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Degeneration of the cervical disc: histology compared with radiography and magnetic resonance imaging

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Abstract Decisions about the treatment of neck pain are largely made on the basis of information gained from plain X-rays and magnetic resonance imaging (MRI), which are used routinely as part of preliminary investigation. We performed a descriptive cadaveric study to compare histology with radiography and MRI. We correlated plain radiography, disc height [Farfan index (FI)] and MRI findings with histology to assess the ability of radiology to detect significant pathologic lesions. The study included 52 motion segments from nine subjects over the age of 50, who underwent routine hospital autopsy. Disc degeneration was assessed by histology, radiography, disc height (FI: anterior disc height plus posterior disc height divided by anterioposterior diameter) and MRI using established grading systems. Most of the discs were classified radiologically as grade 1 (19/52), grade 2 (13/52), grade 3 (9/52) or grade 4 (3/52). Eight of the discs were graded as normal. The distribution of MRI grades was grade 0 (9/36), grade 1 (9/36), grade 2 (7/36), grade 3 (8/36) and grade 4 (3/36). Half of the discs (26/52) showed advanced (grade 4) degeneration histologically. FI correlated with histological grade ($P=0.013$), MRI grade ($P=0.02$) and radiological grade ($P<0.001$) of degeneration. Radiological and histological grade of degeneration showed a weak correlation ($r=0.3$, $P=0.033$). MRI correlated with overall histological grade ($r=0.41$, $P=0.015$, $n=34$). Histological features (e.g., tears, rim lesions, prolapse of nucleus material) were poorly recognised by MRI, which had a sensitivity for disc material prolapse and annulus tears of less than 40%. Our study showed that discs from patients over 50 years are histologically severely degenerated; however, these changes may not be detected by conventional radiography and MRI.

Keywords Cervical spine · Disc degeneration · Histology · Radiography · MRI · Cadaver study

Introduction

Back pain is a significant medical problem in western societies, reaching a peak in adults at around 40–50 years of age. The prevalence of neck and shoulder pain is high—between 18 and 71% of the population. In addition, there is a higher incidence among manual laborers [1]. Autopsy studies have shown that by age 40, all individuals have some degenerative changes of the cervical spine [2].

Decisions about the treatment of neck pain are, to a large extent, made on the basis of information gained

from plain X-rays and magnetic resonance imaging (MRI), which are used routinely as part of the preliminary investigation of affected patients. A few scientific studies have contributed to our knowledge by describing the normal histologic appearance of the lumbar spine from birth to senescence [4–6]. Furthermore, studies have shown the variety of pathologic conditions that could be responsible for pain symptoms, with a differential diagnosis encompassing prolapsed discs, disc degeneration, osteoarthrosis of the apophyseal joints, fractures and dislocations of vertebrae, osteoporosis, and spondylolisthesis [7]. We have not found any studies that have attempted to correlate histologic data with MRI and plain radiography. This is surprising given the high incidence of motor vehicle accident-associated whiplash injury and other causes of neck pain in western countries.

This study was undertaken firstly to describe the histological and radiological features, and grade of degeneration of the cervical discs in patients over 50 years. The second aim of the study was to correlate plain radiography, Farfan index (FI) and MRI findings with histology to assess the ability of radiology to detect significant pathologic lesions.

Methods

Subjects

The study included 54 motion segments from nine subjects over age 50, who underwent routine hospital autopsy. Cervical spine pain or previous surgery was not documented in the medical records of any of the subjects. Taking care to ensure that the musculature and ligaments were kept intact, the cervical spines were removed en bloc, sealed in double thickness polythene bags and frozen at −20°C.

Radiography and MRI

The specimens were thawed to room temperature before radiographic and MR imaging. Six of nine specimens underwent MRI. Anteroposterior and lateral X-rays were obtained from each specimen. The degree of disc degeneration was graded according to the classification system of Kellgren et al. [8, 9] (Table 1). Digitised images of the X-rays were used to calculate the FI [10] as a measure of relative disc height. The FI corresponds to a measure of relative disc height: the addition of anterior and posterior disc heights is divided by the anteroposterior disc diameter. MRI was performed on a 1.5 T Unit (Siemens Vision, Erlangen, Germany). The images were assessed in a blinded fashion by two radiologists and graded according to a classification system that described the features shown in Table 2. Each feature was given equal weighting and the grade assigned to the spine segment was an average value.

