcauley JH, Laslett M, et al. Systematic Review of Tests to Identify the Disc, Sij or Facet Joint as the Source of Low Back Pain. *European Spine Journal*. 2007;16(10):1539-1550.

31. Baker A. Abnormal Magnetic-Resonance Scans of the Lumbar Spine in Asymptomatic Subjects. A Prospective Investigation. Springer London; 2014:245-247.

32. Brinjikji W, Diehn FE, Jarvik JG, Carr CM, Kallmes DF, Murad MH, et al. MRI Findings of Disc Degeneration Are More Prevalent in Adults with Low Back Pain Than in Asymptomatic Controls: A Systematic Review and Meta-Analysis. *American Journal of Neuroradiology*. 2015;36(12):2394-2399.

33. Tonosu J, Oka H, Higashikawa A, Okazaki H, Tanaka S, Matsudaira K. The Associations between Magnetic Resonance Imaging Findings and Low Back Pain: A 10-Year Longitudinal Analysis. *PloS One*. 2017;12(11):e0188057-e0188057.

34. Van Tulder M, Becker A, Bekkering T, Breen A, Del Real M, Hutchinson A, et al. Chapter 3 - European Guidelines for the Management of Acute Nonspecific Low Back Pain in Primary Care. *European Spine Journal*. 2006;15(S2):S169-S191.

35. Koes BW, Van Tulder MW, Thomas S. Diagnosis and Treatment of Low Back Pain. *BMJ*. 2006;332(7555):1430-1434.

36. Kongsted A, Kent P, Axen I, Downie AS, Dunn KM. What Have We Learned from Ten Years of Trajectory Research in Low Back Pain? *BMC Musculoskeletal Disorders*. 2016;17(220):220-220.

37. Oichi T, Taniguchi Y, Oshima Y, Tanaka S, Saito T. Pathomechanism of Intervertebral Disc Degeneration. *Journal of Orthopaedic Research-Spine*. 2020;3(1):e1076.

38. Luoma K, Riihimäki H, Luukkonen R, Raininko R, Viikari-Juntura E, Lamminen A. Low Back Pain in Relation to Lumbar Disc Degeneration. *Spine*. 2000;25(4):487-492.

39. Watanabe T, Otani K, Sekiguchi M, Konno S-I. Relationship between Lumbar Disc Degeneration on MRI and Low Back Pain: A Cross-Sectional Community Study. *Fukushima Journal of Medical Science*. 2022;68(2):97-107.

40. Kleinstück F, Dvorak J, Mannion AF. Are Structural Abnormalities on Magnetic Resonance Imaging a Contraindication to the Successful Conservative Treatment of Chronic Nonspecific Low Back Pain? *Spine*. 2006;31(19):2250-2257.

41. Roberts S, Evans H, Trivedi J, Menage J. Histology and Pathology of the Human Intervertebral Disc. *Journal of Bone and Joint Surgery. American Volume*. 2006;88(Suppl 2):10-14.

42. Bogduk N. Clinical Anatomy of the Lumbar Spine and Sacrum. Elsevier Ltd; 2006. p. 267-268.

43. Kadow T, Sowa G, Vo N, Kang JD. Molecular Basis of Intervertebral Disc Degeneration and Herniations: What Are the Important Translational Questions? *Clinical Orthopaedics and Related Research*. 2015;473(6):1903-1912.

44. Urban JPG, Maroudas A. Swelling of the Intervertebral Disc in Vitro. *Connective Tissue Research*. 1981;9(1):1-10.

45. Freemont AJ, Watkins A, Le Maitre C, Baird P, Jeziorska M, Knight MTN, et al. Nerve Growth Factor Expression and Innervation of the Painful Intervertebral Disc: NGF in Painful Intervertebral Disc. *The Journal of Pathology*. 2002;197(3):286-292.

46. Weiner BK. Difficult Medical Problems: On Explanatory Models and a Pragmatic Alternative. *Medical Hypotheses*. 2007;68(3):474-479.

47. Kauppila LI. Ingrowth of Blood Vessels in Disc Degeneration. Angiographic and Histological Studies of Cadaveric Spines. *Journal of Bone and Joint Surgery. American Volume*. 1995;77(1):26-31.

48. Twomey L, Taylor J. Age Changes in Lumbar Intervertebral Discs. *Acta Orthopaedica*. 1985;56(6):496-499.

49. Beadle O. The Intervertebral Discs: Observations on Their Normal and Morbid Anatomy in Relation to Certain Spinal Deformities. *Journal of the American Medical Association*. 1932;98(14):1212-1212.

50. Boos N, Weissbach S, Rohrbach H, Weiler C, Spratt KF, Nerlich AG. Classification of Age-Related Changes in Lumbar Intervertebral Discs. 2002 Volvo Award in Basic Science. *Spine*. 2002;27(23):2631-2644.

51. Brinjikji W, Luetmer PH, Comstock B, Bresnahan BW, Chen LE, Deyo RA, et al. Systematic Literature Review of Imaging Features of Spinal Degeneration in Asymptomatic Populations. *American Journal of Neuroradiology*. 2015;36(4):811-816.

52. Kjaer P, Leboeuf-Yde C, Korsholm L, Sorensen JS, Bendix T. Magnetic Resonance Imaging and Low Back Pain in Adults: A Diagnostic Imaging Study of 40-Year-Old Men and Women. *Spine*. 2005;30(10):1173-1180.

53. Downie A, Hancock M, Jenkins H, Buchbinder R, Harris I, Underwood M, et al. How Common Is Imaging for Low Back Pain in Primary and Emergency Care? Systematic Review and Meta-Analysis of over 4 Million Imaging Requests across 21 Years. British journal of sports medicine. 2020;54(11):642

54. Balagué FD, Mannion AFP, Pellisé F, Cedraschi CP. Non-Specific Low Back Pain. *The Lancet (British Edition)*. 2012;379(9814):482-491.

55. Swanson BT, Creighton D. The Degenerative Lumbar Disc: Not a Disease, but Still an Important Consideration for OMPT Practice: A Review of the History and Science of Discogenic Instability. *The Journal of Manual & Manipulative Therapy*. 2020;28(4):191-200.

56. COSMIN database of systematic reviews of outcome measurement instruments. Retrieved from https://database.cosmin.nl/

57. Dragsbaek L, Kjaer P, Hancock M, Jensen TS. An Exploratory Study of Different Definitions and Thresholds for Lumbar Disc Degeneration Assessed by MRI and Their Associations with Low Back Pain Using Data from a Cohort Study of a General Population. *BMC Musculoskeletal Disorders*. 2020;21(1):253-253.

58. Niemeläinen R, Videman T, Dhillon SS, Battié MC. Quantitative Measurement of Intervertebral Disc Signal Using MRI. *Clinical Radiology*. 2007;63(3):252-255.

59. Luoma K, Vehmas T, Riihimäki H, Raininko R. Disc Height and Signal Intensity of the Nucleus Pulposus on Magnetic Resonance Imaging as Indicators of Lumbar Disc Degeneration. *Spine*. 2001;26(6):680-686.

60. Griffith JF, Wang Y-XJ, Antonio GE, Choi KC, Yu A, Ahuja AT, et al. Modified Pfirrmann Grading System for Lumbar Intervertebral Disc Degeneration. *Spine*. 2007;32(24):E708-E712.

61. Pfirrmann CWA, Metzdorf A, Zanetti M, Hodler J, Boos N. Magnetic Resonance Classification of Lumbar Intervertebral Disc Degeneration. *Spine*. 2001;26(17):1873-1878.

62. An HS, Anderson PA, Haughton VM, Iatridis JC, Kang JD, Lotz JC, et al. Introduction: Disc Degeneration: Summary. *Spine*. 2004;29(23):2677-2678.

63. Hancock MJ, Maher CG, Jarvik JG, Battié MC, Elliott JM, Jensen TS, et al. Reliability and Validity of Subjective Radiologist Reporting of Temporal Changes in Lumbar Spine MRI Findings. *PM & R*. 2022;14(11):1325-1332.

64. Fardon DF, Williams AL, Dohring EJ, Murtagh FR, Gabriel Rothman SL, Sze GK. Lumbar Disc Nomenclature: Version 2.0: Recommendations of the Combined Task Forces of the North American Spine Society, the American Society of Spine Radiology and the American Society of Neuroradiology. *The Spine Journal*. 2014;14(11):2525-2545.

65. Miyazaki M, Hong SW, Yoon SH, Morishita Y, Wang JC. Reliability of a Magnetic Resonance Imaging-Based Grading System for Cervical Intervertebral Disc Degeneration. *Journal of Spinal Disorders & Techniques*. 2008;21(4):288-292.

66. Urrutia J, Besa P, Campos M, Cikutovic P, Cabezon M, Molina M, et al. The Pfirrmann Classification of Lumbar Intervertebral Disc Degeneration: An Independent Inter- and Intra-Observer Agreement Assessment. *European Spine Journal*. 2016;25(9):2728-2733.

67. Carrino JA, Lurie JD, Herzog R, Tosteson ANA, Tosteson TD, Carragee EJ, et al. Lumbar Spine: Reliability of MR Imaging Findings. *Radiology*. 2009;250(1):161-170.

68. Mchugh ML. Interrater Reliability: The Kappa Statistic. *Biochemia Medica*. 2012;22(3):276-282.

69. Brant-Zawadzki MN, Jensen MC, Obuchowski N, Ross JS, Modic MT. Interobserver and Intraobserver Variability in Interpretation of Lumbar Disc Abnormalities. A Comparison of Two Nomenclatures. *Spine*. Jun 1 1995;20(11):1257-63; discussion 1264.

70. Rim DC. Quantitative Pfirrmann Disc Degeneration Grading System to Overcome the Limitation of Pfirrmann Disc Degeneration Grade. *Korean Journal of Spine*. 2016;13(1):1-8.

71. Videman T, Gibbons LE, Battie MC. Age-and Pathology-Specific Measures of Disc Degeneration. *Spine*. 2008;33(25):2781-2788.

72. Watanabe A, Benneker LM, Boesch C, Watanabe T, Obata T, Anderson SE. Classification of Intervertebral Disk Degeneration with Axial T2 Mapping. *American Journal of Roentgenology (1976)*. 2007;189(4):936-942.

73. Tunset A, Kjaer P, Samir Chreiteh S, Secher Jensen T. A Method for Quantitative Measurement of Lumbar Intervertebral Disc Structures: An Intra- and Inter-Rater Agreement and Reliability Study. *Chiropractic & Manual Therapies*. 2013;21(1):26-26.

74. Salamat S, Hutchings J, Kwong C, Magnussen J, Hancock MJ. The Relationship between Quantitative Measures of Disc Height and Disc Signal Intensity with Pfirrmann Score of Disc Degeneration. *SpringerPlus*. 2016;5(1):829-829.

75. Hu X, Chen M, Pan J, Liang L, Wang Y. Is It Appropriate to Measure Age-Related Lumbar Disc Degeneration on the Mid-Sagittal MR Image? A Quantitative Image Study. *European Spine Journal*. 2018;27(5):1073-1081.

76. Kamei N, Nakamae T, Nakanishi K, Tamura T, Tsuchikawa Y, Morisako T, et al. Evaluation of Intervertebral Disc Degeneration Using T2 Signal Ratio on Magnetic Resonance Imaging. *European Journal of Radiology*. 2022;152:110358-110358.

77. Fyllos AH, Arvanitis DL, Karantanas AH, Varitimidis SE, Hantes M, Zibis AH. Magnetic Resonance Morphometry of the Adult Normal Lumbar Intervertebral Space. *Surgical and Radiologic Anatomy*. 2018;40(9):1055-1061.

78. Koo TK, Li MY. A Guideline of Selecting and Reporting Intraclass Correlation Coefficients for Reliability Research. *Journal of Chiropractic Medicine*. 2016;15(2):155-163.

79. Inoue H, Ohmori K, Miyasaka K, Hosoe H. Radiographic Evaluation of the Lumbosacral Disc Height. *Skeletal Radiology*. 1999;28(11):638-643.

80. Haefeli M, Kalberer F, Saegesser D, Nerlich AG, Boos N, Paesold G. The Course of Macroscopic Degeneration in the Human Lumbar Intervertebral Disc. *Spine*. 2006;31(14):1522-1531.

81. King S, Magnussen J, Elliott J, Hancock MJ. Development of Normalized Quantitative Measures of Lumbar Disc Degeneration. *Journal of Orthopaedic Research- Spine*. 2023:e1278.

82. Sheu A, Diamond T. Diagnostic Tests: Bone Mineral Density: Testing for Osteoporosis. *Australian Prescriber*. 2016;39(2):35-39.

83. Jarman JP, Arpinar VE, Baruah D, Klein AP, Maiman DJ, Tugan Muftuler L. Intervertebral Disc Height Loss Demonstrates the Threshold of Major Pathological Changes During Degeneration. *European Spine Journal*. 2015;24(9):1944-1950.

CHAPTER 2. MRI-BASED GRADING SYSTEMS FOR ASSESSING LUMBAR DISC DEGENERATION: A SCOPING REVIEW

2.1 PREFACE

In Chapter 1 it was shown that different subjective and quantitative grading systems exist for measuring DD on MRI in the lumbar spine. However, the variety of grading systems currently in use, the ways in which these systems are summarised and the different methods used to synthesise them for analysis is currently unknown. It is also unknown whether grading systems for DD have been assessed for measurement properties such as reliability, validity and sensitivity to change. To assess the lack of information regarding the way grading systems are analysed and whether measurement properties have been assessed, it is necessary to investigate the most common grading systems and the ways in which they are used. Chapter 2 presents a scoping review to map the different MRI-based grading systems for DD in the lumbar spine, with an emphasis on how each grading system is summarised for analysis, if measurement properties have been assessed for each grading system and whether associations have been made between DD and clinical variables such as current and future LBP.

The study presented in Chapter 2 has been submitted for publication to The Spine Journal as:

Esposito D, Brown BT, Hancock M, King S, Searant I, Jenkins H. MRI-based grading systems for assessing lumbar disc degeneration: A scoping review.

The study is presented in the format of the submitted manuscript.

No ethics approval was required for this study.

2.2 CO-AUTHOR'S CONTRIBUTION STATEMENT

As co-authors of this paper, MRI-Based Grading Systems for Assessing Lumbar Disc Degeneration: A Scoping Review, we confirm Dean Esposito has made the following contributions:

- Substantial contribution to research design of the study
- Acquisition, analysis and interpretation of the data
- Drafting the paper and revising it critically
- Approved the submitted and final versions

Benjamin Thomas Brown

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MACQUARIE UNIVERSITY
AUTHORSHIP CONTRIBUTION STATEMENT

In accordance with the *Macquarie University Code for the Responsible Conduct of Research* and the *Authorship Standard*, researchers have a responsibility to their colleagues and the wider community to treat others fairly and with respect, to give credit where appropriate to those who have contributed to research.

Note for HDR students: *Where research papers are being included in a thesis, this template must be used to document the contribution of authors to each of the proposed or published research papers. The contribution of the candidate must be sufficient to justify inclusion of the paper in the thesis.*

1. DETAILS OF PUBLICATION & CORRESPONDING AUTHOR

Title of Publication (can be a holding title)		**Publication Status** Choose an item. Submitted for Publication
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Dean Esposito	Department of Chiropractic Faculty of Medicine, Health and Human Sciences	The Journal of Orthopaedic Research (Spine)

2. STUDENTS DECLARATION (if applicable)

Name of HDR thesis author (If the same as corresponding author - write "as above")	Department/Faculty	Thesis title
"as above"	"as above"	MRI-based grading systems for assessing lumbar disc degeneration

Description of HDR thesis author's contribution to planning, execution, and preparation of the work if there are multiple authors

(for example, how much as a percent did you contribute to the conception of the project, the design of methodology or experimental protocol, data collection, analysis, drafting the manuscript, revising it critically for important intellectual content, etc.)

I was a part of 100% of the contribution to planning, execution and preparation of the work of this thesis. We were collaborative in the inception of the project, however I completed all the data collection, analysis, and wrote and drafted the manuscript. It was revised by me critically for important intellectual content

I declare that the above is an accurate description of my contribution to this publication, and the contributions of other authors are as described below.	**Student signature** **Date**	 12/18/2023

3. Description of all other author contributions

Use an Asterisk * to denote if the author is also a current student or HDR candidate.

The HDR candidate or corresponding author must, for each paper, list all authors and provide details of their role in the publication. Where possible, also provide a percentage estimate of the contribution made by each author.

Name and affiliation of author	Intellectual contribution(s) (for example to the: conception of the project, design of methodology/experimental protocol, data collection, analysis, drafting the manuscript, revising it critically for important intellectual content etc.)
Benjamin Brown	Substantial contribution to the study design, acquisition, analysis and interpretation of data and drafting the paper and revising it critically.
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Sam King	Substantial contribution to the study design, analysis and interpretation of data and drafting the paper and revising it critically.
Isaac Searant	Substantial contribution to the study design, analysis and interpretation of data and drafting the paper and revising it critically.
Hazel Jenkins	Substantial contribution to the study design, analysis and interpretation of data and drafting the paper and revising it critically.
	Provide summary for any additional Authors in this cell.

4. Author Declarations

I agree to be named as one of the authors of this work, and confirm:

i. *that I have met the authorship criteria set out in the* Authorship Standard, *accompanying the* Macquarie University Research Code,

ii. *that there are no other authors according to these criteria,*

iii. *that the description in Section 3 or 4 of my contribution(s) to this publication is accurate*

iv. *that I have agreed to the planned authorship order following the* Authorship Standard

Name of author	**Authorised *** By Signature or refer to other written record of approval (eg. pdf of a signed agreement or an email record)	Date
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5. Data storage

The original data for this project are stored in the following location, in accordance with the *Research Data Management Standard* accompanying the *Macquarie University Research Code*.

If the data have been or will be deposited in an online repository, provide the details here with any corresponding DOI.

Data description/format	**Storage Location or DOI**	**Name of custodian** if other than the corresponding author

A copy of this form must be retained by the corresponding author and must accompany the thesis submitted for examination.

2.3 TITLE PAGE

Title: MRI-Based Grading Systems for Assessing Lumbar Disc Degeneration: A Scoping Review

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2.4 ABSTRACT

Background Context: An array of different magnetic resonance imaging (MRI) based grading systems are used to measure disc degeneration (DD) in the lumbar spine. It is currently unclear which grading systems are most commonly used to assess lumbar DD and how these grading systems are applied and reported. It is also unclear if the measurement properties of each grading system have been assessed.

Purpose: The aim of this scoping review was to describe different MRI-based grading systems for DD in the lumbar spine and report which grading systems have been assessed for measurement properties such as reliability, validity and sensitivity to change.

Study Design/Setting: Scoping review.

Methods: A search was conducted in EMBASE, Medline and CINAHL for studies related to MRI-based grading systems for DD in the lumbar spine, conducted in living humans. Data was extracted from each study including the description of the grading system, which levels of the lumbar spine were graded, who graded the degeneration, how the degeneration was summarized for analysis and whether measurement properties such as reliability, validity and sensitivity to change were assessed.

Results: The search identified 569 studies that graded DD. Ninety-three different grading systems were identified, including 63 subjective systems, 25 quantitative systems and five that were unspecified. The Pfirrmann method was used in over 50% of all reports. A range of grading components were used to measure DD, with disc signal intensity (DSI), disc height (DH) and the assessment of the distinctiveness between the annulus and nucleus being most common. Of the grading systems, over 60% were assessed for reliability. The majority of subjective systems and minority of quantitative systems had been assessed for their association with other variables such as LBP. Sensitivity to change was rarely assessed.

Conclusion: A large number of DD grading systems were identified in this review, many of which were infrequently used. There was substantial heterogeneity in the components used in the grading systems, and in the methods of synthesis. This variability in analysis and synthesis may impact upon estimates of association between MRI findings of disc degeneration and LBP.

Keywords: “Magnetic resonance imaging”, “MRI”, “Degenerative disc disease”, “lumbar”, “low back pain”, “intervertebral disc”

2.5 INTRODUCTION

Low back pain (LBP) is a leading cause of global disability [1] with an average lifetime prevalence of between 38-80% [2]. Despite this significant burden, limited progress has been made with regard to effective management of LBP [3,4]. This may be partly due to the inherent difficulty in identifying specific pain generating structure/s, that could serve as a target for treatment [5]. Morphological changes in the lumbar spine are commonly identified on magnetic resonance imaging (MRI) in patients with LBP [5]. However, these same morphological changes are often observed in asymptomatic populations [6,7]. Therefore, the clinical importance of morphological changes observed on MRI in patients with LBP remains unclear.

Disc degeneration (DD) is an example of a morphological change that can be identified on MRI that may be associated with LBP. DD is an umbrella term used to represent a range of intervertebral disc changes, which most commonly includes narrowing of the intervertebral disc space and alterations in disc signal intensity (DSI) [8]. Other changes can include displacement of discal material, tearing of the annulus fibrosis, end-plate changes and osteophytic formation [9]. The clinical relevance of DD for LBP patients is currently uncertain [8]. This may be, in part, due to how changes to the intervertebral disc are measured on MRI [8].

Many different grading systems are used to measure DD in the lumbar spine. These are commonly ordinal-based scales that employ a subjective assessment of different MRI findings to determine the degree of DD. One example is the Pfirrmann method, where DD is subjectively categorized on a five-point scale from I (no degeneration) through to V (severe degeneration) [10,11]. Despite their widespread use and ease of application, subjective grading systems have fundamental limitations; namely, relatively poor inter-rater reliability and sensitivity to change [12,13]. Furthermore, there are obvious shortcomings associated with measuring a continuous process (such as DD) on an ordinal scale, as there are no objective criteria to distinguish the distance/difference between each respective category [14].

Quantitative grading systems on the other hand measure changes to the intervertebral disc more objectively. Most quantitative grading systems measure DSI and/or disc height (DH) to assess DD [9, 15-17]. Although these methods provide a reliable measure of DSI and DH, it is unclear whether these measurements reflect the true severity of DD. For example, measurements of DSI and DH can be impacted by diurnal variation, vertebral level, patient age and height, which may limit their usefulness as measures of between-person severity. Consequently, the variability of factors unrelated to DD on DSI and DH may influence the grading system's ability to measure the true underlying degenerative process. The accuracy and clinical utility of any quantitative measure of DSI and DH may be skewed if these patient-specific factors are not taken into consideration.

Many different grading systems exist that use either subjective or quantitative measurements of DD, with many different variations and modifications. It is currently unclear which grading systems are used to assess lumbar DD and how the grading system is summarized, reported and coded for analysis (each level individually, sum of all levels, worst level, average level, continuous/ordinal/dichotomous). A comprehensive charting of DD grading systems and the method of synthesis used is yet to be presented within the literature.

The aim of this review is to describe different MRI-based grading systems for DD in the lumbar spine. This manuscript will focus on how each grading system was summarized for analysis, if measurement properties have been assessed for each grading system and whether associations have been made between DD and clinical variables such as current and future LBP, and sensitivity to change.

2.6 METHODS

Search strategy

This scoping review was conducted in accordance with recommendations outlined by the Joanna Briggs Institute (JBI) [18] and reported in accordance with the PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines for systematic reviews [19]. The protocol for this scoping review has been published on the Open Science Framework (OSF) [20].

An electronic database search was conducted in EMBASE, Medline and CINAHL from inception to April 5, 2023, for studies relating to MRI-based grading systems for DD in the lumbar spine. The search strategy was developed in conjunction with a faculty librarian at Macquarie University and adapted for each database (Appendix 1.). Backward citation tracking was used to identify studies that described a grading system that had been identified in the primary search.

Inclusion and exclusion criteria

To be included, studies needed to have used a grading system to assess lumbar spine DD on MRI in living humans. For the purposes of this scoping review, a grading system was defined as any subjective or quantitative system that described the presence or absence of disc degeneration or the degree/extent of DD. A subjective grading system was defined as any system that reported on visible intervertebral disc changes that could indicate DD. A quantitative grading system was defined as any system that objectively measured MRI-based components/features of the intervertebral disc on a continuous scale. A number of specialized quantitative MRI techniques and sequences were categorized together and defined as grading systems that measured the water content and tissue composition within the disc using specific sequences such as T2 mapping. Studies were only included if the authors explicitly stated they were using a grading system to measure DD. This decision was made due to inconsistency/uncertainty in the literature regarding whether certain discal changes (e.g., disc herniation) directly reflected the presence or extent

of DD. Studies were excluded if they were unable to be retrieved or translated. We also excluded reviews, and studies that were not peer-reviewed. Conference abstracts were excluded as they did not typically provide a sufficient description of the grading system.

One author (D.E) screened titles in EndNote [21] and removed duplicates and any overtly ineligible citations. The title, abstract and full text screening were performed by two authors independently. Abstracts were screened in Endnote [21] and full studies were screened in Covidence [22]. Any disagreements at the title, abstract and full text screening were discussed between authors. A third author was consulted if a consensus regarding an article's eligibility could not be achieved.

Data extraction

The data extraction tool was adapted from JBI recommendations [19]. One author (D.E) completed the extraction in Covidence [22], with 10% of the extraction conducted by a second author. This 10% was then assessed by the other authors (H.Z, B.B, I.S, S.K and M.H) to check the accuracy of extraction. We extracted the following data from each study including the: year of publication; the country in which the study was conducted in; study setting; and population characteristics. For each grading system we extracted: (1) the name and description of the grading system; (2) how the MRI was performed (supine or weight-bearing); (3) which levels of the lumbar spine were graded; (4) who graded the degeneration; (5) how the disc degeneration was summarized (worst level, each disc level collected and analyzed, sum of all levels, average of all levels); and (6) how the grading system was reported (continuous, ordinal, collected as ordinal but analyzed as dichotomous, collected and analyzed as dichotomous). Finally, we extracted details regarding whether assessment of measurement properties such as reliability (intra-rater, inter-rater), validity (comparison with another grading system, measured association between DD and other variables, including current and future LBP) and sensitivity to change (reporting a change score of the grading system over time) were performed (yes/no).

Data synthesis

The extracted results were exported from Covidence [22] to Excel [23] for data cleaning and synthesis. Descriptive statistics (frequency counts and proportions) were calculated for the year of publication and key sample characteristics including age, location, sample population and setting. The total number of annual publications was calculated for 1986-2022, to ensure a full year of data in the most recent year. The year of publications and key sample characteristics were plotted using a cumulative frequency curve and histogram respectively. The extracted studies were categorized as either a subjective or quantitative grading system. Descriptive statistics (proportions) were calculated for how the grading systems were used/reported (method of synthesis) in different studies, including the proportion of studies that: used different graders of DD (radiologists, surgeons or not specified); assessed different levels of the lumbar spine (the entire spine, singular levels or other); and reported/summarized the grading system differently

(each level individually, worst level, sum of all levels, average across all levels or not specified). The proportion of studies that assessed one or more of the specified measurement properties were also calculated. The results were tabulated into the categories as listed above, and a summary was created for each grading system.

2.7 RESULTS

Included studies

A total of 8070 studies were identified from the literature search, with 569 studies included after full-text screening (Fig.1). The main reasons for full-text exclusion were that a study was only available in conference abstract form (n=89), or that the study did not grade the severity/presence or absence of disc degeneration using a grading system (n=37). Three studies were identified from backwards citation tracking. See Appendix 2. for a complete list of all 569 included studies.

The majority of studies were published after 2010 (443/569, 77.9%) (Fig.2). Studies commonly included adults (419/569, 73.6%) from LBP populations (261/569, 46%) (Fig.3), while the study setting was not clearly reported in 31.3% (178/569) of studies. The studies took place in a variety of different countries including Finland, Japan and the United States of America; however, the most commonly reported study location was China (118/569, 20.7%).

Description of grading systems:

In total, there were 668 reports of grading system use across the 569 studies, as multiple grading systems could be reported within a single study. Ninety-three different grading systems were identified. Of these, 63/93 (67.7%) were classified as subjective grading systems and 25/93 (26.9%) were quantitative. The remaining 5/93 (5.4%) grading systems were categorized as 'unspecified' as the systems lacked a clear classification or description.

Subjective grading systems were used more frequently than quantitative systems (556/668, 83.2% versus, 112/668, 16.8%). The most widely used subjective grading system was the Pfirrmann method [10] (370/668, 55.4%), followed by the Modified Pfirrmann method [11] (42/668, 6.3%) and the Schneiderman classification [24] (30/668, 4.5%). Many of the identified grading systems (60/93, 64.5%) were only reported in single studies. A number of specialized quantitative MRI techniques and sequencing approaches were categorized together and made up 10.8% (72/668) of the reports of grading system use. See Appendix 3 & 4. for descriptions of all 93 grading systems.

The components within each grading system that were used to assess for DD varied considerably (Table 1). The most common components used across all grading systems to measure DD were DSI and DH; however, DH was rarely used as a stand-alone component (seven grading systems used in 1.0% (7/668)

of reports of all grading systems). In the reports of subjective grading systems (n=556), combinations of DSI, DH, structural changes to the disc and the distinction between the boundary between the annulus fibrosis and nucleus pulposus (e.g., Pfirrmann, Modified Pfirrmann) were most commonly used. These features were used in nine grading systems, accounting for 77.5% (431/556) of such reports. Another fourteen grading systems, used within 5.9% (33/556) of reports, used subjective assessment of additional grading components such as endplate changes, Modic changes and high intensity zones (HIZ) as part of the assessment of DD.

In the reports of use of quantitative grading systems (n=112), specialized quantitative MRI techniques and sequences (e.g., T2 mapping, T1 relaxation) were most commonly used (72/112, 64.3%). Ten grading systems, in 17.9% (20/112) of reports of quantitative grading systems utilized measurements of DSI to grade DD, and six grading systems, in 8.9% (10/112) of reports of quantitative grading systems used a combination of quantitative DSI, DH and disc bulging.

Methods used to assess and report the degree of disc degeneration

The methods of synthesis used to report DD grading are presented in Table 1. Radiologists most commonly performed the assessment of DD (273/668, 40.9% across all reports and 236/556, 42.4% for subjective grading systems). However, for the reports of use of quantitative grading systems, the grader was mostly unspecified (61/112, 54.5%). Disc degeneration was usually assessed across all lumbar spine levels (364/668, 54.5%) for both subjective and quantitative grading systems.

A number of different methods were used to synthesize the DD findings for analysis. The grading systems were commonly analyzed at each individual level (409/668, 61.2%) regardless of the type of grading system used. For subjective grading systems, results across multiple levels were sometimes synthesized as the sum of all the levels (80/556, 14.4%) or as the worst score at any level (34/556, 6.1%). It was uncommon for quantitative grading systems to analyze DD using the worst level (3/112, 2.7%), sum of all levels (4/112, 3.6%) or average across all levels (7/112, 6.3%). Of the 183 reports of grading systems using dichotomous summary measures, almost all used a subjective grading system (179/183, 97.8%) and collected the data at an ordinal level before transforming it into a dichotomous variable at each level (153/183, 83.6%). See Appendix 5. for more detail.

Assessment of the measurement properties of the grading systems

The measurement properties that were assessed for the various MRI-based grading systems are presented in Table 2. Intra-rater (204/668, 30.5%) and inter-rater reliability (232/668, 34.7%) were commonly reported across both subjective and quantitative grading systems. Of the 93 grading systems

identified, 33.3% (31/93) had not been assessed for any type of reliability. Sensitivity to change was rarely reported for subjective (61/556, 11.0%) or quantitative grading systems (11/112, 9.8%).

Validity was the most commonly reported measurement property assessed. In subjective grading systems, just under half (257/556, 46.2%) reported associations between DD and other variables including other imaging findings (e.g., degenerative spondylolisthesis, adolescent scoliosis and Modic changes) and patient level data (e.g., age, occupation and genetic factors). While it was less common for quantitative grading systems to measure associations with other variables (38/112, 33.9%), reports of quantitative grading systems were more commonly assessed for validity using a comparative evaluation with another grading system at a single disc level (69/112, 61.6%). The association between LBP and DD was investigated in 16.8% (112/668) of the reports of grading system use. More specifically, 83/668 (12.4%) of reports investigated the association between DD and current LBP, and 29/668 (4.3%) with future LBP. Subjective grading systems were more commonly used to investigate associations between DD and LBP when compared with quantitative grading systems. See Appendix 6. for more detail.

2.8 Discussion

Key Findings

This scoping review comprehensively charted the MRI-based grading systems that measure lumbar DD. We identified 569 studies that reported using MRI-based grading systems to assess for DD. Ninety-three different grading systems were identified, including 63 subjective systems, 25 quantitative systems and five that were unspecified. The subjective MRI-based grading system proposed by Pfirrmann [10] was used more than half the time. Many grading systems (60/93, 64.5%) were only reported once.

There was substantial heterogeneity in the components used to grade DD. Subjective grading systems most commonly used combinations of DSI, DH, structural changes and the distinctiveness of the annulus-nucleus boundary to grade DD, while quantitative grading systems commonly used specialized quantitative MRI techniques and sequences.

A variety of measurement properties of the grading systems were assessed. Intra-rater and or inter-rater reliability were assessed in approximately one-third of reports. Thirty-one of the total 93 grading systems were not assessed for any form of reliability. With regard to validity, studies that used subjective grading systems commonly reported measured associations between DD and other clinical variables such as other imaging findings (degenerative spondylolisthesis, adolescent scoliosis and Modic changes) and patient level data (age, occupation and genetic factors). Studies that used quantitative grading systems were more likely to report a comparative evaluation with another grading system or imaging modality at a single disc level. When the association between DD and LBP was assessed, most studies used a subjective grading system, and assessed for the association with current LBP. Sensitivity to change was rarely assessed.

Comparison to previous literature:

To the authors' knowledge, there are no previous scoping reviews that map the scientific literature on MRI-based grading systems for DD in the lumbar spine. A previous systematic review was conducted to identify and evaluate a range of different grading systems for cervical and lumbar degeneration in the disc and facet joints [25]. Unlike our study, many different imaging modalities were considered including macroscopic, histological, plain radiography, MRI and discography [25]. The review found five different grading systems that measured lumbar DD on MRI [25]. A substantially smaller number of grading systems were identified compared to our study as only studies presenting the original grading system were included in the review. This explained only some of the difference in the number of grading systems identified. Similar to our findings, the five grading systems exhibited a wide array of different grading components.

A scoping review of grading systems for lumbar facet joints on MRI was conducted by Acosta [26], to map the grading systems used to assess inflammatory changes to the lumbar facet joints. Like our study, it found a large variation in the components and scales used to grade facet inflammation. The review identified six grading systems, which had undergone assessment of reliability [26].

Strengths and limitations

The key strength of this study was the inclusive nature of the methodological design. As part of the scoping review, a wide spectrum of grading systems were identified and included in the analysis. Specifically, our study identified grading systems regardless of whether the system had been evaluated for any measurement properties. The inclusion criteria included any subjective or quantitative system that described the presence or absence of disc degeneration or the degree/extent of DD, and therefore focused on the reported use of DD grading systems to more clearly map which grading systems were most commonly used.

Another limitation was the process in which the extraction was completed. Only 10% of the extraction was duplicated by another independent author, and may have resulted in some errors within the extracted data. This was done due to the size of the review and likely did not impact the quality of the information appraised in the review.

One of the limitations of the study was the challenge in defining when a study was considered to have used a grading system to measure DD and therefore met our inclusion criteria. Studies were only included if it was explicitly stated that DD (or a similar term) was being assessed. Some studies described changes to the disc (e.g., disc herniation) without clearly stating that the changes measured were for the purposes of measuring DD. Therefore, this may have resulted in some grading systems being omitted from the review.

Categorizing the specialized quantitative MRI techniques and sequences used to grade DD into more specific categories was challenging. As these specialized quantitative MRI techniques and sequences were commonly used, some nuances regarding how these systems are reported and measured may have been lost by combining them.

Implications and future research

A large number of grading systems were identified in this review, many of which have been infrequently used or assessed. There was substantial heterogeneity in the components used in the grading systems, the thresholds for determining the presence of DD and the method of synthesis. As a result, the comparison of results across different studies is difficult, and may impact the way the grading system is used when making associations with LBP. For example of those studies using the Pfirrmann method [10], 46 studies used a grade higher than three to dichotomize the presence of DD at a single level, while 44 studies used a grade higher than two. In five studies, a grade higher than one was used to demarcate the presence of DD. A more standardized threshold is recommended for systems like the Pfirrmann [10] method when being used to measure for associations with clinical variables such as LBP.

Some of the observed variation in the method of synthesis may also be due to study-specific aims and study designs. For example, if DD was compared to a patient level outcome, such as LBP, a summary measure across disc levels may be required, whereas, comparisons between two alternative grading systems may be assessed at the individual disc level. A wide range of approaches were taken to calculate a summary measure across disc levels, including using the sum of all levels, average across all levels and the worst level in different studies. Using different summary measures to make associations with LBP may also impact the accuracy of these associations. Given that different summary measures are used in a variety of study designs and for a range of different aims, choosing the appropriate method of synthesis may also contribute to the generation of a more robust association between DD and LBP.

There were no quantitative grading systems that were identified in this review that systematically normalized DD scores for patient level factors such as age and disc level. There is preliminary evidence to suggest that normalized quantitative measures of DSI and DH may measure the degenerative process more accurately [27]. Further research is required to investigate the association between normalized quantitative measures and LBP [27].

2.9 CONCLUSION

In this review, we identified a large number of grading systems, many of which were infrequently used. In total, 93 MRI-based grading systems for assessing lumbar DD were identified, including 63 subjective grading systems, 25 quantitative grading systems and five that were unspecified. Subjective grading systems were widely utilized, with the Pfirrmann method used in over 50% of reports. A significant

number of grading systems were only reported in single studies. There was substantial heterogeneity in the components used in the grading systems, however the most common grading components were DSI, DH and the distinctiveness of the annulus-nucleus boundary. There were also significant differences in the methods of synthesis used across studies. The measurement properties of the grading systems (such as reliability) were commonly assessed across the grading systems, while sensitivity to change was rarely examined. When an association with LBP was made, it was usually between a subjective grading system and current LBP. The variability described in both the components used and the methods of synthesis may hinder the ability to draw clear associations with LBP.

Declarations:

1. Ethics approval: Ethics approval was not required for this study
2. Funding: No funding was used to support this study
3. Competing interests: The authors declare no competing interest

2.10 REFERENCES

1. Cieza A, Causey K, Kamenov K, Hanson SW, Chatterji S, Vos T. Global Estimates of the Need for Rehabilitation based on the Global Burden of Disease Study 2019: A Systematic Analysis for the Global Burden of Disease Study 2019. The Lancet (British Edition) 2020;396:2006–17.

2. Walker BF. The Prevalence of Low Back Pain: A Systematic Review of the Literature from 1966 to 1998. Journal of Spinal Disorders 2000;13:205–17.

3. Keller A, Hayden J, Bombardier C, Van Tulder MW. Effect Sizes of Non-Surgical Treatments of Non-Specific Low-Back Pain. European Spine Journal 2007;16:1776–88.

4. Deyo RA. Treatments for Back Pain: Can We Get Past Trivial Effects? Annals of Internal Medicine 2004;141:957–58.

5. Balagué FD, Mannion AFP, Pellisé FMD, Cedraschi CP. Non-Specific Low Back Pain. The Lancet (British Edition) 2012;379:482–91.

6. Baker A. Abnormal Magnetic Resonance Scans of the Lumbar Spine in Asymptomatic Subjects: A Prospective Investigation. In: London: Springer London; 2014, p. 245–47.

7. Brinjikji W, Luetmer PH, Comstock B, Bresnahan BW, Chen LE, Deyo RA, et al. Systematic Literature Review of Imaging Features of Spinal Degeneration in Asymptomatic Populations. American Journal of Neuroradiology 2015;36:811–16.

8. Salamat S, Hutchings J, Kwong C, Magnussen J, Hancock MJ. The Relationship Between Quantitative Measures of Disc Height and Disc Signal Intensity with Pfirrmann Score of Disc Degeneration. SpringerPlus 2016;5:829.

9. Videman T, Gibbons LE, Battie MC. Age-and Pathology-Specific Measures of Disc Degeneration. Spine (Philadelphia, Pa. 1976) 2008;33:2781–88.

10. Pfirrmann CWA, Metzdorf A, Zanetti M, Hodler J, Boos N. Magnetic Resonance Classification of Lumbar Intervertebral Disc Degeneration. Spine 2001;26:1873–78.

11. Griffith JF, Wang Y-XJ, Antonio GE, Choi KC, Yu A, Ahuja AT, et al. Modified Pfirrmann Grading System for Lumbar Intervertebral Disc Degeneration. Spine 2007;32:E708–12.

12. Hancock MJ, Maher CG, Jarvik JG, Battie MC, Elliott JM, Jensen TS, et al. Reliability and Validity of Subjective Radiologist Reporting of Temporal Changes in Lumbar Spine MRI findings. PM & R 2022;14:1325–32.

13. Carrino JA, Lurie JD, Herzog R, Tosteson ANA, Tosteson TD, Carragee EJ, et al. Lumbar Spine: Reliability of MR Imaging Findings. Radiology 2009;250:161–70.

14. Urrutia J, Besa P, Campos M, Cikutovic P, Cabezon M, Molina M, et al. The Pfirrmann Classification of Lumbar Intervertebral Disc Degeneration: An Independent Inter- and Intra-observer Agreement Assessment. European Spine Journal 2016;25:2728–33.

15. Niemeläinen R, Videman T, Dhillon SS, Battie MC. Quantitative Measurement of Intervertebral Disc Signal Using MRI. Clinical Radiology 2007;63:252–55.

16. Watanabe A, Benneker LM, Boesch C, Watanabe T, Obata T, Anderson SE. Classification of Intervertebral Disk Degeneration with Axial T2 mapping. American Journal of Roentgenology (1976) 2007;189:936–42.

17. Tunset A, Kjaer P, Chreiteh SS, Jensen TS. A Method for Quantitative Measurement of Lumbar Intervertebral Disc Structures: An Intra- and Inter-Rater Agreement and Reliability Study. Chiropractic & Manual Therapies 2013;21:26.

18. Aromataris E MZE. JBI Manual for Evidence Synthesis. JBI 2020 [Available from]: http://synthesismanual.jbi.jbi.global.http://doi.org/10.46658/JBIMES-20-01

19. Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. Annals of Internal Medicine 2018;169:467–73.

20. Esposito D, Jenkins H, Brown B, Hancock M, King S, Searant I. MRI-Based Grading Systems for Assessing Lumbar Disc Degeneration: A Scoping Review Protocol 2023. ID:osf.io/3nqst.

21. EndNote for PC software, Version X20 Clarivate Analytics, U.S. [Available from]: https://endnote.com.

22. Covidence Systematic Review Software, Veritas Health Innovation, July 2023, Melbourne, Australia. Available at www.covidence.org.

23. Microsoft Corporation. Microsoft Excel. 2018. Available from: https://office.microsoft.com/excel.

24. Schneiderman G, Flannigan B, Kingston S. Magnetic Resonance Imaging in the Diagnosis of Disc Degeneration: Correlation with Discography. Spine 1987;12(3):276–81.

25. Kettler A, Wilke H-J. Review of Existing Grading Systems for Cervical or Lumbar Disc and Facet Joint Degeneration. European Spine Journal 2006;15:705–18.

26. Acosta JI, Mandell JC, Ermann J, Isaac Z, Zampini JM, DeFilipp M, et al. Grading Systems of Lumbar Facet Joint Inflammatory Changes on Magnetic Resonance Imaging: A Scoping Review. Spine (Philadelphia, Pa. 1976) 2023;48:636–44.

27. King S, Magnussen J, Elliott J, Hancock MJ. Development of Normalized Quantitative Measures of Lumbar Disc Degeneration. Journal of Orthopaedic Research-Spine 2023;127.

2.11 TABLES

Table 1. The proportion of grading systems reported to be used to assess disc degeneration with different methods of synthesis, stratified by the grading system components used to assess for disc degeneration

	DD grading performed by**			L-spine levels reported				Method of synthesis I**				Method of synthesis II			
Grading system components	Proportion of reported use of grading systems % (n/N)	Radiologist % (n/N)	Surgeon % (n/N)	Not specified % (n/N)	Lumbar spine reported (T12-S1)* % (n/N)	Single level reported % (n/N)	Other* % (n/N)	Each level individually % (n/N)	Worst level % (n/N)	Sum of all levels % (n/N)	Average across all levels % (n/N)	Not specified % (n/N)	Continuous % (n/N)	Ordinal % (n/N)	Collected as ordinal but analyzed as dichotomous % (n/N)	Collected and analyzed as dichotomous % (n/N)
Subjective grading systems (all)	**83.2 (556/ 668)**	**42.4 (236/ 556)**	**24.1 (134/ 556)**	**31.8 (177/ 556)**	**53.2 (296/ 556)**	**12.6 (70/ 556)**	**34.4 (191/ 556)**	**58.1 (323/ 556)**	**6.1 (34/ 556)**	**14.4 (80/ 556)**	**3.8 (21/ 556)**	**21.8 (121/ 556)**	**9.4 (52/ 556)**	**58.5 (325/ 556)**	**27.5 (153/ 556)**	**4.7 (26/ 556)**
DSI	3.8 (21/ 556)	57.1 (12/ 21)	19.0 (4/21)	38.1 (8/21)	33.3 (7/21)	19.0 (4/21)	47.7 (10/21)	71.4 (15/21)	4.8 (1/21)	0.0 (0/21)	0.0 (0/21)	23.8 (5/21)	0.0 (0/21)	42.9 (9/21)	14.3 (3/21)	42.9 (9/21)
DH	0.7 (4/556)	75.0 (3/4)	75.0 (3/4)	0.0 (0/4)	75.0 (3/4)	25.0 (1/4)	0.0 (0/4)	50.0 (2/4)	25.0 (1/4)	0.0 (0/4)	25.0 (1/4)	0.0 (0/4)	0.0 (0/4)	75.0 (3/4)	25.0 (1/4)	0.0 (0/4)
DSI and DH	7.9 (44/556)	43.2 (19/44)	18.2 (8/44)	31.8 (14/44)	75.0 (33/44)	4.5 (2/44)	22.7 (10/44)	45.5 (20/44)	4.5 (2/44)	43.2 (19/44)	2.3 (1/44)	11.4 (5/44)	25.0 (11/44)	43.2 (19/44)	25.0 (11/44)	6.8 (3/44)
DSI and/or DH and/or disc bulging and herniation	4.1 (23/556)	60.9 (14/23)	30.4 (7/23)	13.0 (3/23)	43.5 (10/23)	0.0 (0/23)	56.5 (13/23)	34.8 (8/23)	8.7 (2/23)	34.8 (8/23)	8.7 (2/23)	21.7 (5/23)	17.4 (4/23)	60.9 (14/23)	0.0 (0/23)	21.7 (5/23)

DSI and/or DH and/or structural changes, and distinction between AF and NP	77.5 (431/556)	40.4 (174/431)	23.9 (103/431)	32.9 (142/431)	52.4 (226/431)	11.1 (60/431)	33.6 (145/431)	61.3 (264/431)	6.5 (28/431)	9.0 (39/431)	3.7 (16/431)	23.0 (99/431)	5.6 (24/431)	61.3 (264/431)	31.3 (135/431)	1.9 (8/431)
DSI and/or DH and/or osteophytes, end-plate changes, Modic changes and high intensity zones	5.9 (33/556)	42.4 (14/33)	27.3 (9/33)	30.3 (10/33)	51.5 (17/33)	9.1 (3/33)	39.4 (13/33)	42.4 (14/33)	0.0 (0/33)	42.4 (14/33)	3.0 (1/33)	21.2 (7/33)	39.4 (13/33)	48.5 (16/33)	9.1 (3/33)	3.0 (1/33)
Quantitative grading systems (all)	**16.8 (112/668)**	**33.0 (37/ 112)**	**11.6 (13/ 112)**	**54.5 (61/ 112)**	**60.7 (68/ 112)**	**3.6 (4 /112)**	**35.7 (40/ 112)**	**76.8 (86/ 112)**	**2.7 (3/ 112)**	**3.6 (4/ 112)**	**6.3 (7/ 112)**	**13.4 (15/112)**	**92.0 (103/112)**	**6.3 (7/ 112)**	**0.0 (0/ 112)**	**3.6 (4/ 122)**
DSI	17.9 (20/112)	25.0 (5/20)	20.0 (4/20)	65.0 (13/20)	50.0 (10/20)	5.0 (1/20)	45.0 (9/20)	65.0 (13/20)	5.0 (1/20)	0.0 (0/20)	15.0 (3/20)	25.0 (5/20)	75.0 (15/20)	15.0 (3/20)	0.0 (0/20)	10.0 (2/20)
DH	2.7 (3/112)	0.0 (0/3)	0.0 (0/3)	100.0 (3/3)	66.7 (2/3)	0.0 (0/3)	33.3 (1/3)	100.0 (3/3)	0.0 (0/3)	0.0 (0/3)	33.3 (1/3)	0.0 (0/3)	100.0 (3/3)	0.0 (0/3)	0.0 (0/3)	0.0 (0/3)
Disc bulging	3.6 (4/112)	75.0 (3/4)	0.0 (0/4)	25.0 (1/4)	25.0 (1/4)	0.0 (0/4)	75.0 (3/4)	50.0 (2/4)	0.0 (0/4)	0.0 (0/4)	25.0 (1/4)	25.0 (1/4)	50.0 (2/4)	0.0 (0/4)	0.0 (0/4)	50.0 (2/4)
DSI and DH	2.7 (3/112)	66.7 (2/3)	33.3 (1/3)	0.0 (0/3)	66.7 (2/3)	0.0 (0/3)	33.3 (1/3)	66.7 (2/3)	0.0 (0/3)	33.3 (1/3)	0.0 (0/3)	0.0 (0/3)	100.0 (3/3)	0.0 (0/3)	0.0 (0/3)	0.0 (0/3)

DSI, DH, and disc bulging	8.9 (10/112)	20.0 (2/10)	20.0 (2/10)	30.0 (3/10)	80.0 (8/10)	10.0 (1/10)	10.0 (1/10)	70.0 (7/10)	0.0 (0/10)	10.0 (1/10)	0.0 (0/10)	20.0 (2/10)	80.0 (8/10)	20.0 (2/10)	0.0 (0/10)	0.0 (0/10)
Specialized quantitative MRI techniques and sequences	64.3 (72/112)	34.8 (25/72)	8.3 (6/72)	56.9 (41/72)	62.5 (45/72)	2.8 (2/72)	34.7 (25/72)	81.9 (59/72)	2.8 (2/72)	2.8 (2/72)	2.8 (2/72)	9.7 (7/72)	97.2 (70/72)	2.8 (2/72)	0.0 (0/72)	0.0 (0/72)
Summary of subjective and quantitative grading systems	**668**	**40.9 (273/668)**	**22.0 (147/668)**	**35.6 (238/668)**	**54.5 (364/668)**	**11.1 (74/668)**	**34.6 (231/668)**	**61.2 (409/668)**	**5.5 (37/668)**	**12.6 (84/668)**	**4.2 (28/668)**	**20.4 (136/668)**	**23.2 (155/668)**	**49.7 (332/668)**	**22.9 (153/668)**	**4.5 (30/668)**

DSI: disc signal intensity, DH: disc height, AF: annulus fibrosis, NP: nucleus pulposus MRI: magnetic resonance imaging, DD: disc degeneration, LBP: low back pain.
*Included combinations of T12-L5, T12-S1, L1-L5, and L5-S1. Other category includes unspecified, and all other combinations reported
**The total number of responses may exceed the number of reports of grading system use due to the possibility of multiple options

Table 2. The proportion of grading systems reported to be assessed for measurement properties, stratified by the grading system components used to assess for disc degeneration

		Reliability		Sensitivity to change	Validity		
Grading system components	Proportion of reported use of grading systems % (n/N)	Intra-rater reliability % (n/N)	Inter-rater reliability % (n/N)	Use of a change score % (n/N)	Comparative evaluation with another grading system % (n/N)	Measured associations between DD and other variables % (n/N)	Measured associations between DD and LBP % (n/N)
Subjective grading systems (all)	**83.2 (556/ 668)**	**28.1 (156/556)**	**34.5 (192/556)**	**11.0 (61/556)**	**14.6 (81/556)**	**46.2 (257/556)**	**18.0 (100/556)**
DSI	3.8 (21/ 556)	23.8 (5/21)	33.3 (7/21)	0.0 (0/21)	9.5 (2/21)	47.6 (10/21)	28.6 (6/21)
DH	0.7 (4/556)	25.0 (1/4)	50.0 (2/4)	0.0 (0/4)	0.0 (0/4)	75.0 (3/4)	50.0 (2/4)
DSI and DH	7.9 (44/556)	31.8 (14/44)	45.5 (20/44)	11.4 (5/44)	11.4 (5/44)	54.5 (24/44)	31.8 (14/44)
DSI and/or DH and/or disc bulging and herniation	4.1 (23/556)	30.4 (7/23)	39.1 (9/23)	13.0 (3/23)	17.4 (4/23)	52.2 (12/23)	34.8 (8/23)
DSI and/or DH and/or osteophytes, end-plate changes, Modic changes and high intensity zones	5.9 (33/556)	42.4 (14/33)	30.3 (10/33)	18.2 (6/33)	3.0 (1/33)	60.6 (20/33)	30.3 (10/33)

Quantitative grading systems (all)	**16.8 (112/668)**	**42.9 (48/112)**	**35.7 (40/112)**	**9.8 (11/112)**	**61.6 (69/112)**	**33.9 (38/112)**	**10.7 (12/112)**
DSI	17.9 (20/112)	30.0 (6/20)	20.0 (4/20)	25.0 (5/20)	15.0 (3/20)	55.0 (11/20)	25.0 (5/20)
DH	2.7 (3/112)	33.3 (1/3)	0.0 (0/3)	0.0 (0/3)	33.3 (1/3)	66.7 (2/3)	0.0 (0/3)
Disc bulging	3.6 4/112)	75.0 (3/4)	50.0 (2/4)	0.0 (0/4)	0.0 (0/4)	100.0 (4/4)	50.0 (2/4)
DSI and DH	2.7 (3/112)	0.0 (0/3)	33.3 (1/3)	33.3 (1/3	33.3 (1/3	66.7 (2/3)	33.3 (1/3
DSI, DH, and disc bulging	8.9 (10/112)	70.0 (7/10)	70.0 (7/10)	20.0 (2/10)	20.0 (2/10)	60.0 (6/10)	10.0 (1/10)
Specialized quantitative MRI techniques and sequences	64.3 (72/112)	43.1 (31/72)	36.1 (26/72)	4.2 (3/72)	86.1 (62/72)	18.1 (13/72)	4.2 (3/72)
Summary of subjective and quantitative grading systems	**668**	**30.5 (204/668)**	**34.7 (232/668)**	**10.8 (72/668)**	**22.5 (150/668)**	**44.2 (295/668)**	**16.8 (112/668)**

DSI: disc signal intensity, DH: disc height, AF: annulus fibrosis, NP: nucleus pulposus MRI: magnetic resonance imaging, DD: disc degeneration, LBP: low back pain.

2.12 FIGURES

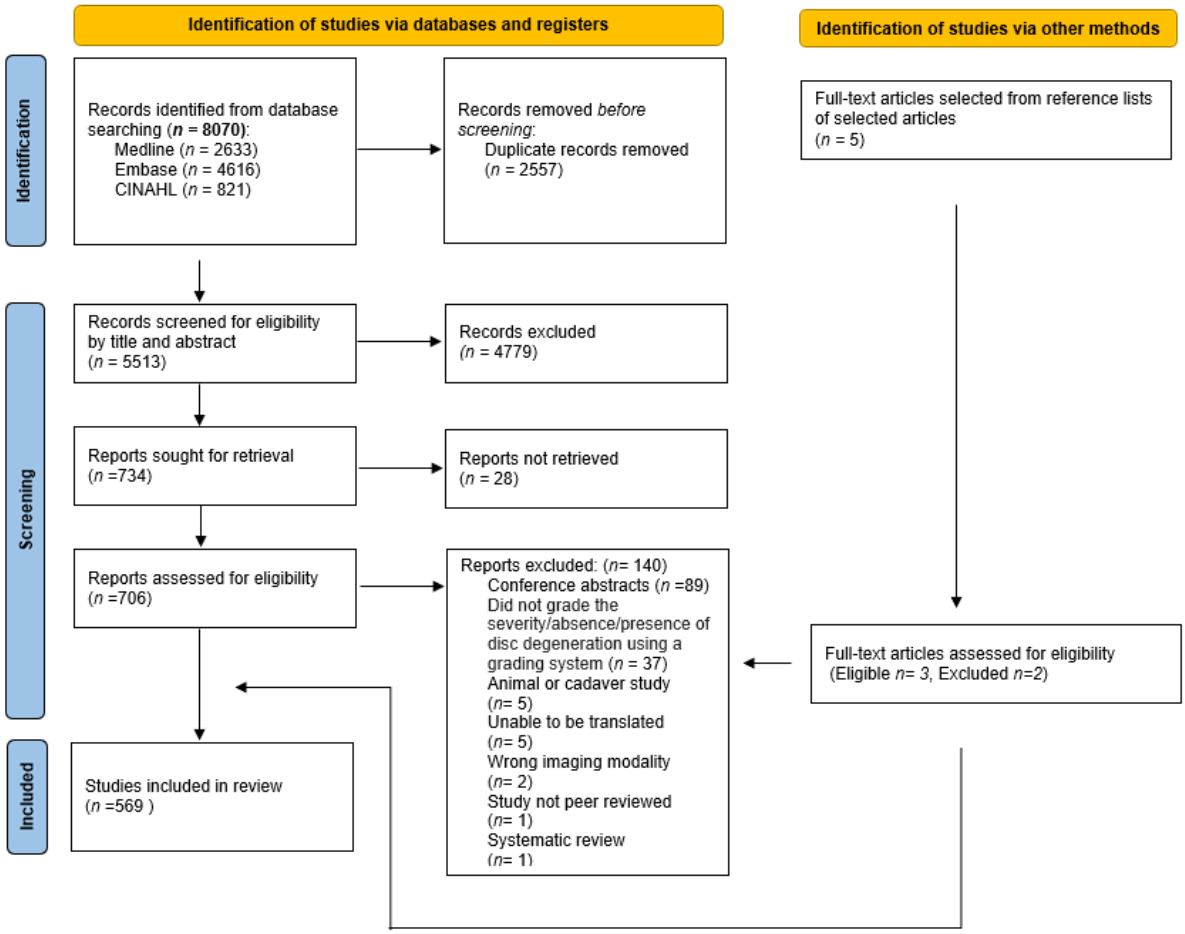
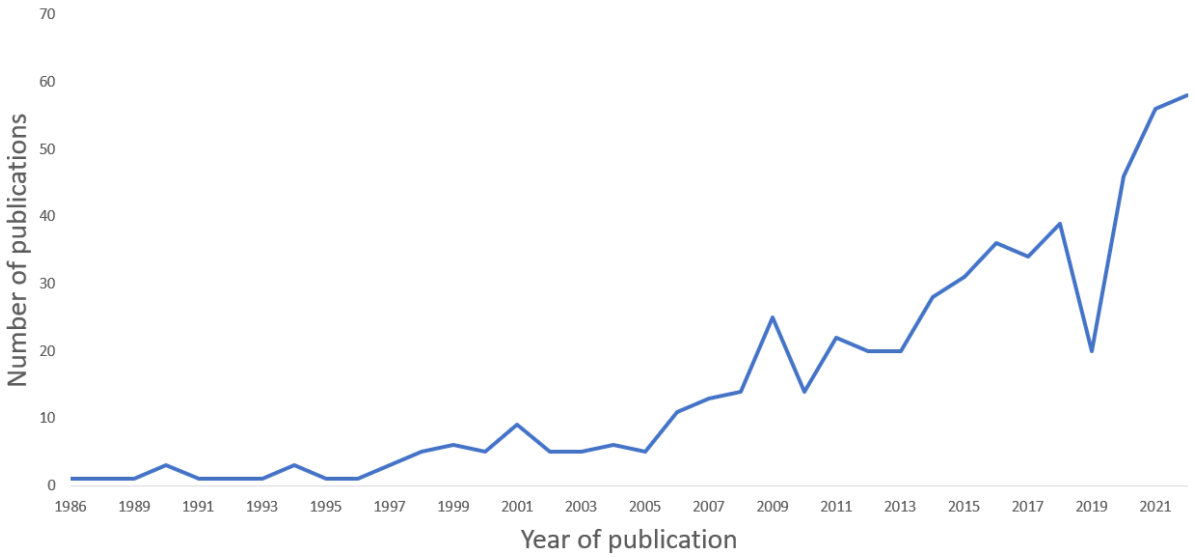
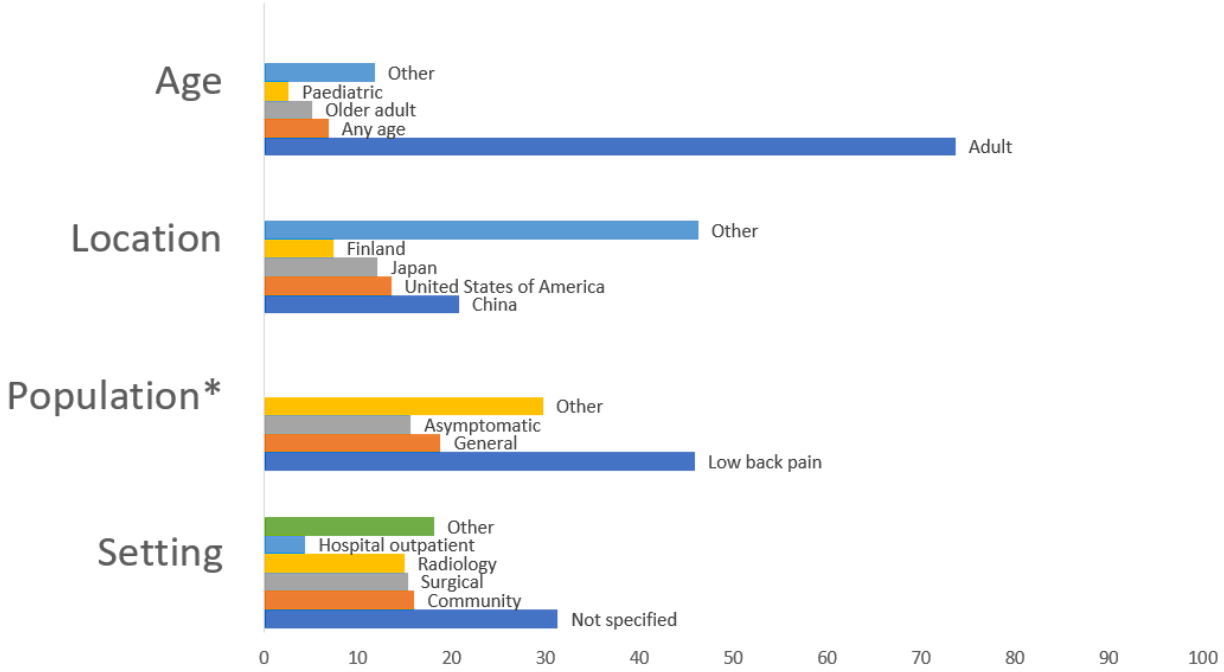


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow chart.



*The reported publications represent completed years.

Figure 2. Annual publication counts of studies that used a grading system to assess lumbar spine DD on MRI in living humans between 1986 and 2022.



*The total number of responses exceeds the study population due to the possibility of multiple options.

Figure 3. Key characteristics summary: Age, location, sample population and setting of included studies that used a grading system to assess lumbar spine DD based on MRI in living humans.

2.13 SUBMITTED SUPPLEMENTARY MATERIAL

Appendix 1. Search strategy

For each database search terms were used for each of the three key domains: magnetic resonance imaging; intervertebral disc degeneration; lumbar vertebrae

Terms with each of the domains were combined with 'or'

The four key domains were combined with 'and'

Search Terms

Medline

1 magnetic resonance imaging/

2 magnetic resonance imaging.mp.

3 magnetic resonance.mp.

4 MRI findings.mp.

5 MR imaging.mp.

6 MRI.mp.

7 1 or 2 or 3 or 4 or 5 or 6

8 intervertebral disc degeneration/

9 intervertebral disc degeneration.mp.

10 intervertebral disk degeneration.mp.

11 ((disc or disk) adj3 (degenerat* or degradat* or disease*)).mp.

12 degenera* disc.mp.

13 degenerat* disk.mp.

14 Disc signal intensity.mp.

15 Disk signal intensity.mp.

16 disc height.mp.

17 disk height.mp.

18 spondylosis.mp.

19 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18

20 lumbar vertebrae/

21 lumbar vertebrae.mp.

22 lumbar vertebra.mp.

23 (lumbar adj2 (spine or vertebrae)).mp.

24 Low back pain.mp.

25 LBP.mp.

26 20 or 21 or 22 or 23 or 24 or 25

27 7 and 19 and 26

EMBASE

1 nuclear magnetic resonance imaging/

2 magnetic resonance imaging.mp.

3 magnetic resonance.mp.

4 MRI findings.mp.

5 MR imaging.mp.

6 MRI.mp.

7 1 or 2 or 3 or 4 or 5 or 6

8 intervertebral disk degeneration/

9 intervertebral disc degeneration.mp.

10 intervertebral disk degeneration.mp.

11 ((disc or disk) adj3 (degenerat* or degradat* or disease*)).mp.

12 degenera* disc.mp.

13 degenerat* disk.mp.

14 Disc signal intensity.mp.

15 Disk signal intensity.mp.

16 disc height.mp.

17 disk height.mp.

18 spondylosis.mp.

19 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18

20 lumbar vertebra/

21 lumbar vertebrae.mp.

22 lumbar vertebra.mp.

23 (lumbar adj2 (spine or vertebrae)).mp.

24 Low back pain.mp.

25 LBP.mp.

26 20 or 21 or 22 or 23 or 24 or 25

27 7 and 19 and 26

CINAHL

S1 (MH "Magnetic Resonance Imaging")

S2 (TI "magnetic resonance imaging" or AB "magnetic resonance imaging")

S3 (TI "MR imaging" or AB "MR imaging")

S4 (TI MRI or AB MRI)

S5 (TI "Magnetic resonance" or AB "magnetic resonance

S6 S1 OR S2 OR S3 OR S4 OR S5

S7 TI (disk or disc) N3 (degenerat* or degrad* or disease*) or AB (disk or disc) N3 (degenerat* or degrad* or disease*)

S8 (TI "degenera* disc" or ab "degenera* disc)

S9 (TI "degenerat* disk" or AB "degenerat* disk")

S10 (TI "intervertebral disc degeneration" or AB "intervertebral disc degeneration")

S11 (TI "disc changes" or AB "disc changes" or (TI "disk changes" or AB "disk changes")

S12 (TI "disc signal intensity" or AB "disc signal intensity") or (TI "disc height" or AB "disc height") or (TI "disk height" or AB "disk height")

S13 S7 OR S8 OR S9 OR S10 OR S11 OR S12

S14 (MH "Lumbar Vertebrae")

S15 (TI (lumbar) N2 (spine or vertebrae) or AB (lumbar) N2 (spine or vertebrae)

S16 (TI LBP or AB LBP) or (TI "low back pain" or AB "low back pain")

S17 S14 OR S15 OR S16

S18 S6 AND S13 AND S17

Appendix 2. Complete list of references for all 569 studies included in scoping review

Grading system name	References
Subjective grading systems	[1-4] [5-7] [8, 9] [10-80] [49, 50, 81-86] [51, 87-332] [74-76, 99, 178, 212, 333-509] [447, 449, 510-540]
Disc signal intensity	[1-21]
Gibson	[1-4]
Decandido	[5-7]
Luoma	[8, 9]
Other	[10-21]
Disc height	[11, 12, 20, 541]
Disc height and disc signal intensity	[22-51, 56-69]
Schneidermann	[22-51]
Jensen	[56-60]
Luoma	[61, 62]
Other	[63-69]
DSI and/or DH and/or disc bulging and herniation	[49, 50, 52-55, 70-86]
Fardon	[70-73]
Solovieva	[52-55]
Witwit	[74-76]
Battie	[77, 78]
Horton and Daftari	[79, 80]

Kanamori	[49, 50]
Videman	[81, 82]
Other	[83-86]
DSI and/or DH and/or herniation, structural changes, and distinction between annulus fibrosis and nucleus fibrosus	[51, 87-332] [74-76, 333-452] [99, 178, 212, 434, 453-490] [491-499] [500-502] [503, 504] [503, 504] [505, 506] [507-509]
Pfirrmann	[51, 87-332] [74-76, 333-452]
Modified Pfirrmann	[99, 178, 212, 434, 453-490]
Thompson	[491-499]
Buirski	[500-502]
Modified Pearce	[503, 504]
Woodend Classification	[505, 506]
Other	[507-509]
DSI and/or DH and/or osteophytes, end-plate changes, Modic changes and high intensity zones (HIZ)	[447, 449, 510-540]
Jarosz Atlas	[447, 449, 510-519]
Pearce	[520-525]
Battie	[526, 527]
Benneker	[528, 529]
Tuft degenerative disc classification	[530, 531]
Other	[532-540]

Quantitative grading systems	[8, 9, 22, 62, 77, 78, 81, 83, 89, 222, 315, 350, 407, 452, 483, 527, 528, 536, 541-559] [23, 24, 51, 73, 92, 104, 106, 113, 114, 119, 120, 122, 137, 162, 165, 170, 172, 185, 186, 199, 212, 222, 225, 226, 228, 254, 261, 264, 270, 271, 275-277, 286, 293, 295, 299, 317, 318, 341, 360, 369, 375, 376, 402, 409, 418-420, 423, 426, 431, 433, 437, 441, 442, 445, 448, 450, 451, 455, 463, 469, 475, 477, 487, 508, 560-564]
Disc signal intensity	[22, 78, 81, 83, 89, 222, 315, 407, 483, 541-551]
Videman	[78, 81, 541-543]
Paajanen	[544-547]
Battie	[83, 548]
Luoma	[483, 549]
Nagashima	[315, 550]
Other	[22, 89, 222, 407, 551]
Disc height	[222, 548, 549]
Disc bulging	[8, 9, 62, 552]
Luoma	[8, 9, 62]
Other	[552]
Disc signal intensity and disc height	[350, 528, 553]
Disc signal intensity, disc height, and disc bulging	[77, 452, 527, 536, 554-559]
Battie	[77, 527, 554]
Feng	[555-557]
Other	[452, 536, 558, 559]

Specialised quantitative MRI techniques and sequences	[23, 24, 51, 73, 92, 104, 106, 113, 114, 119, 120, 122, 137, 162, 165, 170, 172, 185, 186, 199, 212, 222, 225, 226, 228, 254, 261, 264, 270, 271, 275-277, 286, 293, 295, 299, 317, 318, 341, 360, 369, 375, 376, 402, 409, 418-420, 423, 426, 431, 433, 437, 441, 442, 445, 448, 450, 451, 455, 463, 469, 475, 477, 487, 508, 560-564]
Unspecified	[565-569]

References for Appendix 2

1. Dai LY. Orientation and Tropism of Lumbar Facet Joints in Degenerative Spondylolisthesis. International Orthopaedics. 2001;25(1):40-2.

2. Gibson MJ, Buckley J, Mawhinney R, Mulholland RC, Worthington BS. Magnetic Resonance Imaging and Discography in the Diagnosis of Disc Degeneration. A Comparative Study of 50 Discs. Journal of Bone and Joint Surgery - Series B. 1986;68(3):369-73.

3. Hyodo H, Sato T, Sasaki H, Tanaka Y. Discogenic Pain in Acute Nonspecific Low-Back Pain. European Spine Journal. 2005;14(6):573-7.

4. Dai LY. Disc Degeneration in Patients with Lumbar Spondylolysis. Journal of Spinal Disorders. 2000;13(6):478-86.

5. Decandido P, Reinig JW, Dwyer AJ, Thompson KJ, Ducker TB. Magnetic Resonance Assessment of the Distribution of Lumbar Spine Disc Degenerative Changes. Journal of Spinal Disorders. 1988;1(1):9-15.

6. Dimitriadis A, Smith F, Mavrogenis AF, Pope MH, Papagelopoulos PJ, Karantanas A, et al. Effect of Two Sitting Postures on Lumbar Sagittal Alignment and Intervertebral Discs in Runners. Radiologia Medica. 2012;117(4):654-68.

7. Iida T, Abumi K, Kotani Y, Kaneda K. Effects of Aging and Spinal Degeneration on Mechanical Properties of Lumbar Supraspinous and Interspinous Ligaments. Spine Journal: Official Journal of the North American Spine Society. 2002;2(2):95-100.

8. Luoma K, Riihimaki H, Luukkonen R, Raininko R, Viikari-Juntura E, Lamminen A. Low Back Pain in Relation to Lumbar Disc Degeneration. Spine. 2000;25(4):487-92.

9. Luoma K, Riihimaki H, Raininko R, Luukkonen R, Lamminen A, Viikari-Juntura E. Lumbar Disc Degeneration in Relation to Occupation. Scandinavian Journal of Work, Environment & Health. 1998;24(5):358-66.

10. Dimar JR, 2nd, Glassman SD, Carreon LY. Juvenile Degenerative Disc Disease: A Report of 76 Cases Identified by Magnetic Resonance Imaging. Spine Journal: Official Journal of the North American Spine Society. 2007;7(3):332-7.

11. Dragsbaek L, Kjaer P, Hancock M, Jensen TS. An Exploratory Study of Different Definitions and Thresholds for Lumbar Disc Degeneration Assessed by MRI and Their Associations with Low Back Pain Using Data from a Cohort Study of a General Population. BMC Musculoskeletal Disorders. 2020;21(1):253.

12. Fu MC, Buerba RA, Long WD, 3rd, Blizzard DJ, Lischuk AW, Haims AH, et al. Interrater and Intrarater Agreements of Magnetic Resonance Imaging Findings in the Lumbar Spine: Significant Variability across Degenerative Conditions. Spine Journal: Official Journal of the North American Spine Society. 2014;14(10):2442-8.

13. Kotilainen E, Alanen A, Erkintalo M, Valtonen S, Kormano M. Association between Decreased Disc Signal Intensity in Preoperative T2-Weighted MRI and a 5-Year Outcome after Lumbar Minimally Invasive Discectomy. Minimally Invasive Neurosurgery. 2001;44(1):31-6.

14. Linson MA, Crowe CH. Comparison of Magnetic Resonance Imaging and Lumbar Discography in the Diagnosis of Disc Degeneration. Clinical Orthopaedics & Related Research. 1990;(250):160-3.

15. Liuke M, Solovieva S, Lamminen A, Luoma K, Leino-Arjas P, Luukkonen R, et al. Disc Degeneration of the Lumbar Spine in Relation to Overweight. International Journal of Obesity. 2005;29(8):903-8.

16. Madan SS, Rai A, Harley JM. Interobserver Error in Interpretation of the Radiographs for Degeneration of the Lumbar Spine. Iowa Orthopaedic Journal. 2003;23:51-6.

17. Tertti M, Paajanen H, Kujala UM, Alanen A, Salmi TT, Kormano M. Disc Degeneration in Young Gymnasts. A Magnetic Resonance Imaging Study. American Journal of Sports Medicine. 1990;18(2):206-8.

18. Heithoff KB, Gundry CR, Burton CV, Winter RB, Heithoff KB, Gundry CR, et al. Juvenile Discogenic Disease. Spine (03622436). 1994;19(3):335-40.

19. Evans W, Jobe W, Seibert C, Evans W, Jobe W, Seibert C. A Cross-Sectional Prevalence Study of Lumbar Disc Degeneration in a Working Population. Spine (03622436). 1989;14(1):60-4.

20. Ito M, Incorvaia KM, Yu SF, Fredrickson BE, Yuan HA, Rosenbaum AE. Predictive Signs of Discogenic Lumbar Pain on Magnetic Resonance Imaging with Discography Correlation. Spine. 1998;23(11):1252-8; discussion 9-60.

21. Maurer M, Soder RB, Baldisserotto M. Spine Abnormalities Depicted by Magnetic Resonance Imaging in Adolescent Rowers. American Journal of Sports Medicine. 2011;39(2):392-7.

22. Lund T, Schlenzka D, Lohman M, Ristolainen L, Kautiainen H, Klemetti E, et al. The Intervertebral Disc During Growth: Signal Intensity Changes on Magnetic Resonance Imaging and Their Relevance to Low Back Pain. PLoS ONE [Electronic Resource]. 2022;17(10):e0275315.

23. Pang H, Bow C, Cheung JPY, Zehra U, Borthakur A, Karppinen J, et al. The Ute Disc Sign on MRI: A Novel Imaging Biomarker Associated with Degenerative Spine Changes, Low Back Pain, and Disability. Spine (03622436). 2018;42(15).

24. Pang H, Bow C, Cheung JPY, Zehra U, Borthakur A, Karppinen J, et al. The Ute Disc Sign on MRI: A Novel Imaging Biomarker Associated with Degenerative Spine Changes, Low Back Pain, and Disability. Spine (03622436). 2017;42(15).

25. Bakr KI, Sadiq IM, Nooruldeen SA. Lumbosacral MRI Findings in Chronic Lower Back Pain. Indian Journal of Public Health Research and Development. 2019;10(11):2035-40.

26. Cheung KM, Chan D, Karppinen J, Chen Y, Jim JJ, Yip SP, et al. Association of the Taq I Allele in Vitamin D Receptor with Degenerative Disc Disease and Disc Bulge in a Chinese Population. Spine. 2006;31(10):1143-8.

27. Cheung KM, Samartzis D, Karppinen J, Mok FP, Ho DW, Fong DY, et al. Intervertebral Disc Degeneration: New Insights Based on "Skipped" Level Disc Pathology. Arthritis & Rheumatism. 2010;62(8):2392-400.

28. Cheung KMC, Karppinen J, Chan D, Ho DWH, Song YQ, Sham P, et al. Prevalence and Pattern of Lumbar Magnetic Resonance Imaging Changes in a Population Study of One Thousand Forty-Three Individuals. Spine. 2009;34(9):934-40.

29. Higashino K, Matsui Y, Yagi S, Takata Y, Goto T, Sakai T, et al. The Alpha2 Type Ix Collagen Tryptophan Polymorphism Is Associated with the Severity of Disc Degeneration in Younger Patients with Herniated Nucleus Pulposus of the Lumbar Spine. International Orthopaedics. 2007;31(1):107-11.

30. Kanayama M, Togawa D, Takahashi C, Terai T, Hashimoto T. Cross-Sectional Magnetic Resonance Imaging Study of Lumbar Disc Degeneration in 200 Healthy Individuals. Journal of Neurosurgery Spine. 2009;11(4):501-7.

31. Kawaguchi Y, Kanamori M, Ishihara H, Ohmori K, Matsui H, Kimura T. The Association of Lumbar Disc Disease with Vitamin-D Receptor Gene Polymorphism. Journal of Bone & Joint Surgery - American Volume. 2002;84(11):2022-8.

32. Kawaguchi Y, Osada R, Kanamori M, Ishihara H, Ohmori K, Matsui H, et al. Association between an Aggrecan Gene Polymorphism and Lumbar Disc Degeneration. Spine. 1999;24(23):2456-60.

33. Law T, Anthony MP, Chan Q, Samartzis D, Kim M, Cheung KMC, et al. Ultrashort Time-to-Echo MRI of the Cartilaginous Endplate: Technique and Association with Intervertebral Disc Degeneration. Journal of Medical Imaging and Radiation Oncology. 2013;57(4):427-34.

34. Lin WP, Lin JH, Chen XW, Wu CY, Zhang LQ, Huang ZD, et al. Interleukin-10 Promoter Polymorphisms Associated with Susceptibility to Lumbar Disc Degeneration in a Chinese Cohort. Genetics & Molecular Research. 2011;10(3):1719-27.

35. Makino H, Kawaguchi Y, Seki S, Nakano M, Yasuda T, Suzuki K, et al. Lumbar Disc Degeneration Progression in Young Women in Their 20's: A Prospective Ten-Year Follow Up. Journal of Orthopaedic Science. 2017;22(4):635-40.

36. Marchiori DM, Mclean I, Firth R, Tatum R. A Comparison of Radiographic Signs of Degeneration to Corresponding MRI Signal Intensities in the Lumbar Spine. Journal of Manipulative & Physiological Therapeutics. 1994;17(4):238-45.

37. Matsui H, Kanamori M, Ishihara H, Yudoh K, Naruse Y, Tsuji H. Familial Predisposition for Lumbar Degenerative Disc Disease. A Case-Control Study. Spine. 1998;23(9):1029-34.

38. Mok FP, Samartzis D, Karppinen J, Fong DY, Luk KD, Cheung KM. Modic Changes of the Lumbar Spine: Prevalence, Risk Factors, and Association with Disc Degeneration and Low Back Pain in a Large-Scale Population-Based Cohort. Spine Journal: Official Journal of the North American Spine Society. 2016;16(1):32-41.

39. Mok FP, Samartzis D, Karppinen J, Luk KD, Fong DY, Cheung KM. Issls Prize Winner: Prevalence, Determinants, and Association of Schmorl Nodes of the Lumbar Spine with Disc Degeneration: A Population-Based Study of 2449 Individuals. Spine. 2010;35(21):1944-52.

40. Samartzis D, Karppinen J, Chan D, Luk KD, Cheung KM. The Association of Lumbar Intervertebral Disc Degeneration on Magnetic Resonance Imaging with Body Mass Index in Overweight and Obese Adults: A Population-Based Study. Arthritis & Rheumatism. 2012;64(5):1488-96.

41. Samartzis D, Karppinen J, Mok F, Fong DY, Luk KD, Cheung KM. A Population-Based Study of Juvenile Disc Degeneration and Its Association with Overweight and Obesity, Low Back Pain, and Diminished Functional Status. Journal of Bone & Joint Surgery - American Volume. 2011;93(7):662-70.

42. Samartzis D, Mok FPS, Karppinen J, Fong DYT, Luk KDK, Cheung KMC. Classification of Schmorl's Nodes of the Lumbar Spine and Association with Disc Degeneration: A Large-Scale Population-Based MRI Study. Osteoarthritis & Cartilage. 2016;24(10):1753-60.

43. Schistad EI, Bjorland S, Roe C, Gjerstad J, Vetti N, Myhre K, et al. Five-Year Development of Lumbar Disc Degeneration-a Prospective Study. Skeletal Radiology. 2019;48(6):871-9.

44. Song YQ, Ho DW, Karppinen J, Kao PY, Fan BJ, Luk KD, et al. Association between Promoter -1607 Polymorphism of Mmp1 and Lumbar Disc Disease in Southern Chinese. BMC Medical Genetics. 2008;9:38.

45. Sun ZM, Ling M, Huo Y, Chang Y, Li Y, Qin H, et al. Caspase 9 Gene Polymorphism and Susceptibility to Lumbar Disc Disease in the Han Population in Northern China. Connective Tissue Research. 2011;52(3):198-202.

46. Sun ZM, Miao L, Zhang YG, Ming L. Association between the -1562 C/T Polymorphism of Matrix Metalloproteinase-9 Gene and Lumbar Disc Disease in the Young Adult Population in North China. Connective Tissue Research. 2009;50(3):181-5.

47. Watanabe T, Otani K, Sekiguchi M, Konno SI. Relationship between Lumbar Disc Degeneration on MRI and Low Back Pain: A Cross-Sectional Community Study. Fukushima Journal of Medical Science. 2022;68(2):97-107.

48. Zehra U, Cheung JPY, Bow C, Lu W, Samartzis D. Multidimensional Vertebral Endplate Defects Are Associated with Disc Degeneration, Modic Changes, Facet Joint Abnormalities, and Pain. Journal of Orthopaedic Research. 2019;37(5):1080-9.

49. Kanamori M, Nobukiyo M, Suzuki K, Yasuda T, Hori T. Clinical Validity of a New T2-Weighted MRI-Based Grading System for Lumbar Disc Degeneration. International Medical Journal. 2013;20(4):466-9.

50. Masahiko K, Masanori N, Kayo S, Taketoshi Y, Takeshi H. Clinical Validity of a New T2-Weighted MRI-Based Grading System for Lumbar Disc Degeneration. International Medical Journal. 2013;20(4):466-9.

51. Nagy SA, Juhasz I, Komaromy H, Pozsar K, Zsigmond I, Perlaki G, et al. A Statistical Model for Intervertebral Disc Degeneration: Determination of the Optimal T2 Cut-Off Values. Clinical Neuroradiology. 2014;24(4):355-63.

52. Solovieva S, Kouhia S, Leino-Arjas P, Ala-Kokko L, Luoma K, Raininko R, et al. Interleukin 1 Polymorphisms and Intervertebral Disc Degeneration. Epidemiology. 2004;15(5):626-33.

53. Solovieva S, Lohiniva J, Leino-Arjas P, Raininko R, Luoma K, Ala-Kokko L, et al. Intervertebral Disc Degeneration in Relation to the Col9a3 and the Il-1ss Gene Polymorphisms. European Spine Journal. 2006;15(5):613-9.

54. Solovieva S, Lohiniva J, Leino-Arjas P, Raininko R, Luoma K, Ala-Kokko L, et al. Col9a3 Gene Polymorphism and Obesity in Intervertebral Disc Degeneration of the Lumbar Spine: Evidence of Gene-Environment Interaction. Spine (03622436). 2002;27(23):2691-6.

55. Solovieva S, Noponen N, Mannikko M, Leino-Arjas P, Luoma K, Raininko R, et al. Association between the Aggrecan Gene Variable Number of Tandem Repeats Polymorphism and Intervertebral Disc Degeneration. Spine. 2007;32(16):1700-5.

56. Jensen RK, Jensen TS, Kjaer P, Kent P. Can Pathoanatomical Pathways of Degeneration in Lumbar Motion Segments Be Identified by Clustering MRI Findings. BMC Musculoskeletal Disorders. 2013;14 (no pagination).

57. Jensen RK, Kent P, Hancock M. Do MRI Findings Identify Patients with Chronic Low Back Pain and Modic Changes Who Respond Best to Rest or Exercise: A Subgroup Analysis of a Randomised Controlled Trial. Chiropractic & manual therapies. 2015;23:26.

58. Jensen RK, Kent P, Jensen TS, Kjaer P. The Association between Subgroups of MRI Findings Identified with Latent Class Analysis and Low Back Pain in 40-Year-Old Danes. BMC Musculoskeletal Disorders. 2018;19(1):62.

59. Jensen RK, Kjaer P, Jensen TS, Albert H, Kent P. Degenerative Pathways of Lumbar Motion Segments: A Comparison in Two Samples of Patients with Persistent Low Back Pain. PLoS ONE [Electronic Resource]. 2016;11(1):e0146998.

60. Jensen TS, Bendix T, Sorensen JS, Manniche C, Korsholm L, Kjaer P. Characteristics and Natural Course of Vertebral Endplate Signal (Modic) Changes in the Danish General Population. BMC Musculoskeletal Disorders. 2009;10:81.

61. Luoma K, Vehmas T, Gronblad M, Kerttula L, Kaapa E. MRI Follow-up of Subchondral Signal Abnormalities in a Selected Group of Chronic Low Back Pain Patients. European Spine Journal. 2008;17(10):1300-8.

62. Luoma K, Vehmas T, Kerttula L, Gronblad M, Rinne E. Chronic Low Back Pain in Relation to Modic Changes, Bony Endplate Lesions, and Disc Degeneration in a Prospective MRI Study. European Spine Journal. 2016;25(9):2873-81.

63. Borenstein DG, O'mara JW, Jr., Boden SD, Lauerman WC, Jacobson A, Platenberg C, et al. The Value of Magnetic Resonance Imaging of the Lumbar Spine to Predict Low-Back Pain in Asymptomatic Subjects : A Seven-Year Follow-up Study. Journal of Bone & Joint Surgery - American Volume. 2001;83(9):1306-11.

64. Buttermann GR, Mullin WJ. Pain and Disability Correlated with Disc Degeneration Via Magnetic Resonance Imaging in Scoliosis Patients. European Spine Journal. 2008;17(2):240-9.

65. Karppinen J, Paakko E, Paassilta P, Lohiniva J, Kurunlahti M, Tervonen O, et al. Radiologic Phenotypes in Lumbar Mr Imaging for a Gene Defect in the Col9a3 Gene of Type Ix Collagen. Radiology. 2003;227(1):143-8.

66. Lakadamyali H, Tarhan NC, Ergun T, Cakir B, Agildere AM. Stir Sequence for Depiction of Degenerative Changes in Posterior Stabilizing Elements in Patients with Lower Back Pain. AJR American Journal of Roentgenology. 2008;191(4):973-9.

67. Sabnis AB, Chamoli U, Diwan AD. Is L5-S1 Motion Segment Different from the Rest? A Radiographic Kinematic Assessment of 72 Patients with Chronic Low Back Pain. European Spine Journal. 2018;27(5):1127-35.

68. Throckmorton TW, Hilibrand AS, Mencio GA, Hodge A, Spengler DM. The Impact of Adjacent Level Disc Degeneration on Health Status Outcomes Following Lumbar Fusion. Spine. 2003;28(22):2546-50.

69. Leboeuf-Yde C, Kjaer P, Bendix T, Manniche C. Self-Reported Hard Physical Work Combined with Heavy Smoking or Overweight May Result in So-Called Modic Changes. BMC Musculoskeletal Disorders. 2008;9:5.

70. Irurhe NK, Adekola OO, Quadri AR, Menkiti ID, Udenze IC, Awolola NA. The Magnetic Resonance Imaging Scan Findings in Adult Nigerians with Low Back Pain. World Journal of Medical Sciences. 2012;7(4):204-9.

71. Kiil RM, Mistegaard CE, Loft AG, Zejden A, Hendricks O, Jurik AG. Differences in Topographical Location of Sacroiliac Joint MRI Lesions in Patients with Early Axial Spondyloarthritis and Mechanical Back Pain. Arthritis Research & Therapy. 2022;24(1):75.

72. Kim J, Park HJ, Kim MS, Kim JN, Choi YJ, Rho MH, et al. Wedging of Vertebral Bodies at the Thoracolumbar Spine in Healthy Individuals on Whole Body MRI Screening: Correlation with Disc Degeneration and Disc Herniation. Acta Radiologica. 2022;63(7):958-63.

73. Michopoulou SK, Costaridou L, Panagiotopoulos E, Speller R, Panayiotakis G, Todd-Pokropek A. Atlas-Based Segmentation of Degenerated Lumbar Intervertebral Discs from Mr Images of the Spine. IEEE Transactions on Biomedical Engineering. 2009;56(9):2225-31.

74. Witwit W, Thoreson O, Sward Aminoff A, Todd C, Jonasson P, Laxdal G, et al. Young Football Players Have Significantly More Spinal Changes on MRI Compared to Non-Athletes. Translational Sports Medicine. 2020;3(4):288-95.

75. Witwit WA, Hebelka H, Sward Aminoff A, Abrahamson J, Todd C, Baranto A. No Significant Change in MRI Abnormalities or Back Pain Prevalence in the Thoraco-Lumbar Spine of Young Elite Skiers over a 2-Year Follow-Up. Open Access Journal of Sports Medicine. 2022;13:69-76.

76. Witwit WA, Kovac P, Sward A, Agnvall C, Todd C, Thoreson O, et al. Disc Degeneration on MRI Is More Prevalent in Young Elite Skiers Compared to Controls. Knee Surgery, Sports Traumatology, Arthroscopy. 2018;26(1):325-32.

77. Battie MC, Videman T, Gibbons LE, Fisher LD, Manninen H, Gill K. Determinants of Lumbar Disc Degeneration: A Study Relating Lifetime Exposures and Magnetic Resonance Imaging Findings in Identical Twins. Spine. 1995;20(24):2601-12.

78. Videman T, Leppavuori J, Kaprio J, Battie MC, Gibbons LE, Peltonen L, et al. Intragenic Polymorphisms of the Vitamin D Receptor Gene Associated with Intervertebral Disc Degeneration. Spine. 1998;23(23):2477-85.

79. Horton WC, Daftari TK. Which Disc as Visualized by Magnetic Resonance Imaging Is Actually a Source of Pain? A Correlation between Magnetic Resonance Imaging and Discography. Spine (Phila Pa 1976). 1992;17(6 Suppl):S164-71.

80. Boden SD, Riew KD, Yamaguchi K, Branch TP, Schellinger D, Wiesel SW. Orientation of the Lumbar Facet Joints: Association with Degenerative Disc Disease. Journal of Bone & Joint Surgery - American Volume. 1996;78(3):403-11.

81. Videman T, Saarela J, Kaprio J, Nakki A, Levalahti E, Gill K, et al. Associations of 25 Structural, Degradative, and Inflammatory Candidate Genes with Lumbar Disc Desiccation, Bulging, and Height Narrowing. Arthritis & Rheumatism. 2009;60(2):470-81.

82. Videman T, Gibbons LE, Battie MC. Age- and Pathology-Specific Measures of Disc Degeneration. Spine. 2008;33(25):2781-8.

83. Battie MC, Videman T, Levalahti E, Gill K, Kaprio J. Genetic and Environmental Effects on Disc Degeneration by Phenotype and Spinal Level: A Multivariate Twin Study. Spine. 2008;33(25):2801-8.

84. Deng C, Xia W. Effect of Tai Chi Chuan on Degeneration of Lumbar Vertebrae and Lumbar Discs in Middle-Aged and Aged People: A Cross-Sectional Study Based on Magnetic Resonance Images. Journal of International Medical Research. 2018;46(2):578-85.

85. Desigan S, Hall-Craggs MA, Ho CP, Eliahoo J, Porter JB. Degenerative Disc Disease as a Cause of Back Pain in the Thalassaemic Population: A Case-Control Study Using MRI and Plain Radiographs. Skeletal Radiology. 2006;35(2):95-102.

86. Videman T, Battie MC, Gibbons LE, Manninen H, Gill K, Fisher LD, et al. Lifetime Exercise and Disk Degeneration: An MRI Study of Monozygotic Twins. Medicine & Science in Sports & Exercise. 1997;29(10):1350-6.

87. Aaen J, Austevoll IM, Hellum C, Storheim K, Myklebust TA, Banitalebi H, et al. Clinical and MRI Findings in Lumbar Spinal Stenosis: Baseline Data from the Nordsten Study. European Spine Journal. 2022;31(6):1391-8.

88. Aaen J, Banitalebi H, Austevoll IM, Hellum C, Storheim K, Myklebust TA, et al. The Association between Preoperative MRI Findings and Clinical Improvement in Patients Included in the Nordsten Spinal Stenosis Trial. European Spine Journal. 2022;31(10):2777-85.

89. Aavikko A, Lohman M, Ristolainen L, Kautiainen H, Osterman K, Schlenzka D, et al. Issls Prize in Clinical Science 2022: Accelerated Disc Degeneration after Pubertal Growth Spurt Differentiates Adults with Low Back Pain from Their Asymptomatic Peers. European Spine Journal. 2022;31(5):1080-7.

90. Abdalkader M, Guermazi A, Engebretsen L, Roemer FW, Jarraya M, Hayashi D, et al. MRI-Detected Spinal Disc Degenerative Changes in Athletes Participating in the Rio De Janeiro 2016 Summer Olympics Games. BMC Musculoskeletal Disorders. 2020;21(1):45.

91. Abdollah V, Parent EC, Su A, Wachowicz K, Battié MC. The Effects of Axial Loading on the Morphometric and T2 Characteristics of Lumbar Discs in Relation to Disc Degeneration. Clinical Biomechanics. 2021;83:N.PAG-N.PAG.

92. Abou Khadrah RS, Dawoud MF, Abo-Elsafa AA, Elkilany AM. Advanced Trends in Magnetic Resonance Imaging in Assessment of Lumbar Intervertebral Degenerative Disk Disease. Egyptian Journal of Radiology and Nuclear Medicine. 2019;50(1) (no pagination).

93. Ahn TJ, Lee SH, Choi G, Ahn Y, Liu WC, Kim HJ, et al. Effect of Intervertebral Disk Degeneration on Spinal Stenosis During Magnetic Resonance Imaging with Axial Loading. Neurologia Medico-Chirurgica. 2009;49(6):242-7; discussion 7.

94. Akazawa T, Kotani T, Sakuma T, Minami S, Orita S, Fujimoto K, et al. Spinal Fusion on Adolescent Idiopathic Scoliosis Patients with the Level of L4 or Lower Can Increase Lumbar Disc Degeneration with Sagittal Imbalance 35 Years after Surgery. Spine Surgery & Related Research. 2017;1(2):72-7.

95. Akazawa T, Kotani T, Sakuma T, Minami S, Orita S, Inage K, et al. Modic Changes and Disc Degeneration of Nonfused Segments 27 to 45 Years after Harrington Instrumentation for Adolescent Idiopathic Scoliosis: Comparison to Healthy Controls. Spine (03622436). 2017;42(15):N.PAG-N.PAG.

96. Akazawa T, Umehara T, Iinuma M, Asano K, Kuroya S, Torii Y, et al. Spinal Alignments of Residual Lumbar Curve Affect Disc Degeneration after Spinal Fusion in Patients with Adolescent Idiopathic Scoliosis: Follow-up after 5 or More Years. Spine Surgery and Related Research. 2020;4(1):50-6.

97. Akazawa T, Watanabe K, Matsumoto M, Tsuji T, Kawakami N, Kotani T, et al. Modic Changes and Disc Degeneration in Adolescent Idiopathic Scoliosis Patients Who Reach Middle Age without Surgery: Can Residual Deformity Cause Lumbar Spine Degeneration? Journal of Orthopaedic Science. 2018;23(6):884-8.

98. Alicioglu B, Sut N. Synovial Cysts of the Lumbar Facet Joints: A Retrospective Magnetic Resonance Imaging Study Investigating Their Relation with Degenerative Spondylolisthesis. Prague Medical Report. 2009;110(4):301-9.

99. Alkhasawneh MH, Al-Mnayyis A, Bagain Y. Spinal Degeneration and Degenerative Disc Disease Correlation Identified with Magnetic Resonance Imaging. Biomedical and Pharmacology Journal. 2021;14(1):491-6.

100. Alserafy AM, Badran M, El-Nasr AA, El-Fiki A, Halaby W. Pre-Existing Adjacent Level Degeneration Effect on Decision Making in Single Level Lumbar Spondylolisthesis. Journal of Cardiovascular Disease Research. 2021;12(3):1004-10.

101. Alyas F, Turner M, Connell D. MRI Findings in the Lumbar Spines of Asymptomatic, Adolescent, Elite Tennis Players. British Journal of Sports Medicine. 2007;41(11):836-41; discussion 41.

102. Apaydin M, Kalayci OT, Varer M, Sezgin G, Uluc E. Lumbosacral Transitional Vertebra in the Young Men Population with Low Back Pain: Anatomical Considerations and Degenerations. Neuroradiology. 2015;1):S137.

103. Arana E, Royuela A, Kovacs FM, Estremera A, Sarasibar H, Amengual G, et al. Lumbar Spine: Agreement in the Interpretation of 1.5-T Mr Images by Using the Nordic Modic Consensus Group Classification Form. Radiology. 2010;254(3):809-17.

104. Arslan E, Demirci I, Kilincaslan MO, Hacifazlioglu C, Demir T, Demirkale I. Identification of Intervertebral Disc Regeneration with Magnetic Resonance Imaging after a Long-Term Follow-up in Patients Treated with Percutaneous Diode Laser Nucleoplasty: A Retrospective Clinical and Radiological Analysis of 14 Patients. European Spine Journal. 2014;23(5):1044-51.

105. Atalay A, Turhan N, Atalay B. Deconditioning in Chronic Low Back Pain: Might There Be a Relationship between Fitness and Magnetic Resonance Imaging Findings? Rheumatology International. 2012;32(1):21-5.

106. Auerbach JD, Johannessen W, Borthakur A, Wheaton AJ, Dolinskas CA, Balderston RA, et al. In Vivo Quantification of Human Lumbar Disc Degeneration Using T(1rho)-Weighted Magnetic Resonance Imaging. European Spine Journal. 2006;15 Suppl 3:S338-44.

107. Baioni A, Silvestre M, Greggi T, Vommaro F, Lolli F, Scarale A, et al. Does Hybrid Fixation Prevent Junctional Disease after Posterior Fusion for Degenerative Lumbar Disorders? A Minimum 5-Year Follow-up Study. European Spine Journal. 2015;24:855-64.

108. Banno T, Hasegawa T, Yamato Y, Yoshida G, Arima H, Oe S, et al. Disc Degeneration Could Be Recovered after Chemonucleolysis with Condoliase.-1 Year Clinical Outcome of Condoliase Therapy. Journal of Orthopaedic Science. 2022;27(4):767-73.

109. Bao H, Zhu F, Liu Z, Zhu Z, He S, Ding Y, et al. Coronal Curvature and Spinal Imbalance in Degenerative Lumbar Scoliosis: Disc Degeneration Is Associated. Spine. 2014;39(24):E1441-7.

110. Basaran R, Senol M, Ozkanli S, Efendioglu M, Kaner T. Correlation of Matrix Metalloproteinase (Mmp)-1, -2, -3, and -9 Expressions with Demographic and Radiological Features in Primary Lumbar Intervertebral Disc Disease. Journal of Clinical Neuroscience. 2017;41:46-9.

111. Basques BA, Espinoza Orias AA, Shifflett GD, Fice MP, Andersson GB, An HS, et al. The Kinematics and Spondylosis of the Lumbar Spine Vary Depending on the Levels of Motion Segments in Individuals with Low Back Pain. Spine. 2017;42(13):E767-E74.

112. Bazan PL, Borri AE, Medina M. Correlation between the Modic I Sign and Images of Vertebral Instability. Coluna/ Columna. 2021;20(4):264-7.

113. Belykh E, Kalinin AA, Patel AA, Miller EJ, Bohl MA, Stepanov IA, et al. Apparent Diffusion Coefficient Maps in the Assessment of Surgical Patients with Lumbar Spine Degeneration. PLoS ONE [Electronic Resource]. 2017;12(8):e0183697.

114. Benedikter C, Abrar DB, Konieczny M, Schleich C, Bittersohl B. Patterns of Intervertebral Disk Alteration in Asymptomatic Elite Rowers: A T2* MRI Mapping Study. Orthopaedic Journal of Sports Medicine. 2022;10(4).

115. Berg AJ, Ahmadje U, Jayanna HH, Tregouet P, Sanville P, Kapoor V. The Prevalence of Lumbar Disc Degeneration in Symptomatic Younger Patients: A Study of MRI Scans. Journal of Clinical Orthopaedics & Trauma. 2020;11(5):932-6.

116. Bernstein P, Hentschel S, Platzek I, Huhne S, Ettrich U, Hartmann A, et al. Thoracal Flat Back Is a Risk Factor for Lumbar Disc Degeneration after Scoliosis Surgery. Spine Journal: Official Journal of the North American Spine Society. 2014;14(6):925-32.

117. Bezuglov E, Lazarev A, Petrov A, Brodskaia A, Lyubushkina A, Kubacheva K, et al. Asymptomatic Degenerative Changes in the Lumbar Spine among Professional Soccer Players. Spine. 2021;46(2):122-8.

118. Bo R, Yang QG, Duan W, Liu JR, Zhang YS. Correlation between Vertebral Endplate Shape and Intervertebral Disc Degeneration. Chinese Journal of Tissue Engineering Research. 2012;16(24):4413-6.

119. Borthakur A, Maurer PM, Fenty M, Wang C, Berger R, Yoder J, et al. T<Inf>1rho</Inf> Magnetic Resonance Imaging and Discography Pressure as Novel Biomarkers for Disc Degeneration and Low Back Pain. Spine. 2011;36(25):2190-6.

120. Byval'tsev VA, Stepanov IA, Kalinin AA, Belykh EG. Diffusion-Weighted Magnetic Resonance Imaging in the Diagnosis of Intervertebral Disc Degeneration in the Lumbosacral Spine. Vestnik Rentgenologii i Radiologii. 2016;97(6):357-64.

121. Canbay S, Turhan N, Bozkurt M, Arda K, Caglar S. Correlation of Matrix Metalloproteinase-3 Expression with Patient Age, Magnetic Resonance Imaging and Histopathological Grade in Lumbar Disc Degeneration. Turkish Neurosurgery. 2013;23(4):427-33.

122. Cao Y, Guo QW, Wan YD. Significant Association between the T2 Values of Vertebral Cartilage Endplates and Pfirrmann Grading. Orthopaedic Audio-Synopsis Continuing Medical Education [Sound Recording]. 2020;12(4):1164-72.

123. Castro-Mateos I, Hua R, Pozo J, Lazary A, Frangi A, Pozo JM, et al. Intervertebral Disc Classification by Its Degree of Degeneration from T2-Weighted Magnetic Resonance Images. European Spine Journal. 2016;25(9):2721-7.

124. Chen L, Hu X, Zhang J, Battie MC, Lin X, Wang Y. Modic Changes in the Lumbar Spine Are Common Aging-Related Degenerative Findings That Parallel with Disk Degeneration. Clinical Spine Surgery : A Spine Publication. 2018;31(7):312-7.

125. Chen N, Lang N, Yuan H. Ultrashort Echo Time MRI on Cartilaginous Endplates in Lumbar Spine. [Chinese]. Chinese Journal of Medical Imaging Technology. 2019;35(6):899-903.

126. Chen R, Liang X, Huang T, Zhong W, Luo X. Effects of Type 1 Diabetes Mellitus on Lumbar Disc Degeneration: A Retrospective Study of 118 Patients. Journal of Orthopaedic Surgery. 2020;15(1):280.

127. Chen SQ, Li QP, Huang YY, Guo AN, Zhang RF, Ye PP, et al. Different Spinal Subtypes with Varying Characteristics of Lumbar Disc Degeneration at Specific Level with Age: A Study Based on an Asymptomatic Population. Journal of Orthopaedic Surgery. 2020;15(1):3.

128. Cheng Z, Li Y, Li M, Huang J, Liang Y, Lu S, et al. Correlation between Posterior Paraspinal Muscle Atrophy and Lumbar Intervertebral Disc Degeneration in Patients with Chronic Low Back Pain. International Orthopaedics. 2023;47(3):793-801.

129. Chiu CK, Tan CS, Chung WH, Mohamad SM, Kwan MK, Chan CYW. Mid-Long-Term Outcome and Degeneration of the Remaining Unfused Lumbar Intervertebral Disc in Adolescent Idiopathic Scoliosis Patients Who Had Posterior Spinal Fusion Surgery. European Spine Journal. 2021;30(7):1978-87.

130. Collinet A, Charles YP, Ntilikina Y, Tuzin N, Steib JP. Analysis of Intervertebral Discs Adjacent to Thoracolumbar A3 Fractures Treated by Percutaneous Instrumentation and Kyphoplasty. Orthopaedics & traumatology, surgery & research. 2020;106(6):1221-6.

131. Corniola MV, Stienen MN, Joswig H, Smoll NR, Schaller K, Hildebrandt G, et al. Correlation of Pain, Functional Impairment, and Health-Related Quality of Life with Radiological Grading Scales of Lumbar Degenerative Disc Disease. Acta Neurochirurgica. 2016;158(3):499-505.

132. Crewe H, Elliott B, Couanis G, Campbell A, Alderson J. The Lumbar Spine of the Young Cricket Fast Bowler: An MRI Study. Journal of Science and Medicine in Sport. 2012;15(3):190-4.

133. Cubuk R, Kozakcioglu M, Tasali N, Atalay A, Celik L. Lumbar Disc and Facet Degeneration: Correlation with Age and Facet Orientation. Trakya Universitesi Tip Fakultesi Dergisi. 2009;26(1):36-42.

134. Cuellar VG, Cuellar JM, Vaccaro AR, Carragee EJ, Scuderi GJ. Accelerated Degeneration after Failed Cervical and Lumbar Nucleoplasty. Journal of Spinal Disorders & Techniques. 2010;23(8):521-4.

135. Cui J, Zhou R, Tian N, Sui X, Huang M, Hao D, et al. Correlation between Lower Lumbar Multifidus Muscles Fatty Atrophy and Corresponding Level Degenerative Diseases in Patients with Low Back Pain Using MRI. Chinese Journal of Academic Radiology. 2021;4(1):63-70.

136. Cui JH, Kim YC, Lee K, Park GT, Kim KT, Kim SM. Relationship between Facet Joint Tropism and Degeneration of Facet Joints and Intervertebral Discs Based on a Histological Study. Journal of Orthopaedics. 2019;16(2):123-7.

137. Cui YZ, Yang XH, Liu PF, Wang B, Chen WJ. Preliminary Study on Diagnosis of Lumbar Disc Degeneration with Magnetic Resonance T1p, T2 Mapping and Dwi Quantitative Detection Technologies. European Review for Medical & Pharmacological Sciences. 2016;20(16):3344-50.

138. Davies BM, Atkinson RA, Ludwinski F, Freemont AJ, Hoyland JA, Gnanalingham KK. Qualitative Grading of Disc Degeneration by Magnetic Resonance in the Lumbar and Cervical Spine: Lack of Correlation with Histology in Surgical Cases. British Journal of Neurosurgery. 2016;30(4):414-21.

139. Deguchi T, Hashizume H, Nakajima M, Teraguchi M, Akune T, Yamada H, et al. A Population-Based Study Identifies an Association of Thbs2 with Intervertebral Disc Degeneration. Osteoarthritis and Cartilage. 2019;27(10):1501-7.

140. Dehnokhalaji M, Golbakhsh MR, Siavashi B, Talebian P, Javidmehr S, Bozorgmanesh M. Evaluation of the Degenerative Changes of the Distal Intervertebral Discs after Internal Fixation Surgery in Adolescent Idiopathic Scoliosis. Asian Spine Journal. 2018;12(6):1060-8.

141. Ding Y, Chen JY, Yang JC, Li RY, Yin YJ, Chen JT, et al. Disc Degeneration Contributes to the Denser Bone in the Subendplate but Not in the Vertebral Body in Patients with Lumbar Spinal Stenosis or Disc Herniation. Spine Journal: Official Journal of the North American Spine Society. 2023;23(1):64-71.

142. Dogan A, Dogan K, Tasolar S. Magnetic Resonance Imaging Evaluation of the Effects of Cigarette and Maras Powder (Smokeless Tobacco) on Lumbar Disc Degeneration. Clinical Neurology & Neurosurgery. 2019;186:105500.

143. Doktor K, Hartvigsen J, Hancock M, Christensen HW, Fredberg U, Boyle E, et al. Reliability of Reporting Differences in Degenerative MRI Findings of the Lumbar Spine from the Supine to the Upright Position. Skeletal Radiology. 2022;51(11):2141-54.

144. Doktor K, Jensen TS, Christensen HW, Fredberg U, Kindt M, Boyle E, et al. Degenerative Findings in Lumbar Spine MRI: An Inter-Rater Reliability Study Involving Three Raters. Chiropractic & manual therapies. 2020;28(1):8.

145. Doyle AJ, Merrilees M. Synovial Cysts of the Lumbar Facet Joints in a Symptomatic Population: Prevalence on Magnetic Resonance Imaging. Spine. 2004;29(8):874-8.

146. Duran S, Cavusoglu M, Gunaydin E, Sakman B. Ligamentum Flavum Hypertrophy in Elderly Patients with Low Back Pain: A MRI Study. Turk Geriatri Dergisi. 2016;19(2):107-12.

147. Dybvik V, Hermansen E, Banitalebi H, Myklebust TA, Indrekvam K. Is Repeated Preoperative Magnetic Resonance Imaging Necessary before Planned Decompressive Surgery for Lumbar Spinal Stenosis? International Journal of Spine Surgery. 2023;24:24.

148. Eksi MS, Ozcan-Eksi EE, Akkas A, Orhun O, Arslan HN, Zarbizada M, et al. Intradiscal Vacuum Phenomenon and Spinal Degeneration: A Cross-Sectional Analysis of 219 Subjects. Current Medical Research & Opinion. 2022;38(2):255-63.

149. Eksi MS, Ozcan-Eksi EE, Orhun O, Huet SE, Turgut VU, Pamir MN. Association between Facet Joint Orientation/Tropism and Lumbar Intervertebral Disc Degeneration. British Journal of Neurosurgery. 2020:1-8.

150. Eksi MS, Ozcan-Eksi EE, Orhun O, Turgut VU, Pamir MN. Proposal for a New Scoring System for Spinal Degeneration: Mo-Fi-Disc. Clinical Neurology & Neurosurgery. 2020;198:106120.

151. Eksi MS, Ozcan-Eksi EE, Ozmen BB, Turgut VU, Huet SE, Dinc T, et al. Lumbar Intervertebral Disc Degeneration, End-Plates and Paraspinal Muscle Changes in Children and Adolescents with Low-Back Pain. Journal of Pediatric Orthopaedics Part B. 2022;31(1):93-102.

152. Eksi MS, Turgut VU, Berikol G, Ozmen BB, Huet SE, Dinc T, et al. Schmorl's Nodes Could Be Associated with Intervertebral Disc Degeneration at Upper Lumbar Levels and End-Plate Disease at Lower Lumbar Level in Patients with Low Back Pain. Journal of Clinical Neuroscience. 2022;100:66-74.

153. Elfadle AA, Zarad CA, Elmaaty AaA, El-Nagaa BFA, Soliman AY. Correlation between Lumbar Spinal Canal Magnetic Resonance Imaging Grading Systems and Parameters in Lumbar Spinal Canal Compromise. Egyptian Journal of Neurology, Psychiatry and Neurosurgery. 2022;58(1) (no pagination).

154. Enercan M, Kahraman S, Yilar S, Cobanoglu M, Gokcen BH, Karadereler S, et al. Does It Make a Difference to Stop Fusion at L3 Versus L4 in Terms of Disc and Facet Joint Degeneration: An MRI Study with Minimum 5 Years Follow-Up. Spine Deformity. 2016;4(3):237-44.

155. Enoki S, Kuramochi R, Nakajyuku S, Mitsuyama H. The Prevalence of Spondylolysis and Intervertebral Disc Degeneration in Male Pole Vaulters. Journal of Back & Musculoskeletal Rehabilitation. 2022;35(1):147-51.

156. Ergun T, Lakadamyali H, Sahin MS. The Relation between Sagittal Morphology of the Lumbosacral Spine and the Degree of Lumbar Intervertebral Disc Degeneration. Acta Orthopaedica et Traumatologica Turcica. 2010;44(4):293-9.

157. Farshad-Amacker N, Hughes A, Herzog R, Seifert B, Farshad M, Farshad-Amacker NA, et al. The Intervertebral Disc, the Endplates and the Vertebral Bone Marrow as a Unit in the Process of Degeneration. European Radiology. 2017;27(6):2507-20.

158. Farshad-Amacker N, Hughes AP, Aichmair A, Herzog RJ, Farshad M. Determinants of Evolution of Endplate and Disc Degeneration in the Lumbar Spine-a Multifactorial Perspective. Swiss Medical Weekly. 2014;204):30S.

159. Farshad-Amacker NA, Herzog RJ, Hughes AP, Aichmair A, Farshad M. Associations between Lumbosacral Transitional Anatomy Types and Degeneration at the Transitional and Adjacent Segments. Spine Journal: Official Journal of the North American Spine Society. 2015;15(6):1210-6.

160. Farshad-Amacker NA, Hughes AP, Aichmair A, Herzog RJ, Farshad M. Determinants of Evolution of Endplate and Disc Degeneration in the Lumbar Spine: A Multifactorial Perspective. European Spine Journal. 2014;23(9):1863-8.

161. Farshad-Amacker NA, Hughes AP, Aichmair A, Herzog RJ, Farshad M. Is an Annular Tear a Predictor for Accelerated Disc Degeneration? European Spine Journal. 2014;23(9):1825-9.

162. Filippi CG, Duncan CT, Watts R, Nickerson JP, Gonyea JV, Hipko SG, et al. In Vivo Quantification of T1rho in Lumbar Spine Disk Spaces at 3 T Using Parallel Transmission MRI. AJR American Journal of Roentgenology. 2013;201(1):W110-6.

163. Foizer GA, Paiva VC, Nascimento RDD, Gorios C, Cliquet Junior A, Miranda JB. Is There Any Association between the Severity of Disc Degeneration and Low Back Pain? Revista Brasileira de Ortopedia. 2022;57(2):334-40.

164. Folkvardsen S, Magnussen E, Karppinen J, Auvinen J, Larsen R, Wong C, et al. Does Elite Swimming Accelerate Lumbar Intervertebral Disc Degeneration and Increase Low Back Pain? A Cross-Sectional Comparison. European Spine Journal. 2016;25(9):2849-55.

165. Frenken M, Nebelung S, Schleich C, Muller-Lutz A, Radke KL, Kamp B, et al. Non-Specific Low Back Pain and Lumbar Radiculopathy: Comparison of Morphologic and Compositional MRI as Assessed by Gagcest Imaging at 3t. Diagnostics. 2021;11(3):26.

166. Fu CL, Zhang B, Liu Y, Dai M, Zhou X, Fu XX. MRI Comparison of Lumbar Facet Joint Degeneration and Intervertebral Disc Degeneration in Patients with Low Back Pain. [Chinese]. Chinese Journal of Tissue Engineering Research. 2015;19(46):7401-5.

167. Fu L, France A, Xie Y, Fang K, Gan Y, Zhang P. Functional and Radiological Outcomes of Semi-Rigid Dynamic Lumbar Stabilization Adjacent to Single-Level Fusion after 2 Years. Archives of Orthopaedic & Trauma Surgery. 2014;134(5):605-10.

168. Fujita N, Ishihara S, Michikawa T, Azuma K, Suzuki S, Tsuji O, et al. Potential Association of Metabolic and Musculoskeletal Disorders with Lumbar Intervertebral Disc Degeneration: Cross-Sectional Study Using Medical Checkup Data. Journal of Orthopaedic Science. 2020;25(3):384-8.

169. Galbusera F, Niemeyer F, Tao Y, Cina A, Sconfienza LM, Kienle A, et al. Issls Prize in Bioengineering Science 2021: In Vivo Sagittal Motion of the Lumbar Spine in Low Back Pain Patients-a Radiological Big Data Study. European Spine Journal. 2021;30(5):1108-16.

170. Galley J, Balague F. Revisiting Radiographic L5-S1 Parallelism Using MRI T1 Mapping. Journal of the Belgian Society of Radiology. 2018;102(1):59.

171. Gao F, Liu S, Zhang X, Wang X, Zhang J. Automated Grading of Lumbar Disc Degeneration Using a Push-Pull Regularization Network Based on MRI. Journal of Magnetic Resonance Imaging. 2021;53(3):799-806.

172. Gao J, Zhao W, Zhang X, Nong L, Zhou D, Lv Z, et al. MRI Analysis of the Isobar Ttl Internal Fixation System for the Dynamic Fixation of Intervertebral Discs: A Comparison with Rigid Internal Fixation. Journal of Orthopaedic Surgery. 2014;9:43.

173. Gao X, Wang L, Zhang J, Wang P, Shen Y. Long Fusion Arthrodesis Stopping at L5 for Adult Scoliosis: Fate of L5-S1 Disk and Risk Factors for Subsequent Disk Degeneration. Clinical Spine Surgery : A Spine Publication. 2018;31(3):E171-E7.

174. Gautschi OP, Stienen MN, Joswig H, Smoll NR, Schaller K, Corniola MV. The Usefulness of Radiological Grading Scales to Predict Pain Intensity, Functional Impairment, and Health-Related Quality of Life after Surgery for Lumbar Degenerative Disc Disease. Acta Neurochirurgica. 2017;159(2):271-9.

175. Golan JD, Martens F, Griebel J, Lopresti DC, Hess MG, Ahrens M. Long-Term Outcomes Following Lumbar Nucleus Replacement. International Journal of Spine Surgery. 2021;15(6):1096-102.

176. Grannum S, Torrie PA, Miller A, Harding IJ. Risk Factors for the Development of a Mobile Degenerative Spondylolisthesis at L4-L5. Spine Deformity. 2015;3(1):98-104.

177. Green DW, Lawhorne TW, 3rd, Widmann RF, Kepler CK, Ahern C, Mintz DN, et al. Long-Term Magnetic Resonance Imaging Follow-up Demonstrates Minimal Transitional Level Lumbar Disc Degeneration after Posterior Spine Fusion for Adolescent Idiopathic Scoliosis. Spine (03622436). 2011;36(23):1948-54.

178. Griffith JF, Wang YX, Antonio GE, Choi KC, Yu A, Ahuja AT, et al. Modified Pfirrmann Grading System for Lumbar Intervertebral Disc Degeneration. Spine. 2007;32(24):E708-12.

179. Grob A, Loibl M, Jamaludin A, Winklhofer S, Fairbank JCT, Fekete T, et al. External Validation of the Deep Learning System "Spinenet" for Grading Radiological Features of Degeneration on MRIs of the Lumbar Spine. European Spine Journal. 2022;31(8):2137-48.

180. Guo Y, Li C, Shen B, Chen X, Hu T, Wu D. Is Intervertebral Disc Degeneration Associated with Reduction in Serum Ferritin? European Spine Journal. 2022;31(11):2950-9.

181. Guo Y, Li C, Shen B, Zhu Z, Chen X, Hu T, et al. Is There Any Relationship between Plasma Il-6 and Tnf-Alpha Levels and Lumbar Disc Degeneration? A Retrospective Single-Center Study. Disease Markers. 2022;2022:6842130.

182. Guo Y, Zhao H, Lu J, Xu H, Hu T, Wu D. Preoperative Lymphocyte to Monocyte Ratio as a Predictive Biomarker for Disease Severity and Spinal Fusion Failure in Lumbar Degenerative Diseases Patients Undergoing Lumbar Fusion. Journal of Pain Research. 2022;15:2879-91.

183. Hancock M, Maher C, Macaskill P, Latimer J, Kos W, Pik J, et al. MRI Findings Are More Common in Selected Patients with Acute Low Back Pain Than Controls? European Spine Journal. 2012;21(2):240-6.

184. Hancock MJ, Maher CM, Petocz P, Lin C-WC, Steffens D, Luque-Suarez A, et al. Risk Factors for a Recurrence of Low Back Pain. Spine Journal. 2015;15(11):2360-8.

185. Haneder S, Apprich SR, Schmitt B, Michaely HJ, Schoenberg SO, Friedrich KM, et al. Assessment of Glycosaminoglycan Content in Intervertebral Discs Using Chemical Exchange Saturation Transfer at 3.0 Tesla: Preliminary Results in Patients with Low-Back Pain. European Radiology. 2013;23(3):861-8.

186. Haneder S, Ong MM, Budjan JM, Schmidt R, Konstandin S, Morelli JN, et al. 23na-Magnetic Resonance Imaging of the Human Lumbar Vertebral Discs: In Vivo Measurements at 3.0 T in Healthy Volunteers and Patients with Low Back Pain. Spine Journal: Official Journal of the North American Spine Society. 2014;14(7):1343-50.

187. Hangai M, Kaneoka K, Hinotsu S, Shimizu K, Okubo Y, Miyakawa S, et al. Lumbar Intervertebral Disk Degeneration in Athletes. American Journal of Sports Medicine. 2009;37(1):149-55.

188. Hangai M, Kaneoka K, Kuno S, Hinotsu S, Sakane M, Mamizuka N, et al. Factors Associated with Lumbar Intervertebral Disc Degeneration in the Elderly. Spine Journal: Official Journal of the North American Spine Society. 2008;8(5):732-40.

189. Hanhivaara J, Maatta JH, Karppinen J, Niinimaki J, Nevalainen MT. The Association of Lumbosacral Transitional Vertebrae with Low Back Pain and Lumbar Degenerative Findings in MRI: A Large Cohort Study. Spine. 2022;47(2):153-62.

190. Hanimoglu H, Cevik S, Yilmaz H, Kaplan A, Calis F, Katar S, et al. Effects of Modic Type 1 Changes in the Vertebrae on Low Back Pain. World Neurosurgery. 2019;121:e426-e32.

191. Hansen BB, Ciochon UM, Trampedach CR, Christensen AF, Rasti Z, Boesen M. Grading Lumbar Disc Degeneration: A Comparison between Low- and High-Field MRI. Acta Radiologica. 2019;60(12):1636-42.

192. Hasegawa K, Kitahara K, Hara T, Takano K, Shimoda H, Homma T. Evaluation of Lumbar Segmental Instability in Degenerative Diseases by Using a New Intraoperative Measurement System. Journal of Neurosurgery Spine. 2008;8(3):255-62.

193. Hayashi T, Daubs MD, Suzuki A, Scott TP, Phan KH, Ruangchainikom M, et al. Motion Characteristics and Related Factors of Modic Changes in the Lumbar Spine. Journal of Neurosurgery Spine. 2015;22(5):511-7.

194. He X, Liang A, Gao W, Peng Y, Zhang L, Liang G, et al. The Relationship between Concave Angle of Vertebral Endplate and Lumbar Intervertebral Disc Degeneration. Spine. 2012;37(17):E1068-73.

195. Hebelka H, Brisby H, Hansson T. Comparison between Pain at Discography and Morphological Disc Changes at Axial Loaded MRI in Patients with Low Back Pain. European Spine Journal. 2014;23(10):2075-82.

196. Hebelka H, Gunterberg V, Lagerstrand K, Brisby H. Clinical Outcome and MRI Appearance in a Group of Chronic Low Back Pain Patients More Than 10 Years after Discography Evaluation and Consideration for Surgery. BMC Musculoskeletal Disorders. 2023;24(1):138.

197. Hey HWD, Ng NL, Loh KYS, Tan YH, Tan KA, Moorthy V, et al. Sagittal Radiographic Parameters of the Spine in Three Physiological Postures Characterized Using a Slot Scanner and Their Potential Implications on Spinal Weight-Bearing Properties. Asian Spine Journal. 2021;15(1):23-31.

198. Hong C, Lee CG, Song H. Characteristics of Lumbar Disc Degeneration and Risk Factors for Collapsed Lumbar Disc in Korean Farmers and Fishers. Annals of Occupational and Environmental Medicine. 2021;33(1) (no pagination).

199. Hoppe S, Quirbach S, Mamisch TC, Krause FG, Werlen S, Benneker LM. Axial T2 Mapping in Intervertebral Discs: A New Technique for Assessment of Intervertebral Disc Degeneration. European Radiology. 2012;22(9):2013-9.

200. Hornung AL, Barajas JN, Rudisill SS, Aboushaala K, Butler A, Park G, et al. Prediction of Lumbar Disc Herniation Resorption in Symptomatic Patients: A Prospective, Multi-Imaging and Clinical Phenotype Study. Spine Journal: Official Journal of the North American Spine Society. 2023;23(2):247-60.

201. Hsieh CC, Wang JD, Lin RM, Lin CJ, Huang KY. Adjacent Disc and Facet Joint Degeneration in Young Adults with Low-Grade Spondylolytic Spondylolisthesis: A Magnetic Resonance Imaging Study. Journal of the Formosan Medical Association. 2015;114(12):1211-5.

202. Hu J, Zhang Y, Duan C, Peng X, Hu P, Lu H. Feasibility Study for Evaluating Early Lumbar Facet Joint Degeneration Using Axial T<Inf>1</Inf>Rho, T<Inf>2</Inf>, and T2* Mapping in Cartilage. Journal of Magnetic Resonance Imaging. 2017;46(2):468-75.

203. Hu JK, Morishita Y, Montgomery SR, Hymanson H, Taghavi CE, Do D, et al. Kinematic Evaluation of Association between Disc Bulge Migration, Lumbar Segmental Mobility, and Disc Degeneration in the Lumbar Spine Using Positional Magnetic Resonance Imaging. Global Spine Journal. 2011;1(1):43-8.

204. Huang Y, Liu J, Guo L, Meng Y, Hao D, Du J. "Temporary" Short Segment Fixation in Treating Adolescent Lumbar Spondylolysis. World Neurosurgery. 2019;123:e77-e84.

205. Huang Y, Wang L, Zeng X, Chen J, Zhang Z, Jiang Y, et al. Association of Paraspinal Muscle Csa and Pdff Measurements with Lumbar Intervertebral Disk Degeneration in Patients with Chronic Low Back Pain. Frontiers in Endocrinology. 2022;13:792819.

206. Ibrahim M, Arockiaraj J, Amritanand R, Venkatesh K, David KS. Recurrent Lumbar Disc Herniation: Results of Revision Surgery and Assessment of Factors That May Affect the Outcome. A Non-Concurrent Prospective Study. Asian Spine Journal. 2015;9(5):728-36.

207. Identeg F, Lagerstrand K, Hedelin H, Senorski EH, Sansone M, Hebelka H. Low Occurrence of MRI Spinal Changes in Elite Climbing Athletes; a Cross-Sectional Study. BMC Sports Science, Medicine and Rehabilitation. 2023;15(1):29.

208. Iguchi T, Nishida K, Ozaki T, Kitagawa A, Tsumura N, Kakutani K, et al. Grade Three Disc Degeneration Is a Critical Stage for Anterior Spondylolisthesis in Lumbar Spine. European Spine Journal. 2012;21(11):2134-9.

209. Iii WS, Orias AaE, Shifflett GD, Lee JYB, Siemionow K, Gandhi S, et al. Image-Based Markers Predict Dynamic Instability in Lumbar Degenerative Spondylolisthesis. Neurospine. 2020;17(1):221-7.

210. Illeez OG, Ulger FEB, Aktas I. The Effect of Transitional Vertebrae and Spina Bifida Occulta on Disc Herniation, Disc Degeneration, and End-Plate Changes in Pediatric Patients with Low Back Pain. Acta Orthopaedica Belgica. 2022;88(2):275-83.

211. Imagama S, Kawakami N, Kanemura T, Matsubara Y, Tsuji T, Ohara T, et al. Radiographic Adjacent Segment Degeneration at Five Years after L4/5 Posterior Lumbar Interbody Fusion with Pedicle Screw Instrumentation: Evaluation by Computed Tomography and Annual Screening with Magnetic Resonance Imaging. Journal of Spinal Disorders and Techniques. 2013;19.

212. Iriondo C, Pedoia V, Majumdar S. Lumbar Intervertebral Disc Characterization through Quantitative MRI Analysis: An Automatic Voxel-Based Relaxometry Approach. Magnetic Resonance in Medicine. 2020;84(3):1376-90.

213. Jain A, Jain S, Barasker SK, Agrawal A. Predictors of Discogenic Pain in Magnetic Resonance Imaging: A Retrospective Study of Provocative Discography Performed by Posterolateral Approach. The Korean journal of pain. 2021;34(4):447-53.

214. Jakkepally S, Viswanathan VK, Shetty AP, Hajare S, Kanna RM, Rajasekaran S. The Analysis of Progression of Disc Degeneration in Distal Unfused Segments and Evaluation of Long-Term Functional Outcome in Adolescent Idiopathic Scoliosis Patients Undergoing Long-Segment Instrumented Fusion. Spine Deformity. 2022;10(2):343-50.

215. Jamaludin A, Kadir T, Zisserman A. Spinenet: Automated Classification and Evidence Visualization in Spinal MRIs. Medical Image Analysis. 2017;41:63-73.

216. Jamaludin A, Kadir T, Zisserman A, Mccall I, Williams FMK, Lang H, et al. Age and Disc Degeneration in Low Back Pain: Automated Analysis Enables a Magnetic Resonance Imaging Comparison of Large Cross-Sectional Cohorts of Symptomatic and Asymptomatic Subjects. medRxiv. 2021;08.

217. Jamaludin A, Kadir T, Zisserman A, Mccall I, Williams FMK, Lang H, et al. Issls Prize in Clinical Science 2023: Comparison of Degenerative MRI Features of the Intervertebral Disc between Those with and without Chronic Low Back Pain. An Exploratory Study of Two Large Female Populations Using Automated Annotation. European Spine Journal. 2023;30:30.

218. Jamaludin A, Lootus M, Kadir T, Zisserman A, Urban J, Battie MC, et al. Issls Prize in Bioengineering Science 2017: Automation of Reading of Radiological Features from Magnetic Resonance Images (MRIs) of the Lumbar Spine without Human Intervention Is Comparable with an Expert Radiologist. European Spine Journal. 2017;26(5):1374-83.

219. Janardhana AP, Rajagopal, Rao S, Kamath A. Correlation between Clinical Features and Magnetic Resonance Imaging Findings in Lumbar Disc Prolapse. Indian Journal of Orthopaedics. 2010;44(3):263-9.

220. Jang SY, Kong MH, Hymanson HJ, Jin TK, Song KY, Wang JC. Radiographic Parameters of Segmental Instability in Lumbar Spine Using Kinetic MRI. Journal of Korean Neurosurgical Society. 2009;45(1):24-31.

221. Jang TW, Ahn YS, Byun J, Lee JI, Kim KH, Kim Y, et al. Lumbar Intervertebral Disc Degeneration and Related Factors in Korean Firefighters. BMJ Open. 2016;6(6):e011587.

222. Jarman JP, Arpinar VE, Baruah D, Klein AP, Maiman DJ, Muftuler LT. Intervertebral Disc Height Loss Demonstrates the Threshold of Major Pathological Changes During Degeneration. European Spine Journal. 2015;24(9):1944-50.

223. Jeng CM, Cheng TC, Kung CH, Hsu HC. Yoga and Disc Degenerative Disease in Cervical and Lumbar Spine: An Mr Imaging-Based Case Control Study. European Spine Journal. 2011;20(3):408-13.

224. Jha SC, Takata Y, Abe M, Yamashita K, Tezuka F, Sakai T, et al. High Intensity Zone in Lumbar Spine and Its Correlation with Disc Degeneration. Journal of Medical Investigation. 2017;64(1.2):39-42.

225. Ji Y, Hong W, Liu M, Liang Y, Deng Y, Ma L. Intervertebral Disc Degeneration Associated with Vertebral Marrow Fat, Assessed Using Quantitative Magnetic Resonance Imaging. Skeletal Radiology. 2020;49(11):1753-63.

226. Jiang Y, Yu L, Luo X, Lin Y, He B, Wu B, et al. Quantitative Synthetic MRI for Evaluation of the Lumbar Intervertebral Disk Degeneration in Patients with Chronic Low Back Pain. European Journal of Radiology. 2020;124:108858.

227. Jung M, Rospleszcz S, Loffler MT, Walter SS, Maurer E, Jungmann PM, et al. Association of Lumbar Vertebral Bone Marrow and Paraspinal Muscle Fat Composition with Intervertebral Disc Degeneration: 3t Quantitative MRI Findings from the Population-Based Kora Study. European Radiology. 2023;33(3):1501-12.

228. Kamei N, Nakamae T, Nakanishi K, Tamura T, Tsuchikawa Y, Morisako T, et al. Evaluation of Intervertebral Disc Degeneration Using T2 Signal Ratio on Magnetic Resonance Imaging. European Journal of Radiology. 2022;152:110358.

229. Kaneoka K, Shimizu K, Hangai M, Okuwaki T, Mamizuka N, Sakane M, et al. Lumbar Intervertebral Disk Degeneration in Elite Competitive Swimmers: A Case Control Study. American Journal of Sports Medicine. 2007;35(8):1341-5.

230. Kanna RM, Hajare S, Thippeswamy PB, Shetty AP, Rajasekaran S. Advanced Disc Degeneration, Bi-Planar Instability and Pathways of Peri-Discal Gas Suffusion Contribute to Pathogenesis of Intradiscal Vacuum Phenomenon. European Spine Journal. 2022;31(3):755-63.

231. Kanna RM, Shetty AP, Rajasekaran S. Patterns of Lumbar Disc Degeneration Are Different in Degenerative Disc Disease and Disc Prolapse Magnetic Resonance Imaging Analysis of 224 Patients. Spine Journal: Official Journal of the North American Spine Society. 2014;14(2):300-7.

232. Keorochana G, Taghavi CE, Lee KB, Yoo JH, Liao JC, Fei Z, et al. Effect of Sagittal Alignment on Kinematic Changes and Degree of Disc Degeneration in the Lumbar Spine: An Analysis Using Positional MRI. Spine. 2011;36(11):893-8.

233. Khodair SA, Ghieda UE, Eltomey MA. Relationship of Lumbosacral Spine Morphometrics and Lumber Disc Degenerative Disease in Young Adults Using Magnetic Resonance Imaging. Egyptian Journal of Radiology and Nuclear Medicine. 2014;45(2):461-6.

234. Kilic G, Senol S, Baspinar S, Kilic E, Ozgocmen S. Degenerative Changes of Lumbar Spine and Their Clinical Implications in Patients with Axial Spondyloarthritis. Clinical Rheumatology. 2023;42(1):111-6.

235. Kim HJ, Suh BG, Lee DB, Lee GW, Kim DW, Kang KT, et al. The Influence of Pain Sensitivity on the Symptom Severity in Patients with Lumbar Spinal Stenosis. Pain Physician. 2013;16(2):135-44.

236. Kim HJ, Suh BG, Lee DB, Park JY, Kang KT, Chang BS, et al. Gender Difference of Symptom Severity in Lumbar Spinal Stenosis: Role of Pain Sensitivity. Pain Physician. 2013;16(6):E715-23.

237. Kim JY, Ryu DS, Paik HK, Ahn SS, Kang MS, Kim KH, et al. Paraspinal Muscle, Facet Joint, and Disc Problems: Risk Factors for Adjacent Segment Degeneration after Lumbar Fusion. Spine Journal: Official Journal of the North American Spine Society. 2016;16(7):867-75.

238. Kim SY, Lee IS, Kim BR, Lim JH, Lee J, Koh SE, et al. Magnetic Resonance Findings of Acute Severe Lower Back Pain. Annals of Rehabilitation Medicine. 2012;36(1):47-54.

239. Kleinstuck F, Dvorak J, Mannion AF. Are "Structural Abnormalities" on Magnetic Resonance Imaging a Contraindication to the Successful Conservative Treatment of Chronic Nonspecific Low Back Pain? Spine. 2006;31(19):2250-7.

240. Kobayashi K, Sato K, Ando T. Factors Associated with Disc Degeneration Based on Pfirrmann Criteria after Condoliase Treatment for Lumbar Disc Herniation. Journal of Orthopaedic Science. 2022;24:24.

241. Kobayashi K, Sato K, Ando T, Ando K. MRI Characteristics of Disc Degeneration after Condoliase Injection in Young Patients: A Consecutive Case Series. Journal of Orthopaedic Science. 2023;04:04.

242. Kojima T, Kubo S, Tajima N, Mitsuhashi R, Nozaki S, Chosa E. Lumbar Intervertebral Disc Degeneration in Professional Surfers. Sports Orthopaedics and Traumatology. 2018;34(3):261-4.

243. Kong MH, Morishita Y, He W, Miyazaki M, Zhang H, Wu G, et al. Lumbar Segmental Mobility According to the Grade of the Disc, the Facet Joint, the Muscle, and the Ligament Pathology by Using Kinetic Magnetic Resonance Imaging. Spine. 2009;34(23):2537-44.

244. Kovacs FM, Royuela A, Jensen TS, Estremera A, Amengual G, Muriel A, et al. Agreement in the Interpretation of Magnetic Resonance Images of the Lumbar Spine. Acta Radiologica. 2009;50(5):497-506.

245. Kraft CN, Pennekamp PH, Becker U, Young M, Diedrich O, Luring C, et al. Magnetic Resonance Imaging Findings of the Lumbar Spine in Elite Horseback Riders: Correlations with Back Pain, Body Mass Index, Trunk/Leg-Length Coefficient, and Riding Discipline. American Journal of Sports Medicine. 2009;37(11):2205-13.

246. Krug R, Joseph GB, Han M, Fields A, Cheung J, Mundada M, et al. Associations between Vertebral Body Fat Fraction and Intervertebral Disc Biochemical Composition as Assessed by Quantitative MRI. Journal of Magnetic Resonance Imaging. 2019;50(4):1219-26.

247. Kuisma M, Karppinen J, Haapea M, Lammentausta E, Niinimaki J, Tervonen O. Modic Changes in Vertebral Endplates: A Comparison of Mr Imaging and Multislice Ct. Skeletal Radiology. 2009;38(2):141-7.

248. Kuisma M, Karppinen J, Haapea M, Niinimaki J, Ojala R, Heliovaara M, et al. Are the Determinants of Vertebral Endplate Changes and Severe Disc Degeneration in the Lumbar Spine the Same? A Magnetic Resonance Imaging Study in Middle-Aged Male Workers. BMC Musculoskeletal Disorders. 2008;9:51.

249. Kuo C-H, Huang W-C, Wu J-C, Tu T-H, Fay L-Y, Wu C-L, et al. Radiological Adjacent-Segment Degeneration in L4-5 Spondylolisthesis: Comparison between Dynamic Stabilization and Minimally Invasive Transforaminal Lumbar Interbody Fusion. Journal of Neurosurgery: Spine. 2018:1-9.

250. Lagerback T, Kastrati G, Moller H, Jensen K, Skorpil M, Gerdhem P. MRI Characteristics at a Mean of Thirteen Years after Lumbar Disc Herniation Surgery in Adolescents: A Case-Control Study. JB & JS Open Access. 2021;6(4):Oct-Dec.

251. Lao L, Daubs MD, Scott TP, Lord EL, Cohen JR, Yin R, et al. Effect of Disc Degeneration on Lumbar Segmental Mobility Analyzed by Kinetic Magnetic Resonance Imaging. Spine. 2015;40(5):316-22.

252. Lao L, Daubs MD, Takahashi S, Lord EL, Cohen JR, Zhong G, et al. Kinetic Magnetic Resonance Imaging Analysis of Lumbar Segmental Motion at Levels Adjacent to Disc Herniation. European Spine Journal. 2016;25(1):222-9.

253. Latif R, Imran S, Ahmad I, Ilyas MS, Aziz A, Zehra U. Vertebral Endplate Changes Correlate with Presence of Cartilaginous Endplate in the Herniated Disc Tissue: Factor Predicting Failure of Conservative Treatment. Asian Spine Journal. 2022;16(2):212-20.

254. Latz D, Frenken M, Schiffner E, Knautz M, Quante WA, Windolf J, et al. Assessment of Glycosaminoglycan Content in Intervertebral Discs of Patients with Leg Length Discrepancy: A Pilot Study. Journal of Orthopaedics. 2019;16(5):363-7.

255. Lee CS, Ha JK, Kim DG, Hwang CJ, Lee DH, Cho JH. The Clinical Importance of Lumbosacral Transitional Vertebra in Patients with Adolescent Idiopathic Scoliosis. Spine. 2015;40(17):E964-70.

256. Lee J, Kim J, Shin JS, Lee YJ, Kim MR, Jeong SY, et al. Long-Term Course to Lumbar Disc Resorption Patients and Predictive Factors Associated with Disc Resorption. Evidence-based Complementary and Alternative Medicine. 2017;2017 (no pagination).

257. Lee JW, Choi SW, Park SH, Lee GY, Kang HS, Lee JW, et al. Mr-Based Outcome Predictors of Lumbar Transforaminal Epidural Steroid Injection for Lumbar Radiculopathy Caused by Herniated Intervertebral Disc. European Radiology. 2013;23(1):205-11.

258. Lee K, Shin JS, Lee J, Lee YJ, Kim MR, Seong I, et al. Lumbar Intervertebral Disc Space Height in Disc Herniation and Degeneration Patients Aged 20 to 25. International Journal of Clinical and Experimental Medicine. 2017;10(4):6828-36.

259. Lee SE, Jahng TA, Kim HJ. Clinical Experiences of Non-Fusion Dynamic Stabilization Surgery for Adjacent Segmental Pathology after Lumbar Fusion. International Journal of Spine Surgery. 2016;10:8.

260. Lee SM, Lee GW. The Impact of Generalized Joint Laxity on the Clinical and Radiological Outcomes of Single-Level Posterior Lumbar Interbody Fusion. Spine Journal: Official Journal of the North American Spine Society. 2015;15(5):809-16.

261. Li X, Xie Y, Lu R, Zhang Y, Li Q, Kober T, et al. Q-Dixon and Grappatini T2 Mapping Parameters: A Whole Spinal Assessment of the Relationship between Osteoporosis and Intervertebral Disc Degeneration. Journal of Magnetic Resonance Imaging. 2022;55(5):1536-46.

262. Li Y, Lord E, Cohen Y, Ruangchainikom M, Wang B, Lv G, et al. Effects of Sagittal Endplate Shape on Lumbar Segmental Mobility as Evaluated by Kinetic Magnetic Resonance Imaging. Spine. 2014;39(17):E1035-41.

263. Liang J, Dong Y, Zhao H. Risk Factors for Predicting Symptomatic Adjacent Segment Degeneration Requiring Surgery in Patients after Posterior Lumbar Fusion. Journal of Orthopaedic Surgery. 2014;9:97.

264. Liang X, Xie R, Hou B, Li Y, Xiong Y, Yin C, et al. Feasibility Study for Evaluating Lumbar Intervertebral Disc Degeneration Using Histogram Analysis of T2 Values. European Spine Journal. 2020;29(10):2600-8.

265. Liawrungrueang W, Kim P, Kotheeranurak V, Jitpakdee K, Sarasombath P. Automatic Detection, Classification, and Grading of Lumbar Intervertebral Disc Degeneration Using an Artificial Neural Network Model. Diagnostics. 2023;13(4):10.

266. Lippross S, Girmond P, Luders KA, Austein F, Braunschweig L, Luders S, et al. Smaller Intervertebral Disc Volume and More Disc Degeneration after Spinal Distraction in Scoliotic Children. Journal of Clinical Medicine. 2021;10(10) (no pagination).

267. Liu C, Liang G, Deng Z, Tan J, Zheng Q, Lyu FJ. The Upregulation of Cox2 in Human Degenerated Nucleus Pulposus: The Association of Inflammation with Intervertebral Disc Degeneration. Mediators of Inflammation. 2021;2021:2933199.

268. Liu T, Wang Y, Xu Z, Wu T, Zang X, Li M, et al. Application Study of 3d Lava-Flex on Lumbar Intervertebral Disc Degeneration. European Journal of Medical Research. 2021;26(1):43.

269. Liu X, Pan F, Ba Z, Wang S, Wu D. The Potential Effect of Type 2 Diabetes Mellitus on Lumbar Disc Degeneration: A Retrospective Single-Center Study. Journal of Orthopaedic Surgery. 2018;13(1):52.

270. Liu ZZ, Chen JY, Cai ZX, Jiang XH, Zhang Y, Yang ZH, et al. MRI of Lumbar Intervertebral Disc Degeneration: Correlation of Tlrho Value with Pfirrmann Grade and T2 Value. [Chinese]. Chinese Journal of Medical Imaging Technology. 2014;30(2):260-4.

271. Liu ZZ, Wen HQ, Zhu YQ, Zhao BL, Kong QC, Chen JY, et al. Short-Term Effect of Lumbar Traction on Intervertebral Discs in Patients with Low Back Pain: Correlation between the T2 Value and Odi/Vas Score. Cartilage. 2021;13(1_suppl):414S-23S.

272. Lorenc T, Burzykowski T. Relationship among the Foraminal Area and Demographic and Clinical Characteristics of Patients with Low Back Pain. World Neurosurgery. 2022;160:e520-e8.

273. Lorenc T, Glinkowski WM, Golebiowski M. Axially Loaded Magnetic Resonance Imaging Identification of the Factors Associated with Low Back-Related Leg Pain. Journal of Clinical Medicine. 2021;10(17):29.

274. Louie PK, Orias AaE, Fogg LF, Labelle M, An HS, Andersson GBJ, et al. Changes in Lumbar Endplate Area and Concavity Associated with Disc Degeneration. Spine. 2018;43(19):E1127-E34.

275. Ma H, Zhang X, Guo Y, Du Y, Wang R, Niu G. Intravoxel Incoherent Motion Mr Imaging in the Quantitative Evaluation of Lumbar Disc Degeneration. [Chinese]. Journal of Xi'an Jiaotong University (Medical Sciences). 2020;41(6):901-5.

276. Ma J, Wang R, Yu Y, Xu X, Duan H, Yu N. Is Fractal Dimension a Reliable Imaging Biomarker for the Quantitative Classification of an Intervertebral Disk? European Spine Journal. 2020;29(5):1175-80.

277. Maasumi K, Tehranzadeh J, Muftuler LT, Gardner V, Hasso AN. Assessment of the Correlation between Apparent Diffusion Coefficient and Intervertebral Disk Degeneration Using 3 Tesla MRI. Neuroradiology Journal. 2011;24(4):593-602.

278. Maatta J, Kautiainen H, Leinonen V, Niinimaki J, Jarvenpaa S, Koskelainen T, et al. Association of Modic Changes with Health-Related Quality of Life among Patients Referred to Spine Surgery. Scandinavian Journal of Pain. 2014;5(1):36-40.

279. Maatta JH, Karppinen J, Paananen M, Bow C, Luk KDK, Cheung KMC, et al. Refined Phenotyping of Modic Changes: Imaging Biomarkers of Prolonged Severe Low Back Pain and Disability. Medicine. 2016;95(22):e3495.

280. Maatta JH, Karppinen JI, Luk KD, Cheung KM, Samartzis D. Phenotype Profiling of Modic Changes of the Lumbar Spine and Its Association with Other MRI Phenotypes: A Large-Scale Population-Based Study. Spine Journal: Official Journal of the North American Spine Society. 2015;15(9):1933-42.

281. Machino M, Nakashima H, Ito K, Tsushima M, Ando K, Kobayashi K, et al. Influence of Age and Gender on Intervertebral Disk Degeneration and Height in the Thoracolumbar Spine. Spine Surgery and Related Research. 2022;6(4):379-87.

282. Majeed SA, Seshadrinath NaK, Binoy KR, Raji L. Lumbar Disc Herniation: Is There an Association between Histological and Magnetic Resonance Imaging Findings? Indian Journal of Orthopaedics. 2016;50(3):234-42.

283. Mallow GM, Zepeda D, Kuzel TG, Barajas JN, Aboushaala K, Nolte MT, et al. Issls Prize in Clinical Science 2022: Epidemiology, Risk Factors and Clinical Impact of Juvenile Modic Changes in Paediatric Patients with Low Back Pain. European Spine Journal. 2022;31(5):1069-79.

284. Manabe H, Sakai T, Omichi Y, Sugiura K, Morimoto M, Tezuka F, et al. Role of Growth Plate (Apophyseal Ring Fracture) in Causing Modic Type Changes in Pediatric Low Back Pain Patients. European Spine Journal. 2021;30(9):2565-9.

285. Mardare M, Oprea M, Popa I, Zazgyva A, Niculescu M, Poenaru D. Sagittal Balance Parameters Correlate with Spinal Conformational Type and MRI Changes in Lumbar Degenerative Disc Disease: Results of a Retrospective Study. European Journal of Orthopaedic Surgery & Traumatology. 2016;26(7):735-43.

286. Marinelli NL, Haughton VM, Anderson PA. T2 Relaxation Times Correlated with Stage of Lumbar Intervertebral Disk Degeneration and Patient Age. Ajnr: American Journal of Neuroradiology. 2010;31(7):1278-82.

287. Martin JT, Oldweiler AB, Kosinski AS, Spritzer CE, Soher BJ, Erickson MM, et al. Lumbar Intervertebral Disc Diurnal Deformations and T2 and T1rho Relaxation Times Vary by Spinal Level and Disc Region. European Spine Journal. 2022;31(3):746-54.

288. Martin JT, Wesorick B, Oldweiler AB, Kosinski AS, Goode AP, Defrate LE. In Vivo Fluid Transport in Human Intervertebral Discs Varies by Spinal Level and Disc Region. JOR Spine. 2022;5(2):e1199.

289. Maurer E, Klinger C, Lorbeer R, Hefferman G, Schlett CL, Peters A, et al. Association between Cardiovascular Risk Factors and Degenerative Disc Disease of the Thoracolumbar Spine in the General Population: Results from the Kora MRI Study. Acta Radiologica. 2022;63(6):750-9.

290. Maurer E, Klinger C, Lorbeer R, Rathmann W, Peters A, Schlett CL, et al. Long-Term Effect of Physical Inactivity on Thoracic and Lumbar Disc Degeneration-an MRI-Based Analysis of 385 Individuals from the General Population. Spine Journal: Official Journal of the North American Spine Society. 2020;20(9):1386-96.

291. Mazza E, Marcia S, Mondaini F, Piras E, Giordan N, Torri T, et al. Efficacy and Safety of a Novel Hydrogel (Hyadd4-G) in Degenerative Disc Disease Patients: A Multicentric Open Label Study. European Review for Medical & Pharmacological Sciences. 2020;24(5):2692-703.

292. Mcsweeney TP, Tiulpin A, Saarakkala S, Niinimaki J, Windsor R, Jamaludin A, et al. External Validation of Spinenet, an Open-Source Deep Learning Model for Grading Lumbar Disk Degeneration MRI Features, Using the Northern Finland Birth Cohort 1966. Spine. 2023;48(7):484-91.

293. Meadows KD, Peloquin JM, Newman HR, Cauchy PJK, Vresilovic EJ, Elliott DM. MRI-Based Measurement of in Vivo Disc Mechanics in a Young Population Due to Flexion, Extension, and Diurnal Loading. JOR Spine. 2023;6(1):e1243.

294. Menezes-Reis R, Bonugli GP, Dalto VF, Da Silva Herrero CFP, Aparecido Defino HL, Nogueira-Barbosa MH, et al. Association between Lumbar Spine Sagittal Alignment and L4-L5 Disc Degeneration among Asymptomatic Young Adults. Spine (03622436). 2016;41(18):E1081-E7.

295. Menezes-Reis R, Salmon CE, Carvalho CS, Bonugli GP, Chung CB, Nogueira-Barbosa MH. T1rho and T2 Mapping of the Intervertebral Disk: Comparison of Different Methods of Segmentation. Ajnr: American Journal of Neuroradiology. 2015;36(3):606-11.

296. Mera Y, Teraguchi M, Hashizume H, Oka H, Muraki S, Akune T, et al. Association between Types of Modic Changes in the Lumbar Region and Low Back Pain in a Large Cohort: The Wakayama Spine Study. European Spine Journal. 2021;30(4):1011-7.

297. Mertimo T, Karppinen J, Niinimaki J, Blanco R, Maatta J, Kankaanpaa M, et al. Association of Lumbar Disc Degeneration with Low Back Pain in Middle Age in the Northern Finland Birth Cohort 1966. BMC Musculoskeletal Disorders. 2022;23(1):359.

298. Mesregah MK, Lee H, Roberts S, Gardner C, Shah I, Buchanan IA, et al. Evaluation of Facet Joints and Segmental Motion in Patients with Different Grades of L5/S1 Intervertebral Disc Degeneration: A Kinematic MRI Study. European Spine Journal. 2020;29(10):2609-18.

299. Michopoulou S, Costaridou L, Vlychou M, Speller R, Todd-Pokropek A. Texture-Based Quantification of Lumbar Intervertebral Disc Degeneration from Conventional T2-Weighted MRI. Acta Radiologica. 2011;52(1):91-8.

300. Middendorp M, Vogl TJ, Kollias K, Kafchitsas K, Khan MF, Maataoui A. Association between Intervertebral Disc Degeneration and the Oswestry Disability Index. Journal of Back & Musculoskeletal Rehabilitation. 2017;30(4):819-23.

301. Miki T, Naoki F, Takashima H, Takebayashi T. Associations between Paraspinal Muscle Morphology, Disc Degeneration, and Clinical Features in Patients with Lumbar Spinal Stenosis. Progress in Rehabilitation Medicine. 2020;5:20200015.

302. Milgrom Y, Milgrom C, Constantini N, Applbaum Y, Radeva-Petrova D, Finestone AS. The Effect of Very High Versus Very Low Sustained Loading on the Lower Back and Knees in Middle Life. BioMed Research International. 2013;2013:921830.

303. Min HK, He W, Tsai YD, Chen NF, Keorochana G, Do DH, et al. Relationship of Facet Tropism with Degeneration and Stability of Functional Spinal Unit. Yonsei Medical Journal. 2009;50(5):624-9.

304. Min HK, Hymanson HJ, Kwan YS, Dong KC, Yong EC, Do HY, et al. Kinetic Magnetic Resonance Imaging Analysis of Abnormal Segmental Motion of the Functional Spine Unit: Clinical Article. Journal of Neurosurgery: Spine. 2009;10(4):357-65.

305. Minetama M, Kawakami M, Teraguchi M, Matsuo S, Enyo Y, Nakagawa M, et al. MRI Grading of Spinal Stenosis Is Not Associated with the Severity of Low Back Pain in Patients with Lumbar Spinal Stenosis. BMC Musculoskeletal Disorders. 2022;23(1):857.

306. Minetama M, Kawakami M, Teraguchi M, Matsuo S, Sumiya T, Nakagawa M, et al. Endplate Defects, Not the Severity of Spinal Stenosis, Contribute to Low Back Pain in Patients with Lumbar Spinal Stenosis. The spine journal : official journal of the North American Spine Society. 2021;29.

307. Morishita Y, Buser Z, D'oro A, Shiba K, Wang JC. Clinical Relationship of Degenerative Changes between the Cervical and Lumbar Spine. Asian Spine Journal. 2018;12(2):343-8.

308. Morishita Y, Ohta H, Naito M, Matsumoto Y, Huang G, Tatsumi M, et al. Kinematic Evaluation of the Adjacent Segments after Lumbar Instrumented Surgery: A Comparison between Rigid Fusion and Dynamic Non-Fusion Stabilization. European Spine Journal. 2011;20(9):1480-5.

309. Moser M, Adl Amini D, Albertini Sanchez L, Oezel L, Haffer H, Muellner M, et al. The Association between Vertebral Endplate Defects, Subchondral Bone Marrow Changes, and Lumbar Intervertebral Disc Degeneration: A Retrospective, 3-Year Longitudinal Study. European Spine Journal. 2023;11:11.

310. Muellner M, Haffer H, Chiapparelli E, Dodo Y, Tan ET, Shue J, et al. Differences in Lumbar Paraspinal Muscle Morphology in Patients with Sagittal Malalignment Undergoing Posterior Lumbar Fusion Surgery. European Spine Journal. 2022;31(11):3109-18.

311. Muftuler LT, Jarman JP, Yu HJ, Gardner VO, Maiman DJ, Arpinar VE. Association between Intervertebral Disc Degeneration and Endplate Perfusion Studied by Dce-MRI. European Spine Journal. 2015;24(4):679-85.

312. Munarriz PM, Paredes I, Alen JF, Castano-Leon AM, Cepeda S, Hernandez-Lain A, et al. [Assessment of the Correlation between Histological Degeneration and Radiological and Clinical Parameters in a Series of Patients Who Underwent Lumbar Disc Herniation Surgery]. Neurocirugia (English Edition). 2018;29(2):79-85.

313. Munns JJ, An HS, Oias AaE, Andersson GJ, Takatori BR, Inoue N. Ligamentum Flavum Hyperthropy Related to Disc Degeneration. Spine Journal. 2010;1):76S.

314. Murata K, Akeda K, Takegami N, Cheng K, Masuda K, Sudo A. Morphology of Intervertebral Disc Ruptures Evaluated by Vacuum Phenomenon Using Multi-Detector Computed Tomography: Association with Lumbar Disc Degeneration and Canal Stenosis. BMC Musculoskeletal Disorders. 2018;19(1):164.

315. Nagashima M, Abe H, Amaya K, Matsumoto H, Yanaihara H, Nishiwaki Y, et al. A Method for Quantifying Intervertebral Disc Signal Intensity on T2-Weighted Imaging. Acta Radiologica. 2012;53(9):1059-65.

316. Niemeyer F, Galbusera F, Tao Y, Kienle A, Beer M, Wilke HJ. A Deep Learning Model for the Accurate and Reliable Classification of Disc Degeneration Based on MRI Data. Investigative Radiology. 2021;56(2):78-85.

317. Niinimaki JL, Parviainen O, Ruohonen J, Ojala RO, Kurunlahti M, Karppinen J, et al. In Vivo Quantification of Delayed Gadolinium Enhancement in the Nucleus Pulposus of Human Intervertebral Disc. Journal of Magnetic Resonance Imaging. 2006;24(4):796-800.

318. Niu G, Yang J, Wang R, Dang S, Wu EX, Guo Y. Mr Imaging Assessment of Lumbar Intervertebral Disk Degeneration and Age-Related Changes: Apparent Diffusion Coefficient Versus T2 Quantitation. Ajnr: American Journal of Neuroradiology. 2011;32(9):1617-23.

319. Nohara A, Kawakami N, Seki K, Tsuji T, Ohara T, Saito T, et al. The Effects of Spinal Fusion on Lumbar Disc Degeneration in Patients with Adolescent Idiopathic Scoliosis: A Minimum 10-Year Follow-Up. Spine Deformity. 2015;3(5):462-8.

320. Nordberg CL, Boesen M, Fournier GL, Bliddal H, Hansen P, Hansen BB. Positional Changes in Lumbar Disc Herniation During Standing or Lumbar Extension: A Cross-Sectional Weight-Bearing MRI Study. European Radiology. 2021;31(2):804-12.

321. Ohashi M, Watanabe K, Hirano T, Hasegawa K, Katsumi K, Tashi H, et al. Impact of the Flexibility of the Spinal Deformity on Low Back Pain and Disc Degeneration in Adult Patients Nonoperatively Treated for Adolescent Idiopathic Scoliosis with Thoracolumbar or Lumbar Curves. Spine Deformity. 2022;10(1):133-40.

322. Oldweiler AB, Martin JT. In Vivo Relationships between Lumbar Facet Joint and Intervertebral Disc Composition and Diurnal Deformation. Clinical Biomechanics. 2021;88:105425.

323. Oprea M, Popa I, Cimpean AM, Raica M, Poenaru DV. Microscopic Assessment of Degenerated Intervertebral Disc: Clinical Implications and Possible Therapeutic Challenge. In Vivo. 2015;29(1):95-102.

324. Otluoglu GD, Konya D, Toktas ZO. The Influence of Mechanic Factors Idisc Degeneration Disease as a Determinant for Surgical Indication. Neurospine. 2020;17(1):215-20.

325. Ozcan-Eksi EE, Eksi MS, Akcal MA. Severe Lumbar Intervertebral Disc Degeneration Is Associated with Modic Changes and Fatty Infiltration in the Paraspinal Muscles at All Lumbar Levels, except for L1-L2: A Cross-Sectional Analysis of 50 Symptomatic Women and 50 Age-Matched Symptomatic Men. World Neurosurgery. 2019;122:e1069-e77.

326. Ozcan-Eksi EE, Eksi MS, Turgut VU, Canbolat C, Pamir MN. Reciprocal Relationship between Multifidus and Psoas at L4-L5 Level in Women with Low Back Pain. British journal of neurosurgery. 2020:1-9.

327. Ozcan-Eksi EE, Kara M, Berikol G, Orhun O, Turgut VU, Eksi MS. A New Radiological Index for the Assessment of Higher Body Fat Status and Lumbar Spine Degeneration. Skeletal Radiology. 2022;51(6):1261-71.

328. Ozcan-Eksi EE, Turgut VU, Kucuksuleymanoglu D, Eksi MS. Obesity Could Be Associated with Poor Paraspinal Muscle Quality at Upper Lumbar Levels and Degenerated Spine at Lower Lumbar Levels: Is This a Domino Effect? Journal of Clinical Neuroscience. 2021;94:120-7.

329. Ozcan-Eksi EE, Yayla A, Orhun O, Turgut VU, Arslan HN, Eksi MS. Is the Distribution Pattern of Modic Changes in Vertebral End-Plates Associated with the Severity of Intervertebral Disc Degeneration?: A Cross-Sectional Analysis of 527 Caucasians. World Neurosurgery. 2021;150:e298-e304.

330. Paholpak P, Dedeogullari E, Lee C, Tamai K, Barkoh K, Sessumpun K, et al. Do Modic Changes, Disc Degeneration, Translation and Angular Motion Affect Facet Osteoarthritis of the Lumbar Spine. European Journal of Radiology. 2018;98:193-9.

331. Carrino JA, Lurie JD, Herzog R, Tosteson ANA, Tosteson TD, Carragee EJ, et al. Lumbar Spine: Reliability of Mr Imaging Findings. Radiology. 2009;250(1):161-70.

332. Duran S, Cavusoglu M, Hatipoglu HG, Sozmen Ciliz D, Sakman B. Association between Measures of Vertebral Endplate Morphology and Lumbar Intervertebral Disc Degeneration. Canadian Association of Radiologists Journal. 2017;68(2):210-6.

333. Pan J, Lu X, Yang G, Han Y, Tong X, Wang Y. Lumbar Disc Degeneration Was Not Related to Spine and Hip Bone Mineral Densities in Chinese: Facet Joint Osteoarthritis May Confound the Association. Archives of Osteoporosis. 2017;12(1):20.

334. Papic M, Papic V, Kresoja M, Munteanu V, Mikov I, Cigic T. Relation between Grades of Intervertebral Disc Degeneration and Occupational Activities of Patients with Lumbar Disc Herniation. Vojnosanitetski Pregled. 2017;74(12):1121-7.

335. Pappou IP, Cammisa FP, Jr., Girardi FP. Correlation of End Plate Shape on MRI and Disc Degeneration in Surgically Treated Patients with Degenerative Disc Disease and Herniated Nucleus Pulposus. Spine Journal: Official Journal of the North American Spine Society. 2007;7(1):32-8.

336. Park C, Ryu K, Jee W. Degenerative Changes of Discs and Facet Joints in Lumbar Total Disc Replacement Using Prodisc Ii: Minimum Two-Year Follow-Up. Spine (03622436). 2008;33(16):1755-61.

337. Pfirrmann CWA, Metzdorf A, Elfering A, Hodler J, Boos N. Effect of Aging and Degeneraton on Disc Volume and Shape: A Quantitative Study in Asymptomatic Volunteers. Journal of Orthopaedic Research. 2006;24(5):1086-94.

338. Pfirrmann CWA, Metzdorf A, Zanetti M, Hodler J, Boos N. Magnetic Resonance Classification of Lumbar Intervertebral Disc Degeneration. Spine (Philadelphia, Pa 1976). 2001;26(17):1873-8.

339. Pinson H, Hallaert G, Herregodts P, Everaert K, Couvreur T, Caemaert J, et al. Outcome of Anterior Lumbar Interbody Fusion: A Retrospective Study of Clinical and Radiologic Parameters. World Neurosurgery. 2017;103:772-9.

340. Rajasekaran S, Kanna RM, Senthil N, Raveendran M, Ranjani V, Cheung KM, et al. Genetic Susceptibility of Lumbar Degenerative Disc Disease in Young Indian Adults. European Spine Journal. 2015;24(9):1969-75.

341. Raudner M, Schreiner MM, Juras V, Weber M, Stelzeneder D, Kronnerwetter C, et al. Prediction of Lumbar Disk Herniation and Clinical Outcome Using Quantitative Magnetic Resonance Imaging: A 5-Year Follow-up Study. Investigative Radiology. 2019;54(3):183-9.

342. Raudner M, Toth DF, Schreiner MM, Hilbert T, Kober T, Juras V, et al. Synthetic T₂-Weighted Images of the Lumbar Spine Derived from an Accelerated T₂ Mapping Sequence: Comparison to Conventional T₂W Turbo Spin Echo. Magnetic Resonance Imaging. 2021;84:92-100.

343. Ravikanth R. Magnetic Resonance Evaluation of Lumbar Disc Degenerative Disease as an Implication of Low Back Pain: A Prospective Analysis. Neurology India. 2020;68(6):1378-84.

344. Reyes-Sanchez A, Zarate-Kalfopulos B, Ramirez-Mora I, Rosales-Olivarez LM, Alpizar-Aguirre A, Sanchez-Bringas G. Posterior Dynamic Stabilization of the Lumbar Spine with the Accuflex Rod System as a Stand-Alone Device: Experience in 20 Patients with 2-Year Follow-Up. European Spine Journal. 2010;19(12):2164-70.

345. Rigal J, Thelen T, Byrne F, Cogniet A, Boissière L, Aunoble S, et al. Prospective Study Using Anterior Approach Did Not Show Association between Modic 1 Changes and Low Grade Infection in Lumbar Spine. European Spine Journal. 2016;25(4):1000-5.

346. Roberts S, Gardner C, Jiang Z, Abedi A, Buser Z, Wang JC. Analysis of Trends in Lumbar Disc Degeneration Using Kinematic MRI. Clinical Imaging. 2021;79:136-41.

347. Rodriguez-Soto AE, Berry DB, Jaworski R, Jensen A, Chung CB, Niederberger B, et al. The Effect of Training on Lumbar Spine Posture and Intervertebral Disc Degeneration in Active-Duty Marines. Ergonomics. 2017;60(8):1055-63.

348. Roller BL, Boutin RD, O'gara TJ, Knio ZO, Jamaludin A, Tan J, et al. Accurate Prediction of Lumbar Microdecompression Level with an Automated MRI Grading System. Skeletal Radiology. 2021;50(1):69-78.

349. Ruangchainikom M, Daubs MD, Suzuki A, Xiong C, Hayashi T, Scott TP, et al. Patterns of Lumbar Disc Degeneration: Magnetic Resonance Imaging Analysis in Symptomatic Subjects. Asian Spine Journal. 2021;15(6):799-807.

350. Salamat S, Hutchings J, Kwong C, Magnussen J, Hancock MJ. The Relationship between Quantitative Measures of Disc Height and Disc Signal Intensity with Pfirrmann Score of Disc Degeneration. Springerplus. 2016;5(1):829.

351. Salo S, Hurri H, Rikkonen T, Sund R, Kroger H, Sirola J. Association between Severe Lumbar Disc Degeneration and Self-Reported Occupational Physical Loading. Journal of Occupational Health. 2022;64(1):e12316.

352. Salo S, Leinonen V, Rikkonen T, Vainio P, Marttila J, Honkanen R, et al. Association between Bone Mineral Density and Lumbar Disc Degeneration. Maturitas. 2014;79(4):449-55.

353. Sandor Z, Rathonyi GK, Dinya E. Assessment of Lumbar Lordosis Distribution with a Novel Mathematical Approach and Its Adaptation for Lumbar Intervertebral Disc Degeneration. Computational & Mathematical Methods in Medicine. 2020;2020:7312125.

354. Sandor Z, Rathonyi GK, Dinya E. Relationship between the Distribution of Lumbar Lordosis and the Average Degeneration of Intervertebral Discs. [Hungarian]. Orvosi Hetilap. 2020;161(31):1286-92.

355. Schroeder GD, Mendoza M, Daley E, La Bella C, Savage JW, Patel AA, et al. The Role of Athletic Activity on Structural Lumbar Abnormalities in Adolescent Patients with Symptomatic Low Back Pain. Spine Journal. 2014;1):S139.

356. Schwarz-Nemec U, Friedrich KM, Prayer D, Trattnig S, Schwarz FK, Weber M, et al. Lumbar Intervertebral Disc Degeneration as a Common Incidental Finding in Young Pregnant Women as Observed on Prenatal Magnetic Resonance Imaging. Journal of Women's Health. 2020;29(5):713-20.

357. Seyithanoglu MH, Kitis S, Ozer OF, Kocyigit A, Dundar T, Gundag Papaker M, et al. Comparison of the Biochemical and Radiological Criteria for Lumbar Disc Degeneration. Neurologia i Neurochirurgia Polska. 2018;52(5):570-4.

358. Sharma A, Pilgram T, Wippold FJ, 2nd. Association between Annular Tears and Disk Degeneration: A Longitudinal Study. Ajnr: American Journal of Neuroradiology. 2009;30(3):500-6.

359. Sharma A, Sargar K, Salter A. Temporal Evolution of Disc in Young Patients with Low Back Pain and Stress Reaction in Lumbar Vertebrae. Ajnr: American Journal of Neuroradiology. 2017;38(8):1647-52.

360. Sharma A, Walk RE, Tang SY, Eldaya R, Owen PJ, Belavy DL. Variability of T2-Relaxation Times of Healthy Lumbar Intervertebral Discs Is More Homogeneous within an Individual Than across Healthy Individuals. Ajnr: American Journal of Neuroradiology. 2020;41(11):2160-5.

361. Shu-Hua Y, Orías AaE, Chien-Chou P, Senoo I, Andersson GBJ, An HS, et al. Spatial Geometric and Magnetic Resonance Signal Intensity Changes with Advancing Stages of Nucleus Pulposus Degeneration. BMC Musculoskeletal Disorders. 2017;18:1-6.

362. Singh R, Kumar P, Wadhwani J, Yadav RK, Khanna M, Kaur S. A Comparative Study to Evaluate Disc Degeneration on Magnetic Resonance Imaging in Patients with Chronic Low Back Pain and Asymptomatic Individuals. Journal of Orthopaedics, Trauma and Rehabilitation. 2021;28(no pagination).

363. Smith A, Hancock M, O'hanlon S, Krieser M, O'sullivan P, Cicuttini F, et al. The Association between Different Trajectories of Low Back Pain and Degenerative Imaging Findings in Young Adult Participants within the Raine Study. Spine (Philadelphia, Pa 1976). 2022;47(3):269-76.

364. Soh J, Lee JC, Shin BJ. Analysis of Risk Factors for Adjacent Segment Degeneration Occurring More Than 5 Years after Fusion with Pedicle Screw Fixation for Degenerative Lumbar Spine. Asian Spine Journal. 2013;7(4):273-81.

365. Son S, Lee SG, Kim WK, Ahn Y, Jung JM. Disc Height Discrepancy between Supine and Standing Positions as a Screening Metric for Discogenic Back Pain in Patients with Disc Degeneration. Spine Journal: Official Journal of the North American Spine Society. 2021;21(1):71-9.

366. Song J, Pan F, Kong C, Sun X, Wang Y, Wang W, et al. Does the Sagittal Spinal Profile Differ between the Elderly Chinese Populations with and without Lumbar Disc Herniation? Asian Journal of Surgery. 2022;45(12):2719-24.

367. Song Q, Liu X, Chen DJ, Lai Q, Tang B, Zhang B, et al. Evaluation of MRI and Ct Parameters to Analyze the Correlation between Disc and Facet Joint Degeneration in the Lumbar Three-Joint Complex. Medicine. 2019;98(40):e17336.

368. Splendiani A, Bruno F, Marsecano C, Arrigoni F, Di Cesare E, Barile A, et al. Modic I Changes Size Increase from Supine to Standing MRI Correlates with Increase in Pain Intensity in Standing Position: Uncovering the "Biomechanical Stress" and "Active Discopathy" Theories in Low Back Pain. European Spine Journal. 2019;28(5):983-92.

369. Stelzeneder D, Welsch GH, Kovacs BK, Goed S, Paternostro-Sluga T, Vlychou M, et al. Quantitative T2 Evaluation at 3.0T Compared to Morphological Grading of the Lumbar Intervertebral Disc: A Standardized Evaluation Approach in Patients with Low Back Pain. European Journal of Radiology. 2012;81(2):324-30.

370. Stosch-Wiechert K, Wuertz-Kozak K, Hitzl W, Szeimies U, Stabler A, Siepe CJ. Clinical and Radiological Mid- to Long-Term Investigation of Anterior Lumbar Stand-Alone Fusion: Incidence of Reoperation and Adjacent Segment Degeneration. Brain & Spine. 2022;2:100924.

371. Su Y, Ren D, Liu D, Li J, Wang T, Qi W, et al. Effects of Endplate Healing Morphology on Intervertebral Disc Degeneration after Pedicle Screw Fixation for Thoracolumbar Fractures. Medicine. 2021;100(17):e25636.

372. Sudhir G, Jayabalan V, Sellayee S, Gadde S, Kailash K. Is There an Interdependence between Paraspinal Muscle Mass and Lumbar Disc Degeneration? A MRI Based Study at 2520 Levels in 504 Patients. Journal of Clinical Orthopaedics & Trauma. 2021;22:101576.

373. Sun S, Tan ET, Mintz DN, Sahr M, Endo Y, Nguyen J, et al. Evaluation of Deep Learning Reconstructed High-Resolution 3d Lumbar Spine MRI. European Radiology. 2022;32(9):6167-77.

374. Takahashi S, Lord EL, Hayashi T, Cohen JR, Lao L, Yao Q, et al. Radiologic Factors Associated with the Dynamic Change of Dural Sac Diameter in Lumbar Spine: A Kinematic MRI Study. Clinical Spine Surgery : A Spine Publication. 2017;30(6):E827-E32.

375. Takashima H, Yoshimoto M, Ogon I, Takebayashi T, Imamura R, Akatsuka Y, et al. T1rho, T2, and T2* Relaxation Time Based on Grading of Intervertebral Disc Degeneration. Acta Radiologica. 2022.

376. Takashima H, Yoshimoto M, Ogon I, Terashima Y, Imamura R, Akatsuka Y, et al. Lumbar Disc Degeneration Assessment Using T2* Relaxation Time with Ultra-Short Te. Magnetic Resonance Imaging. 2020;73:11-4.

377. Takatalo J, Karppinen J, Nayha S, Taimela S, Niinimaki J, Blanco Sequeiros R, et al. Association between Adolescent Sport Activities and Lumbar Disk Degeneration among Young Adults. Scandinavian Journal of Medicine & Science in Sports. 2017;27(12):1993-2001.

378. Takatalo J, Karppinen J, Niinimäki J, Taimela S, Näyhä S, Järvelin MR, et al. Prevalence of Degenerative Imaging Findings in Lumbar Magnetic Resonance Imaging among Young Adults. Spine (03622436). 2009;34(16):1716-21.

379. Takatalo J, Karppinen J, Niinimaki J, Taimela S, Nayha S, Mutanen P, et al. Does Lumbar Disc Degeneration on Magnetic Resonance Imaging Associate with Low Back Symptom Severity in Young Finnish Adults? Spine. 2011;36(25):2180-9.

380. Takatalo J, Karppinen J, Taimela S, Niinimaki J, Laitinen J, Blanco Sequeiros R, et al. Body Mass Index Is Associated with Lumbar Disc Degeneration in Young Finnish Males: Subsample of Northern Finland Birth Cohort Study 1986. BMC Musculoskeletal Disorders. 2013;14:87.

381. Takatalo J, Karppinen J, Taimela S, Niinimaki J, Laitinen J, Sequeiros RB, et al. Association of Abdominal Obesity with Lumbar Disc Degeneration--a Magnetic Resonance Imaging Study. PLoS ONE [Electronic Resource]. 2013;8(2):e56244.

382. Takegami N, Akeda K, Murata K, Yamada J, Sudo A. Association between Non-Traumatic Vertebral Fractures and Adjacent Discs Degeneration: A Cross-Sectional Study and Literature Review. BMC Musculoskeletal Disorders. 2020;21(1):781.

383. Takeuchi M, Nagamachi A, Adachi K, Inoue K, Tamaki Y, Omichi Y, et al. Prevalence of High-Intensity Zones in the Lumbar Spine According to Age and Their Correlation with Other Degenerative Findings on Magnetic Resonance Imaging. Spine Surgery & Related Research. 2018;2(4):299-303.

384. Tan Y, Aghdasi BG, Montgomery SR, Inoue H, Lu C, Wang JC. Kinetic Magnetic Resonance Imaging Analysis of Lumbar Segmental Mobility in Patients without Significant Spondylosis. European Spine Journal. 2012;21(12):2673-9.

385. Tarnoki AD, Tarnoki DL, Olah C, Szily M, Kovacs DT, Dienes A, et al. Lumbar Spine Abnormalities in Patients with Obstructive Sleep Apnoea. Scientific Reports. 2021;11(1):16233.

386. Teichtahl AJ, Finnin MA, Wang Y, Wluka AE, Urquhart DM, O'sullivan R, et al. The Natural History of Modic Changes in a Community-Based Cohort. Joint, Bone, Spine: Revue du Rhumatisme. 2017;84(2):197-202.

387. Teichtahl AJ, Urquhart DM, Wang Y, Wluka AE, Heritier S, Cicuttini FM. A Dose-Response Relationship between Severity of Disc Degeneration and Intervertebral Disc Height in the Lumbosacral Spine. Arthritis Research & Therapy. 2015;17:297.

388. Teichtahl AJ, Urquhart DM, Wang Y, Wluka AE, O'sullivan R, Jones G, et al. Lumbar Disc Degeneration Is Associated with Modic Change and High Paraspinal Fat Content - a 3.0t Magnetic Resonance Imaging Study. BMC Musculoskeletal Disorders. 2016;17(1):439.

389. Teraguchi M, Cheung JPY, Karppinen J, Bow C, Hashizume H, Luk KDK, et al. Lumbar High-Intensity Zones on MRI: Imaging Biomarkers for Severe, Prolonged Low Back Pain and Sciatica in a Population-Based Cohort. Spine Journal: Official Journal of the North American Spine Society. 2020;20(7):1025-34.

390. Teraguchi M, Samartzis D, Hashizume H, Yamada H, Muraki S, Oka H, et al. Classification of High Intensity Zones of the Lumbar Spine and Their Association with Other Spinal MRI Phenotypes: The Wakayama Spine Study. PLoS ONE [Electronic Resource]. 2016;11(9):e0160111.

391. Teraguchi M, Yoshimura N, Hashizume H, Muraki S, Yamada H, Oka H, et al. Metabolic Syndrome Components Are Associated with Intervertebral Disc Degeneration: The Wakayama Spine Study. PLoS ONE. 2016;11(2) (no pagination).

392. Teraguchi M, Yoshimura N, Hashizume H, Muraki S, Yamada H, Oka H, et al. The Association of Combination of Disc Degeneration, End Plate Signal Change, and Schmorl Node with Low Back Pain in a Large Population Study: The Wakayama Spine Study. Spine Journal: Official Journal of the North American Spine Society. 2015;15(4):622-8.

393. Teraguchi M, Yoshimura N, Hashizume H, Yamada H, Oka H, Minamide A, et al. Progression, Incidence, and Risk Factors for Intervertebral Disc Degeneration in a Longitudinal Population-Based Cohort: The Wakayama Spine Study. Osteoarthritis & Cartilage. 2017;25(7):1122-31.

394. Tonosu J, Oka H, Higashikawa A, Okazaki H, Tanaka S, Matsudaira K. The Associations between Magnetic Resonance Imaging Findings and Low Back Pain: A 10-Year Longitudinal Analysis. PLoS ONE [Electronic Resource]. 2017;12(11):e0188057.

395. Tonosu J, Oka H, Matsudaira K, Higashikawa A, Okazaki H, Tanaka S. The Relationship between Findings on Magnetic Resonance Imaging and Previous History of Low Back Pain. Journal of pain research. 2017;10:47-52.

396. Toren L, Hebelka H, Kasperska I, Brisby H, Lagerstrand K. With Axial Loading During MRI Diurnal T2-Value Changes in Lumbar Discs Are Neglectable: A Cross Sectional Study. BMC Musculoskeletal Disorders. 2018;19(1) (no pagination).

397. Torrie PaG, Mckay G, Bryne R, Morris SJ, Harding IJ. The Influence of Lumbar Spine Subtype on Lumbar Intervertebral Disc Degeneration in Young and Middle-Aged Adults. European Spine Journal. 2014;1):S131.

398. Udby PM, Ohrt-Nissen S, Bendix T, Brorson S, Carreon LY, Andersen MO. The Association of MRI Findings and Long-Term Disability in Patients with Chronic Low Back Pain. Global Spine Journal. 2021;11(5):633-9.

399. Urrutia J, Besa P, Campos M, Cikutovic P, Cabezon M, Molina M, et al. The Pfirrmann Classification of Lumbar Intervertebral Disc Degeneration: An Independent Inter- and Intra-Observer Agreement Assessment. European Spine Journal. 2016;25(9):2728-33.

400. Urrutia J, Besa P, Lobos D, Campos M, Arrieta C, Andia M, et al. Lumbar Paraspinal Muscle Fat Infiltration Is Independently Associated with Sex, Age, and Inter-Vertebral Disc Degeneration in Symptomatic Patients. Skeletal Radiology. 2018;47(7):955-61.

401. Urrutia J, Zamora T, Prada C. The Prevalence of Degenerative or Incidental Findings in the Lumbar Spine of Pediatric Patients: A Study Using Magnetic Resonance Imaging as a Screening Tool. European Spine Journal. 2016;25(2):596-601.

402. Vadala G, Russo F, Battisti S, Stellato L, Martina F, Del Vescovo R, et al. Early Intervertebral Disc Degeneration Changes in Asymptomatic Weightlifters Assessed by T1rho-Magnetic Resonance Imaging. Spine. 2014;39(22):1881-6.

403. Vaga S, Brayda-Bruno M, Perona F, Fornari M, Raimondi MT, Petruzzi M, et al. Molecular Mr Imaging for the Evaluation of the Effect of Dynamic Stabilization on Lumbar Intervertebral Discs. European Spine Journal. 2009;18 Suppl 1:40-8.

404. Van Den Heuvel MM, Oei EHG, Renkens JJM, Bierma-Zeinstra SMA, Van Middelkoop M. Structural Spinal Abnormalities on MRI and Associations with Weight Status in a General Pediatric Population. The spine journal : official journal of the North American Spine Society. 2020;09.

405. Van Den Heuvel MM, Oei EHG, Renkens JJM, Bierma-Zeinstra SMA, Van Middelkoop M. Structural Spinal Abnormalities on MRI and Associations with Weight Status in a General Pediatric Population. Spine Journal: Official Journal of the North American Spine Society. 2021;21(3):465-76.

406. Videbaek TS, Egund N, Christensen FB, Grethe Jurik A, Bunger CE. Adjacent Segment Degeneration after Lumbar Spinal Fusion: The Impact of Anterior Column Support: A Randomized Clinical Trial with an Eight- to Thirteen-Year Magnetic Resonance Imaging Follow-Up. Spine. 2010;35(22):1955-64.

407. Videman T, Battie MC, Gibbons LE, Gill K. A New Quantitative Measure of Disc Degeneration. Spine Journal: Official Journal of the North American Spine Society. 2017;17(5):746-53.

408. Violante FS, Zompatori M, Lovreglio P, Apostoli P, Marinelli F, Bonfiglioli R. Is Age More Than Manual Material Handling Associated with Lumbar Vertebral Body and Disc Changes? A Cross-Sectional Multicentre MRI Study. BMJ Open. 2019;9(9):e029657.

409. Waldenberg C, Hebelka H, Brisby H, Lagerstrand KM. MRI Histogram Analysis Enables Objective and Continuous Classification of Intervertebral Disc Degeneration. European Spine Journal. 2018;27(5):1042-8.

410. Walter BA, Mageswaran P, Mo X, Boulter DJ, Mashaly H, Nguyen XV, et al. Mr Elastography-Derived Stiffness: A Biomarker for Intervertebral Disc Degeneration. Radiology. 2017;285(1):167-75.

411. Walter SS, Lorbeer R, Hefferman G, Schlett CL, Peters A, Rospleszcz S, et al. Correlation between Thoracolumbar Disc Degeneration and Anatomical Spinopelvic Parameters in Supine Position on MRI. PLoS ONE [Electronic Resource]. 2021;16(6):e0252385.

412. Wan ZY, Zhang J, Shan H, Liu TF, Song F, Samartzis D, et al. Epidemiology of Lumbar Degenerative Phenotypes of Children and Adolescents: A Large-Scale Imaging Study. Global Spine Journal. 2023;13(3):599-608.

413. Wang J, Zhou Y, Zhang ZF, Li CQ, Zheng WJ, Liu J. Radiological Study on Disc Degeneration of Thoracolumbar Burst Fractures Treated by Percutaneous Pedicle Screw Fixation. European Spine Journal. 2013;22(3):489-94.

414. Wang S, Yang D, Zheng G, Cao J, Zhao F, Shi J, et al. MRI Changes of Adjacent Segments after Transforaminal Lumbar Interbody Fusion (Tlif) and Foraminal Endoscopy: A Case-Control Study. Medicine. 2022;101(41):e31093.

415. Wang Y, Wang H, Lv F, Ma X, Xia X, Jiang J. Asymmetry between the Superior and Inferior Endplates Is a Risk Factor for Lumbar Disc Degeneration. Journal of Orthopaedic Research. 2018;36(9):2469-75.

416. Wang ZX, An P, Li Y, Kim SH. Analysis of Lumbar Spine MRI in Asymptomatic Chinese Adults. [Chinese]. Chinese Journal of Interventional Imaging and Therapy. 2012;9(5):371-5.

417. Wedatilake T, Palmer A, Fernquest S, Redgrave A, Arnold L, Kluzek S, et al. Association between Hip Joint Impingement and Lumbar Disc Disease in Elite Rowers. BMJ Open Sport & Exercise Medicine. 2021;7(4):e001063.

418. Welsch GH, Trattnig S, Paternostro-Sluga T, Bohndorf K, Goed S, Stelzeneder D, et al. Parametric T2 and T2 Mapping Techniques to Visualize Intervertebral Disc Degeneration in Patients with Low Back Pain: Initial Results on the Clinical Use of 3.0 Tesla MRI. Skeletal Radiology. 2011;40(5):543-51.

419. Wollschlager LM, Nebelung S, Schleich C, Muller-Lutz A, Radke KL, Frenken M, et al. Evaluating Lumbar Intervertebral Disc Degeneration on a Compositional Level Using Chemical Exchange Saturation Transfer: Preliminary Results in Patients with Adolescent Idiopathic Scoliosis. Diagnostics. 2021;11(6) (no pagination).

420. Wu LL, Liu LH, Rao SX, Wu PY, Zhou JJ. Ultrashort Time-to-Echo T2 and T2 Relaxometry for Evaluation of Lumbar Disc Degeneration: A Comparative Study. BMC Musculoskeletal Disorders. 2022;23(1):524.

421. Xiao L, Ni C, Shi J, Wang Z, Wang S, Zhang J, et al. Analysis of Correlation between Vertebral Endplate Change and Lumbar Disc Degeneration. Medical Science Monitor. 2017;23:4932-8.

422. Xingwang Y, Fei C, Chuning D, Jeffrey W, Yanlin T, Yao X, et al. Kinetic Magnetic Resonance Imaging Analysis of Thoracolumbar Segmental Mobility in Patients without Significant Spondylosis. Medicine. 2020;99(2):1-6.

423. Xiong X, Zhou Z, Figini M, Shangguan J, Zhang Z, Chen W. Multi-Parameter Evaluation of Lumbar Intervertebral Disc Degeneration Using Quantitative Magnetic Resonance Imaging Techniques. American Journal Of Translational Research. 2018;10(2):444-54.

424. Yabe Y, Hagiwara Y, Tsuchiya M, Onoda Y, Yoshida S, Onoki T, et al. Factors Associated with Thickening of the Ligamentum Flavum on Magnetic Resonance Imaging in Patients with Lumbar Spinal Canal Stenosis. Spine. 2022;47(14):1036-41.

425. Yang H, Liu H, Li Z, Zhang K, Wang J, Wang H, et al. Low Back Pain Associated with Lumbar Disc Herniation: Role of Moderately Degenerative Disc and Annulus Fibrous Tears. International journal of clinical and experimental medicine. 2015;8(2):1634-44.

426. Yang L, Sun C, Gong T, Li Q, Chen X, Zhang X. T1rho, T2 and T2 Mapping of Lumbar Intervertebral Disc Degeneration: A Comparison Study. BMC Musculoskeletal Disorders. 2022;23(1):1135.

427. Yang S, Lassalle L, Mekki A, Appert G, Rannou F, Nguyen C, et al. Can T2-Weighted Dixon Fat-Only Images Replace T1-Weighted Images in Degenerative Disc Disease with Modic Changes on Lumbar Spine MRI? European Radiology. 2021;31(12):9380-9.

428. Yang Z, Griffith JF, Leung PC, Lee R, Yang Z, Griffith JF, et al. Effect of Osteoporosis on Morphology and Mobility of the Lumbar Spine. Spine (03622436). 2009;34(3):E115-21.

429. Yin R, Lord EL, Cohen JR, Buser Z, Lao L, Zhong G, et al. Distribution of Schmorl Nodes in the Lumbar Spine and Their Relationship with Lumbar Disk Degeneration and Range of Motion. Spine. 2015;40(1):E49-53.

430. Yin R, Wang JC, Lord EL, Cohen JR, Takahashi S. Distribution of Schmorl's Nodes in the Lumbar Spine and Their Relationship with Lumbar Disc Degeneration and Range of Motion. Spine Journal. 2014;1):S108.

431. Yoon MA, Hong SJ, Kang CH, Ahn KS, Kim BH. T1rho and T2 Mapping of Lumbar Intervertebral Disc: Correlation with Degeneration and Morphologic Changes in Different Disc Regions. Magnetic Resonance Imaging. 2016;34(7):932-9.

432. Young-Min O, Jong-Pil E, Oh Y-M, Eun J-P. Clinical Impact of Sagittal Spinopelvic Parameters on Disc Degeneration in Young Adults. Medicine. 2015;94(42):1-5.

433. Yu HJ, Bahri S, Gardner V, Muftuler LT. In Vivo Quantification of Lumbar Disc Degeneration: Assessment of Adc Value Using a Degenerative Scoring System Based on Pfirrmann Framework. European Spine Journal. 2015;24(11):2442-8.

434. Yu LP, Qian WW, Yin GY, Ren YX, Hu ZY. MRI Assessment of Lumbar Intervertebral Disc Degeneration with Lumbar Degenerative Disease Using the Pfirrmann Grading Systems. PLoS ONE [Electronic Resource]. 2012;7(12):e48074.

435. Yucekul A, Akpunarli B, Durbas A, Zulemyan T, Havlucu I, Ergene G, et al. Does Vertebral Body Tethering Cause Disc and Facet Joint Degeneration? A Preliminary MRI Study with Minimum Two Years Follow-Up. Spine Journal: Official Journal of the North American Spine Society. 2021;21(11):1793-801.

436. Zehra U, Cheung JPY, Bow C, Crawford RJ, Luk KDK, Lu W, et al. Spinopelvic Alignment Predicts Disc Calcification, Displacement, and Modic Changes: Evidence of an Evolutionary Etiology for Clinically-Relevant Spinal Phenotypes. JOR Spine. 2020;3(1):e1083.

437. Zeng F, Zha Y, Li L, Xing D, Gong W, Hu L, et al. A Comparative Study of Diffusion Kurtosis Imaging and T2 Mapping in Quantitative Detection of Lumbar Intervertebral Disk Degeneration. European Spine Journal. 2019;28(9):2169-78.

438. Zhang F, Wang H, Xu H, Shao M, Lu F, Jiang J, et al. Radiologic Analysis of Kinematic Characteristics of Modic Changes Based on Lumbar Disc Degeneration Grade. World Neurosurgery. 2018;114:e851-e6.

439. Zhang J, Zhao F, Wang FL, Yang YF, Zhang C, Cao Y, et al. Identification of Lumbar Disc Disease Hallmarks: A Large Cross-Sectional Study. Springerplus. 2016;5(1):1973.

440. Zhang K, Li M, Pei X, Yuan H. Regression between Mr Findings of Lumbar Elements and Chronic Low Back Pain. [Chinese]. Chinese Journal of Radiology (China). 2014;48(12):1019-23.

441. Zhang W, Ma X, Wang Y, Zhao J, Zhang X, Gao Y, et al. Assessment of Apparent Diffusion Coefficient in Lumbar Intervertebral Disc Degeneration. European Spine Journal. 2014;23(9):1830-6.

442. Zhang X, Yang L, Gao F, Yuan Z, Lin X, Yao B, et al. Comparison of T1rho and T2* Relaxation Mapping in Patients with Different Grades of Disc Degeneration at 3t Mr. Medical Science Monitor. 2015;21:1934-41.

443. Zhao B, Huang W, Lu X, Ma X, Wang H, Lu F, et al. Association between Roussouly Classification and Characteristics of Lumbar Degeneration. World Neurosurgery. 2022;163:e565-e72.

444. Zhou L, Li C, Zhang H. Correlation between Bone Mineral Density of Different Sites and Lumbar Disc Degeneration in Postmenopausal Women. 2022;1(13):e28947.

445. Zobel BB, Vadalà G, Del Vescovo R, Battisti S, Martina FM, Stellato L, et al. T1ρ Magnetic Resonance Imaging Quantification of Early Lumbar Intervertebral Disc Degeneration in Healthy Young Adults. Spine (03622436). 2012;37(14):1224-30.

446. Zou J, Yang H, Miyazaki M, Morishita Y, Wei F, Mcgovern S, et al. Dynamic Bulging of Intervertebral Discs in the Degenerative Lumbar Spine. 2009;1(23):2545-50.

447. Munir S, Freidin MB, Rade M, Maatta J, Livshits G, Williams FMK. Endplate Defect Is Heritable, Associated with Low Back Pain and Triggers Intervertebral Disc Degeneration: A Longitudinal Study from Twinsuk. Spine. 2018;43(21):1496-501.

448. Perry J, Haughton V, Anderson PA, Wu Y, Fine J, Mistretta C. The Value of T2 Relaxation Times to Characterize Lumbar Intervertebral Disks: Preliminary Results. Ajnr: American Journal of Neuroradiology. 2006;27(2):337-42.

449. Rade M, Maatta JH, Freidin MB, Airaksinen O, Karppinen J, Williams FMK. Vertebral Endplate Defect as Initiating Factor in Intervertebral Disc Degeneration. Spine. 2018;43(6):412-9.

450. Togao O, Hiwatashi A, Wada T, Yamashita K, Kikuchi K, Tokunaga C, et al. A Qualitative and Quantitative Correlation Study of Lumbar Intervertebral Disc Degeneration Using Glycosaminoglycan Chemical Exchange Saturation Transfer, Pfirrmann Grade, and T1-Rho. Ajnr: American Journal of Neuroradiology. 2018;39(7):1369-75.

451. Wang YX, Zhao F, Griffith JF, Mok GS, Leung JC, Ahuja AT, et al. T1rho and T2 Relaxation Times for Lumbar Disc Degeneration: An in Vivo Comparative Study at 3.0-Tesla MRI. European Radiology. 2013;23(1):228-34.

452. Huang J, Shen H, Wu J, Hu X, Zhu Z, Lv X, et al. Spine Explorer: A Deep Learning Based Fully Automated Program for Efficient and Reliable Quantifications of the Vertebrae and Discs on Sagittal Lumbar Spine Mr Images. Spine Journal: Official Journal of the North American Spine Society. 2020;20(4):590-9.

453. Chadha M, Srivastava A, Kumar V, Tandon A. Disc Degeneration in Lumbar Spine of Asymptomatic Young Adults: A Descriptive Cross-Sectional Study. Indian Journal of Orthopaedics. 2022;56(6):1083-9.

454. Chao L, Hongliang C, Liangwei M, Weiyang Y, Kejun Z, Feijun L, et al. Association between Menopause and Lumbar Disc Degeneration: An MRI Study of 1,566 Women and 1,382 Men. Menopause (10723714). 2017;24(10):1136-44.

455. Coppock JA, Zimmer NE, Englander ZA, Danyluk ST, Kosinski AS, Spritzer CE, et al. In Vivo Intervertebral Disc Mechanical Deformation Following a Treadmill Walking "Stress Test" Is Inversely Related to T1rho Relaxation Time. Osteoarthritis & Cartilage. 2023;31(1):126-33.

456. Coskun H, Turan A, Kaplanoglu H, Kaplanoglu V. Frequency of Hypoplasia of the Vertebral Body at L5, and Its Relationship with Degeneration in Patients with Low Back Pain. Turkish Neurosurgery. 2022;32(4):641-8.

457. Deane JA, Lim AKP, Mcgregor AH, Strutton PH. Understanding the Impact of Lumbar Disc Degeneration and Chronic Low Back Pain: A Cross-Sectional Electromyographic Analysis of Postural Strategy During Predicted and Unpredicted Postural Perturbations. PLoS ONE [Electronic Resource]. 2021;16(4):e0249308.

458. Dujic MK, Recnik G, Milcic M, Bosnjak E, Rupreht M. MRI Assessment of the Early Disc Degeneration Two Levels above Fused Lumbar Spine Segment: A Comparison after Unilateral and Bilateral

Transforaminal Lumbar Interbody Fusion (Tlif) Procedure. Journal of Clinical Medicine. 2022;11(14):07.

459. Garcia Isidro M, Ferreiro Perez A, Fernandez Lopez-Pelaez MS, Moeinvaziri M, Fernandez Garcia P. Differences in MRI Measurements of Lateral Recesses and Foramina in Degenerative Lumbar Segments in Upright Versus Decubitus Symptomatic Patients. Radiologia. 2021;01:01.

460. Guan J, Liu T, Yu X, Feng N, Jiang G, Li W, et al. Isobar Hybrid Dynamic Stabilization with Posterolateral Fusion in Mild and Moderate Lumbar Degenerative Disease. BMC Musculoskeletal Disorders. 2023;24(1):217.

461. Guo R, Yang X, Zhong Y, Lai Q, Gao T, Lai F, et al. Correlations between Modic Change and Degeneration in 3-Joint Complex of the Lower Lumbar Spine: A Retrospective Study. Medicine. 2018;97(38):e12496.

462. Hafeez R, Memon I. MRI Grading of Lumbar Spine Degenerative Disc Disease Using a Modified Pfirrmann Grading System. Journal of the Liaquat University of Medical and Health Sciences. 2022;21(4):281-4.

463. Huang L, Liu Y, Ding Y, Wu X, Zhang N, Lai Q, et al. Quantitative Evaluation of Lumbar Intervertebral Disc Degeneration by Axial T2 Mapping. Medicine. 2017;96(51):e9393.

464. Jang HJ, Park JY, Parkkuh SU, Chin DK, Kim KS, Cho YE, et al. The Fate of Proximal Junctional Vertebral Fractures after Long-Segment Spinal Fixation: Are There Predictable Radiologic Characteristics for Revision Surgery? Journal of Korean Neurosurgical Society. 2021;64(3):437-46.

465. Karadag MK, Akinci AT, Basak AT, Hekimoglu M, Yildirim H, Akyoldas G, et al. Preoperative Magnetic Resonance Imaging Abnormalities Predictive of Lumbar Herniation Recurrence after Surgical Repair. World Neurosurgery. 2022;165:e750-e6.

466. Kim KT, Lee DH, Cho DC, Sung JK, Kim YB. Preoperative Risk Factors for Recurrent Lumbar Disk Herniation in L5-S1. Journal of Spinal Disorders & Techniques. 2015;28(10):E571-7.

467. Kim SJ, Lee TH, Lim SM. Prevalence of Disc Degeneration in Asymptomatic Korean Subjects. Part 1 : Lumbar Spine. Journal of Korean Neurosurgical Society. 2013;53(1):31-8.

468. Lee JW, Kim HC, Kim SI, Min HK, Ha KY, Park HY, et al. Effects of Bone Cement Augmentation for Uppermost Instrumented Vertebra on Adjacent Disc Segment Degeneration in Lumbar Fusions. World Neurosurgery. 2023;171:e31-e7.

469. Li L, Zhou Z, Xiong W, Fang J, Li Y, Jiao Z, et al. Characterization of the Microstructure of the Intervertebral Disc in Patients with Chronic Low Back Pain by Diffusion Kurtosis Imaging. European Spine Journal. 2019;28(11):2517-25.

470. Li R, Wang Z, Ma L, Yang D, Xie D, Zhang B, et al. Lumbar Vertebral Endplate Defects on Magnetic Resonance Imaging in Degenerative Spondylolisthesis: Novel Classification, Characteristics, and Correlative Factor Analysis. World Neurosurgery. 2020;141:e423-e30.

471. Li X, Zhao R, Rudd S, Ding W, Yang S. Correlation Analysis between Tamoxifen and Lumbar Intervertebral Disc Degeneration: A Retrospective Case-Control Study. Pain Research and Management. 2022;2022 (no pagination).

472. Lin RH, Chen HC, Pan HC, Chen HT, Chang CC, Tzeng CY, et al. Efficacy of Percutaneous Endoscopic Lumbar Discectomy for Pediatric Lumbar Disc Herniation and Degeneration on Magnetic Resonance Imaging: Case Series and Literature Review. Journal of International Medical Research. 2021;49(1):300060520986685.

473. Liu HY, Zhou J, Wang B, Wang HM, Jin ZH, Zhu ZG, et al. Comparison of Topping-Off and Posterior Lumbar Interbody Fusion Surgery in Lumbar Degenerative Disease: A Retrospective Study. Chinese Medical Journal. 2012;125(22):3942-6.

474. Lou C, Chen HL, Feng XZ, Xiang GH, Zhu SP, Tian NF, et al. Menopause Is Associated with Lumbar Disc Degeneration: A Review of 4230 Intervertebral Discs. Climacteric. 2014;17(6):700-4.

475. Luo Y, Wang J, Zhang H, Yue M, Lu Z, Sun B. Feasibility of Dual Energy Ct Virtual Non-Calcium Imaging for Evaluation on Lumbar Intervertebral Disc Degeneration. [Chinese]. Chinese Journal of Medical Imaging Technology. 2021;37(7):1064-8.

476. Pan W, Wang J, Liu J, Lu Y, Huang B. [Modified MRI Short Time Inversion Recovery Sequence Grading System for Lumbar Intervertebral Disc Degeneration]. Chung-Kuo Hsiu Fu Chung Chien Wai Ko Tsa Chih/Chinese Journal of Reparative & Reconstructive Surgery. 2012;26(12):1430-4.

477. Pandit P, Talbott JF, Pedoia V, Dillon W, Majumdar S. T1rho and T2 -Based Characterization of Regional Variations in Intervertebral Discs to Detect Early Degenerative Changes. Journal of Orthopaedic Research. 2016;34(8):1373-81.

478. Rahmani MS, Takahashi S, Hoshino M, Takayama K, Sasaoka R, Tsujio T, et al. The Degeneration of Adjacent Intervertebral Discs Negatively Influence Union Rate of Osteoporotic Vertebral Fracture: A Multicenter Cohort Study. Journal of Orthopaedic Science. 2018;23(4):627-34.

479. Saifuddin A, Rajakulasingam R, Santiago R, Siddiqui M, Khoo M, Pressney I. Comparison of Lumbar Degenerative Disc Disease Using Conventional Fast Spin Echo T₂W MRI and T₂ Fast Spin Echo Dixon Sequences. British Journal of Radiology. 2021;94(1121):20201438.

480. Sezer C, Acikalin R. Unilateral Dynamic Stabilization in Recurrent Lumbar Disc Herniation. Turkish Neurosurgery. 2023;33(2):334-40.

481. Shinohara Y, Sasaki F, Ohmura T, Itoh T, Endo T, Kinoshita T. Evaluation of Lumbar Intervertebral Disc Degeneration Using Dual Energy Ct Virtual Non-Calcium Imaging. European Journal of Radiology. 2020;124:108817.

482. Sun D, Liu P, Cheng J, Ma Z, Liu J, Qin T. Correlation between Intervertebral Disc Degeneration, Paraspinal Muscle Atrophy, and Lumbar Facet Joints Degeneration in Patients with Lumbar Disc Herniation. BMC Musculoskeletal Disorders. 2017;18(1):167.

483. Wang YL, Wang XY, Fang BD, Chi YL, Xu HZ, Wu LJ, et al. L5-S1 Disc Degeneration and the Anatomic Parameters of the Iliac Crest: Imaging Study. European Spine Journal. 2015;24(11):2481-7.

484. Wang YX, Griffith JF, Ma HT, Kwok AW, Leung JC, Yeung DK, et al. Relationship between Gender, Bone Mineral Density, and Disc Degeneration in the Lumbar Spine: A Study in Elderly Subjects Using an Eight-Level MRI-Based Disc Degeneration Grading System. Osteoporosis International. 2011;22(1):91-6.

485. Wang YX, Kwok AW, Griffith JF, Leung JC, Ma HT, Ahuja AT, et al. Relationship between Hip Bone Mineral Density and Lumbar Disc Degeneration: A Study in Elderly Subjects Using an Eight-Level MRI-Based Disc Degeneration Grading System. Journal of Magnetic Resonance Imaging. 2011;33(4):916-20.

486. Wang YXJ, Griffith JF, Ma HT, Kwok AWL, Leung JCS, Yeung DKW, et al. Relationship between Gender, Bone Mineral Density, and Disc Degeneration in the Lumbar Spine: A Study in Elderly Subjects Using an Eight-Level MRI-Based Disc Degeneration Grading System. Osteoporosis International. 2011;22(1):91-6.

487. Wei Z, Lombardi AF, Lee RR, Wallace M, Masuda K, Chang EY, et al. Comprehensive Assessment of in Vivo Lumbar Spine Intervertebral Discs Using a 3d Adiabatic T<Inf>1rho</Inf> Prepared Ultrashort Echo Time (Ute-Adiab-T<Inf>1rho</Inf>) Pulse Sequence. Quantitative Imaging in Medicine and Surgery. 2022;12(1):269-80.

488. Wu J, Liu YY, Jin HJ, Wang Z, Liu MY, Liu P. Fate of the Intervertebral Disc and Analysis of Its Risk Factors Following High-Energy Traumatic Thoracic and Lumbar Fractures: MRI Results of Minimum Five Years after Injury. European Spine Journal. 2022;31(6):1468-78.

489. Yang L, Mu L, Huang K, Zhang T, Mei Z, Zeng W, et al. Abdominal Adipose Tissue Thickness Measured Using Magnetic Resonance Imaging Is Associated with Lumbar Disc Degeneration in a Chinese Patient Population. Oncotarget. 2016;7(50):82055-62.

490. Zhang Y, Patiman, Liu B, Zhang R, Ma X, Guo H. Correlation between Intervertebral Disc Degeneration and Bone Mineral Density Difference: A Retrospective Study of Postmenopausal Women Using an Eight-Level MRI-Based Disc Degeneration Grading System. BMC Musculoskeletal Disorders. 2022;23(1):833.

491. Edmondston SJ, Song S, Bricknell RV, Davies PA, Fersum K, Humphries P, et al. MRI Evaluation of Lumbar Spine Flexion and Extension in Asymptomatic Individuals. Manual Therapy. 2000;5(3):158-64.

492. Fujiwara A, Tamai K, An HS, Kurihashi A, Lim TH, Yoshida H, et al. The Relationship between Disc Degeneration, Facet Joint Osteoarthritis, and Stability of the Degenerative Lumbar Spine. Journal of Spinal Disorders. 2000;13(5):444-50.

493. Fujiwara A, Tamai K, Kurihashi A, Yoshida H, Saotome K. Relationship between Morphology of Iliolumbar Ligament and Lower Lumbar Disc Degeneration. Journal of Spinal Disorders. 1999;12(4):348-52.

494. Fujiwara A, Tamai K, Yamato M, An HS, Yoshida H, Saotome K, et al. The Relationship between Facet Joint Osteoarthritis and Disc Degeneration of the Lumbar Spine: An MRI Study. European Spine Journal. 1999;8(5):396-401.

495. Fukuta S, Miyamoto K, Suzuki K, Maehara H, Inoue T, Hara A, et al. Abundance of Calpain and Aggrecan-Cleavage Products of Calpain in Degenerated Human Intervertebral Discs. Osteoarthritis & Cartilage. 2011;19(10):1254-62.

496. Il Youp C, Si Young P, Jong Hoon P, Seung Woo S, Soon Hyuck L, Cho IY, et al. MRI Findings of Lumbar Spine Instability in Degenerative Spondylolisthesis. Journal of Orthopaedic Surgery (10225536). 2017;25(2):1-5.

497. Murata M, Morio Y, Kuranobu K. Lumbar Disc Degeneration and Segmental Instability: A Comparison of Magnetic Resonance Images and Plain Radiographs of Patients with Low Back Pain. Archives of Orthopaedic & Trauma Surgery. 1994;113(6):297-301.

498. Nanjo Y, Morio Y, Nagashima H, Hagino H, Teshima R. Correlation between Bone Mineral Density and Intervertebral Disk Degeneration in Pre- and Postmenopausal Women. Journal of Bone & Mineral Metabolism. 2003;21(1):22-7.

499. Ochia RS, Inoue N, Takatori R, Andersson GB, An HS. In Vivo Measurements of Lumbar Segmental Motion During Axial Rotation in Asymptomatic and Chronic Low Back Pain Male Subjects. Spine. 2007;32(13):1394-9.

500. Buirski G, Silberstein M, Buirski G, Silberstein M. The Symptomatic Lumbar Disc in Patients with Low-Back Pain. Magnetic Resonance Imaging Appearances in Both a Symptomatic and Control Population. Spine (03622436). 1993;18(13):1808-11.

501. Ishida Y, Ohmori K, Inoue H, Suzuki K. Delayed Vertebral Slip and Adjacent Disc Degeneration with an Isthmic Defect of the Fifth Lumbar Vertebra. Journal of Bone & Joint Surgery - British Volume. 1999;81(2):240-4.

502. Omair A, Holden M, Lie BA, Reikeras O, Brox JI. Treatment Outcome of Chronic Low Back Pain and Radiographic Lumbar Disc Degeneration Are Associated with Inflammatory and Matrix Degrading Gene Variants: A Prospective Genetic Association Study. BMC Musculoskeletal Disorders. 2013;14:105.

503. Chen JY, Ding Y, Lv RY, Liu QY, Huang JB, Yang ZH, et al. Correlation between Mr Imaging and Discography with Provocative Concordant Pain in Patients with Low Back Pain. Clinical Journal of Pain. 2011;27(2):125-30.

504. Lim CH, Jee WH, Son BC, Kim DH, Ha KY, Park CK. Discogenic Lumbar Pain: Association with Mr Imaging and Ct Discography. European Journal of Radiology. 2005;54(3):431-7.

505. Lei D, Rege A, Koti M, Smith FW, Wardlaw D. Painful Disc Lesion: Can Modern Biplanar Magnetic Resonance Imaging Replace Discography? Journal of Spinal Disorders & Techniques. 2008;21(6):430-5.

506. Karadimas EJ, Siddiqui M, Smith FW, Wardlaw D. Positional MRI Changes in Supine Versus Sitting Postures in Patients with Degenerative Lumbar Spine. Journal of Spinal Disorders and Techniques. 2006;19(7):495-500.

507. Butler D, Trafimow JH, Andersson GB, Mcneill TW, Huckman MS. Discs Degenerate before Facets. Spine (Phila Pa 1976). 1990;15(2):111-3.

508. Kealey SM, Aho T, Delong D, Barboriak DP, Provenzale JM, Eastwood JD. Assessment of Apparent Diffusion Coefficient in Normal and Degenerated Intervertebral Lumbar Disks: Initial Experience. Radiology. 2005;235(2):569-74.

509. Kjaer P, Leboeuf-Yde C, Sorensen JS, Bendix T. An Epidemiologic Study of MRI and Low Back Pain in 13-Year-Old Children. Spine. 2005;30(7):798-806.

510. Fabiane SM, Ward KJ, Iatridis JC, Williams FMK. Does Type 2 Diabetes Mellitus Promote Intervertebral Disc Degeneration? European Spine Journal. 2016;25(9):2716-20.

511. Livshits G, Ermakov S, Popham M, Macgregor AJ, Sambrook PN, Spector TD, et al. Evidence That Bone Mineral Density Plays a Role in Degenerative Disc Disease: The Uk Twin Spine Study. Annals of the Rheumatic Diseases. 2010;69(12):2102-6.

512. Livshits G, Ermakov S, Popham M, Macgregor AJ, Sambrook PN, Spector TD, et al. Lumbar Disc Degeneration and Genetic Factors Are the Main Risk Factors for Low Back Pain: The Uk Twin Spine Study. Osteoarthritis and Cartilage. 2010;2):S42.

513. Maatta JH, Wadge S, Macgregor A, Karppinen J, Williams FMK. Issls Prize Winner: Vertebral Endplate (Modic) Change Is an Independent Risk Factor for Episodes of Severe and Disabling Low Back Pain. Spine. 2015;40(15):1187-93.

514. Macgregor AJ, Andrew T, Sambrook PN, Spector TD. Structural, Psychological, and Genetic Influences on Low Back and Neck Pain: A Study of Adult Female Twins. Arthritis & Rheumatism. 2004;51(2):160-7.

515. Mellor F, Morris A, Breen A. An in Vivo Study Exploring Correlations between Early-to-Moderate Disc Degeneration and Flexion Mobility in the Lumbar Spine. European Spine Journal. 2020;29(10):2619-27.

516. Sambrook PN, Macgregor AJ, Spector TD. Genetic Influences on Cervical and Lumbar Disc Degeneration: A Magnetic Resonance Imaging Study in Twins. Arthritis & Rheumatism. 1999;42(2):366-72.

517. Shambrook J, Mcnee P, Clare Harris E, Kim M, Sampson M, Palmer KT, et al. Clinical Presentation of Low Back Pain and Association with Risk Factors According to Findings on Magnetic Resonance Imaging. Pain. 2011;152(7):1659-65.

518. Williams FM, Manek NJ, Sambrook PN, Spector TD, Macgregor AJ. Schmorl's Nodes: Common, Highly Heritable, and Related to Lumbar Disc Disease. Arthritis & Rheumatism. 2007;57(5):855-60.

519. Williams FMK, Popham M, Sambrook PN, Jones AF, Spector TD, Macgregor AJ. Progression of Lumbar Disc Degeneration over a Decade: A Heritability Study. Annals of the Rheumatic Diseases. 2011;70(7):1203-7.

520. Boos N, Dreier D, Hilfiker E, Schade V, Kreis R, Hora J, et al. Tissue Characterization of Symptomatic and Asymptomatic Disc Herniations by Quantitative Magnetic Resonance Imaging. Journal of Orthopaedic Research. 1997;15(1):141-9.

521. Danielsson AJ, Cederlund CG, Ekholm S, Nachemson AL. The Prevalence of Disc Aging and Back Pain after Fusion Extending into the Lower Lumbar Spine. A Matched Mr Study Twenty-Five Years after Surgery for Adolescent Idiopathic Scoliosis. Acta Radiologica. 2001;42(2):187-97.

522. Elfering A, Semmer N, Birkhofer D, Zanetti M, Hodler J, Boos N. Risk Factors for Lumbar Disc Degeneration: A 5-Year Prospective MRI Study in Asymptomatic Individuals. Spine. 2002;27(2):125-34.

523. Masui T, Yukawa Y, Nakamura S, Kajino G, Matsubara Y, Kato F, et al. Natural History of Patients with Lumbar Disc Herniation Observed by Magnetic Resonance Imaging for Minimum 7 Years. Journal of Spinal Disorders & Techniques. 2005;18(2):121-6.

524. Oishi Y, Shimizu K, Katoh T, Nakao H, Yamaura M, Furuko T, et al. Lack of Association between Lumbar Disc Degeneration and Osteophyte Formation in Elderly Japanese Women with Back Pain. Bone. 2003;32(4):405-11.

525. Weishaupt D, Zanetti M, Hodler J, Min K, Fuchs B, Pfirrmann CWA, et al. Painful Lumbar Disk Derangement: Relevance of Endplate Abnormalities at Mr Imaging. Radiology. 2001;218(2):420-7.

526. Battie MC, Videman T, Levalahti E, Gill K, Kaprio J. Heritability of Low Back Pain and the Role of Disc Degeneration. Pain. 2007;131(3):272-80.

527. Battie MC, Videman T, Gibbons LE, Manninen H, Gill K, Pope M, et al. Occupational Driving and Lumbar Disc Degeneration: A Case-Control Study. Lancet. 2002;360(9343):1369-74.

528. Bechara BP, Agarwal V, Boardman J, Perera S, Weiner DK, Vo N, et al. Correlation of Pain with Objective Quantification of Magnetic Resonance Images in Older Adults with Chronic Low Back Pain. Spine. 2014;39(6):469-75.

529. Mariconda M, Galasso O, Imbimbo L, Lotti G, Milano C. Relationship between Alterations of the Lumbar Spine, Visualized with Magnetic Resonance Imaging, and Occupational Variables. European Spine Journal. 2007;16(2):255-66.

530. Burke SM, Hwang SW, Mehan WA, Jr., Bedi HS, Ogbuji R, Riesenburger RI. Reliability of the Modified Tufts Lumbar Degenerative Disc Classification between Neurosurgeons and Neuroradiologists. Journal of Clinical Neuroscience. 2016;29:111-6.

531. Riesenburger RI, Safain MG, Ogbuji R, Hayes J, Hwang SW. A Novel Classification System of Lumbar Disc Degeneration. Journal of Clinical Neuroscience. 2015;22(2):346-51.

532. Battie MC, Levalahti E, Videman T, Burton K, Kaprio J. Heritability of Lumbar Flexibility and the Role of Disc Degeneration and Body Weight. Journal of Applied Physiology. 2008;104(2):379-85.

533. Djurasovic M, Carreon LY, Crawford CH, 3rd, Zook JD, Bratcher KR, Glassman SD. The Influence of Preoperative MRI Findings on Lumbar Fusion Clinical Outcomes. European Spine Journal. 2012;21(8):1616-23.

534. Frobin W, Brinckmann P, Kramer M, Hartwig E. Height of Lumbar Discs Measured from Radiographs Compared with Degeneration and Height Classified from Mr Images. European Radiology. 2001;11(2):263-9.

535. Kilitci A, Asan Z, Yuceer A, Aykanat O, Durna F. Comparison of the Histopathological Differences between the Spinal Material and Posterior Longitudinal Ligament in Patients with Lumbar Disc Herniation: A Focus on the Etiopathogenesis. Annals of Saudi Medicine. 2021;41(2):115-20.

536. Luoma K, Vehmas T, Raininko R, Luukkonen R, Riihimaki H. Lumbosacral Transitional Vertebra: Relation to Disc Degeneration and Low Back Pain. Spine. 2004;29(2):200-5.

537. Thalgott JS, Albert TJ, Vaccaro AR, Aprill CN, Giuffre JM, Drake JS, et al. A New Classification System for Degenerative Disc Disease of the Lumbar Spine Based on Magnetic Resonance Imaging, Provocative Discography, Plain Radiographs and Anatomic Considerations. Spine Journal: Official Journal of the North American Spine Society. 2004;4(6 Suppl):167S-72S.

538. Videman T, Battie MC, Gibbons LE, Kaprio J, Koskenvuo M, Kannus P, et al. Disc Degeneration and Bone Density in Monozygotic Twins Discordant for Insulin-Dependent Diabetes Mellitus. Journal of Orthopaedic Research. 2000;18(5):768-72.

539. Videman T, Battié MC, Ripatti S, Gill K, Manninen H, Kaprio J, et al. Determinants of the Progression in Lumbar Degeneration: A 5-Year Follow-up Study of Adult Male Monozygotic Twins. Spine (03622436). 2006;31(6):671-8.

540. Jiang X, Chen D, Li Z, Lou Y. Correlation between Lumbar Spine Facet Joint Orientation and Intervertebral Disk Degeneration: A Positional MRI Analysis. Journal of Neurological Surgery. 2019;80(4):255-61.

541. Videman T, Levalahti E, Battie MC. The Effects of Anthropometrics, Lifting Strength, and Physical Activities in Disc Degeneration. Spine. 2007;32(13):1406-13.

542. Videman T, Gibbons LE, Kaprio J, Battie MC. Challenging the Cumulative Injury Model: Positive Effects of Greater Body Mass on Disc Degeneration. Spine Journal: Official Journal of the North American Spine Society. 2010;10(1):26-31.

543. Videman T, Gibbons LE, Battie MC. Age-and Pathology-Specific Measures of Disc Degeneration. Spine (Philadelphia, Pa 1976). 2008;33(25):2781-8.

544. Paajanen H, Haapasalo H, Kotilainen E, Aunapuu M, Kettunen J. Proliferation Potential of Human Lumbar Disc after Herniation. Journal of Spinal Disorders. 1999;12(1):57-60.

545. Saaksjarvi S, Kerttula L, Luoma K, Paajanen H, Waris E. Disc Degeneration of Young Low Back Pain Patients: A Prospective 30-Year Follow-up MRI Study. Spine. 2020;45(19):1341-7.

546. Tertti MO, Salminen JJ, Paajanen HE, Terho PH, Kormano MJ. Low-Back Pain and Disk Degeneration in Children: A Case-Control Mr Imaging Study. Radiology. 1991;180(2):503-7.

547. Waris E, Eskelin M, Hermunen H, Kiviluoto O, Paajanen H. Disc Degeneration in Low Back Pain: A 17-Year Follow-up Study Using Magnetic Resonance Imaging. Spine. 2007;32(6):681-4.

548. Hancock MJ, Battie MC, Videman T, Gibbons L. The Role of Back Injury or Trauma in Lumbar Disc Degeneration: An Exposure-Discordant Twin Study. Spine. 2010;35(21):1925-9.

549. Luoma K, Vehmas T, Riihimäki H, Raininko R, Luoma K, Vehmas T, et al. Disc Height and Signal Intensity of the Nucleus Pulposus on Magnetic Resonance Imaging as Indicators of Lumbar Disc Degeneration. Spine (03622436). 2001;26(6):680-6.

550. Nagashima M, Abe H, Amaya K, Matsumoto H, Yanaihara H, Nishiwaki Y, et al. Risk Factors for Lumbar Disc Degeneration in High School American Football Players: A Prospective 2-Year Follow-up Study. American Journal of Sports Medicine. 2013;41(9):2059-64.

551. Ding WY, Yang DL, Cao LZ, Sun YP, Zhang W, Xu JX, et al. Intervertebral Disc Degeneration and Bone Density in Degenerative Lumbar Scoliosis: A Comparative Study between Patients with Degenerative Lumbar Scoliosis and Patients with Lumbar Stenosis. Chinese Medical Journal. 2011;124(23):3875-8.

552. Harada A, Okuizumi H, Miyagi N, Genda E. Correlation between Bone Mineral Density and Intervertebral Disc Degeneration. Spine. 1998;23(8):857-61; discussion 62.

553. Su Y, Ren D, Chen Y, Geng L, Yao S, Wu H, et al. Effect of Endplate Reduction on Endplate Healing Morphology and Intervertebral Disc Degeneration in Patients with Thoracolumbar Vertebral Fracture. European Spine Journal. 2023;32(1):55-67.

554. Hu X, Chen M, Pan J, Liang L, Wang Y. Is It Appropriate to Measure Age-Related Lumbar Disc Degeneration on the Mid-Sagittal Mr Image? A Quantitative Image Study. European Spine Journal. 2018;27(5):1073-81.

555. Feng Z, Liu Y, Wei W, Hu S, Wang Y. Type Ii Modic Changes May Not Always Represent Fat Degeneration: A Study Using Mr Fat Suppression Sequence. Spine. 2016;41(16):E987-E94.

556. Feng Z, Liu Y, Yang G, Battie MC, Wang Y. Lumbar Vertebral Endplate Defects on Magnetic Resonance Images: Classification, Distribution Patterns, and Associations with Modic Changes and Disc Degeneration. Spine. 2018;43(13):919-27.

557. Lv B, Yuan J, Ding H, Wan B, Jiang Q, Luo Y, et al. Relationship between Endplate Defects, Modic Change, Disc Degeneration, and Facet Joint Degeneration in Patients with Low Back Pain. BioMed Research International. 2019;2019:9369853.

558. Lu X, Zhu Z, Pan J, Feng Z, Lv X, Battie MC, et al. Traumatic Vertebra and Endplate Fractures Promote Adjacent Disc Degeneration: Evidence from a Clinical Mr Follow-up Study. Skeletal Radiology. 2022;51(5):1017-26.

559. Oktay AB, Albayrak NB, Akgul YS. Computer Aided Diagnosis of Degenerative Intervertebral Disc Diseases from Lumbar Mr Images. Computerized Medical Imaging & Graphics. 2014;38(7):613-9.

560. Byvaltsev VA, Stepanov IA, Kalinin AA, Belykh EG. Quantitative Assessment of the Degree of Degenerative Change in Intervertebral Disks Using Diffusion-Weighted Images. Biomedical Engineering. 2017;51(4):275-9.

561. Cavusoglu M, Pazahr S, Ciritsis AP, Rossi C. Quantitative ²³ Na-MRI of the Intervertebral Disk at 3 T. NMR in Biomedicine. 2022;35(8):e4733.

562. Meadows KD, Johnson CL, Peloquin JM, Spencer RG, Vresilovic EJ, Elliott DM. Impact of Pulse Sequence, Analysis Method, and Signal to Noise Ratio on the Accuracy of Intervertebral Disc T ₂ Measurement. JOR Spine. 2020;3(3):e1102.

563. Shen S, Wang H, Shi CZ, Guan SY, Liu SR. Mr T2[*]Mapping in Lumbar Intervertebral Discs of Young Volunteers. [Chinese]. Chinese Journal of Medical Imaging Technology. 2010;26(11):2164-7.

564. Vaga S, Raimondi MT, Caiani EG, Costa F, Giordano C, Perona F, et al. Quantitative Assessment of Intervertebral Disc Glycosaminoglycan Distribution by Gadolinium-Enhanced MRI in Orthopedic Patients. Magnetic Resonance in Medicine. 2008;59(1):85-95.

565. Park JB, Chang H, Kim KW, Park SJ. Facet Tropism: A Comparison between Far Lateral and Posterolateral Lumbar Disc Herniations. Spine. 2001;26(6):677-9.

566. Bajpai J, Saini S, Singh R. Clinical Correlation of Magnetic Resonance Imaging with Symptom Complex in Prolapsed Intervertebral Disc Disease: A Cross-Sectional Double Blind Analysis. Journal of Craniovertebral Junction & Spine. 2013;4(1):16-20.

567. Manav V, Ilhan D, Mercan H, Kilic A, Polat AK, Aksu AEK. Association between Intervertebral Disc Degeneration and Behcet's Disease. Dermatologic Therapy. 2022;35(7):e15585.

568. Sivas FA, Ciliz D, Erel U, Inal EE, Özoran K, Sakman B. Abnormal Lumbar Magnetic Resonance Imaging in Asymptomatic Individuals. Turkish Journal of Physical Medicine & Rehabilitation. 2009;55(2):73-7.

569. Hupli M, Heinonen R, Vanharanta H. Height Changes among Chronic Low Back Pain Patients During Intense Physical Exercise. Scandinavian Journal of Medicine & Science in Sports. 1997;7(1):32-7.

Appendix 3. Subjective grading systems for lumbar disc degeneration on MRI

MRI-based grading systems that used disc signal intensity alone in the assessment of disc degeneration in the lumbar spine

Table 1. Grading system for lumbar disc degeneration proposed by Decandido [1].

Grading components	Grade	Description (visual brightness of the disc)
Visual brightness of the disc	1	Normal
	2	Mild loss*
	3	Moderate loss*
	4	Severe

*Mild and moderate loss were described as intermediate signal intensities between the two extremes.

Table 2. Grading system for lumbar disc degeneration proposed by Dimar [2].

Grading components	Description
Disc signal intensity	Any form of reduction was considered disc degeneration

Table 3. Grading system for lumbar disc degeneration proposed by Evans [3].

Grading components	Grade	Description
Disc signal intensity	Normal	A normal disc signal was described as high or bright signal
	Abnormal	A decreased, black, or gray signal was interpreted as evidence of degeneration or dehydration

Table 4. Grading system for lumbar disc degeneration as reported in Dragsbaek [4].

Grading components	Grade	Description
Disc signal intensity	0	Homogenously hyperintense
	1	Hyperintense with visible intranuclear cleft
	2	Intermediate signal intensity
	3	Hypointense

Proposed by Eyre [5].

Table 5. Grading system for lumbar disc degeneration proposed by Fu [6].

Grading Components	Grade	Description
Disc hydration	0	Normal
	1	Partially reduced
	2	Completely black disc

Table 6. Grading system for lumbar disc degeneration proposed by Gibson [7].

Grade	Description*
0	Pure, hyperintense signal (normal)
1	Early degeneration
2	Moderate degeneration
3	Severe degeneration
4	Total loss of nuclear signal/hypointense (dark)

*Degeneration was graded according to a 5-point scale, ranging from 0 = normal to 4 = total loss of nuclear signal.

Table 7. Grading system for lumbar disc degeneration proposed by Heithoff [8].

Grading Component	Description
Disc dehydration	Presence of lumbar degenerative disc disease as manifested by greater than 50% degenerative disc dehydration compared with normal discs

Table 8. Grading system for lumbar disc degeneration proposed by Ito [9].

Grading components	Description
Nuclear signal intensity	Normal
	Moderate loss
	Severe

Table 9. Grading system for lumbar disc degeneration proposed by Kotilainen [10].

Grading components	Grade	Description
Visual brightness of the discs on a T2-weighted image in comparison to the signal intensity of the lumbar vertebrae	No degeneration	Not specified
	Mild	Not specified
	Severe	Not specified

Table 10. Grading system for lumbar disc degeneration proposed by Linson [11].

Grading components	Grade	Description
Disc signal intensity*	Mild, moderate, or marked	Mild, moderate, and marked decrease in signal intensity were classified as being abnormal with no differentiation as to the degree of abnormality

*Signal intensity was compared with the adjacent disc spaces in the same patient

Table 11. Grading system for lumbar disc degeneration proposed by Liuke [12].

Grading components	Grade	Description
Disc signal intensity	Bright	Discs with a nucleus pulposus brighter or as bright as CSF were classified as having normal intensity
	Dark	Discs with a nucleus pulposus darker than CSF were classified as having decreased signal intensity

Table 12. Grading system for lumbar disc degeneration proposed by Luoma [13].

Grading components	Grade	Description
Signal intensity of the nucleus pulposus*	1	Bright
	2	Grey
	3	Dark
	4	Black

*Signal intensity was visually estimated using CSF in the adjacent dural sac as an intensity reference.

Table 13. Grading system for lumbar disc degeneration as reported in Madan [14].

Grading components	Grade	Description
Disc signal intensity	Bright (1)	High signal intensity appearance (bright) normal
	Gray (2)	Intermediate intensity appearance for early degenerative change
	Dark (3)	Low signal appearance for well-established degenerative change

Proposed by Marchiori [15].

Table 14. Grading system for lumbar disc degeneration proposed by Maurer [16].

Grading components	Description
Disc signal intensity	Disc degeneration/desiccation was diagnosed when there was a decrease in disc signal intensity on T2-weighted images

Table 15. Grading system for lumbar disc degeneration proposed by Tertti [17]

Grading Components	Grade	Description
Disc signal intensity	Healthy/well hydrated	High signal intensity
	Abnormal/degenerated	Over 50% decrease of MR signal intensity was detected when compared to the maximal signal intensity of the lumbar discs

Grading systems that used disc height alone in the assessment of disc degeneration

Table 16. Grading system for lumbar disc degeneration proposed by Fu [6].

Grading Components	Grade	Description
Disc space height	0	Normal
	1	Mild, reduced <50%
	2	Moderate/severe, reduced ≥50%

Table 17. Grading system for lumbar disc degeneration proposed by Ito [9].

Grading components	Description
Disc narrowing	Normal
	Moderate narrowing
	Severe narrowing

Table 18. Grading system for lumbar disc degeneration proposed by Raininko [18].

Grading components	Grade	Description
Disc height	0	Disc higher than the disc above
	1	Disc as high as the disc above (if normal)
	2	Disc narrower than the disc above (if normal)
	3	Endplates almost in contact

Table 19. Grading system for lumbar disc degeneration proposed by Videman [19].

Grading components	Grade	Description
Disc height	0-4	Disc height narrowing was determined from qualitative evaluations of films using a 4-point scale which was not specified

Grading systems that used disc signal intensity and disc height in the assessment of disc degeneration

Table 20. Grading system for lumbar disc degeneration proposed by Borenstein [20].

Grade	Description
0	Normal
1	Mild (slight dehydration of the disc on T2-weighted images)
2	Moderate (disc dehydration and mild loss of disc height
3	Severe (total disc dehydration with nearly complete loss of disc height)

Table 21. Grading system for lumbar disc degeneration proposed by Butterman [21].

Grading components	Description
Disc dehydration	Description not specified
Disc narrowing	Description not specified

Table 22. Grading system for lumbar disc degeneration proposed by Jensen [22].

Grading components	Grade	Description
Disc signal intensity	1	Hyper-intense with visible intra-nuclear cleft
	2	Intermediate signal intensity
	3	Hypo-intense
Disc height*	1	Disc higher than the one above
	2	Disc as high as the disc above (if normal)
	3	Disc narrower than the disc above (if normal)
	4	Endplates almost in contact

Used in a latent class analysis. Intervertebral disc was categorised as being degenerated if its disc signal intensity was grade 3, or its disc height was graded as 3 or 4. *Disc height measured using the system by Raininko [18].

Table 23. Grading system for lumbar disc degeneration proposed by Lakadamyali [23].

Grading component	Description
Signal intensity	Considered as any loss of signal intensity of the disc
Disc height	Considered as any disc height loss of the disc

Table 24. Grading system for lumbar disc degeneration proposed by Leboeuf-Yde [24].

Grading components	Description
Disc height	Grade 2 or 3
Disc signal	Grade 3

Disc degeneration was defined as either reduced disc height or signal intensity.

Table 25. Grading system for lumbar disc degeneration proposed by Luoma [25].

Grading components	Grade	Description
Signal intensity	0-5	If the signal intensity of both nucleus pulposus and annulus fibrosis was very dark like that of cortical bone, the disc signal intensity was classified as severely decreased. If signal intensity in nucleus pulposus was bright (normal or increased signal) but that of annulus very dark in a disc with a decreased height, the disc signal intensity was classified as increased
Disc height	0-4	Disc height (anterior, posterior, and middle) was visually estimated as normal (higher than, or as high as the upper not degenerated disc space), slightly decreased (<33% lower than the upper disc space), clearly decreased (34–66% lower), or strongly decreased (>66% or lower)

Table 26. Grading system for lumbar disc degeneration proposed by Sabnis [26].

Grading components	Grade	Description
Disc signal intensity and disc height	0	Normal disc with a bright homogeneous centre and disc height preserved
	1	Mildly inhomogeneous disc but disc height preserved
	2	Mildly homogeneous disc with a disc height loss of <50%
	3	Black disc with a disc height loss of <50%
	4	Black disc with a disc height loss of >50%

Each disc was assigned weight per the following protocols; (i) No points, if the disc was normal (bright homogenous centre and normal disc height compared with adjacent level discs); (ii) One point when the disc was inhomogeneous (but not entirely black), and two points when the disc was entirely black; (iii) One point for a disc height loss of <50% (compared with the cephalad disc height), and two points for a disc height loss of >50%. Points were added to give an overall grade (0-4) to each disc.

Table 27. Grading system for lumbar disc degeneration proposed by Schneidermann [27].

Grade	Description
Normal	No signal changes
1	Slight decrease in signal intensity of the nucleus pulposis
2	Hypointense nucleus pulposis with normal disc height
3	Hypointense nucleus pulposus with disc space narrowing

Table 28. Grading system for lumbar disc degeneration as reported in Karppinen [28].

Grading components	Grade	Description
Disc signal intensity and disc height	Mild	A decrease in signal intensity of the nucleus pulposus on T2-weighted images
	Moderate	Hypo-intense nucleus pulposus on T2-weighted images
	Severe	Hypointense nucleus pulposus with narrowing of the disc space

Proposed by Stadnik [29].

Table 29. Grading system for lumbar disc degeneration proposed by Throckmorton [30].

Grading components	Grade	Description
Hydration status and disc height	Normal	The hydration status and height of the intervertebral disc was evaluated. Discs with normal hydration and height were considered normal
	Degenerated	Endplates were considered degenerated if there was either a significant increase or decrease in signal intensities. If either the discs or the endplates were diagnosed as degenerated, the disc was classified as degenerated

MRI-based grading systems that used any combination of disc signal intensity and bulge, disc height and bulge, and disc signal intensity, disc height and bulge in the assessment of disc degeneration in the lumbar spine

Table 30. Grading system for lumbar disc degeneration proposed by Battie [31].

Grading components	Grade	Description
Disc height	0	Normal
	1	Mild*
	2	Moderate*
	3	Severe*
Disc Bulging	0	Normal
	1	Mild
	2	Moderate
	3	Severe

*Mild, moderate, and severe were described as progressive degrees of abnormality.

Table 31. Grading system for lumbar disc degeneration proposed by Battie [32].

Grading components	Grade	Description
Disc signal intensity	0	Normal
	1	Mild*
	2	Moderate*
	3	Severe*
Disc height narrowing	0	Normal
	1	Mild
	2	Moderate
	3	Severe
Disc Bulging	0	Normal
	1	Mild
	2	Moderate
	3	Severe

*Mild, moderate, and severe were described as progressive degrees of abnormality.

Table 32. Grading system for lumbar disc degeneration proposed by Deng [33].

Grading components	Description
Disc signal intensity	Low
Herniation	Present

Table 33. Grading system for lumbar disc degeneration proposed by Desigan [34].

Grading components	Grade	Description
MRI scoring for disc appearance	0	Normal appearance
	1	Some loss of signal but disc structure still visible
	2	Significant signal loss with loss of structure but no loss of disc height or loss of disc height with normal structure
	3	Loss of disc height and signal
	4	Loss of disc height and signal with annular disruption
MRI scoring for disc protrusion	0	Normal
	1	Annular disc bulge
	2	Focal disc protrusion
	3	Disc extrusion

Table 34. Grading system for lumbar disc degeneration proposed by Fardon [35].

Grading description	Grade	Description
Disc herniation and signal intensity changes*	0	No sign of disc degeneration or herniation
	1	Loss of water content and/or disc height
	2	Disc protrusion
	3	Disc extrusion

As reported in Kiil [36]

Table 35. Grading system for lumbar disc degeneration proposed by Horton and Daftari [37].

Grading components	Grade	Description
Nuclear intensity	White	Homogenous, hypointense signal was defined
	Speckled	A speckled pattern consisted of dark signal and two or more areas of light signal
Bulge	Flat	A straight or minimally convex posterior annulus
	Bulged	A convex annulus that encroached the anterior thecal sac
	Torn	Definite discontinuity in the signal of the posterior annulus or posterior longitudinal ligament

When the two grading components were combined, each disc could be classified into nine possible patterns.

Table 36. Grading system for lumbar disc degeneration proposed by Kanamori [38].

Grade	I	II	III	IV
Signal intensity	High	High-moderate	Moderate-low	Absent
Disc bulging	Normal	Rupture of the posterior annulus	Protrusion or extrusions of the disc materials	

Table 37. Grading system for lumbar disc degeneration proposed by Solovieva [39].

Quantitative components	Description
Disc signal intensity	Cerebrospinal fluid at the corresponding disc level was used as a signal intensity reference. Intensity lower than that of the adjacent cerebrospinal fluid was considered a positive finding and was called a dark nucleus pulposus
Disc height	Graded on a 4-point scale (0 = normal, 1 = slightly decreased, 2 = distinctly decreased, and 3 = severely decreased)
Disc bulging	Bulge anterior or posteriorly

Table 38. Grading system for lumbar disc degeneration proposed by Videman [40].

Grading components	Grade	Description
Disc height narrowing	0	Normal- typically disc higher than the upper disc
	1	Slight- disc as high as the upper disc if it is normal
	2	Moderate- disc narrower than the upper disc if it is normal
	3	Severe- endplates almost in contact
Disc bulging	0	None- normal contour of the disc
	1	Slight- approximately 1.51 ± 1mm
	2	Moderate- approximately 3.5 ± 1mm
	3	Severe- ≥4.5 mm

Table 39. Grading system for lumbar disc degeneration proposed by Videman [41].

Grading components	Grade	Description
Disc height	0-3	0 equalling normal and 1 through 3 representing progressive degrees of abnormality
Disc bulging (anteriorly and posteriorly)	0-3	0 equalling normal and 1 through 3 representing progressive degrees of abnormality (if bulging was detected both anteriorly and posteriorly, the larger of the ratings was used
Signal Intensity	0-3	0 equalling normal and 1 through 3 representing progressive degrees of abnormality

Table 40. Grading system for lumbar disc degeneration proposed by WitWit [42].

Grading components	Grade	Description
Disc signal reduction/ degeneration	0	Normal
	1	Slight reduction as compared to normal appearing adjacent discs
	2	Moderate reduction
	3	Severe reduction (complete or near complete lack of signal)
Disc height	0	Normal
	1	Reduction ≤ 50%
	2	Reduction 50%-90%
	3	Reduction > 90%
Disc bulging	0	Normal
	1	Bulging disc

Disc degeneration as a separate category was defined as a combination and/or either of reduced disc signal, reduced disc height and disc bulging

MRI-based grading systems that used disc signal intensity and/or disc height, herniation, structural changes of the disc and the distinction between the annulus fibrosis and nucleus pulposus in the assessment of disc degeneration in the lumbar spine

Table 41. Grading system for lumbar disc degeneration proposed by Buirski [43].

Buirski pattern	Description
1	Thickened cleft with no prolapse/bulge, and normal disc intensity and disc height
2	Thickened cleft with no prolapse/bulge, reduced disc intensity and normal disc height
3	Normal cleft, disc intensity and disc height, with prolapse/bulge
4	Thickened cleft, prolapsed/bulge, and reduced disc intensity and disc height
5	Thickened or incomplete cleft, with prolapse/bulge with focal signal voids disc intensity and moderately reduced disc
6	Cleft not visible, with prolapse/bulge, and significant disc signal intensity and severe disc height

Table 42. Grading system for lumbar disc degeneration proposed by Butler [44].

Grading components	Grade	Description
Nuclear intensity, disc height, distinction between the annulus fibrosis and nucleus pulposus and herniation	Normal	Well-preserved disc space without evidence of collapse, Smooth borders of both annulus and nucleus pulposus, no evidence of disc herniation, and a clear white signal of the disc on the T2-weighted image
	Degenerated	Discs not fulfilling this criterion were considered degenerated

Table 43. Grading system for lumbar disc degeneration proposed by Griffith [45].

Grade	Signal From Nucleus and Inner Fibres of Annulus	Distinction Between Inner and Outer Fibres of Annulus at Posterior Aspect of Disc	Height of Disc
1	Uniformly hyperintense, equal to CSF	Distinct	Normal
2	Hyperintense (>presacral fat and <CSF) ± Hypointense intranuclear cleft	Distinct	Normal
3	Hyperintense though < Presacral fat	Distinct	Normal
4	Mildly hyperintense (slightly>outer fibres of annulus)	Indistinct	Normal
5	Hypointense (= outer fibres of annulus)	Indistinct	Normal
6	Hypointense	Indistinct	<30% reduction in disc height
7	Hypointense	Indistinct	30%-60% reduction in disc height
8	Hypointense	Indistinct	>60% reduction in disc height

More commonly referred to as the modified Pfirrmann.

Table 44. Grading system for lumbar disc degeneration proposed by Kealey [46].

Grading components	Description
Loss of disc height Reduction in signal intensity on a T2-weighted image Loss of distinctness of the intranuclear cleft	Discs with only one of these findings were defined as mildly degenerated, while those with at least two findings were defined as severely degenerated

Table 45. Grading system for lumbar disc degeneration proposed by Kjaer [47].

Grading components	Grade	Description
Signal intensity	0	Homogenous hyperintense
	1	Hyperintense with visible intranuclear cleft
	2	Intermediate signal intensity
	3	Hypointense
Nuclear shape	0	Round or kidney shaped, 0<60% of sagittal or coronal diameter of the disc
	1	Slightly lobulated or irregular
	2	Severely irregular shape and small, less than 25% of the area of the disc
	3	Not seen in a disc of low signal intensity
Disc height	0	Disc higher than the upper disc
	1	Disc as high as the upper disc (if normal)
	2	Disc narrower than the upper disc (if normal)
	3	Endplates almost in contact

Table 46. Grading system for lumbar disc degeneration proposed by Lei [48].

Grade	Description
Grade 1	White nuclear signal, normal height bean shape nucleus, annular margins well defined, no tears
Grade 2	Speckled nuclear signal, height reduced <10%, distortion of nuclear shape, small radial tears not reaching the PLL on axial views
Grade 3	Speckled or dark nucleus, height reduced by 10%-50%, radial tears extending up to or torn PLL on sagittal/axial views
Grade 4	Dark nucleus, height reduced by >50%, no difference between appearance of annulus and nucleus ± complex tears

Described as the Woodend classification

Table 47. Grading system for lumbar disc degeneration as reported in Chen [49] and Lim [50].

Grading component	Grade	Description
Disc signal intensity and distinction between the annulus and nucleus	I	Preserved differentiation of the nucleus pulposus from the annulus, homogeneously hyperintense signal of the nucleus pulposus
	II	Preserved differentiation of the nucleus pulposus from the annulus, hyperintense signal of the nucleus pulposus with a horizontal dark band
	III	Mild degeneration, blurred differentiation of the nucleus pulposus from the annulus, slightly decreased signal of the nucleus pulposus with minor irregularities
	IV	Moderate degeneration, a loss of differentiation of the nucleus pulposus from the annulus, moderately decreased signal of the nucleus pulposus with hypointense zones
	V	Severe degeneration, a loss of differentiation of the nucleus pulposus from the annulus, hypointense signal of the nucleus pulposus with or without horizontal hyperintense band

Proposed by Pearce [5]

Table 48. Grading system for lumbar disc degeneration proposed by Pfirrmann [51].

Grade	Distinction of nucleus and annulus	Signal intensity	Height of intervertebral disc
I	Clear	Hyperintense, isointense to cerebrospinal fluid	Normal
II	Clear	Hyperintense, isointense to cerebrospinal fluid	Normal
III	Unclear	Intermediate	Normal to slightly decreased
IV	Lost	Intermediate to hypointense	Normal to moderately decreased
V	Lost	Hypointense	Collapsed disc space

Table 49. Grading system for lumbar disc degeneration proposed by Thompson [5].

Grading components	Grade	Description
Disc signal intensity, Disc height, and distinction between the annulus fibrosis and nucleus pulposis	1	Homogeneous, bright nucleus pulposus and homogenous dark gray annulus fibrosis
	2	Horizontal dark bands extended across the annulus fibrosis
	3	Diminished signal intensity of annulus fibrosis and nucleus pulposus indistinguishable from the annulus fibrosis
	4	Further reduced signal intensity of the nucleus pulposus and some bright and dark signals
	5	Diminished disc height

MRI-based grading systems that used disc signal intensity and/or disc height, in combination with osteophytes, end-plate changes, modic changes and high intensity zones in the assessment of disc degeneration in the lumbar spine

Table 50. Grading system for lumbar disc degeneration proposed by Battie [52].

Grading components	Grade	Description
Disc height reduction	0	Normal
	1	Mild*
	2	Moderate*
	3	Severe*
Disc signal intensity	1	Normal
	2	Mild*
	3	Severe*
Disc bulging	0	Normal
	1	Mild
	2	Moderate
	3	Severe
Anterior osteophytes	0	Normal
	1	Mild
	2	Moderate
	3	Severe
Schmorl's Nodes	0	Normal
	1	Mild
	2	Moderate
	3	Severe

As reported in Videman [53].

Table 51. Grading system for lumbar disc degeneration proposed by Battie [54].

Grading components	Grade	Description
Disc height narrowing	0	Normal
	1	Mild*
	2	Moderate*
	3	Severe*
Disc Bulging	0	Normal
	1	Mild
	2	Moderate
	3	Severe
Osteophytes	0	Normal
	1	Mild
	2	Moderate
	3	Severe

*Mild, moderate, and severe were described as progressive degrees of abnormality.

Table 52. Grading system for lumbar disc degeneration proposed by Battie [55].

Grading components	Grade	Description
Disc height reduction	0	Normal
	1	Mild*
	2	Moderate*
	3	Severe*
Disc bulging	0	Normal
	1	Mild
	2	Moderate
	3	Severe
Anterior osteophytes	0	Normal
	1	Mild
	2	Moderate
	3	Severe
Schmorl's Nodes	0	Normal
	1	Mild
	2	Moderate
	3	Severe

*Mild, moderate, and severe were described as progressive degrees of abnormality.

Table 53. Grading system for lumbar disc degeneration as reported in Bechara [56].

Grading components	Grade	Description
T2 Signal Intensity Loss	0 (Healthy)- 3 (Pathologic)	Decreased signal intensity
Nucleus Pulposus Shape	0 (Healthy)- 3 (Pathologic)	Abnormal shape of the nucleus pulposis
Modic Changes	0 (Healthy)- 3 (Pathologic)	Abnormalities in vertebral endplates indicating degeneration
Osteophytes	0 (Healthy)- 3 (Pathologic)	Formation of bone spurs, often associated with degeneration

Proposed by Benneker [57].

Table 54. Grading system for lumbar disc degeneration proposed by Djurasovic [58].

Grading Components	Grade	Description
Disc desiccation	Present	Not specified
High intensity zone	Present	Area of increased T2 signal, isointense to CSF
Modic changes	Type I	Hypointensity on T1-weighted images and hyperintensity on T2-weighted images
	Type II	Hyperintensity on T1-weighted images and isointensity or slight hyperintensity on T2-weighted images
	Type III	Hypointensity on both T1 and T2-weighted images

Table 55. Grading system for lumbar disc degeneration proposed by Frobin [59].

	Nucleus signal	Prolapse detected	Bone marrow signal
A	No signal loss	No prolapse	No intensity change
B	No signal loss	Prolapse	No intensity change
C	No signal loss	No prolapse	Intensity change
D	No signal loss	Prolapse	Intensity change
E	Moderate signal loss	No prolapse	No intensity change
F	Moderate signal loss	Prolapse	No intensity change
G	Moderate signal loss	No prolapse	Intensity change
H	Moderate signal loss	Prolapse	Intensity change
I	Total signal loss	No prolapse	No intensity change
J	Total signal loss	Prolapse	No intensity change
K	Total signal loss	No prolapse	Intensity change
L	Total signal loss	Prolapse	Intensity change

Table 56. Grading system for lumbar disc degeneration as reported in Sambrook [60].

Grading components	Grade	Description
Disc signal intensity	0	Normal
	1	Mild*
	2	Moderate*
	3	Severe*
Disc height narrowing	0	Normal
	1	Mild
	2	Moderate
	3	Severe
Disc bulging	0	Normal
	1	Mild
	2	Moderate
	3	Severe
Anterior osteophytes	0	Normal
	1	Mild
	2	Moderate
	3	Severe

Proposed by Jarosz [61].

*Mild, moderate, and severe were described as progressive degrees of abnormality.

Table 57. Grading system for lumbar disc degeneration proposed by Jiang [62].

Grading Components	Grade	Description
Disc signal intensity, disc height, herniation and osteophytic change	1	Hyperintense signal in the nucleus, with normal disc height
	2	Intermediate signal in the nucleus, with a slight decrease in disc height
	3	Hypointense signal in the nucleus, with a decrease in disc height and evidence of disc herniation/osteophyte
	4	Hypointense signal in the nucleus, with a collapsed disc height and disc herniation/osteophyte

Table 58. Grading system for lumbar disc degeneration proposed by Kilitchi [63].

Radiological (MRI) parameters	Score 0	Score 1	Score 2
Height loss	0 (none)	1 (mild/moderate)	2 (severe)
Osteophyte formation	0 (none)	1 (mild/moderate)	2 (severe)
Endplate sclerosis	0 (none)	1 (mild/moderate)	3 (severe)

Table 59. Grading system for lumbar disc degeneration proposed by Luoma [64].

Grading components	Grade	Description
Size and shape of the nuclear complex	1	Regular shape, size< 60% of the sagittal diameter of the disc
	2	Regular shape, size >60% of the sagittal diameter of the disc
	3	Irregular shaggy borders, size <60% of the sagittal diameter of the disc
	4	Dark, no clear border with annulus fibrosis
Border between the outer annulus fibrosis and nuclear complex	1	Smooth, concave border anteriorly and posteriorly
	2	Shaggy or irregular border anteriorly and/or posteriorly
	3	Not distinguishable anteriorly or posteriorly; dark nuclear complex
Homogeneity of annulus fibrosis	1	Homogeneous, regular, dark lamellar structure anteriorly and posteriorly
	2	Inhomogeneous, irregular structure anteriorly and/or posteriorly
	3	No clear border to nuclear complex; dark nuclear complex
Homogeneity of nuclear complex	1	Normal, homogeneous, bright, or light grey
	2	Inhomogeneous
	3	Homogeneous, dark
Regularity of the horizontal intranuclear cleft (INC)	1	None
	2	Regular thin, grey
	3	Regular thick, dark
	4	Irregular thick, dark
	5	Not distinguishable; dark nuclear complex
Dark dot in the INC	1	No dot
	2	Clear dot in the INC
	3	Not distinguishable; dark nuclear complex
Defect in the vertebral endplates	1	No clear endplate defect
	2	Distinct indentation on the vertebral endplate with clear-cut edges

Table 60. Grading system for lumbar disc degeneration as reported in Boos [65].

Grading components	Grade	Description
Disc signal intensity, morphological aspects of the nucleus pulposis, annulus fibrosis and vertebral bodies	I-V	Grade I represents a normal adolescent disc; grade II, a normal adult disc; grades III-V represent increasing degenerative changes

Proposed by Eyre [5].

Table 61. Grading system for lumbar disc degeneration proposed by Thalgott [66].

Classification of lumbar degenerative disc disease
A, anterior column
Normal T2-weighted signal on MRI
Lordotic in sagittal plane
Domed end plates
Normal density of endplates
No internal disc disruption/not painful
No herniation
No intersegmental motion
No loss of disc height
B, anterior column
Dehydration in T2-weighted signal on MRI, otherwise, normal anatomy
May have loss of lordosis in sagittal plane
May have slight sclerosis of endplates
May have internal disc disruption/may be painful
May have herniation
Slight increase in intersegmental motion
No loss of disc height
C, anterior column
Severe dehydration in T2-weighted signal on MRI nonlordotic in sagittal plane
May have sclerosis of endplates
Loss of endplate domed shape with irregularity of endplate surface
Internal disc disruption/painful
May have herniation
Increased intersegmental motion
Loss of disc height
D, anterior column
Severe dehydration in T2-weighted signal on MRI
Neutral to kyphotic in sagittal plane
Sclerosis of endplates
Total loss of end plate anatomy
Total internal disc disruption/painful
Herniation likely
No intersegmental motion
Total collapse of disc space with loss of posterior arch
May have anterior osteophytes
E, anterior column
Sagittal plane translational deformity
Isthmic/Lytic spondylolisthesis, Grades I-V

Subcategory of disc A-D
Motion of segment resulting from pars defect
Degenerative spondylolisthesis, Grades I-II
All have Grade C or D discs
May have end plate-on-end plate contact
F, coronal plane deformity
End plate irregularity
Degenerative aetiology
All C and D discs
Osteophytes
Posterior column
1 No facet joint degeneration
2 Facet joint degeneration/no stenosis
3 Facet joint degeneration with stenosis
A Presence of central stenosis
B Presence of lateral stenosis
C Presence of foraminal stenosis

Table 62. Grading system for lumbar disc degeneration proposed by Tufts [67].

Radiographic criteria	Description	Points assigned by original classification	Modified classification
Disc structure and brightness	Presence of a distinct annulus fibrosis and nucleus; nucleus T2-weighted signal isointense to CSF	0	0
	Lack of a distinction of annulus fibrosis and nucleus pulposus; nucleus pulposus T2-weighted signal completely hypointense to CSF but not completely black	1	1
	Lack of a distinction of annulus fibrosis and nucleus pulposus; nucleus pulposus T2-weighted signal completely hypointense (black or dark disc)	2	2
Modic changes	No Type I or Type II changes	0	0
	Type I or Type II changes present	1	1
Disc height	Greater or equal to 5mm	0	0
	Less than 5 mm	1	1
High intensity zone	Absent	0	Removed
	Present	1	Removed

This includes both the original and modified system as reported in Burke [68].

Table 63. Grading system for lumbar disc degeneration proposed by Videman [69].

Grading components	Grade	Description
Disc height	0-3	0 equalling normal and 1 through 3 representing progressive degrees of abnormality
Disc bulging (anteriorly and posteriorly)	0-3	0 equalling normal and 1 through 3 representing progressive degrees of abnormality (if bulging was detected both anteriorly and posteriorly, the larger of the ratings was used
Disc herniation, high intensity zones, osteophytes, upper endplate irregularities and fatty degeneration of the vertebrae	0-3	0 equalling normal and 1 through 3 representing progressive degrees of abnormality

MRI-based grading systems that did not specify the grading components used to measure disc degeneration

Table 64. Grading system for lumbar disc degeneration proposed by Bajpai [70].

Grading components	Grade
Not specified	1-5

Table 65 Grading system for lumbar disc degeneration as reported in Park [71].

Grading components	Grade
Unspecified	Degenerative status was classified into five grades according to the criteria of Frymoyer and Moskowitz

Table 66. Grading system for lumbar disc degeneration proposed by Manev [72].

Grading components	Description
Single level disc degeneration	Not specified
Multi-level disc degeneration	Not specified

Table 67. Grading system for lumbar disc degeneration proposed by Hupli [73].

Grading components	Description
Disc degeneration	Not specified

Table 68. Grading system for lumbar disc degeneration proposed by Sivas [74].

Grading components	Grade
Unspecified	Disc degeneration was graded between 1-5 whereby grade 1 and 2 were considered normal, and grade 3-5 was accepted as the presence of degeneration

References for Appendix 3

1. Decandido P, Reinig JW, Dwyer AJ, Thompson KJ, Ducker TB. Magnetic Resonance Assessment of the Distribution of Lumbar Spine Disc Degenerative Changes. Journal of Spinal Disorders. 1988;1(1):9-15.

2. Dimar JR, 2nd, Glassman SD, Carreon LY. Juvenile Degenerative Disc Disease: A Report of 76 Cases Identified by Magnetic Resonance Imaging. Spine Journal: Official Journal of the North American Spine Society. 2007;7(3):332-7.

3. Evans W, Jobe W, Seibert C, Evans W, Jobe W, Seibert C. A Cross-Sectional Prevalence Study of Lumbar Disc Degeneration in a Working Population. Spine (03622436). 1989;14(1):60-4.

4. Dragsbaek L, Kjaer P, Hancock M, Jensen TS. An Exploratory Study of Different Definitions and Thresholds for Lumbar Disc Degeneration Assessed by Mri and Their Associations with Low Back Pain Using Data from a Cohort Study of a General Population. BMC Musculoskeletal Disorders. 2020;21(1):253.

5. Eyre D, ; Nemya P.; Buckwalter. Intervertebral Disk: Basic Science Perspectives. New perspectives on low back pain. 1989.

6. Fu MC, Buerba RA, Long WD, 3rd, Blizzard DJ, Lischuk AW, Haims AH, et al. Interrater and Intrarater Agreements of Magnetic Resonance Imaging Findings in the Lumbar Spine: Significant Variability across Degenerative Conditions. Spine Journal: Official Journal of the North American Spine Society. 2014;14(10):2442-8.

7. Gibson MJ, Buckley J, Mawhinney R, Mulholland RC, Worthington BS. Magnetic Resonance Imaging and Discography in the Diagnosis of Disc Degeneration. A Comparative Study of 50 Discs. Journal of Bone and Joint Surgery - Series B. 1986;68(3):369-73.

8. Heithoff KB, Gundry CR, Burton CV, Winter RB, Heithoff KB, Gundry CR, et al. Juvenile Discogenic Disease. Spine (03622436). 1994;19(3):335-40.

9. Ito M, Incorvaia KM, Yu SF, Fredrickson BE, Yuan HA, Rosenbaum AE. Predictive Signs of Discogenic Lumbar Pain on Magnetic Resonance Imaging with Discography Correlation. Spine. 1998;23(11):1252-8; discussion 9-60.

10. Kotilainen E, Alanen A, Erkintalo M, Valtonen S, Kormano M. Association between Decreased Disc Signal Intensity in Preoperative T2-Weighted Mri and a 5-Year Outcome after Lumbar Minimally Invasive Discectomy. Minimally Invasive Neurosurgery. 2001;44(1):31-6.

11. Linson MA, Crowe CH. Comparison of Magnetic Resonance Imaging and Lumbar Discography in the Diagnosis of Disc Degeneration. Clinical Orthopaedics & Related Research. 1990;(250):160-3.

12. Liuke M, Solovieva S, Lamminen A, Luoma K, Leino-Arjas P, Luukkonen R, et al. Disc Degeneration of the Lumbar Spine in Relation to Overweight. International Journal of Obesity. 2005;29(8):903-8.

13. Luoma K, Riihimaki H, Luukkonen R, Raininko R, Viikari-Juntura E, Lamminen A. Low Back Pain in Relation to Lumbar Disc Degeneration. Spine. 2000;25(4):487-92.

14. Madan SS, Rai A, Harley JM. Interobserver Error in Interpretation of the Radiographs for Degeneration of the Lumbar Spine. Iowa Orthopaedic Journal. 2003;23:51-6.

15. Marchiori DM, Mclean I, Firth R, Tatum R. A Comparison of Radiographic Signs of Degeneration to Corresponding Mri Signal Intensities in the Lumbar Spine. Journal of Manipulative & Physiological Therapeutics. 1994;17(4):238-45.

16. Maurer M, Soder RB, Baldisserotto M. Spine Abnormalities Depicted by Magnetic Resonance Imaging in Adolescent Rowers. American Journal of Sports Medicine. 2011;39(2):392-7.

17. Tertti M, Paajanen H, Kujala UM, Alanen A, Salmi TT, Kormano M. Disc Degeneration in Young Gymnasts. A Magnetic Resonance Imaging Study. American Journal of Sports Medicine. 1990;18(2):206-8.

18. Raininko R, Manninen H, Battie MC, Gibbons LE, Gill K, Fisher LD. Observer Variability in the Assessment of Disc Degeneration on Magnetic Resonance Images of the Lumbar and Thoracic Spine. Spine. 1995;20(9):1029-35.

19. Videman T, Levalahti E, Battie MC. The Effects of Anthropometrics, Lifting Strength, and Physical Activities in Disc Degeneration. Spine. 2007;32(13):1406-13.

20. Borenstein DG, O'mara JW, Jr., Boden SD, Lauerman WC, Jacobson A, Platenberg C, et al. The Value of Magnetic Resonance Imaging of the Lumbar Spine to Predict Low-Back Pain in Asymptomatic Subjects : A Seven-Year Follow-up Study. Journal of Bone & Joint Surgery - American Volume. 2001;83(9):1306-11.

21. Buttermann GR, Mullin WJ, Buttermann GR, Mullin WJ. Pain and Disability Correlated with Disc Degeneration Via Magnetic Resonance Imaging in Scoliosis Patients. European Spine Journal. 2008;17(2):240-9.

22. Jensen RK, Kent P, Jensen TS, Kjaer P. The Association between Subgroups of Mri Findings Identified with Latent Class Analysis and Low Back Pain in 40-Year-Old Danes. BMC Musculoskeletal Disorders. 2018;19(1):62.

23. Lakadamyali H, Tarhan NC, Ergun T, Cakir B, Agildere AM. Stir Sequence for Depiction of Degenerative Changes in Posterior Stabilizing Elements in Patients with Lower Back Pain. AJR American Journal of Roentgenology. 2008;191(4):973-9.

24. Leboeuf-Yde C, Kjaer P, Bendix T, Manniche C. Self-Reported Hard Physical Work Combined with Heavy Smoking or Overweight May Result in So-Called Modic Changes. BMC Musculoskeletal Disorders. 2008;9:5.

25. Luoma K, Vehmas T, Kerttula L, Gronblad M, Rinne E. Chronic Low Back Pain in Relation to Modic Changes, Bony Endplate Lesions, and Disc Degeneration in a Prospective Mri Study. European Spine Journal. 2016;25(9):2873-81.

26. Sabnis AB, Chamoli U, Diwan AD. Is L5-S1 Motion Segment Different from the Rest? A Radiographic Kinematic Assessment of 72 Patients with Chronic Low Back Pain. European Spine Journal. 2018;27(5):1127-35.

27. Schneiderman G, Flannigan B, Kingston S, Thomas J, Dillin WH, Watkins RG, et al. Magnetic Resonance Imaging in the Diagnosis of Disc Degeneration: Correlation with Discography. Spine (03622436). 1987;12(3):276-81.

28. Karppinen J, Paakko E, Paassilta P, Lohiniva J, Kurunlahti M, Tervonen O, et al. Radiologic Phenotypes in Lumbar Mr Imaging for a Gene Defect in the Col9a3 Gene of Type Ix Collagen. Radiology. 2003;227(1):143-8.

29. Stadnik TW, Lee RR, Coen HL, Neirynck EC, Buisseret TS, Osteaux MJC. Annular Tears and Disk Herniation: Prevalence and Contrast Enhancement on Mr Images in the Absence of Low Back Pain or Sciatica. Radiology. 1998;206(1):49-55.

30. Throckmorton TW, Hilibrand AS, Mencio GA, Hodge A, Spengler DM. The Impact of Adjacent Level Disc Degeneration on Health Status Outcomes Following Lumbar Fusion. Spine. 2003;28(22):2546-50.

31. Battie MC, Videman T, Levalahti E, Gill K, Kaprio J. Genetic and Environmental Effects on Disc Degeneration by Phenotype and Spinal Level: A Multivariate Twin Study. Spine. 2008;33(25):2801-8.

32. Battie MC, Videman T, Gibbons LE, Fisher LD, Manninen H, Gill K. Determinants of Lumbar Disc Degeneration: A Study Relating Lifetime Exposures and Magnetic Resonance Imaging Findings in Identical Twins. Spine. 1995;20(24):2601-12.

33. Deng C, Xia W. Effect of Tai Chi Chuan on Degeneration of Lumbar Vertebrae and Lumbar Discs in Middle-Aged and Aged People: A Cross-Sectional Study Based on Magnetic Resonance Images. Journal of International Medical Research. 2018;46(2):578-85.

34. Desigan S, Hall-Craggs MA, Ho CP, Eliahoo J, Porter JB. Degenerative Disc Disease as a Cause of Back Pain in the Thalassaemic Population: A Case-Control Study Using Mri and Plain Radiographs. Skeletal Radiology. 2006;35(2):95-102.

35. Fardon DF, Milette PC. Nomenclature and Classification of Lumbar Disc Pathology. Recommendations of the Combined Task Forces of the North American Spine Society, American Society of Spine Radiology, and American Society of Neuroradiology. Spine (Philadelphia, Pa 1976). 2001;26(5):E93-E113.

36. Kiil RM, Mistegaard CE, Loft AG, Zejden A, Hendricks O, Jurik AG. Differences in Topographical Location of Sacroiliac Joint Mri Lesions in Patients with Early Axial Spondyloarthritis and Mechanical Back Pain. Arthritis Research & Therapy. 2022;24(1):75.

37. Horton WC, Daftari TK. Which Disc as Visualized by Magnetic Resonance Imaging Is Actually a Source of Pain? A Correlation between Magnetic Resonance Imaging and Discography. Spine (Phila Pa 1976). 1992;17(6 Suppl):S164-71.

38. Kanamori M, Nobukiyo M, Suzuki K, Yasuda T, Hori T. Clinical Validity of a New T2-Weighted Mri-Based Grading System for Lumbar Disc Degeneration. International Medical Journal. 2013;20(4):466-9.

39. Solovieva S, Lohiniva J, Leino-Arjas P, Raininko R, Luoma K, Ala-Kokko L, et al. Col9a3 Gene Polymorphism and Obesity in Intervertebral Disc Degeneration of the Lumbar Spine: Evidence of Gene-Environment Interaction. Spine (03622436). 2002;27(23):2691-6.

40. Videman T, Gibbons LE, Battie MC. Age-and Pathology-Specific Measures of Disc Degeneration. Spine (Philadelphia, Pa 1976). 2008;33(25):2781-8.

41. Videman T, Battie MC, Gibbons LE, Manninen H, Gill K, Fisher LD, et al. Lifetime Exercise and Disk Degeneration: An Mri Study of Monozygotic Twins. Medicine & Science in Sports & Exercise. 1997;29(10):1350-6.

42. Witwit WA, Kovac P, Sward A, Agnvall C, Todd C, Thoreson O, et al. Disc Degeneration on Mri Is More Prevalent in Young Elite Skiers Compared to Controls. Knee Surgery, Sports Traumatology, Arthroscopy. 2018;26(1):325-32.

43. Buirski G, Silberstein M, Buirski G, Silberstein M. The Symptomatic Lumbar Disc in Patients with Low-Back Pain. Magnetic Resonance Imaging Appearances in Both a Symptomatic and Control Population. Spine (03622436). 1993;18(13):1808-11.

44. Butler D, Trafimow JH, Andersson GB, Mcneill TW, Huckman MS. Discs Degenerate before Facets. Spine (Phila Pa 1976). 1990;15(2):111-3.

45. Griffith JF, Wang YX, Antonio GE, Choi KC, Yu A, Ahuja AT, et al. Modified Pfirrmann Grading System for Lumbar Intervertebral Disc Degeneration. Spine. 2007;32(24):E708-12.

46. Kealey SM, Aho T, Delong D, Barboriak DP, Provenzale JM, Eastwood JD. Assessment of Apparent Diffusion Coefficient in Normal and Degenerated Intervertebral Lumbar Disks: Initial Experience. Radiology. 2005;235(2):569-74.

47. Kjaer P, Leboeuf-Yde C, Sorensen JS, Bendix T. An Epidemiologic Study of Mri and Low Back Pain in 13-Year-Old Children. Spine. 2005;30(7):798-806.

48. Lei D, Rege A, Koti M, Smith FW, Wardlaw D. Painful Disc Lesion: Can Modern Biplanar Magnetic Resonance Imaging Replace Discography? Journal of Spinal Disorders & Techniques. 2008;21(6):430-5.

49. Chen JY, Ding Y, Lv RY, Liu QY, Huang JB, Yang ZH, et al. Correlation between Mr Imaging and Discography with Provocative Concordant Pain in Patients with Low Back Pain. Clinical Journal of Pain. 2011;27(2):125-30.

50. Lim CH, Jee WH, Son BC, Kim DH, Ha KY, Park CK. Discogenic Lumbar Pain: Association with Mr Imaging and Ct Discography. European Journal of Radiology. 2005;54(3):431-7.

51. Pfirrmann CW, Metzdorf A, Zanetti M, Hodler J, Boos N. Magnetic Resonance Classification of Lumbar Intervertebral Disc Degeneration. Spine. 2001;26(17):1873-8.

52. Battie MC, Videman T, Gibbons LE, Manninen H, Gill K, Pope M, et al. Occupational Driving and Lumbar Disc Degeneration: A Case-Control Study. Lancet. 2002;360(9343):1369-74.

53. Videman T, Battie MC, Gibbons LE, Kaprio J, Koskenvuo M, Kannus P, et al. Disc Degeneration and Bone Density in Monozygotic Twins Discordant for Insulin-Dependent Diabetes Mellitus. Journal of Orthopaedic Research. 2000;18(5):768-72.

54. Battie MC, Levalahti E, Videman T, Burton K, Kaprio J. Heritability of Lumbar Flexibility and the Role of Disc Degeneration and Body Weight. Journal of Applied Physiology. 2008;104(2):379-85.

55. Battie MC, Videman T, Levalahti E, Gill K, Kaprio J. Heritability of Low Back Pain and the Role of Disc Degeneration. Pain. 2007;131(3):272-80.

56. Bechara BP, Agarwal V, Boardman J, Perera S, Weiner DK, Vo N, et al. Correlation of Pain with Objective Quantification of Magnetic Resonance Images in Older Adults with Chronic Low Back Pain. Spine. 2014;39(6):469-75.

57. Benneker LM, Heini PF, Anderson SE, Alini M, Ito K. Correlation of Radiographic and Mri Parameters to Morphological and Biochemical Assessment of Intervertebral Disc Degeneration. European Spine Journal. 2005;14(1):27-35.

58. Djurasovic M, Carreon LY, Crawford CH, 3rd, Zook JD, Bratcher KR, Glassman SD. The Influence of Preoperative Mri Findings on Lumbar Fusion Clinical Outcomes. European Spine Journal. 2012;21(8):1616-23.

59. Frobin W, Brinckmann P, Kramer M, Hartwig E. Height of Lumbar Discs Measured from Radiographs Compared with Degeneration and Height Classified from Mr Images. European Radiology. 2001;11(2):263-9.

60. Sambrook PN, Macgregor AJ, Spector TD. Genetic Influences on Cervical and Lumbar Disc Degeneration: A Magnetic Resonance Imaging Study in Twins. Arthritis & Rheumatism. 1999;42(2):366-72.

61. Jarosz J, Bingham J, Pemberton J, Sambrook P, Spector T. An Atlas for Scoring Cervical and Lumbar Disc Degeneration. London: Springer Verlag; 1997.

62. Jiang X, Chen D, Li Z, Lou Y. Correlation between Lumbar Spine Facet Joint Orientation and Intervertebral Disk Degeneration: A Positional Mri Analysis. Journal of Neurological Surgery. 2019;80(4):255-61.

63. Kilitci A, Asan Z, Yuceer A, Aykanat O, Durna F. Comparison of the Histopathological Differences between the Spinal Material and Posterior Longitudinal Ligament in Patients with Lumbar Disc Herniation: A Focus on the Etiopathogenesis. Annals of Saudi Medicine. 2021;41(2):115-20.

64. Luoma K, Vehmas T, Raininko R, Luukkonen R, Riihimaki H. Lumbosacral Transitional Vertebra: Relation to Disc Degeneration and Low Back Pain. Spine. 2004;29(2):200-5.

65. Boos N, Dreier D, Hilfiker E, Schade V, Kreis R, Hora J, et al. Tissue Characterization of Symptomatic and Asymptomatic Disc Herniations by Quantitative Magnetic Resonance Imaging. Journal of Orthopaedic Research. 1997;15(1):141-9.

66. Thalgott JS, Albert TJ, Vaccaro AR, Aprill CN, Giuffre JM, Drake JS, et al. A New Classification System for Degenerative Disc Disease of the Lumbar Spine Based on Magnetic Resonance Imaging, Provocative Discography, Plain Radiographs and Anatomic Considerations. Spine Journal: Official Journal of the North American Spine Society. 2004;4(6 Suppl):167S-72S.

67. Riesenburger RI, Safain MG, Ogbuji R, Hayes J, Hwang SW. A Novel Classification System of Lumbar Disc Degeneration. Journal of Clinical Neuroscience. 2015;22(2):346-51.

68. Burke SM, Hwang SW, Mehan WA, Jr., Bedi HS, Ogbuji R, Riesenburger RI. Reliability of the Modified Tufts Lumbar Degenerative Disc Classification between Neurosurgeons and Neuroradiologists. Journal of Clinical Neuroscience. 2016;29:111-6.

69. Videman T, Battié MC, Ripatti S, Gill K, Manninen H, Kaprio J, et al. Determinants of the Progression in Lumbar Degeneration: A 5-Year Follow-up Study of Adult Male Monozygotic Twins. Spine (03622436). 2006;31(6):671-8.

70. Bajpai J, Saini S, Singh R. Clinical Correlation of Magnetic Resonance Imaging with Symptom Complex in Prolapsed Intervertebral Disc Disease: A Cross-Sectional Double Blind Analysis. Journal of Craniovertebral Junction & Spine. 2013;4(1):16-20.

71. Park JB, Chang H, Kim KW, Park SJ. Facet Tropism: A Comparison between Far Lateral and Posterolateral Lumbar Disc Herniations. Spine. 2001;26(6):677-9.

72. Manav V, Ilhan D, Mercan H, Kilic A, Polat AK, Aksu AEK. Association between Intervertebral Disc Degeneration and Behcet's Disease. Dermatologic Therapy. 2022;35(7):e15585.

73. Hupli M, Heinonen R, Vanharanta H. Height Changes among Chronic Low Back Pain Patients During Intense Physical Exercise. Scandinavian Journal of Medicine & Science in Sports. 1997;7(1):32-7.

74. Sivas FA, Ciliz D, Erel U, Inal EE, Özoran K, Sakman B. Abnormal Lumbar Magnetic Resonance Imaging in Asymptomatic Individuals. Turkish Journal of Physical Medicine & Rehabilitation / Turkiye Fiziksel Tip ve Rehabilitasyon Dergisi. 2009;55(2):73-7.

Appendix 4. Quantitative grading systems for lumbar disc degeneration on magnetic resonance imaging

MRI-based grading systems that used CSF-adjusted disc signal intensity alone in the assessment of disc degeneration in the lumbar spine

Table 1. Grading system for lumbar disc degeneration proposed by Aavikko [1].

Quantitative components	Description
CSF-adjusted disc signal intensity	An ellipsoid region of interest (ROI) was digitally marked from each nucleus pulposus. As an internal reference, the SI of the adjacent cerebrospinal fluid was used, resulting in a disc to CSF-SI ratio (SINDAHL)

Table 2. Grading system for lumbar disc degeneration as reported in Battie [2].

Quantitative components	Description
CSF-adjusted disc signal intensity	Ratio of the mean signal intensity of the entire disc to the adjacent CSF signal intensity. Calculated by drawing outlines of vertebrae, discs, and the adjacent CSF samples

Proposed by Battie [3]

Table 3. Grading system for lumbar disc degeneration proposed by Ding [4].

Grading components	Grades
Quantitative normalised disc signal intensity (Gray value and pixels of the nucleus pulposus and gray value of CSF in adjoining domains was measured. The average relative signal intensity was divided into four grades by hierarchical clustering analysis)	0-4

Table 4. Grading system for lumbar disc degeneration proposed by Jarman [5].

Quantitative components	Description
Normalised disc signal intensity	A semi-quantitative measure was derived by using the mean voxel intensity in each nucleus pulposus. Then another ROI was drawn in the uniform region of the gray matter of the spinal cord and the mean intensity was calculated. Then, the mean intensity in each disc was divided by the mean intensity in the spinal cord gray matter to obtain a metric that can be compared across subjects.

Table 5. Grading system for lumbar disc degeneration proposed by Luoma [6].

Quantitative components	Description
Computerised analysis of the signal intensity of the nucleus pulposus	For signal intensity measurements, the spatially dependent inhomogeneity of the signal intensity in the surface coil images were corrected by a computerised method. Regions of interest above and below the central intranuclear cleft in each nucleus pulposus and in cerebrospinal fluid (CSF) in the anterior part of the adjacent dural sac behind each vertebra were defined, and their signal intensities measured.

Table 6. Grading system for lumbar disc degeneration proposed by Lund [7].

Quantitative components	Description
CSF-adjusted disc signal intensity	The signal intensity of the disc was assessed quantitatively by a computerised method with a region of interest (ROI) marked digitally from each nucleus pulposus. As an internal reference, the SI of the adjacent CSF was used for a disc to CSF-SI ratio. For the ROI of the CSF at every level, the area in the anterior dural sac immediately posterior to the disc was chosen to exclude the effect of the nerve roots.

Table 7. Grading system for lumbar disc degeneration proposed by Nagashima [8].

Quantitative components	Description
CSF-adjusted disc signal intensity	The intervertebral area was defined as the quadrangle formed by the anterior and posterior edges of the upper and lower endplates in contact with the intervertebral disc to be measured. A shape similar to the intervertebral area but with one fourth of the area was drawn. The geometric shape centre of the shape was matched to the centre of intensity, and this shape was used as the region of interest for measuring intensity of the nucleus pulposus. The signal intensity of the nucleus pulposis was expressed as a percentage of the intensity of the CSF.

The degree of disc degeneration was defined as the mean signal intensity of the 6 intervertebral discs from T12-L1 to L5-S1.

Table 8. Grading system for lumbar disc degeneration proposed by Paajanen [9].

Grading components	Description
CSF-adjusted disc signal intensity	A region of interest (ROI) was determined in the nucleus pulposus of each disc from T12-L1 to L5-S1. The disc with the highest SI value was regarded as the healthiest in each subject and used as a reference point. A relative SI value was calculated as a percentage of the reference disc.

Disc signal intensity was graded ordinally using a 3-point scale from bright/normal to absent/marked degeneration.

Table 9. Grading system for lumbar disc degeneration proposed by Videman [10].

Grading components	Description
CSF-adjusted disc signal intensity	Disc signal intensity was measured using a midsagittal disc signal, which was adjusted according to the signal intensity of an adjacent cerebrospinal fluid sample extracted from digital MRI data, using a custom-designed image analysis program (Spine Examiner)

Table 10. Grading system for lumbar disc degeneration proposed by Videman [11].

Quantitative components	Description
Disc signal intensity	Used a ratio of the mean signal strength in the nucleus area to the mean in the annulus region. SpIn (for spine insight) were conducted, which passed through the centre of the disc between the two end plates. Nucleus and annulus regions were defined as preset proportions of the axial disc area. The first axial measure, Axial SpIn1, was based on the ratio of the mean signal of the central 75% of the disc area, including the entire nucleus area, to the outer annulus region, which was the ring along the perimeter of the disc comprising 25% of the total disc area. One was subtracted from the ratio and then multiplied by 10 to create informative scores. Axial SpIn2 was constructed to determine if weighting regions of the nucleus and inner annulus equally would improve measurement. The central 25% of the total disc area represented the nucleus, the ring along the perimeter of the disc comprising 25% of the total disc area represented the outer annulus, and the intermediate area comprising 50% of the disc represented the inner annulus. The mean signal of each was divided by the mean signal strength of the outer annulus, and one was subtracted. The scores for each region were averaged and then multiplied by 10.

MRI-based grading systems that used quantitative disc height alone in the assessment of disc degeneration in the lumbar spine

Table 11. Grading system for lumbar disc degeneration proposed by Luoma [6].

Quantitative components	Description
Disc height	The anterior and posterior heights of the intervertebral discs were measured in the middle line of the disc from the proton density-weighted sagittal images. The shortest distance between the anterior and posterior edge of the neighbouring end plates was measured with MRI software. Their mean-distance was considered to represent the disc height

Table 12. Grading system for lumbar disc degeneration as reported in Hancock [12].

Quantitative components	Description
Disc height	Quantitative height was obtained from the midsagittal section by dividing the disc area contained between the theoretical vertebral borders (corners) by the diameter of the area

Proposed by Battie [2].

Table 13. Grading system for lumbar disc degeneration proposed by Jarman [5].

Quantitative components	Description
Disc height index	The proximal and distal vertebral body height and intervertebral height were measured from the anterior, middle, and posterior portions of each respective disc level on T2 images. The measurements were performed on the midsagittal slice. The corners of the vertebral bodies and the midpoints of the endplates were marked. The measurement lines were drawn between those landmarks and distance measurements were taken

MRI-based grading systems that used quantitative measurements of disc bulging in the assessment of disc degeneration in the lumbar spine

Table 14. Grading system for lumbar disc degeneration proposed by Harada [13].

Quantitative components	Description
Anterior and posterior bulge of the intervertebral disc	The magnitude of disc bulges was measured in the middle line of the disc from the proton density-weighted sagittal images. A bulge of ≥3.2 mm was considered positive for degenerative disc disease

Table 15. Grading system for lumbar disc degeneration proposed by Luoma [14].

Quantitative components	Description
Disc bulge ratio using the disc area	Disc areas were measured and the average of the four-disc areas were used as a disc area. Two lines connecting the middle points of the anterior and posterior borders of two adjacent vertebral bodies were drawn. The anterior and posterior areas protruding from these lines were measured. The average was obtained of the protruding areas in the four discs and used as a bulging disc area. The disc bulge ratio was calculated from the ratio of the bulging disc area and disc area

MRI-based grading systems that used CSF-adjusted disc signal intensity, and quantitative disc height in the assessment of disc degeneration in the lumbar spine

Table 16. Grading system for lumbar disc degeneration proposed by Bechara [15].

Quantitative components	Description
Disc area	Percent area parameter for each disc was calculated as the area of that disc divided by the sum of all disc areas in that subject
Sum of pixel intensities	Calculated as a percentage of the total sum intensity across all discs for each subject respectively
MRI index parameter	This was calculated as a product of the disc's area and sum intensity. Lower values indicate a degenerated disc while higher values indicate a healthy disc

Discs were segmented according to atlas-based segmentation using fuzzy c-means algorithm.

Table 17. Grading system for lumbar disc degeneration as reported by Salamat [16].

Quantitative components	Description
Disc signal intensity	3 different measures of disc signal intensity were used. A raw disc signal intensity measure, a ratio adjusted for brightness of CSF at the same level, and a ratio adjusted for brightest level of CSF at any of the 5 spinal levels. Raw signal intensity was recorded for each disc area as defined above for measurement of disc height. Ratio 1 was calculated by dividing the raw disc signal intensity for each vertebral level by the signal intensity of the CSF at the adjacent level. Ratio 2 was calculated by dividing the raw disc signal intensity by the signal intensity of the most intense CSF at any of the 5 spinal levels.
Disc height	3 different measures of disc height were used. A raw disc height measure, a ratio adjusted for each person's height, and a ratio adjusted for height of the vertebral body about the disc. Raw disc height was measured by dividing the disc area by horizontal length. Disc area was defined by using the freehand region of interest measurement tool and tracing around the disc starting along the anterior longitudinal ligament. Ratio 1 was calculated by dividing the raw disc height for each vertebral level by the total body height of the participant. Ratio 2 was calculated by dividing the raw disc height by the height of the vertebral body above the disc. The height of the vertebral body above was calculated in a similar matter to disc height

CSF adjusted disc signal intensity and disc height as proposed by Battie [3].

Table 18. Grading system for lumbar disc degeneration proposed by Su [17].

Quantitative components	Description
CSF adjusted disc signal intensity	The intervertebral disc signals in the anterior, middle, and posterior regions of the nucleus pulposus were measured and averaged and further adjusted by the adjacent CSF signal
Disc height*	Disc height was defined as the average of the anterior, middle, and posterior heights of the nonconvex portion of the disc

MRI-based grading systems that used CSF-adjusted disc signal intensity, quantitative disc height, and quantitative measurements of disc bulging in the assessment of disc degeneration in the lumbar spine

Table 19. Grading system for lumbar disc degeneration as reported in Hu [18].

Quantitative components	Description
CSF-adjusted disc signal intensity	Ratio of the mean signal intensity of the entire disc to the adjacent CSF signal intensity. Calculated by drawing outlines of vertebrae, discs, and the adjacent CSF samples
Disc height	Mean of the four height measurements: 1) Anterior corners of the adjacent vertebrae, 2) posterior corners of the adjacent vertebrae, 3) distances on either side of the nucleus
Disc bulging	Relative degree was indicated by measuring disc width at its centre point. Computer drawn lines based on a standard algorithm

Proposed by Battie [3].

Table 20. Grading system for lumbar disc degeneration proposed by Feng [19].

Quantitative components	Description
CSF-adjusted disc signal intensity	The mean disc signal intensity was acquired by defining a ROI for the intervertebral disc, which was further adjusted for adjacent CSF signal intensity
Disc height	Disc height was defined as the mean of anterior, middle, and posterior height of the intervertebral disc
Disc bulging	Disc bulging, which includes anterior and posterior bulging, was measured as the area of the portion of the disc that exceeds the anterior and posterior edges of vertebral bodies

Table 21. Grading system for lumbar disc degeneration proposed by Huang [20].

Category	Parameter
Diameter	Superior vertebra diameter Middle vertebra diameter Inferior vertebra diameter Middle disc diameter
Height	Anterior vertebra height Middle vertebra height Posterior vertebra height Anterior disc height Middle disc height Posterior disc height
Area	Vertebra area Disc area Anterior disc bulging area Posterior disc bulging area
Signal	Mean vertebra signal intensity SD of vertebra signal intensity Mean disc signal intensity Mean signal of adjacent CSF

Signal intensity was measured pixel by pixel in a defined ROI and thus, there are mean and standard deviation for signal intensity measurement

Table 22. Grading system for lumbar disc degeneration proposed by Lu [21].

Quantitative components	Description
Disc height	Disc height was defined as the mean of anterior, middle, and posterior heights of the non-convex portion of the disc
Disc bulging	Disc bulging included anterior and posterior bulging, which was measured as the area of the disc that exceeded the anterior or posterior edges of the adjacent vertebral bodies
CSF-adjusted disc signal intensity	Disc signals were sampled in the anterior, middle, and posterior regions of the nucleus pulposus, which were averaged and further adjusted using adjacent CSF signal

Acquired on a mid-sagittal T2W MR image.

Table 23. Grading system for lumbar disc degeneration proposed by Luoma [22].

Quantitative components	Description
CSF-adjusted disc signal intensity	The signal intensity of each nucleus pulposus was quantified by comparing it with cerebrospinal fluid.
Disc height	The means of the anterior and posterior heights were called disc heights
Disc bulging	A bulge measuring ≥3.2mm was considered a positive finding

Table 24. Grading system for lumbar disc degeneration proposed by Oktay [23].

Quantitative components	Description
Automation and computer aided grading for intensity, planar shape, and herniation	A novel method for automated diagnosis of degenerative disc disease using midsagittal MR images. The discs are first localised and segmented. Then, intensity, shape, context, and texture features of the discs are extracted with various techniques. A Support Vector Machine classifier is applied to classify the discs as normal or degeneration. The segmentation used planar shape (disc height), intensity (CSF adjusted signal intensity), and shape (herniation)

Table 25. Specialised quantitative MRI techniques and sequences

Quantitative components	Description
Disc signal intensity	A clustering of grading systems that measure the water content and tissue composition within the disc using specific techniques and sequences. These commonly included T1 and T2 mapping and relaxation techniques.

References for Appendix 4

1. Aavikko A, Lohman M, Ristolainen L, Kautiainen H, Osterman K, Schlenzka D, et al. Issls Prize in Clinical Science 2022: Accelerated Disc Degeneration after Pubertal Growth Spurt Differentiates Adults with Low Back Pain from Their Asymptomatic Peers. European Spine Journal. 2022;31(5):1080-7.

2. Battie MC, Videman T, Levalahti E, Gill K, Kaprio J. Genetic and Environmental Effects on Disc Degeneration by Phenotype and Spinal Level: A Multivariate Twin Study. Spine. 2008;33(25):2801-8.

3. Battie MC, Videman T, Gibbons LE, Fisher LD, Manninen H, Gill K. Determinants of Lumbar Disc Degeneration: A Study Relating Lifetime Exposures and Magnetic Resonance Imaging Findings in Identical Twins. Spine. 1995;20(24):2601-12.

4. Ding WY, Yang DL, Cao LZ, Sun YP, Zhang W, Xu JX, et al. Intervertebral Disc Degeneration and Bone Density in Degenerative Lumbar Scoliosis: A Comparative Study between Patients with Degenerative Lumbar Scoliosis and Patients with Lumbar Stenosis. Chinese Medical Journal. 2011;124(23):3875-8.

5. Jarman JP, Arpinar VE, Baruah D, Klein AP, Maiman DJ, Muftuler LT. Intervertebral Disc Height Loss Demonstrates the Threshold of Major Pathological Changes During Degeneration. European Spine Journal. 2015;24(9):1944-50.

6. Luoma K, Vehmas T, Riihimäki H, Raininko R, Luoma K, Vehmas T, et al. Disc Height and Signal Intensity of the Nucleus Pulposus on Magnetic Resonance Imaging as Indicators of Lumbar Disc Degeneration. Spine (03622436). 2001;26(6):680-6.

7. Lund T, Schlenzka D, Lohman M, Ristolainen L, Kautiainen H, Klemetti E, et al. The Intervertebral Disc During Growth: Signal Intensity Changes on Magnetic Resonance Imaging and Their Relevance to Low Back Pain. PLoS ONE [Electronic Resource]. 2022;17(10):e0275315.

8. Nagashima M, Abe H, Amaya K, Matsumoto H, Yanaihara H, Nishiwaki Y, et al. Risk Factors for Lumbar Disc Degeneration in High School American Football Players: A Prospective 2-Year Follow-up Study. American Journal of Sports Medicine. 2013;41(9):2059-64.

9. Paajanen H, Erkintalo M, Kuusela T, Dahlstrom S, Kormano M. Magnetic Resonance Study of Disc Degeneration in Young Low-Back Pain Patients. Spine. 1989;14(9):982-5.

10. Videman T, Saarela J, Kaprio J, Nakki A, Levalahti E, Gill K, et al. Associations of 25 Structural, Degradative, and Inflammatory Candidate Genes with Lumbar Disc Desiccation, Bulging, and Height Narrowing. Arthritis & Rheumatism. 2009;60(2):470-81.

11. Videman T, Battie MC, Gibbons LE, Gill K. A New Quantitative Measure of Disc Degeneration. Spine Journal: Official Journal of the North American Spine Society. 2017;17(5):746-53.

12. Hancock MJ, Battie MC, Videman T, Gibbons L. The Role of Back Injury or Trauma in Lumbar Disc Degeneration: An Exposure-Discordant Twin Study. Spine. 2010;35(21):1925-9.

13. Harada A, Okuizumi H, Miyagi N, Genda E. Correlation between Bone Mineral Density and Intervertebral Disc Degeneration. Spine. 1998;23(8):857-61; discussion 62.

14. Luoma K, Riihimaki H, Luukkonen R, Raininko R, Viikari-Juntura E, Lamminen A. Low Back Pain in Relation to Lumbar Disc Degeneration. Spine. 2000;25(4):487-92.

15. Bechara BP, Agarwal V, Boardman J, Perera S, Weiner DK, Vo N, et al. Correlation of Pain with Objective Quantification of Magnetic Resonance Images in Older Adults with Chronic Low Back Pain. Spine. 2014;39(6):469-75.

16. Salamat S, Hutchings J, Kwong C, Magnussen J, Hancock MJ. The Relationship between Quantitative Measures of Disc Height and Disc Signal Intensity with Pfirrmann Score of Disc Degeneration. Springerplus. 2016;5(1):829.

17. Su Y, Ren D, Chen Y, Geng L, Yao S, Wu H, et al. Effect of Endplate Reduction on Endplate Healing Morphology and Intervertebral Disc Degeneration in Patients with Thoracolumbar Vertebral Fracture. European Spine Journal. 2023;32(1):55-67.

18. Hu X, Chen M, Pan J, Liang L, Wang Y. Is It Appropriate to Measure Age-Related Lumbar Disc Degeneration on the Mid-Sagittal Mr Image? A Quantitative Image Study. European Spine Journal. 2018;27(5):1073-81.

19. Feng Z, Liu Y, Wei W, Hu S, Wang Y. Type Ii Modic Changes May Not Always Represent Fat Degeneration: A Study Using Mr Fat Suppression Sequence. Spine. 2016;41(16):E987-E94.

20. Huang J, Shen H, Wu J, Hu X, Zhu Z, Lv X, et al. Spine Explorer: A Deep Learning Based Fully Automated Program for Efficient and Reliable Quantifications of the Vertebrae and Discs on Sagittal Lumbar Spine Mr Images. Spine Journal: Official Journal of the North American Spine Society. 2020;20(4):590-9.

21. Lu X, Zhu Z, Pan J, Feng Z, Lv X, Battie MC, et al. Traumatic Vertebra and Endplate Fractures Promote Adjacent Disc Degeneration: Evidence from a Clinical Mr Follow-up Study. Skeletal Radiology. 2022;51(5):1017-26.

22. Luoma K, Vehmas T, Raininko R, Luukkonen R, Riihimaki H. Lumbosacral Transitional Vertebra: Relation to Disc Degeneration and Low Back Pain. Spine. 2004;29(2):200-5.

23. Oktay AB, Albayrak NB, Akgul YS. Computer Aided Diagnosis of Degenerative Intervertebral Disc Diseases from Lumbar Mr Images. Computerized Medical Imaging & Graphics. 2014;38(7):613-9.

Appendix 5. The proportion of all grading systems reported to be used to assess disc degeneration with different methods of synthesis, stratified by the grading system components used to assess for disc degeneration

		DD grading performed by**				L-spine levels reported			Methods of synthesis I**				Methods of synthesis II			
Grading system components	Proportion of reported use of grading systems % (n/N)	Radiologist % (n/N)	Surgeon % (n/N)	Not specified % (n/N)	Lumbar spine reported (T12-S1)* % (n/N)	Single level reported % (n/N)	Other* % (n/N)	Each level individually % (n/N)	Worst level % (n/N)	Sum of all levels % (n/N)	Average across all levels % (n/N)	Not specified % (n/N)	Continuous % (n/N)	Ordinal % (n/N)	Collected as ordinal but analysed as dichotomous % (n/N)	Collected and analysed as dichotomous % (n/N)
Subjective grading systems	**83.2 (556/668)**	**42.4 (236/556)**	**24.1 (134/556)**	**31.8 (177/556)**	**53.2 (296/556)**	**12.6 (70/556)**	**34.4 (191/556)**	**58.1 (323/556)**	**6.1 (34/556)**	**14.4 (80/556)**	**3.8 (21/556)**	**21.8 (121/556)**	**9.4 (52/556)**	**58.5 (325/556)**	**27.5 (153/556)**	**4.7 (26/556)**
DSI	**3.8 (21/556)**	**57.1 (12/21)**	**19.0 (4/21)**	**38.1 (8/21)**	**33.3 (7/21)**	**19.0 (4/21)**	**47.7 (10/21)**	**71.4 (15/21)**	**4.8 (1/21)**	**0.0 (0/21)**	**0.0 (0/21)**	**23.8 (5/21)**	**0.0 (0/21)**	**42.9 (9/21)**	**14.3 (3/21)**	**42.9 (9/21)**
Gibson	19.0 (4/21)	0.0 (0/4)	25.0 (1/4)	75.0 (3/4)	25.0 (1/4)	50.0 (2/4)	25.0 (1/4)	75.0 (3/4)	0.0 (0/4)	0.0 (0/4)	0.0 (0/4)	25.0 (1/4)	0.0 (0/4)	100.0 (4/4)	0.0 (0/4)	0.0 (0/4)
Decandido	14.3 (3/21)	33.3 (1/3)	33.3 (1/3)	66.7 (2/3)	66.7 (2/3)	33.3 (1/3)	0.0 (0/3)	66.7 (2/3)	0.0 (0/3)	0.0 (0/3)	0.0 (0/3)	33.3 (1/3)	0.0 (0/3)	66.7 (2/3)	0.0 (0/3)	33.3 (1/3)
Luoma	9.5 (2/21)	100.0 (2/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	100.0 (2/2)	100.0 (2/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	50.0 (1/2)	50.0 (1/2)
Other***	57.1 (12/21)	75.0 (9/12)	16.7 (2/12)	25.0 (3/12)	33.3 (4/12)	8.3 (1/12)	58.3 (7/12)	66.7 (8/12)	8.3 (1/12)	0.0 (0/12)	0.0 (0/12)	25.0 (3/12)	0.0 (0/12)	25.0 (3/12)	16.7 (2/12)	58.3 (7/12)
DH	**0.7 (4/556)**	**75.0 (3/4)**	**75.0 (3/4)**	**0.0 (0/4)**	**75.0 (3/4)**	**25.0 (1/4)**	**0.0 (0/4)**	**50.0 (2/4)**	**25.0 (1/4)**	**0.0 (0/4)**	**25.0 (1/4)**	**0.0 (0/4)**	**25.0 (1/4)**	**75.0 (3/4)**	**25.0 (1/4)**	**0.0 (0/4)**

DSI and DH	**7.9 (44/556)**	**43.2 (19/44)**	**18.2 (8/44)**	**31.8 (14/44)**	**75.0 (33/44)**	**4.5 (2/44)**	**22.7 (10/44)**	**45.5 (20/44)**	**4.5 (2/44)**	**43.2 (19/44)**	**2.3 (1/44)**	**11.4 (5/44)**	**25.0 (11/44)**	**43.2 (19/44)**	**25.0 (11/44)**	**6.8 (3/44)**
Schneidermann	68.2 (30/44)	23.3 (7/30)	26.7 (8/30)	40 (12/30)	76.7 (23/30)	3.3 (1/30)	20.0 (6/30)	33.3 (10/30)	3.3 (1/30)	60.0 (18/30)	3.3 (1/30)	6.7 (2/30)	33.3 (10/30)	43.3 (13/30)	23.3 (7/30)	0.0 (0/30)
Jensen	11.4 (5/44)	100.0 (5/5)	0.0 (0/5)	0.0 (0/5)	100.0 (5/5)	0.0 (0/5)	0.0 (0/5)	60.0 (3/5)	20.0 (1/5)	0.0 (0/5)	0.0 (0/5)	20.0 (1/5)	20.0 (1/5)	40.0 (2/5)	40.0 (2/5)	0.0 (0/5)
Luoma	4.5 (2/44)	100.0 (2/2)	0.0 (0/2)	0.0 (0/2)	50.0 (1/2)	0.0 (0/2)	50.0 (1/2)	50.0 (1/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	50.0 (1/2)	0.0 (0/2)	100.0 (2/2)	0.0 (0/2)	0.0 (0/2)
Other***	15.9 (7/44)	71.4 (5/7)	0.0 (0/7)	28.6 (2/7)	57.1 (4/7)	14.3 (1/7)	42.9 (3/7)	85.7 (6/7)	0.0 (0/7)	14.3 (1/7)	0.0 (0/7)	14.3 (1/7)	0.0 (0/7)	28.6 (2/7)	28.6 (2/7)	42.9 (3/7)
DSI and/or DH and/or disc bulging and herniation	**4.1 (23/556)**	**60.9 (14/23)**	**30.4 (7/23)**	**13.0 (3/23)**	**43.5 (10/23)**	**0.0 (0/23)**	**56.5 (13/23)**	**34.8 (8/23)**	**8.7 (2/23)**	**34.8 (8/23)**	**8.7 (2/23)**	**21.7 (5/23)**	**17.4 (4/23)**	**60.9 (14/23)**	**0.0 (0/23)**	**21.7 (5/23)**
Fardon	17.4 (4/23)	50.0 (2/4)	25.0 (1/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	100.0 (4/4)	50.0 (2/4)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	50.0 (2/4)	0.0 (0/2)	25.0 (1/2)	0.0 (0/2)	75.0 (3/4)
Solovieva	17.4 (4/23)	100.0 (4/4)	0.0 (0/4)	0.0 (0/4)	0.0 (0/4)	0.0 (0/4)	100.0 (4/4)	25.0 (1/4)	0.0 (0/4)	100.0 (4/4)	0.0 (0/4)	0.0 (0/4)	0.0 (0/4)	100.0 (4/4)	0.0 (0/4)	0.0 (0/4)
Witwit	13.0 (3/23)	100.0 (3/3)	0.0 (0/3)	0.0 (0/3)	100.0 (3/3)	0.0 (0/3)	0.0 (0/3)	66.7 (2/3)	0.0 (0/3)	0.0 (0/3)	0.0 (0/3)	33.3 (1/3)	0.0 (0/3)	66.7 (2/3)	0.0 (0/3)	33.3 (1/3)
Battie	8.7 (2/23)	50.0 (1/2)	50.0 (1/2)	50.0 (1/2)	50.0 (1/2)	0.0 (0/2)	50.0 (1/2)	50.0 (1/2)	0.0 (0/2)	50.0 (1/2)	0.0 (0/2)	0.0 (0/2)	50.0 (1/2)	50.0 (1/2)	0.0 (0/2)	0.0 (0/2)
Horton and Daftari	8.7 (2/23)	50.0 (1/2)	0.0 (0/2)	50.0 (1/2)	0.0 (0/2)	0.0 (0/2)	100.0 (2/2)	50.0 (1/2)	0.0 (0/2)	50.0 (1/2)	0.0 (0/2)	0.0 (0/2)	50.0 (1/2)	50.0 (1/2)	0.0 (0/2)	0.0 (0/2)
Kanamori	8.7 (2/23)	0.0 (0/2)	100.0 (2/2)	0.0 (0/2)	100.0 (2/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	100.0 (2/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	100.0 (2/2)	0.0 (0/2)	0.0 (0/2)
Videman	8.7 (2/23)	0.0 (0/2)	50.0 (1/2)	50.0 (1/2)	50.0 (1/2)	0.0 (0/2)	50.0 (1/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	50.0 (1/2)	50.0 (1/2)	0.0 (0/2)	100.0 (2/2)	0.0 (0/2)	0.0 (0/2)
Other***	17.4 (4/23)	75.0 (3/4)	50.0 (2/4)	0.0 (0/4)	75.0 (3/4)	0.0 (0/4)	25.0 (1/4)	25.0 (1/4)	0.0 (0/4)	50.0 (2/4)	25.0 (1/4)	25.0 (1/4)	50.0 (2/4)	25.0 (1/4)	0.0 (0/4)	25.0 (1/4)

DSI and/or DH and/or herniation, and/or structural changes, and/or distinction between AF and NP	**77.5 (431/556)**	**40.4 (174/431)**	**23.9 (103/431)**	**32.9 (142/431)**	**52.4 (226/431)**	**11.1 (60/431)**	**33.6 (145/431)**	**61.3 (264/431)**	**6.5 (28/431)**	**9.0 (39/431)**	**3.7 (16/431)**	**23.0 (99/431)**	**5.6 (24/431)**	**61.3 (264/431)**	**31.3 (135/431)**	**1.9 (8/431)**
Pfirrmann	85.8 (370/431)	40.3 (149/370)	23.5 (87/370)	32.2 (119/370)	54.1 (200/370)	13.0 (48/370)	33.0 (122/370)	61.6 (228/370)	6.2 (23/370)	9.7 (36/370)	4.3 (16/370)	22.2 (82/370)	5.9 (22/370)	59.5 (220/370)	30.3 (122/370)	1.6 (6/370)
Modified Pfirrmann	9.7 (42/431)	50.0 (21/42)	33.3 (14/42)	28.6 (12/42)	40.5 (17/42)	26.2 (11/42)	33.3 (14/42)	54.8 (23/42)	9.5 (4/42)	2.4 (1/42)	0.0 (0/42)	33.3 (14/42)	4.8 (2/42)	76.2 (32/42)	16.7 (7/42)	2.4 (1/42)
Thompson	2.1 (9/431)	0.0 (0/9)	22.2 (2/9)	66.7 (6/9)	44.4 (4/9)	0.0 (0/9)	55.6 (5/9)	66.7 (6/9)	0.0 (0/9)	11.1 (1/9)	0.0 (0/9)	22.2 (2/9)	0.0 (0/9)	77.8 (7/9)	22.2 (2/9)	0.0 (0/9)
Buirski	0.7 (3/431)	0.0 (0/3)	0.0 (0/3)	66.7 (2/3)	33.3 (1/3)	0.0 (0/3)	66.7 (2/3)	66.7 (2/3)	0.0 (0/3)	0.0 (0/3)	0.0 (0/3)	33.3 (1/3)	0.0 (0/3)	33.3 (1/3)	66.7 (2/3)	0.0 (0/3)
Modified Pearce	0.5 (2/431	100.0 (2/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	100.0 (2/2)	100.0 (2/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	100.0 (2/2)	0.0 (0/2)	0.0 (0/2)
Woodend Classification	0.5 (2/431	0.0 (0/2)	0.0 (0/2)	100.0 (2/2)	50.0 (1/2)	50.0 (1/2)	0.0 (0/2)	50.0 (1/2)	50.0 (1/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	100.0 (2/2)	0.0 (0/2)	0.0 (0/2)
Other***	0.7 (3/431)	66.7 (2/3)	0.0 (0/3)	33.3 (1/3)	100 (3/3)	0.0 (0/3)	0.0 (0/3)	66.7 (2/3)	0.0 (0/3)	33.3 (1/3)	0.0 (0/3)	0.0 (0/3)	0.0 (0/3)	0.0 (0/3)	66.7 (2/3)	33.3 (1/3)
DSI and/or DH and/or osteophytes, end-plate changes, Modic changes and high intensity zones (HIZ)	**5.9 (33/556)**	**42.4 (14/33)**	**27.3 (9/33)**	**30.3 (10/33)**	**51.5 (17/33)**	**9.1 (3/33)**	**39.4 (13/33)**	**42.4 (14/33)**	**0.0 (0/33)**	**42.4 (14/33)**	**3.0 (1/33)**	**21.2 (7/33)**	**39.4 (13/33)**	**48.5 (16/33)**	**9.1 (3/33)**	**3.0 (1/33)**
Jarosz Atlas	36.4 (12/33)	16.7 (2/12)	0.0 (0/12)	58.3 (7/12)	58.3 (7/12)	0.0 (0/12)	41.7 (5/12)	33.3 (4/12)	0.0 (0/12)	91.7 (11/12)	0.0 (0/12)	0.0 (0/12)	75.0 (9/12)	16.7 (2/12)	8.3 (1/12)	0.0 (0/12)

Pearce	18.2 (6/33)	66.7 (4/6)	16.7 (1/6)	16.7 (1/6)	16.7 (1/6)	16.7 (1/6)	66.7 (4/6)	33.3 (2/6)	0.0 (0/6)	0.0 (0/6)	0.0 (0/6)	66.7 (4/6)	0.0 (0/6)	66.7 (4/6)	33.3 (2/6)	0.0 (0/6)
Battie	6.1 (2/33)	50.0 (1/2)	100.0 (2/2)	0.0 (0/2)	100.0 (2/2)	0.0 (0/2)	0.0 (0/2)	50.0 (1/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	50.0 (1/2)	0.0 (0/2)	100.0 (2/2)	0.0 (0/2)	0.0 (0/2)
Benneker	6.1 (2/33)	100.0 (2/2)	0.0 (0/2)	0.0 (0/2)	100.0 (2/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	100.0 (2/2)	0.0 (0/2)	0.0 (0/2)	100.0 (2/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)
Tuft degenerative disc classification	6.1 (2/33)	50.0 (1/2)	100.0 (2/2)	0.0 (0/2)	100.0 (2/2)	0.0 (0/2)	0.0 (0/2)	100.0 (2/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	50.0 (1/2)	50.0 (1/2)	0.0 (0/2)	0.0 (0/2)
Other	27.3 (9/33)	44.4 (4/9)	44.4 (4/9)	22.2 (2/9)	33.3 (3/9)	22.2 (2/9)	44.4 (4/9)	55.6 (5/9)	0.0 (0/9)	11.1 (1/9)	11.1 (1/9)	22.2 (2/9)	11.1 (1/9)	77.8 (7/9)	0.0 (0/9)	11.1 (1/9)
Quantitative grading systems	**16.8 (112/668)**	**33.0 (37/112)**	**11.6 (13/112)**	**54.5 (61/112)**	**60.7 (68/112)**	**3.6 (4/112)**	**35.7 (40/112)**	**76.8 (86/112)**	**2.7 (3/112)**	**3.6 (4/112)**	**6.3 (7/112)**	**13.4 (15/112)**	**92.0 (103/112)**	**6.3 (7/112)**	**0.0 (0/112)**	**3.6 (4/112)**
DSI	**17.9 (20/112)**	**25.0 (5/20)**	**20.0 (4/20)**	**65.0 (13/20)**	**50.0 (10/20)**	**5.0 (1/20)**	**45.0 (9/20)**	**65.0 (13/20)**	**5.0 (1/20)**	**0.0 (0/20)**	**15.0 (3/20)**	**25.0 (5/20)**	**75.0 (15/20)**	**15.0 (3/20)**	**0.0 (0/20)**	**10.0 (2/20)**
Videman	25.0 (5/20)	0.0 (0/5)	0.0 (0/5)	100.0 (5/5)	80.0 (4/5)	0.0 (0/5)	20.0 (1/5)	40.0 (2/5)	0.0 (0/5)	0.0 (0/5)	40.0 (2/5)	20.0 (1/5)	100.0 (5/5)	0.0 (0/5)	0.0 (0/5)	0.0 (0/5)
Paajanen	20.0 (4/20)	0.0 (0/4)	0.0 (0/4)	100.0 (4/4)	0.0 (0/4)	0.0 (0/4)	100.0 (4/4)	25.0 (1/4)	0.0 (0/4)	0.0 (0/4)	0.0 (0/4)	75.0 (3/4)	0.0 (0/4)	50.0 (2/4)	0.0 (0/4)	50.0 (2/4)
Battie	10.0 (2/20)	0.0 (0/2)	50.0 (1/2)	50.0 (1/2)	100.0 (2/2)	0.0 (0/2)	0.0 (0/2)	100.0 (2/2)	50.0 (1/2)	0.0 (0/2)	0.0 (0/2)	50.0 (1/2)	100.0 (2/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)
Luoma	10.0 (2/20)	100.0 (2/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	50.0 (1/2)	50.0 (1/2)	100.0 (2/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	100.0 (2/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)
Nagashima	10.0 (2/20)	0.0 (0/2)	0.0 (0/2)	100.0 (2/2)	100.0 (2/2)	0.0 (0/2)	0.0 (0/2)	50.0 (1/2)	0.0 (0/2)	0.0 (0/2)	50.0 (1/2)	0.0 (0/2)	100.0 (2/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)
Other***	25.0 (5/20)	60.0 (3/5)	60.0 (3/5)	20.0 (1/5)	40.0 (2/5)	0.0 (0/5)	60.0 (3/5)	100.0 (5/5)	0.0 (0/5)	0.0 (0/5)	0.0 (0/5)	0.0 (0/5)	80.0 (4/5)	20.0 (1/5)	0.0 (0/5)	0.0 (0/5)

DH	**2.7 (3/112)**	**0.0 (0/3)**	**0.0 (0/3)**	**100 (3/3)**	**66.7 (2/3)**	**0.0 (0/3)**	**33.3 (1/3)**	**100 (3/3)**	**0.0 (0/3)**	**0.0 (0/3)**	**33.3 (1/3)**	**0.0 (0/3)**	**100 (3/3)**	**0.0 (0/3)**	**0.0 (0/3)**	**0.0 (0/3)**
Disc bulging	**3.6 (4/112)**	**75.0 (3/4)**	**0.0 (0/4)**	**25.0 (1/4)**	**25.0 (1/4)**	**0.0 (0/4)**	**75.0 (3/4)**	**50.0 (2/4)**	**0.0 (0/4)**	**0.0 (0/4)**	**25.0 (1/4)**	**25.0 (1/4)**	**50.0 (2/4)**	**0.0 (0/4)**	**0.0 (0/4)**	**50.0 (2/4)**
Luoma	75.0 (3/4)	100 (3/3)	0.0 (0/3)	0.0 (0/3)	0.0 (0/3)	0.0 (0/3)	100 (3/3)	66.7 (2/3)	0.0 (0/3)	0.0 (0/3)	0.0 (0/3)	33.3 (1/3)	0.0 (0/3)	33.3 (1/3)	0.0 (0/3)	66.7 (2/3)
Other***	25.0 (1/4)	0.0 (0/1)	0.0 (0/1)	100.0 (1/1)	100.0 (1/1)	0.0 (0/1)	0.0 (0/1)	0.0 (0/1)	0.0 (0/1)	0.0 (0/1)	100.0 (1/1)	0.0 (0/1)	100.0 (1/1)	0.0 (0/1)	0.0 (0/1)	0.0 (0/1)
DSI and DH	**2.7 (3/112)**	**66.7 (2/3)**	**33.3 (1/3)**	**0.0 (0/3)**	**66.7 (2/3)**	**0.0 (0/3)**	**33.3 (1/3)**	**66.7 (2/3)**	**0.0 (0/3)**	**33.3 (1/3)**	**0.0 (0/3)**	**0.0 (0/3)**	**100 (3/3)**	**0.0 (0/3)**	**0.0 (0/3)**	**0.0 (0/3)**
DSI, DH, and disc bulging	**8.9 (10/112)**	**20.0 (2/10)**	**20.0 (2/10)**	**30.0 (3/10)**	**80.0 (8/10)**	**10.0 (1/10)**	**10.0 (1/10)**	**70.0 (7/10)**	**0.0 (0/10)**	**10.0 (1/10)**	**0.0 (0/10)**	**20.0 (2/10)**	**80.0 (8/10)**	**20.0 (2/10)**	**0.0 (0/10)**	**0.0 (0/10)**
Battie	30.0 (3/10)	0.0 (0/3)	0.0 (0/3)	66.7 (2/3)	100 (3/3)	0.0 (0/3)	0.0 (0/3)	33.3 (1/3)	0.0 (0/3)	33.3 (1/3)	0.0 (0/3)	33.3 (1/3)	66.7 (2/3)	33.3 (1/3)	0.0 (0/3)	0.0 (0/3)
Feng	30.0 (3/10)	0.0 (0/3)	0.0 (0/3)	33.3 (1/3)	66.7 (2/3)	0.0 (0/3)	33.3 (1/3)	66.7 (2/3)	0.0 (0/3)	0.0 (0/3)	0.0 (0/3)	33.3 (1/3)	100 (3/3)	0.0 (0/3)	0.0 (0/3)	0.0 (0/3)
Other	40.0 (4/10)	50.0 (2/4)	50.0 (2/4)	0.0 (0/4)	75.0 (3/4)	25.0 (1/4)	0.0 (0/4)	100.0 (4/4)	0.0 (0/4)	0.0 (0/4)	0.0 (0/4)	0.0 (0/4)	75.0 (3/4)	25.0 (1/4)	0.0 (0/4)	0.0 (0/4)
Specialized quantitative MRI techniques and sequences	**64.3 (72/112)**	**34.8 (25/72)**	**8.3 (6/72)**	**56.9 (41/72)**	**62.5 (45/72)**	**2.8 (2/72)**	**34.7 (25/72)**	**81.9 (59/72)**	**2.8 (2/72)**	**2.8 (2/72)**	**2.8 (2/72)**	**9.7 (7/72)**	**97.2 (70/76)**	**2.8 (2/72)**	**0.0 (0/72)**	**0.0 (0/72)**
Summary of subjective and quantitative grading systems	**668**	**40.9 (273/668)**	**22.0 (147/668)**	**35.6 (238/668)**	**54.5 (364/668)**	**11.1 (74/668)**	**34.6 (231/668)**	**61.2 (409/668)**	**5.5 (37/668)**	**12.6 (84/668)**	**4.2 (28/668)**	**20.4 (136/668)**	**23.2 (155/668)**	**49.7 (332/668)**	**22.9 (153/668)**	**4.5 (30/668)**

DSI: disc signal intensity, DH: disc height, AF: annulus fibrosis, NP: nucleus pulposus, MRI: magnetic resonance imaging

*Included combinations of T12-L5, T12-S1, L1-L5, and L5-S1. 'Other' category includes unspecified, and all other combinations reported

** The total number of responses may exceed the number of reports of grading system use due to the possibility of multiple options

*** Grading systems listed into the 'Other' category were used in <2 studies

Appendix 6. The proportion of grading systems reported to be assessed for measurement properties, stratified by the grading system components used to assess for disc degeneration

		Reliability		Sensitivity to change		Validity	
Grading system components	Proportion of reported use of grading systems % (n/N)	Intra-rater reliability % (n/N)	Inter-rater reliability % (n/N)	Use of a change score % (n/N)	Comparative evaluation with another grading system % (n/N)	Measured associations between DD and other variables % (n/N)	Measured associations between DD and LBP % (n/N)
Subjective grading system	**83.2 (556/668)**	**28.1 (156/556)**	**34.5 (192/556)**	**11.0 (61/556)**	**14.6 (81/556)**	**46.2 (257/556)**	**18.0 (100/556)**
DSI	**3.8 (21/556)**	**23.8 (5/21)**	**33.3 (7/21)**	**0.0 (0/21)**	**9.5 (2/21)**	**47.6 (10/21)**	**28.6 (6/21)**
Gibson	19.0 (4/21)	25.0 (1/4)	25.0 (1/4)	0.0 (0/4)	0.0 (0/4)	25.0 (1/4)	25.0 (1/4)
Decandido	14.3 (3/21)	0.0 (0/3)	0.0 (0/3)	0.0 (0/3)	0.0 (0/3)	66.7 (2/3)	0.0 (0/3)
Luoma	9.5 (2/21)	100.0 (2/2)	50.0 (1/2)	0.0 (0/2)	0.0 (0/2)	100.0 (2/2)	50.0 (1/2)
Other*	57.1 (12/21)	16.7 (2/12)	41.7 (5/12)	0.0 (0/12)	16.7 (2/12)	41.7 (5/12)	33.3 (4/12)
DH	**0.7 (4/556)**	**25.0 (1/4)**	**50.0 (2/4)**	**0.0 (0/4)**	**0.0 (0/4)**	**75.0 (3/4)**	**50.0 (2/4)**
DSI and DH	**7.9 (44/556)**	**31.8 (14/44)**	**45.5 (20/44)**	**11.4 (5/44)**	**11.4 (5/44)**	**54.5 (24/44)**	**31.8 (14/44)**
Schneidermann	68.2 (30/44)	20.0 (6/30)	40.0 (12/30)	10.0 (3/30)	16.7 (5/30)	53.3 (16/30)	33.3 (10/30)
Jensen	11.4 (5/44)	80.0 (4/5)	80.0 (4/5)	0.0 (0/5)	0.0 (0/5)	60.0 (3/5)	20.0 (1/5)
Luoma	4.5 (2/44)	100.0 (2/2)	100.0 (2/2)	50.0 (1/2)	0.0 (0/2)	50.0 (1/2)	50.0 (1/2)
Other*	15.9 (7/44)	28.6 (2/7)	28.6 (2/7)	14.3 (1/7)	0.0 (0/7)	57.1 (4/7)	28.6 (2/7)

DSI and/or DH and/or disc bulging and herniation	**4.1 (23/556)**	**30.4 (7/23)**	**39.1 (9/23)**	**13.0 (3/23)**	**17.4 (4/23)**	**52.2 (12/23)**	**34.8 (8/23)**
Fardon	17.4 (4/23)	0.0 (0/4)	25.0 (1/4)	0.0 (0/4)	25.0 (1/4)	50.0 (2/4)	25.0 (1/4)
Solovieva	17.4 (4/23)	0.0 (0/4)	100.0 (4/4)	0.0 (0/4)	0.0 (0/4)	0.0 (0/4)	0.0 (0/4)
Witwit	13.0 (3/23)	100.0 (3/3)	33.3 (1/3)	100.0 (3/3)	0.0 (0/3)	100.0 (3/3)	100.0 (3/3)
Battie	8.7 (2/23)	50.0 (1/2)	100.0 (2/2)	0.0 (0/2)	0.0 (0/2)	100.0 (2/2)	0.0 (0/2)
Horton and Daftari	8.7 (2/23)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	50.0 (1/2)	50.0 (1/2)	50.0 (1/2)
Kanamori	8.7 (2/23)	100.0 (2/2)	100.0 (2/2)	0.0 (0/2)	100.0 (2/2)	100.0 (2/2)	100.0 (2/2)
Videman	8.7 (2/23)	50.0 (1/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)
Other*	17.4 (4/23)	0.0 (0/4)	0.0 (0/4)	0.0 (0/4)	0.0 (0/4)	50.0 (2/4)	25.0 (1/4)
DSI and/or DH and/or herniation, structural changes, and distinction between AF and NP	**77.5 (431/556)**	**26.7 (115/431)**	**33.4 (144/431)**	**10.9 (47/431)**	**16.0 (69/431)**	**43.6 (188/431)**	**13.9 (60/431)**
Pfirrmann	85.8 (370/431)	27.3 (101/370)	34.6 (128/370)	11.1 (41/370)	15.1 (56/370)	44.3 (164/370)	14.3 (53/370)
Modified Pfirrmann	9.7 (42/431)	21.4 (9/42)	26.2 (11/42)	14.3 (6/42)	21.4 (9/42)	33.3 (14/42)	0.0 (0/42)
Thompson	2.1 (9/431)	33.3 (3/9)	33.3 (3/9)	0.0 (0/9)	11.1 (1/9)	11.1 (1/9)	11.1 (1/9)
Buirski	0.7 (3/431)	0.0 (0/3)	0.0 (0/3)	0.0 (0/3)	0.0 (0/3)	100.0 (3/3)	33.3 (1/3)
Modified Pearce	0.5 (2/431)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	50.0 (1/2)	100.0 (2/2)	100.0 (2/2)
Woodend Classification	0.5 (2/431)	50.0 (1/2)	50.0 (1/2)	0.0 (0/2)	50.0 (1/2)	100.0 (2/2)	100.0 (2/2)
Other*	0.7 (3/431)	33.3 (1/3)	33.3 (1/3)	0.0 (0/3)	33.3 (1/3)	66.7 (2/3)	33.3 (1/3)

DSI and/or DH and/or osteophytes, end-plate changes, Modic changes and high intensity zones	**5.9 (33/556)**	**42.4 (14/33)**	**30.3 (10/33)**	**18.2 (6/33)**	**3.0 (1/33)**	**60.6 (20/33)**	**30.3 (10/33)**
Jarosz Atlas	36.4 (12/33)	33.3 (4/12)	16.7 (2/12)	25.0 (3/12)	0.0 (0/12)	75.0 (9/12)	33.3 (4/12)
Pearce	18.2 (6/33)	16.7 (1/6)	16.7 (1/6)	33.3 (2/6)	0.0 (0/6)	66.7 (4/6)	33.3 (2/6)
Battie	6.1 (2/33)	50.0 (1/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	100.0 (2/2)	50.0 (1/2)
Benneker	6.1 (2/33)	50.0 (1/2)	50.0 (1/2)	0.0 (0/2)	0.0 (0/2)	100.0 (2/2)	100.0 (2/2)
Tuft degenerative disc classification	6.1 (2/33)	100.0 (2/2)	100.0 (2/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)
Other*	27.3 (9/33)	55.6 (5/9)	44.4 (4/9)	11.1 (1/9)	11.1 (1/9)	33.3 (3/9)	11.1 (1/9)
Quantitative grading systems	**16.8 (112/668)**	**42.9 (48/112)**	**35.7 (40/112)**	**9.8 (11/112)**	**61.6 (69/112)**	**33.9 (38/112)**	**10.7 (12/112)**
DSI	**17.9 (20/112)**	**30.0 (6/20)**	**20.0 (4/20)**	**25.0 (5/20)**	**15.0 (3/20)**	**55.0 (11/20)**	**25.0 (5/20)**
Videman	25.0 (5/20)	20.0 (1/5)	40.0 (2/5)	0.0 (0/5)	0.0 (0/5)	80.0 (4/5)	0.0 (0/5)
Paajanen	20.0 (4/20)	25.0 (1/4)	0.0 (0/4)	50.0 (2/4)	0.0 (0/4)	50.0 (2/4)	50.0 (2/4)
Battie	10.0 (2/20)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	100.0 (2/2)	0.0 (0/2)
Luoma	10.0 (2/20)	50.0 (1/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)	0.0 (0/2)
Nagashima	10.0 (2/20)	50.0 (1/2)	50.0 (1/2)	50.0 (1/2)	50.0 (1/2)	50.0 (1/2)	50.0 (1/2)
Other*	25.0 (5/20)	40.0 (2/5)	20.0 (1/5)	40.0 (2/5)	40.0 (2/5)	40.0 (2/5)	40.0 (2/5)
DH	**2.7 (3/112)**	**33.3 (1/3)**	**0.0 (0/3)**	**0.0 (0/3)**	**33.3 (1/3)**	**66.7 (2/3)**	**0.0 (0/3)**
Disc bulging	**3.6 (4/112)**	**75.0 (3/4)**	**50.0 (2/4)**	**0.0 (0/4)**	**0.0 (0/4)**	**100.0 (4/4)**	**50.0 (2/4)**

Luoma	75.0 (3/4)	100.0 (3/3)	33.3 (1/3)	0.0 (0/3)	0.0 (0/3)	100.0 (3/3)	66.7 (2/3)
Other*	25.0 (1/4)	0.0 (0/1)	100.0 (1/1)	0.0 (0/1)	0.0 (0/1)	100.0 (1/1)	0.0 (0/1)
DSI and DH	**2.7 (3/112)**	**0.0 (0/3)**	**33.3 (1/3)**	**33.3 (1/3)**	**33.3 (1/3)**	**66.7 (2/3)**	**33.3 (1/3)**
DSI, DH, and disc bulging	**8.9 (10/112)**	**70.0 (7/10)**	**70.0 (7/10)**	**20.0 (2/10)**	**20.0 (2/10)**	**60.0 (6/10)**	**10.0 (1/10)**
Battie	30.0 (3/10)	66.7 (2/3)	66.7 (2/3)	0.0 (0/3)	33.3 (1/3)	66.7 (2/3)	0.0 (0/3)
Feng	30.0 (3/10)	33.3 (1/3)	33.3 (1/3)	33.3 (1/3)	0.0 (0/3)	100.0 (3/3)	33.3 (1/3)
Other*	40.0 (4/10)	100.0 (4/4)	100.0 (4/4)	25.0 (1/4)	25.0 (1/4)	25.0 (1/4)	0.0 (0/4)
Specialized quantitative MRI techniques and sequences	**64.3 (72/112)**	**43.1 (31/72)**	**36.1 (26/72)**	**4.2 (3/72)**	**86.1 (62/72)**	**18.1 (13/72)**	**4.2 (3/72)**
Summary of subjective and quantitative grading systems	**668**	**30.5 (204/668)**	**34.7 (232/668)**	**10.8 (72/668)**	**22.5 (150/668)**	**44.2 (295/668)**	**16.8 (112/668)**

DSI: disc signal intensity, DH: disc height, AF: annulus fibrosis, NP: nucleus pulposus, MRI: magnetic resonance imaging, DD: disc degeneration

*Grading systems listed into the 'Other' category were used in <2 studies

CHAPTER 3. TESTING THE PREDICTIVE VALIDITY OF FIVE MRI-BASED GRADING SYSTEMS FOR LUMBAR DISC DEGENERATION

3.1 PREFACE

In Chapter 2 a substantial number of different grading systems for lumbar DD were identified, many of which were used to make associations with LBP. The systems used different grading components, different methods of synthesis and varied in the ways they were summarised for analysis, potentially resulting in different results when drawing conclusions about LBP outcomes. The predictive validity of different grading systems was not clearly assessed and may be influenced by the variability identified in the grading and analysis of these systems. It is currently unclear which grading system is the most predictive of LBP. Chapter 3 will investigate the predictive validity of the most commonly identified grading systems in their ability to predict an episode of recurrent LBP. These systems will be compared against new normalised quantitative measures to see if they have stronger associations with LBP outcomes.

The study presented in Chapter 3 has been submitted for publication to The Journal of Orthopaedic Research (Spine) as:

Esposito D, Hancock M, Brown BT, King S, Jenkins H. Testing the predictive validity of five MRI-based grading systems for lumbar disc degeneration.

The study is presented in the format of the submitted manuscript.

An ethics amendment for the study presented in Chapter 3 was obtained to add D.E as an investigator to a previously approved ethics application. This was completed through the Macquarie University Human Research Ethics Committee on the 21st of March 2023; Reference number: 52023580946889 (Appendices: Appendix 1)

3.2 CO-AUTHOR CONTRIBUTION STATEMENT

As co-authors of this paper, Testing the predictive validity of five MRI-based grading systems for lumbar disc degeneration, we confirm Dean Esposito has made the following contributions:

- Substantial contribution to research design of the study
- Acquisition, analysis and interpretation of the data
- Drafting the paper and revising it critically
- Approved the submitted and final versions

Mark Jonathan Hancock

Date: 18.12.2023

Benjamin Thomas Brown

Date: 18.12.2023

Samuel Stuart Graham King

Date: 18.12.2023

Hazel Jenkins

Date: 18.12.2023

MACQUARIE University

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AUTHORSHIP CONTRIBUTION STATEMENT

In accordance with the *Macquarie University Code for the Responsible Conduct of Research* and the *Authorship Standard*, researchers have a responsibility to their colleagues and the wider community to treat others fairly and with respect, to give credit where appropriate to those who have contributed to research.

Note for HDR students: *Where research papers are being included in a thesis, this template must be used to document the contribution of authors to each of the proposed or published research papers. The contribution of the candidate must be sufficient to justify inclusion of the paper in the thesis.*

Title of Publication (can be a holding title)		**Publication Status** Choose an item. Submitted for Publication
Testing the predictive validity of five MRI-based grading systems for lumbar disc degeneration		☐ In Progress or Unpublished work for thesis submission ☐ Submitted for Publication ☐ Accepted for Publication ☐ Published
Name of **corresponding author**	Department/Faculty	**Publication details:** indicate the name of the journal/ conference/ publisher/other outlet
Dean Esposito	Department of Chiropractic Faculty of Medicine, Health and Human Sciences	JOR (Spine)

2. STUDENTS DECLARATION (if applicable)

Name of HDR thesis author (If the same as corresponding author - write "as above")	Department/Faculty	Thesis title
"as above"	"as above"	MRI-based grading systems for assessing lumbar disc degeneration

Description of HDR thesis author's contribution to planning, execution, and preparation of the work if there are multiple authors

(for example, how much as a percent did you contribute to the conception of the project, the design of methodology or experimental protocol, data collection, analysis, drafting the manuscript, revising it critically for important intellectual content, etc.)

For this study, I contributed 100% to the analysis and drafting of the manuscript, including revising it critically for important intellectual content. I also had a substantial contribution to the research design of the study.

I declare that the above is an accurate description of my contribution to this publication, and the contributions of other authors are as described below.	**Student signature** **Date**	 12/18/2023

3. Description of all other author contributions

Use an Asterisk * to denote if the author is also a current student or HDR candidate.

The HDR candidate or corresponding author must, for each paper, list all authors and provide details of their role in the publication. Where possible, also provide a percentage estimate of the contribution made by each author.

Name and affiliation of author	Intellectual contribution(s) (for example to the: conception of the project, design of methodology/experimental protocol, data collection, analysis, drafting the manuscript, revising it critically for important intellectual content etc.)
Mark Hancock	Substantial contribution to the study design, acquisition, analysis and interpretation of data and drafting the paper and revising it critically.
Benjamin Brown	Substantial contribution to the study design, analysis and interpretation of data and drafting the paper and revising it critically.
Sam King	Substantial contribution to the study design, acquisition, and drafting the paper and revising it critically.
Hazel Jenkins	Substantial contribution to the study design, analysis and interpretation of data and drafting the paper and revising it critically.
	Provide summary for any additional Authors in this cell.

4. Author Declarations

I agree to be named as one of the authors of this work, and confirm:

i. *that I have met the authorship criteria set out in the* Authorship Standard, *accompanying the* Macquarie University Research Code,

ii. *that there are no other authors according to these criteria,*

iii. *that the description in Section 3 or 4 of my contribution(s) to this publication is accurate*

iv. *that I have agreed to the planned authorship order following the* Authorship Standard

Name of author	**Authorised *** By Signature or refer to other written record of approval (eg. pdf of a signed agreement or an email record)	Date
Mark Hancock		12/18/2023
Benjamin Brown		12/18/2023
Sam King		12/18/2023
Hazel Jenkins		12/18/2023
		12/18/2023
	Provide other written record of approval for additional authors (eg. pdf of a signed agreement or an email record)	

5. Data storage

The original data for this project are stored in the following location, in accordance with the *Research Data Management Standard* accompanying the *Macquarie University Research Code*.

If the data have been or will be deposited in an online repository, provide the details here with any corresponding DOI.

Data description/format	**Storage Location or DOI**	**Name of custodian** if other than the corresponding author

A copy of this form must be retained by the corresponding author and must accompany the thesis submitted for examination.

3.3 TITLE PAGE

Title: Testing the predictive validity of five MRI-based grading systems for lumbar disc degeneration

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3.4 ABSTRACT

Background: Lumbar disc degeneration (DD) is commonly associated with low back pain (LBP); however, the relationship remains uncertain, potentially due to differences in the way DD has been measured across studies. A valid measure of DD is needed to accurately measure the extent of DD. This study aimed to assess the predictive validity of different methods of measuring DD including qualitative, quantitative and new normalized measures.

Methods: The study used de-identified data from 76 participants who had recovered from LBP. Magnetic resonance imaging (MRI) scans of the lumbar spine were performed and assessed at baseline and participants were followed for one-year to assess if a recurrence occurred. Multivariate Cox regression survival analysis evaluated the predictive validity of five MRI-based grading systems, using separate cox regression models for both the average and worst summary measures.

Results: The analysis demonstrated no differences in the predictive validity of the five DD grading systems in regard to LBP recurrence; however, variations in the point estimates suggested that the grading components, normalization and method of analysis appeared to influence the direction and magnitude of effect between DD and LBP recurrence.

Conclusion: No difference in the predictive validity of different grading systems for DD was observed. However, the components used to grade DD, normalization and how the grading system was summarized for analysis may influence the measurement of associations with clinical outcomes of LBP. Standardization of a grading system measure for DD is therefore recommended.

Keywords: "recurrence", "disc degeneration", "grading system", "disc height", "disc signal intensity", "quantitative measures", "predictive validity", "normalization"

3.5 INTRODUCTION

Lumbar disc degeneration (DD) is one factor that may contribute to the development or recurrence of low back pain (LBP). While magnetic resonance imaging (MRI) findings of DD are seen in both symptomatic and asymptomatic populations, these changes are more common in patients with LBP[1-3]. Research investigating whether DD is a predictor for future LBP is limited, and the relationship remains uncertain[4,5]. This may, in part, be due to the difficulties associated with measuring changes to the intervertebral disc (IVD) using MRI[6].

The most common MRI methods for grading DD typically employ ordinal-based scales that combine visual assessment of disc signal intensity (DSI), disc height (DH) and structural changes to the IVD (e.g., distinctiveness between the boundary between the annulus fibrosis and nucleus pulposus) to grade DD[7,8]. The Pfirrmann classification is the most commonly used method, whereby DD is graded on a scale between I and V[8]. Although straightforward to implement, these subjective classification systems are limited by relatively poor inter-rater reliability, validity concerns and lack of sensitivity to change[7-9].

Quantitative grading systems represent a more reliable measure of DD compared to subjective approaches, as they can be used to measure IVD changes more objectively. For example, quantitative systems do not rely on visual assessments of DD as do subjective methods, but rather they measure changes to the IVD on a continuous scale using distance between structures and brightness[10,11]. Most quantitative grading systems focus on the measurement of DSI and/or DH to assess DD, as structural changes to the IVD are difficult to quantify[12-15]. Although DSI and DH can be reliably measured, these measures may be susceptible to the influence of intrinsic (e.g., age, and disc level) and extrinsic (e.g., MRI sequence) factors. The added noise introduced by these factors may impact upon the validity of these measures, which may potentially influence the grading system's ability to measure the true extent of the underlying degeneration[16]. In a recent study by King *et al*[16], a normalization process, controlling for intrinsic and extrinsic factors, was developed in an attempt to overcome this noise and improve validity. Quantitative measures of DSI and DH were adjusted for factors such as age, cerebrospinal fluid (CSF), vertebral body height and disc level in the assessment of DD. It was found that normalized quantitative measures markedly changed where an individual was placed within the distribution of DD severity[16]. The findings of this study suggest that normalized measures of DSI and DH may be a more valid measure of DD.

The way in which subjective and quantitative grading systems are summarized for analysis is highly variable between different studies and may account for some of the variability in LBP research. For example, a study by Lund[17] found no association between DSI and LBP when using the grade of the worst/most degenerated disc in adolescents. In contrast, a study by Erkinatalo *et al*[18] measured DSI using a dichotomized summary measure, and showed a positive correlation between DD and LBP. These

examples highlight that the way in which grading systems are summarized for analysis may explain some of the inconsistencies that have been identified when investigating the association between DD and LBP. If a valid method of grading and analyzing DD can be established, more robust estimates of the association between DD and LBP can be made.

To more clearly understand the relationship between DD and LBP, it is important to identify grading systems and methods of analysis that are clinically relevant. How well a grading system predicts LBP, identifies favourable responses to treatment and distinguishes between patients with and without LBP are all clinically relevant outcomes. In this study, the predictive validity of the most commonly used subjective and quantitative grading systems were tested, including new normalized quantitative measures of DSI and DH. The systems were assessed to look for differences in their ability to predict a recurrence of LBP using an existing dataset reporting LBP recurrence.

The aims of this study were to assess: i) the predictive validity of five different MRI-based grading systems for DD in the lumbar spine (raw quantitative measures of DSI, raw quantitative measures of DH, normalized quantitative measures of DSI, normalized quantitative measures of DH and the Pfirrmann classification) for predicting a future recurrence of LBP and: ii) whether normalized quantitative measures of DSI and DH are different to raw quantitative measures of DSI and DH in predicting a recurrent episode of LBP.

3.6 MATERIALS AND METHODS

Study design and participants

This study used de-identified data from a previous observational study[19] investigating 76 participants who had recently recovered from an episode of LBP. At baseline, MRI scans of the lumbar spine were performed on all participants[19]. Participants also completed questionnaires detailing potential risk factors for recurrence, including age and the number of previous episodes[19]. The MRI scans were assessed for DD using the Pfirrmann classification[19], raw quantitative measures of DSI and DH[16] and normalized quantitative measures of DSI and DH[16]. Participants were subsequently monitored every two months over a period of one year to determine if and when they had a recurrence of LBP[19]. No additional information was gathered for this secondary analysis.

Participants were included if they had recently recovered from an episode of acute, non-specific LBP lasting more than 24 hours[19]. Participants were excluded if they had a contraindication to MRI, had undergone previous spinal surgery or were unable to complete the primary electronic follow-up either through text message or email[19]. No further exclusion criteria were applied for this secondary analysis. This study was approved by the Macquarie University Human Ethics Committee (Ref No:52023580946889).

Imaging process

All MRI images were taken using a single high-field strength, 3.0 T, Siemens, Magnetom Verio system (Siemens Australia, Victoria, Australia), equipped with a multichannel phased array spine surface coil[19]. A standardized imaging protocol was implemented for all participants[19]. This included sagittal fast spin echo T1 (TR 650ms, TE 6.3ms) and T2 (TR 4500 ms, TE 101 ms), sagittal short tau inversion recovery (STIR) (TR 3800 ms, TE 35 ms, TI 215 ms), and axial T2 (TR 5000 ms, TE 116 ms) scans[19]. All sequences had a thickness of 4mm and an interslice space of 1mm[19]. The sagittal sequences utilized a 320mm field of view (FOV), while axial sequences utilized a 200-mm FOV[19].

Predictor variables (measures of DD)

Five different grading systems for DD were previously performed on all disc levels and used as predictor variables in the current study, as described in Table 1. These included: i) raw quantitative measures of DSI; ii) normalized quantitative measures of DSI; iii) raw quantitative measures of DH; iv) normalized quantitative measures of DH; and v) the Pfirrmann classification.

Collection of quantitative raw, and normalized measures, and Pfirrmann scores

Raw quantitative MRI measures of DSI and DH were obtained from all five levels of the lumbar spine across the 76 MRI scans (380 measurements in total)[16]. The measurements were taken using a midsagittal view and reported by a researcher[16]. The researcher underwent training with an experienced radiologist and MRI data extraction commenced only after the researcher exhibited high levels of intra-rater reliability (ICC)[16].

Patient specific variables, as described in Table 2, were used to normalize the raw quantitative measures of DSI and DH[16]. In a previous study, a normalization process was undertaken to create Z-scores for each individual lumbar spine level (L1-L5)[16]. Full details of the normalization process have been published previously[16].

The Pfirrmann scores were graded by an experienced radiologist for each individual lumbar level (L1-L2 to L5-S1)[19]. The radiologist adhered to a standardized protocol and was given detailed instructions for how to score DD changes[19].

Summary measures:

Summary measures for analysis were created for each of the five grading systems to enable evaluation of the predictive value for a recurrence of pain for each individual. For each grading system we used two summary measures: 1) the average score across all lumbar levels and 2) the worst score at any lumbar level.

Raw and normalized quantitative measures of DSI and DH were recoded so that a higher score always indicated a greater severity of DD across all predictors (DSI_i and DH_i), to optimize interpretation of findings.

Outcome measure:

The primary outcome was the time (in days) to a recurrent episode of LBP as per the original study. Recurrence was defined as "the return of LBP lasting at least 24 hours with a pain intensity of 3 or more on a 0-10 numerical pain rating scale that also caused at least moderate impact on daily activity"[19].

Statistical analysis

Multivariate Cox regression survival analysis was used to estimate the predictive validity of each of the five grading systems in SPSS (version 29)[20]. One non-MRI variable (previous number of episodes of LBP) was also added as a confounder in the model. This additional confounder was selected as it is the strongest known predictor of a recurrence of LBP[19,21].

For each of the five grading systems, separate Cox regression models were built for both the average and worst summary measures using SPSS (version 29)[20]. A concordance statistic was computed in R (version 4.2.3)[22] to assess the discrimination, or predictive value, of each of the models in predicting a recurrent episode of LBP. The hazard (HR) and 95% confidence interval (95%CI) was calculated to assess the direction and magnitude of effect of the association between DD and LBP recurrence. A HR of >1 indicated an increased risk of a recurrence of LBP with increasing DD, while a HR of <1 indicated a decreased risk. To assess whether normalized measures of DSI and DH are different to raw measures of DSI and DH in predicting a recurrent episode of LBP, we specifically compared the results between normalized and raw measurements for the same measure of DD (e.g., DSI). Due to the small sample size, the focus was on the concordance statistic and effect size estimates, rather than statistical significance. The analysis was descriptive in nature as the HRs and concordance statistics for each of the models were not formally compared. The syntax used in SPSS and R is presented in Appendix 1.

3.7 RESULTS

Participant characteristics

Most of the participants were male (61%) and had a mean age of 45 years[19]. Of the 76 participants, 29 (38%) experienced an episode of activity limiting LBP, or recurrence, during the one-year follow-up period [19]. Baseline characteristics are described in Table 3.

Intra-rater reliability of raw quantitative measures and Pfirrmann classification

The intra-rater reliability of raw quantitative measures of DSI and DH were excellent for all measurements (ICC = ≥0.95)[16]. The intra-rater reliability of the primary MRI findings, which included the Pfirrmann classification ranged from good to fair[19].

Disc degeneration grading systems as predictors of recurrence of low back pain

The predictive validity of the ten models are summarized in Table 4. The concordance statistic showed similar levels of discrimination between the ten models (Range: C= 0.637-0.679), with no apparent differences when comparing raw and normalized measures for both DSI and DH.

None of the ten DD models showed statistically significant associations with recurrence of LBP based on HRs. However, the point estimates and the direction of effect varied substantially between some of the different models. For example, the point estimate for raw DH_i (average across all levels) suggested slightly increased risk of LBP recurrence with DD (HR 1.08, 95% CI 0.74-1.59), while the point estimate for normalized DH_i suggested decreased risk (HR 0.68, 95% CI 0.38-1.21). The point estimates for DSI_i also appeared different for raw (HR 1.00, 95% CI 0.99-1.01) and normalized values (HR 1.39, 95% CI 0.78-2.47).

The use of different summary measures for DD also influenced the direction of effect. For example, when normalized DH_i was graded using an average across all spinal levels, there was a HR of 0.68 (95% CI 0.38-1.21), indicating a decreased risk of LBP recurrence. In contrast, a HR indicating slightly increased risk of LBP recurrence was calculated when the worst score at any spinal level was used (HR of 1.09, 95% CI 0.68-1.75). This was the same for the Pfirrmann classification with a HR of 0.85 (95% CI 0.46-1.58) for the average score across all spinal levels, compared to a HR of 1.02 (95% CI 0.66-1.58) when the worst score at any level was used.

The grading components used to measure DD also influenced the direction of effect, with different directions of effect between the Pfirrmann classification (HR of 0.85, 95% CI 0.46-1.58) that used multiple components for grading (DSI, DH, and the distinction of the annulus-nucleus boundary) compared to normalized DSI_i (HR 1.39, 95% CI 0.78-2.47) when an average across all levels was used.

3.8 DISCUSSION

Summary of key findings

We assessed the predictive validity of five different MRI-based grading systems for DD (using ten models) in predicting a recurrence of LBP. The concordance statistics were similar for each of the models assessed. In addition, no differences in the concordance statistic were seen when raw versus normalized measures

of DSI and DH were used. These findings suggest that no one grading system, including new normalized measures, had superior predictive value in respect to assessing the recurrence of LBP.

Although there were no differences observed in overall predictive value according to the concordance statistics, some potentially important results were highlighted by the effect estimates (HRs) for the different measures of DD. For example, both normalized measures of DSI showed a suggested higher risk of LBP recurrence compared to the raw quantitative measures of DSI. This result may indicate that the normalization of raw quantitative measures of DSI may increase the strength of the association between DD and LBP recurrence. However, wide confidence intervals, likely due to the small sample size, highlight the uncertainty in these estimates.

The selection of different summary measures (average versus worst), and the number of grading components, also appeared to influence the strength and direction of association with LBP recurrence. Using DH and the Pfirrmann as an example, the direction of effect changed depending on whether an average score across all spinal levels or the worst score at any spinal level was used. The grading component used to assess DD also changed the direction of effect, with systems that used multiple grading components (Pfirrmann) showing a different direction of effect compared to those based solely on DSI. Overall, these findings suggest that the grading components (DSI, DH and structural changes), normalization process and the summary approach for analysis may have an impact on the predictive validity of DD grading systems.

Comparison to previous literature

Our study identified that the method of analysis of a grading system for DD, specifically the chosen summary approach, may affect the predictive validity for recurrence of LBP. In the current literature, there is substantial heterogeneity in the way grading systems are summarized for analysis (e.g., the summary measures used), in studies investigating the relationship between DD and future LBP[23]. When associations between LBP and DD are made, a range of different thresholds for the presence and absence of DD are used, which may impact the accuracy of estimates of the association. For example, Dragsbaek *et al*[23] found that the association between DD and LBP was highly dependent on different definitions and thresholds for what constitutes DD. This study differed from ours in that our outcome was a recurrence of LBP while Dragsbaek *et al*[23] used the year in which the patient had LBP. We also included normalized measures of DD as well as quantitative and qualitative measurements.

Among the five measures of DD that we explored, the Pfirrmann was unique in that it was the only system that combined measurements of DSI, DH and assessment of structural components of the IVD to measure DD. As no single measure displayed clear superiority, it remains relatively unclear if measures that use multiple grading components are better than grading systems that utilize single features such as DSI and

DH. Previous studies have investigated the relationship between quantitative measures of DSI and DH with the Pfirrmann classification, with one study identifying a strong association between quantitative measures and Pfirrmann[6]. The authors found that quantitative measures of DSI were strongly associated with Pfirrmann scores, except between grades of four and five, while DH was only associated with more severe degeneration on Pfirrmann[6]. Importantly, the study did not normalize the quantitative measures.

Strengths and limitations

The main strength of this study was the inclusion of data from a previously conducted study that used quantitative grading systems, including new normalized quantitative measures to grade DD. Quantitative measures demonstrate high reliability and have the potential to provide a better understanding of the importance of DD in LBP outcomes. The use of a LBP-specific definition of recurrence was also an important strength, as it is likely that the predictive validity of the system is influenced by the definition of recurrence that is used.

The key limitation of the study was the small sample size, meaning that potentially important differences between the discrimination of the grading systems may not have been captured. Equally the uncertainty in differences we identified in effect estimates (HRs) based on the grading components, normalization and summary measures used for analysis may also have been due to the small sample size. It is important to note that the study population of the original study was not representative of the LBP population generally. Further, some of the participants only experienced a couple of episodes of pain recurrence. As a result of this, there is a chance that some episodes of recurrence might have been missed during the follow up period in the original study.

When assessing future LBP and the potential factors that may predict future episodes, a range of other factors must be considered. Within this study, only the number of previous episodes of recurrence was considered as a non-MRI predictor variable within the regression models. Other factors could include the occurrence of new MRI findings at a similar time to a pain recurrence, the effects of conservative management administered during an episode of LBP prior to inclusion within the study or the level of understanding and knowledge by the patient of degenerative changes such as DD on MRI.

Implications

The findings of our study indicate that the grading system components, normalization process and method of analysis likely impact the predictive validity of a grading system for DD. It is reasonable to suggest that the selection of the components used for grading, and the way in which systems are summarized for analysis, do matter when measuring the true association between DD and future LBP. The use of different grading components, as well as different summary methods, may explain some of the variance in the studies that have investigated this association previously. It is important to identify the most valid grading system/s as this will improve our understanding of the true association between DD and LBP. The use of different thresholds when measuring DSI and DH quantitatively may also be important when determining whether one grading system is more valid than another, but this was not explored in the current study.

When looking more closely at the difference between raw and normalized measures of DSI, preliminary findings showed that a normalized measure of DSI may be more clinically relevant (i.e., showed a stronger HR effect size) compared to their raw DSI measures. Considering these potential differences, normalization may be important in creating more valid quantitative grading systems.

Future directions

The association between DD and LBP is complex, and further investigation is required to explore if different grading systems increase the strength of association between DD and LBP recurrence. Normalized grading systems need to be tested in larger, high-quality studies to determine whether they are more predictive of future LBP compared to raw quantitative measures of DSI and DH, and thus whether they have improved predictive validity. Future studies should also investigate the validity of grading systems for DD in relation to other clinically relevant outcomes such as identifying favourable outcomes for treatments of LBP, and whether different grading systems are better at distinguishing between individuals with or without LBP. This study only investigated one form of validity. An assessment of the other types of validity is also required.

3.9 CONCLUSION

This study tested the predictive validity of five different MRI-based methods of measuring DD for predicting a recurrence of LBP. Our preliminary findings suggest that the components that make up a grading system, whether measures have been normalized and the method of analysis may impact the predictive validity of a grading system for DD. Studies involving larger cohorts are however required to determine whether this is the case.

3.10 REFERENCES

1. Baker A. Abnormal Magnetic-Resonance Scans of the Lumbar Spine in Asymptomatic Subjects. A Prospective Investigation. Springer London; 2014:245-247.

2. Tonosu J, Oka H, Higashikawa A, Okazaki H, Tanaka S, Matsudaira K. The Associations between Magnetic Resonance Imaging Findings and Low Back Pain: A 10-Year Longitudinal Analysis. *PloS One*. 2017;12(11):e0188057-e0188057. doi:10.1371/journal.pone.0188057

3. Brinjikji W, Diehn FE, Jarvik JG, Carr CM, Kallmes DF, Murad MH, et al. MRI Findings of Disc Degeneration Are More Prevalent in Adults with Low Back Pain Than in Asymptomatic Controls: A Systematic Review and Meta-Analysis. *American Journal of Neuroradiology*. 2015;36(12):2394-2399. doi:10.3174/ajnr.A4498

4. Brinjikji W, Luetmer PH, Comstock B, Bresnahan BW, Chen LE, Deyo RA, et al. Systematic Literature Review of Imaging Features of Spinal Degeneration in Asymptomatic Populations. *American Journal of Neuroradiology*. 2015;36(4):811-816. doi:10.3174/ajnr.A4173

5. Han CS, Maher CG, Steffens D, Diwan A, Magnussen J, Hancock EC, et al. Some Magnetic Resonance Imaging Findings May Predict Future Low Back Pain and Disability: A Systematic Review. *Journal of Physiotherapy*. 2023;69(2):79-92. doi:10.1016/j.jphys.2023.02.007

6. Salamat S, Hutchings J, Kwong C, Magnussen J, Hancock MJ. The Relationship between Quantitative Measures of Disc Height and Disc Signal Intensity with Pfirrmann Score of Disc Degeneration. *SpringerPlus*. 2016;5(1):829-829. doi:10.1186/s40064-016-2542-5

7. Griffith JF, Wang Y-XJ, Antonio GE, Choi KC, Yu A, Ahuja AT, et al. Modified Pfirrmann Grading System for Lumbar Intervertebral Disc Degeneration. *Spine*. 2007;32(24):E708-E712. doi:10.1097/BRS.0b013e31815a59a0

8. Pfirrmann CWA, Metzdorf A, Zanetti M, Hodler J, Boos N. Magnetic Resonance Classification of Lumbar Intervertebral Disc Degeneration. *Spine.* 2001;26(17):1873-1878. doi:10.1097/00007632-200109010-00011

9. Rim DC. Quantitative Pfirrmann Disc Degeneration Grading System to Overcome the Limitation of Pfirrmann Disc Degeneration Grade. *Korean Journal of Spine*. 2016;13(1):1-8. doi:10.14245/kjs.2016.13.1.1

10. Jarman JP, Arpinar VE, Baruah D, Klein AP, Maiman DJ, Tugan Muftuler L. Intervertebral Disc Height Loss Demonstrates the Threshold of Major Pathological Changes During Degeneration. *European Spine Journal*. 2015;24(9):1944-1950. doi:10.1007/s00586-014-3564-8

11. Luoma K, Vehmas T, Riihimäki H, Raininko R. Disc Height and Signal Intensity of the Nucleus Pulposus on Magnetic Resonance Imaging as Indicators of Lumbar Disc Degeneration. *Spine*. 2001;26(6):680-686. doi:10.1097/00007632-200103150-00026

12. Niemeläinen R, Videman T, Dhillon SS, Battié MC. Quantitative Measurement of Intervertebral Disc Signal Using MRI. *Clinical Radiology*. 2007;63(3):252-255. doi:10.1016/j.crad.2007.08.012

13. Videman T, Gibbons LE, Battie MC. Age-and Pathology-Specific Measures of Disc Degeneration. *Spine*. 2008;33(25):2781-2788. doi:10.1097/brs.0b013e31817e1d11

14. Watanabe A, Benneker LM, Boesch C, Watanabe T, Obata T, Anderson SE. Classification of Intervertebral Disk Degeneration with Axial T2 Mapping. *American Journal of Roentgenology (1976)*. 2007;189(4):936-942. doi:10.2214/AJR.07.2142

15. Tunset A, Kjaer P, Samir Chreiteh S, Secher Jensen T. A Method for Quantitative Measurement of Lumbar Intervertebral Disc Structures: An Intra- and Inter-Rater Agreement and Reliability Study. *Chiropractic & Manual Therapies*. 2013;21(1):26-26. doi:10.1186/2045-709X-21-26

16. King S, Magnussen J, Elliott J, Hancock MJ. Development of Normalized Quantitative Measures of Lumbar Disc Degeneration. *Journal of Orthopaedic Research-Spine*. 2023:e1278. doi:https://doi.org/10.1002/jsp2.1278

17. Lund T, Schlenzka D, Lohman M, Ristolainen L, Kautiainen H, Klemetti E, et al. The Intervertebral Disc During Growth: Signal Intensity Changes on Magnetic Resonance Imaging and Their Relevance to Low Back Pain. *PloS one*. 2022;17(10):e0275315-e0275315. doi:10.1371/journal.pone.0275315

18. Erkintalo MO, Salminen JJ, Alanen AM, Paajanen HE, Kormano MJ. Development of Degenerative Changes in the Lumbar Intervertebral Disk: Results of a Prospective Mr Imaging Study in Adolescents with and without Low Back Pain. *Radiology*. Aug 1995;196(2):529-33. doi:10.1148/radiology.196.2.7617872

19. Hancock MJPB, Maher CMPF, Petocz PP, Lin C-WCP, Steffens DP, Luque-Suarez AP, et al. Risk Factors for a Recurrence of Low Back Pain. *The Spine Journal*. 2015;15(11):2360-2368. doi:10.1016/j.spinee.2015.07.007

20. IBM Corp. IBM SPSS Statistics for Windows. Version 27.0 [software]. Armonk, NY: IBM Corp; 2020.

21. Stanton TR, Henschke N, Maher CG, Refshauge KM, Latimer J, Mcauley JH. After an Episode of Acute Low Back Pain, Recurrence Is Unpredictable and Not as Common as Previously Thought. *Spine*. 2008;33(26):2923-2928. doi:10.1097/brs.0b013e31818a3167

22. R Core Team. R: A language and environment for statistical computing. Version 4.2.3 [software]. Vienna, Austria: R Foundation for Statistical Computing. Available at: URL. Accessed [June, 2023].

23. Dragsbaek L, Kjaer P, Hancock M, Jensen TS. An Exploratory Study of Different Definitions and Thresholds for Lumbar Disc Degeneration Assessed by MRI and Their Associations with Low Back Pain Using Data from a Cohort Study of a General Population. *BMC Musculoskeletal Disorders*. 2020;21(1):253-253. doi:10.1186/s12891-020-03268-4

3.11 TABLES

Table 1. Magnetic resonance imaging grading system predictors including method of initial scoring and summary measures used

DD grading system predictors	Method of scoring	Summary measure
Raw quantitative DSI	Measured as the mean signal intensity within the disc at each lumbar level (L1-L5)[16]	Worst score at any lumbar level (L1-L5) Average score across all five lumbar levels
Normalized quantitative DSI	Measured as the mean signal intensity within the disc at each lumbar level (1-5), transformed into a z-score through normalization formula for each lumbar level (L1-L5)[16]	Worst score at any lumbar level (L1-L5) Average score across all five lumbar levels
Raw quantitative DH	Measured as the mean anterior, middle, and posterior disc height for each lumbar level (L1-L5)[16]	Worst score at any lumbar level (L1-L5) Average score across all five lumbar levels
Normalized quantitative DH	Measured as the mean anterior, middle, and posterior disc height for each lumbar level (1-5), transformed into a z-score through normalization formula for each lumbar level (L1-L5)[16]	Worst score at any lumbar level (L1-L5) Average score across all five lumbar levels
Pfirrmann classification	Rated on the Pfirrmann scale between I and V for each lumbar level (L1-L5)[19]	Worst score at any lumbar level (L1-L5) Average score across all five lumbar levels

DSI: Disc signal intensity, DH: Disc height

Table 2. Normalization variables for disc signal intensity and disc height[16]

Normalization variables for DSI	Normalization variables for DH
CSF signal intensity (mean signal intensity of CSF region with a minimum area of 1cm^2)	Lumbar height (sum of means of anterior, middle and posterior L1-L4 and L4-S1 heights (mm)
Age (years)	Disc level (level of the disc between L1-L2 and L5-S1)
Disc level (level of the disc between L1-L2 and L5-S1)	

DSI: Disc signal intensity, DH: Disc height, CSF: Cerebro-spinal fluid.

Table 3. Baseline characteristics and variable data

Variable	Participants (n=76)
Age, mean (SD), y	45.6 (12.8)
Male gender, n (%)	46 (60.5)
Number of previous episodes, median (IQR)	2.5 (1-7.8)
Raw quantitative DSI, mean (SD)	142 SI (53 SI)
Raw quantitative DH, mean (SD)	9.9mm (1.8mm)

DSI: disc signal intensity, DH: disc height, SI: signal intensity, mm: millimeters

Table 4. Multivariate hazard ratios (HRs) for disc degeneration grading system predictors of a recurrence of low back pain

Predictor variable	Scoring method **Average score across all spinal levels (1-5)** Recurrence of LBP: HR (95% CI)	Concordance statistic	Scoring method **Worst score at any spinal level (1-5)** Recurrence of LBP: HR (95% CI)	Concordance statistic
Raw quantitative DSI_i	1.00 (0.99-1.01)	**0.672**	1.00 (0.99-1.01)	**0.657**
Normalized quantitative DSI_i	1.39 (0.78-2.47)	**0.660**	1.27 (0.72-2.23)	**0.642**
Raw quantitative DH_i	1.08 (0.74-1.59)	**0.651**	0.91 (0.66-1.24)	**0.679**
Normalized quantitative DH_i	0.68 (0.38-1.21)	**0.653**	1.09 (0.68-1.75)	**0.637**
Pfirrmann classification	0.85 (0.46-1.58)	**0.679**	1.02 (0.66-1.58)	**0.671**

DSI_i: Disc signal intensity (inversed), DH_i: Disc height (inversed)

3.12 SUBMITTED SUPPLEMENTARY MATERIAL

Appendix 1. SPSS and R Script syntax for each separate Cox regression model for both the average and worst summary measures

Raw_Quant_DH_worst cox

```
 COXREG DaystoADL_Recurrence
 /STATUS=Recurrence_ADL_Y_N(1)
 /METHOD=ENTER previous_lbp_number Raw_Quant_DH_worst_inverse_mm
 /PRINT=CI(95)
 /CRITERIA=PIN(.05) POUT(.10) ITERATE(20).
```

Raw Quant DH Avg cox

```
COXREG DaystoADL_Recurrence
 /STATUS=Recurrence_ADL_Y_N(1)
 /METHOD=ENTER previous_lbp_number Raw_Quant_DH_average_inverse_mm
 /PRINT=CI(95)
 /CRITERIA=PIN(.05) POUT(.10) ITERATE(20).
```

Raw Quant DSI Worst cox

```
COXREG DaystoADL_Recurrence
 /STATUS=Recurrence_ADL_Y_N(1)
 /METHOD=ENTER previous_lbp_number Raw_Quant_DSI_worst_inverse
 /PRINT=CI(95)
 /CRITERIA=PIN(.05) POUT(.10) ITERATE(20).
```

Raw quant DSI average cox

```
COXREG DaystoADL_Recurrence
 /STATUS=Recurrence_ADL_Y_N(1)
 /METHOD=ENTER previous_lbp_number Raw_Quant_DSI_average_inverse
 /PRINT=CI(95)
 /CRITERIA=PIN(.05) POUT(.10) ITERATE(20).
```

Normalised quant DH worst cox

```
COXREG DaystoADL_Recurrence
 /STATUS=Recurrence_ADL_Y_N(1)
 /METHOD=ENTER previous_lbp_number Norm_Quant_DH_worst_inverse
 /PRINT=CI(95)
 /CRITERIA=PIN(.05) POUT(.10) ITERATE(20).
```

Normalised Quant DH average cox

```
COXREG DaystoADL_Recurrence
 /STATUS=Recurrence_ADL_Y_N(1)
 /METHOD=ENTER previous_lbp_number Norm_Quant_DH_average_inverse
 /PRINT=CI(95)
 /CRITERIA=PIN(.05) POUT(.10) ITERATE(20).
```

Normalised Quant DSI worst cox

```
COXREG DaystoADL_Recurrence
/STATUS=Recurrence_ADL_Y_N(1)
  /METHOD=ENTER previous_lbp_number Norm_Quant_DSI_worst_inverse
  /PRINT=CI(95)
  /CRITERIA=PIN(.05) POUT(.10) ITERATE(20).
```

Normalised quant DSI average cox

```
COXREG DaystoADL_Recurrence
  /STATUS=Recurrence_ADL_Y_N(1)
  /METHOD=ENTER previous_lbp_number Norm_Quant_DSI_average_inverse
  /PRINT=CI(95)
  /CRITERIA=PIN(.05) POUT(.10) ITERATE(20).
```

Pfirrmann worst score cox

```
COXREG DaystoADL_Recurrence
  /STATUS=Recurrence_ADL_Y_N(1)
  /METHOD=ENTER previous_lbp_number MRI_DD_worst
  /PRINT=CI(95)
  /CRITERIA=PIN(.05) POUT(.10) ITERATE(20).
```

Pfirrmann average score cox

```
COXREG DaystoADL_Recurrence
  /STATUS=Recurrence_ADL_Y_N(1)
  /METHOD=ENTER previous_lbp_number MRI_DD_average
  /PRINT=CI(95)
  /CRITERIA=PIN(.05) POUT(.10) ITERATE(20).
```

```
# Load the relevant libraries

library(survival)
library(ranger)
library(ggplot2)
library(dplyr)
library(ggfortify)

# Set working directory
# Read in data
dat1<-read.csv("dat1.csv")
head(dat1)

# Column headers
names(dat1)

# Turn data into factors where necessary
dat1$MRI_DD_worst<-as.factor(dat1$MRI_DD_worst)
levels(dat1$MRI_DD_worst)<-c("Pfirrmann 2", "Pfirrmann 3", "Pfirrmann 4", "Pfirrmann
5")

# Model 1: Raw Quant DH Worst
m1 <- coxph(Surv(DaystoADL_Recurrence, Recurrence_ADL_Y_N) ~ previous_lbp_number +
Raw_Quant_DH_worst , method= "exact", data = dat1)
summary(m1) # Exponentiated coefficient = Hazard ratio, 95% CI = Coefficient plus or
minus 1.96 * SE. Then exponentiate these two numbers to get the 95% CI for the HR.

# Model 2: Raw Quant DH Avg
m2 <- coxph(Surv(DaystoADL_Recurrence, Recurrence_ADL_Y_N) ~ previous_lbp_number +
Raw_Quant_DH_average, method= "exact", data = dat1)
summary(m2)

# Model 3: Raw Quant DSI Worst
m3 <- coxph(Surv(DaystoADL_Recurrence, Recurrence_ADL_Y_N) ~ previous_lbp_number +
Raw_Quant_DSI_worst, method= "exact", data = dat1)
summary(m3)

# Model 4: Raw Quant DSI Avg
m4 <- coxph(Surv(DaystoADL_Recurrence, Recurrence_ADL_Y_N) ~ previous_lbp_number +
Raw_Quant_DSI_average, method= "exact", data = dat1)
summary(m4)

# Model 5: Norm_Quant_DSI_worst
m5 <- coxph(Surv(DaystoADL_Recurrence, Recurrence_ADL_Y_N) ~ previous_lbp_number +
Norm_Quant_DSI_worst, method= "exact", data = dat1)
summary(m5)

# Model 6: Norm_Quant_DSI_Avg
m6 <- coxph(Surv(DaystoADL_Recurrence, Recurrence_ADL_Y_N) ~ previous_lbp_number +
Norm_Quant_DSI_average, method= "exact", data = dat1)
summary(m6)

# Model 7: MRI_DD_worst
m7 <- coxph(Surv(DaystoADL_Recurrence, Recurrence_ADL_Y_N) ~ previous_lbp_number +
MRI_DD_worst, method= "exact", data = dat1)
summary(m7)

# Model 8: MRI_DD_average
m8 <- coxph(Surv(DaystoADL_Recurrence, Recurrence_ADL_Y_N) ~ previous_lbp_number +
MRI_DD_average, method= "exact", data = dat1)
summary(m8)

# Model 9: Norm_Quant_DH_worst
m9 <- coxph(Surv(DaystoADL_Recurrence, Recurrence_ADL_Y_N) ~ previous_lbp_number +
Norm_Quant_DH_worst, method= "exact", data = dat1)
summary(m9)

# Model 10: Norm_Quant_DH_average
m10 <- coxph(Surv(DaystoADL_Recurrence, Recurrence_ADL_Y_N) ~ previous_lbp_number +




Norm_Quant_DH_average, method= "exact", data = dat1)
summary(m10)
```

CHAPTER 4 DISCUSSION AND CONCLUSIONS

4.1 PREFACE

The primary aim of this thesis was to identify and describe MRI-based grading systems for lumbar DD and to assess the predictive validity of five of these systems in predicting a recurrent episode of LBP. A scoping review was performed (Chapter 2) to describe the most common grading systems, their methods of synthesis and the measurement properties assessed. The predictive validity of five different grading systems for DD, including the preliminary analysis of new normalised measures were assessed in Chapter 3.

4.2 MAIN FINDINGS

4.2.1 GRADING SYSTEMS FOR DISC DEGENERATION ARE NUMEROUS AND USE HETEROGENOUS GRADING COMPONENTS AND METHODS OF SYNTHESIS

In Chapter 2 a scoping review was performed to identify and describe different MRI-based grading systems for DD in the lumbar spine. The review identified 569 studies reporting on 93 individual grading systems for DD. Of these, 63 were subjective, 25 were quantitative and five were unspecified. The subjective system proposed by Pfirrmann [1] was used in more than half of the reports of MRI-based grading systems. The review did not identify any studies that systematically normalised quantitative DD scores to account for intrinsic factors such as age, disc level and vertebral body height.

There was a large variety of different grading components used to grade DD in the included studies. Subjective systems most commonly included combinations of DSI, DH and the distinctiveness of the annulus-nucleus boundary to grade DD. Quantitative grading systems typically assessed DD by measuring DSI with specialised MRI techniques and sequences.

A number of different methods were used to synthesise the DD measures for analysis. A dichotomous summary measure was frequently used in reports of subjective grading use, with data commonly collected at an ordinal level before being transformed into a dichotomous variable at each level. The thresholds for dichotomisation were not consistent between studies. Over 60% of subjective and quantitative systems were measured at each individual level of the lumbar spine. When analysis was required across multiple levels (e.g., using the system to measure patient level outcomes such as LBP), subjective grading systems synthesised DD measures as the sum of all spinal levels, or as the worst score at any level. It was uncommon for quantitative grading systems to measure DD using summary measures, as the systems were rarely used to measure patient level outcomes.

A variety of measurement properties were assessed across the different grading systems. Intra-rater and or inter-rater reliability was assessed in approximately one-third of reports of grading system use. In

regard to the measurement of validity, subjective systems commonly reported measured associations between DD and other clinical variables such as other imaging findings (degenerative spondylolisthesis, adolescent scoliosis and Modic changes) and patient level data (age, occupation and genetic factors). Studies that used quantitative grading systems were more likely to report a comparative evaluation with another grading system or imaging modality at a single disc level. Sensitivity to change was rarely reported for both subjective (11.0%) and quantitative grading systems (9.8%). The association between LBP (mostly 'current LBP') and DD was investigated in 16.8% of the reports of grading system use.

4.2.2. There is no discernable difference in the predictive validity of five lumbar disc degeneration grading systems; however, the different grading systems may influence the magnitude and direction of effect

In order to assess if the use of different grading systems resulted in different associations with clinical outcomes of LBP, we assessed the predictive validity of five different MRI-based grading systems for DD in predicting a recurrence of LBP. We included qualitative, quantitative and normalised grading systems with an emphasis on comparing quantitative measures of DSI and DH with normalised measures of DSI and DH (Chapter 3). One of the main findings of the secondary analysis was that there was no discernable difference in the discrimination, or predictive value, of the DD models that were appraised. Additionally, no differences were seen when raw versus normalised measures of DSI and DH were specifically compared.

The study provided evidence that, when assessing DD as a predictor for LBP recurrence, the size and direction of effect may be altered by different grading system factors, such as the normalisation of DSI and DH. The point estimates, including both the magnitude and direction of effect, varied between some of the different models assessed. When the normalisation of DSI and DH were used to grade DD, the strength and direction of the association changed when compared to raw quantitative grading of DD. In particular, the normalisation of DSI appeared to strengthen the magnitude of effect in the expected direction (i.e., increased severity of DSI loss resulting in more recurrence); however, wide confidence intervals reflect the uncertainty of this finding.

The way the grading system was summarised for analysis (e.g., the summary measure used) was also found to change the direction and magnitude of effect. When a normalised measure of DH and Pfirrmann classification were used to grade DD, the direction of effect changed depending on whether an average across all spinal levels was used compared to the worst score at any level.

The grading components used to measure DD also influenced the direction of effect, with different directions of effect observed between the Pfirrmann classification that used multiple components for

grading (DSI, DH and the distinction between the annulus-nucleus boundary) compared to normalised DSI when the same summary measure was used.

4.3 COMPARISON TO PREVIOUS LITERATURE

As seen in Chapter 2 substantial heterogeneity was identified in the components that are used to grade DD using MRI. These results were consistent with a number of studies investigating the heterogeneity of different grading system components [2]. A systematic review by Kettler *et al.* [2] identified a range of different grading systems for DD on MRI, with large variability in the design and components used within the systems. In contrast to our study, Kettler *et al.* [2] found significantly fewer MRI-based grading systems used to measure DD. This was attributed, in part to the age of the Kettler *et al.* [2] review, but also to the fact that only studies presenting the original grading system were included in the review, with the exclusion of systems that represented a variant of a previously reported grading system. This was an important difference to our study in that our methodological design allowed for the inclusion of grading system variants, and thus a larger number of grading systems for DD were included. Similarly to our study, none of the grading systems used normalised measures to grade DD that had been normalised for multiple intrinsic factors (e.g., age, disc level and vertebral body height).

The Pfirrmann classification was identified in Chapter 2 as the most common subjective grading system. It was also the only system used in Chapter 3 that combined measurements of DSI and DH to measure DD. As no grading system was shown to be more predictive of a recurrence of LBP in Chapter 3, it remains unclear if a system like the Pfirrmann that combines several measures of DD is superior to grading systems that are based on single IVD features such as DSI or DH. A previous study by Salamat and Hutchings *et al.* [3] found strong associations between individual components (e.g., DSI) of DD and those same components measured within the Pfirrmann system. The study concluded that quantitative DSI could be used in the place of Pfirrmann when sensitivity to change and reliability was an important determinant [3]. In Chapter 3 we found that one of the Pfirrmann models (average of all spinal levels) had a different direction of effect compared to any of the DSI models, regardless of whether the measure was normalised or unnormalised. Thus, the summary measure must also be considered along with the components themselves when measuring LBP outcomes.

It was identified in Chapter 3 that certain factors (such as the way the grading system is summarised for analysis) may impact the magnitude and direction of effect when measuring associations with clinical outcomes of LBP. In Chapter 2, it was found that a large variability exists in the way grading systems are summarised for analysis, and this variability was common in studies investigating the relationship between DD and LBP. A study by Dragsbaek *et al* [4] found similar results, concluding that the association between LBP and DD was highly dependent on thresholds of DD that were used, the age of the individual and the components used in the measure. The Dragsbaek *et al* [4] study differed from that used in Chapter

The need for a more standardised method of analysis of DD grading systems was highlighted in Chapter 2 and 3. The most appropriate summary measure for analysis also needs to be considered when assessing the validity of different grading systems. It is recommended that consistent methods of analysis are used when assessing associations between DD and LBP outcomes. A systematic review investigating whether MRI findings can predict future LBP found that poor associations were identified between LBP and MRI findings, likely due to the inconsistency of LBP assessment, outcome measures, MRI protocols and thresholds for positive findings [5]. Although our study did not focus on the specific association between DD and LBP, it was likely that the predictive validity of different DD grading systems was also impacted upon by some of these factors.

4.4 STRENGTHS AND LIMITATIONS

One strength of this thesis was the sensitivity of the search terms which assisted in identifying commonly used grading systems. In Chapter 2 the broad inclusion criteria of the review led to the identification and description of a wide variety of different subjective and quantitative MRI-based grading systems for DD. The implications of the broad inclusion was that we were confident that the review comprehensively identified all of the currently utilised systems for DD on MRI. By mapping the most common grading systems, and their grading components, the most relevant grading systems and components could be selected for comparison in Chapter 3.

This thesis was the first to compare the predictive validity of five different grading systems, including the direct comparison of normalised measures to raw quantitative measures of DSI and DH. An important strength was the ability to apply each grading system to the same cohort of people using the same summary measures. This allowed the results to be directly compared between both the components of the systems and the summary measure approach.

In Chapter 2, one of the main limitations was categorising the specialized quantitative MRI techniques and sequences used to grade DD into more specific categories. As these specialised quantitative MRI techniques and sequences were commonly used, some nuances regarding how these systems are reported and measured may have been lost by combining them.

The main limitation was the size of the sample used in Chapter 3. As the sample was small, potentially important differences between the five grading systems of DD may have been missed. Due to the size of the sample, we refrained from directly performing statistical comparisons between the different grading systems. Rather, the focus was on the descriptive analysis of differences in the magnitude and direction of the effect estimates of the five MRI-based grading systems (ten models). The precision of the effect estimates (HRs) that we identified are low, as evidenced by the wide confidence intervals. For this reason, definitive conclusions cannot be reached. Further studies using larger cohorts are required to confirm whether the predictive validity is influenced by these factors. These could include cohorts such as the RAINE cohort, which include thousands of participants with MRI data.

4.5 RESEARCH AND CLINICAL IMPLICATIONS

The work in this thesis led to the identification of a range of factors that may contribute to the observed variance in results of studies investigating the association between clinical outcomes of LBP and MRI-based grading systems for DD. In Chapter 3 preliminary results were presented that showed that the normalisation of DSI and DH is likely to impact the direction and magnitude of effect for a recurrence of LBP, but may not have superior discriminative capacity. If future research demonstrates the normalisation of quantitative measures of DD result in stronger associations with LBP, then they should become the standard in that type of research and may contribute to a better understanding of associations between DD and LBP.

The predictive validity of the grading system may also be dependent on the way the grading system is summarised for analysis. This is important, as the differences between studies investigating the association of LBP with DD may actually be attributed to variability in the method of analysis, rather than relationship between LBP and DD itself [6-8]. The most appropriate (valid) grading system and summary measure when measuring associations with LBP is currently unknown, which makes it difficult to draw accurate conclusions. A consensus document from a combined task force has previously been used to provide standardised terminology for clinicians and researchers regarding DD [9]. Although some of the recommendations broadly consider measures for DD, a specific recommendation for the most appropriate method for measuring DD has not yet been identified [9]. This is a key area for future research.

Sensitivity to change was found to be poorly reported across both subjective and quantitative grading system use. Grading systems that are sensitive to change may provide more clinical utility when drawing associations with LBP, as DD is a condition that is gradual and changes over time. A study by Panagopoulos *et al.* [10] found a large proportion of MRI findings changed in both patients with and without LBP, highlighting the importance of a grading system to be sensitive to change. Intervertebral disc changes should ideally be measured on a continuous versus dichotomous scale, in order to avoid the loss of information pertaining to the progression of IVD changes associated with DD that may contribute to LBP.

4.5.1 FUTURE RESEARCH

Future research should prioritise high quality studies to accurately determine whether normalised measures are more predictive of LBP recurrence. More specifically, analyses should assess normalised measures using larger sample sizes to gauge whether normalised measures are more valid than raw quantitative or qualitative measures. If this premise is correct, normalised measures may provide more clinically relevant information for practitioners. This thesis provides a preliminary analysis of normalised grading approaches for DD using a very specific clinical outcome (LBP recurrence). Further studies should

also consider whether normalised measures can better identify favourable responses to treatment for LBP and better distinguish between patients with or without LBP [11].

Studies should investigate the most appropriate summary measures to analyse and report DD grading systems. It is currently unknown which summary measure is the most valid. Deeper exploration into whether commonly used grading systems show high levels of discriminative, predictive and concurrent validity is required. Further study into the standardisation of grading system application may provide more consistent findings when investigating the association between DD and future LBP.

Making comparisons between the different grading systems is challenging due to the sheer number of different grading systems in the literature. Research efforts focusing on the validity and sensitivity to change of existing grading systems should be prioritised, rather than the creation of new grading systems. The former will help in establishing which systems should be used to measure associations between DD and LBP outcomes.

4.6 CONCLUSIONS

This thesis comprehensively described the most common grading systems for DD, and assessed the predictive validity of five different grading systems. It was found that a large number of grading systems exist to assess DD, with many infrequently used. Substantial heterogeneity was seen in both the components used for grading, as well as in the methods of synthesis used across studies. Some measurement properties were commonly assessed across different systems (e.g., reliability); however, sensitivity to change was rarely assessed across both subjective and quantitative systems. The importance of normalisation, and the way a system is summarised for analysis were demonstrated, with potential for these factors to influence the direction and magnitude of effect of association between DD and LBP recurrence. Preliminary findings supported the use of normalised DSI measures as a potentially valid measure of DD; however, definitive conclusions are unable to be reached. The variability described in the summary approaches and the components used to grade DD may hinder the ability to draw conclusions about the association between DD and LBP. Future research should focus on validating and standardising a grading system to assess DD, in order to better understand its influence on LBP.

4.7 REFERENCES

1. Pfirrmann CWA, Metzdorf A, Zanetti M, Hodler J, Boos N. Magnetic Resonance Classification of Lumbar Intervertebral Disc Degeneration. *Spine*. 2001;26(17):1873-1878.

2. Kettler A, Wilke HJ. Review of Existing Grading Systems for Cervical or Lumbar Disc and Facet Joint Degeneration. *European Spine Journal*. 2006;15(6):705-718.

3. Salamat S, Hutchings J, Kwong C, Magnussen J, Hancock MJ. The Relationship between Quantitative Measures of Disc Height and Disc Signal Intensity with Pfirrmann Score of Disc Degeneration. *SpringerPlus*. 2016;5(1):829-829.

4. Dragsbaek L, Kjaer P, Hancock M, Jensen TS. An Exploratory Study of Different Definitions and Thresholds for Lumbar Disc Degeneration Assessed by MRI and Their Associations with Low Back Pain Using Data from a Cohort Study of a General Population. *BMC Musculoskeletal Disorders*. 2020;21(1):253-253.

5. Han CS, Maher CG, Steffens D, Diwan A, Magnussen J, Hancock EC, et al. Some Magnetic Resonance Imaging Findings May Predict Future Low Back Pain and Disability: A Systematic Review. *Journal of Physiotherapy*. 2023;69(2):79-92.

6. Chou D, Samartzis D, Bellabarba C, Patel A, Luk KDK, Kisser JMS, et al. Degenerative Magnetic Resonance Imaging Changes in Patients with Chronic Low Back Pain: A Systematic Review. *Spine*. 2011;36(21):S43-S53.

7. Petit A, Roquelaure Y. Low Back Pain, Intervertebral Disc and Occupational Diseases. *International Journal of Occupational Safety and Ergonomics*. 2015;21(1):15-19.

8. Swanson BT, Creighton D. The Degenerative Lumbar Disc: Not a Disease, but Still an Important Consideration for OMPT Practice: A Review of the History and Science of Discogenic Instability. *The Journal of Manual & Manipulative Therapy*. 2020;28(4):191-200.

9. Fardon DF, Williams AL, Dohring EJ, Murtagh FR, Gabriel Rothman SL, Sze GK. Lumbar Disc Nomenclature: Version 2.0: Recommendations of the Combined Task Forces of the North American Spine Society, the American Society of Spine Radiology and the American Society of Neuroradiology. *The Spine Journal*. 2014;14(11):2525-2545.

10. Panagopoulos J, Magnussen JS, Hush J, Maher CG, Crites-Battie M, Jarvik JG, et al. Prospective Comparison of Changes in Lumbar Spine MRI Findings over Time between Individuals with Acute Low Back Pain and Controls: An Exploratory Study. *American Journal of Neuroradiology*. 2017;38(9):1826-1832.

11. King S, Magnussen J, Elliott J, Hancock MJ. Development of Normalized Quantitative Measures of Lumbar Disc Degeneration. *Journal of Orthopaedic Research-Spine*. 2023:e1278.

APPENDICES

5.1 APPENDIX 1: ETHICS AMENDMENT FOR CHAPTER 3

To: Mark Hancock
Cc: Alaa Qanber Ali; Daniel Edward Gonzalez; Geoffrey Wilson; Petar Peric; Richard White; Sam King; John Magnussen; Dean Esposito (HDR); Benjamin Cronin; Mark Hancock

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MACQUARIE University
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Dear Prof Hancock

RE: 52023580946889 - Relationship between lumbar muscle imaging and patient factors.

Your amendment request has been approved.

You may access the application by logging into the Human Research Ethics Management System.

Kind regards,

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