Table 2 Criteria for grading degenerative disc disease by MRI

	Grade
Osteophytes and/or disc narrowing	0/1
Disc prolapse	0/1
Annular tears	0/1
Decrease of signal intensity	0/1
Sum	0–4

Histology

Immediately after X-ray and MRI, the motion segments were divided with a bandsaw by cutting the discs and facet joints into parasagittal slices approximately 5 mm thick. The blocks were photographed, fixed for 48 h in a solution with 4% formalin and 3% Dextran and then immersed in a solution comprising 15% EDTA and 0.5% paraformaldehyde until complete decalcification was confirmed by radiography. All slices were processed into paraffin wax using standard methods, and tissue sections of 5 mm thickness were stained by haematoxylin and eosin (H&E) for histological examination. For each level, three disc sections representing the mid-, left- and right-parasagittal areas of the disc, were classified by two readers according to the grading system used in previous studies for histological changes in the lumbar spine [11] (Table 3). The grade given for each individual section was obtained by taking the worst characteristic feature observed; the overall grade for each level was the average of all sections analysed.

Table 1 Criteria for grading degenerative disc disease by radiography

Grade	Criteria
0	Absence of degeneration in the disc
1	Minimal anterior osteophytosis
2	Definite anterior osteophytosis; possible narrowing of the disc space; some sclerosis of vertebral plates
3	Moderate narrowing of the disc space; definite sclerosis of the vertebral plates; osteophytosis
4	Severe narrowing of the disc space; sclerosis of the vertebral plates; multiple large osteophytes

Table 3 Grading system of histological changes in cervical discs (*BEP* bony endplate, *CEP* cartilaginous endplate)

Grade	Anulus fibrosus	Nucleus pulposus	Cartilage end-plate	Margins/subchondral bone
1	Intact lamellae	Homogenety	Uniform thickness	Even thickness of BEP
	Narrow inter-lamellar matrix	Absence of clefting	Intact attachment to bone	Lamellar bone only
	Intact anulus attachment		Uniform calcification $<1/5$ of depth	Distinct junction with CEP
	Vessels only in outer 1/3		Uniform cell distribution	Few vascular intrusions into CEP
2	Minor lamellar splitting and disorganization	Minor clefting	Minor cartilage thinning	Slightly uneven BEP
	Minor widening of matrix	Minor cell necrosis	Small transverse fissures	Schmorl's nodes
	Minor disorganization of attachment	Minor posterior displacement of anulus	Irregular thickening of calcified zone	Minimal remodelling of BEP
	Rim lesion without reparative reaction	Minor chondrone formation	Few invading vascular channels	Small marginal osteophytes
			Small chondrones	
3	Moderate lamellar disorganization	Moderate clefting	Marked cartilage thinning	Moderately uneven BEP
	Moderate widening of matrix	Moderate cell necrosis	Marked thickening of calcified zone	Vascularised Schmorl's nodes
	Moderate fissuring of attachment	Cystic degeneration	Many transverse fissures	Moderate traecular thickening
	Radiating tears, not involving outer 1/3	Posterior displaement within annulus	Many vascular channels	Defect in bone lamellae
	Minimal chondroid metaplasia	Centripetal extension of collagen	Many chondrones	Minimal fibrosis tissue in marrow spaces
	Cystic degeneration	Moderate chondrone formation		Medium-sized osteophytes
	Vessels in outer and middle 1/3			
	Rim with minor reparative reaction			
4	Extensive lamellar disorganisation	Complete loss of nucleus	Total loss of cartilage	Marked uneven BEP
	Radiating tears extending into outer 1/3	Loose body formation	Calcification of residual cartilage	Ossified Schmorl's nodes
	Extensive chondroid metaplasia	Marked chondrone formation	Widespread fissuring	Large osteophytes
	Vessles in all zones			Marked trabecular thickening
	Rim lesion with marked reparative reaction			Marked fibrosis of marrow spaces
				Cartilage formation

Statistics

The data were analysed using cross-tabulation, correlation analysis, paired *t*-tests (significance $P = 0.05$) and frequency plots.

Results

Plain X-ray

Most of the discs were classified as grade 1 (19/52), grade 2 (13/52), grade 3 (9/52) or grade 4 (3/52). Eight of the discs were graded as normal. A total of 29% (16/54) of the discs showed moderate to severe posterior, and 20% (11/54) showed moderate to severe anterior osteophytosis. Moderate to severe sclerosis was noted in 26% (14/54) of the vertebral end plates, and 15% (8/54) of the disc spaces were moderately to severely narrowed (Table 1). The FI tended to be lowest at level 5/6.

Magnetic resonance imaging

The distribution of MRI grades was: grade 0 (10/36), grade 1 (8/36), grade 2 (7/36), grade 3 (8/36) and grade 4 (3/34) with a trend towards more advanced pathology in the discs at C4–5 and C5–6. Radiating tears (Fig. 1) were observed in 40% (14/36) of the discs, bulging prolapse in 31% (11/36) (Figs. 2 and 3), osteophytosis and disc space narrowing in 42% (15/36) and loss of signal intensity in 53% (19/36).

Histology

Half of the discs (26/52) showed advanced (grade 4) degeneration. Radiating tears of the annulus were

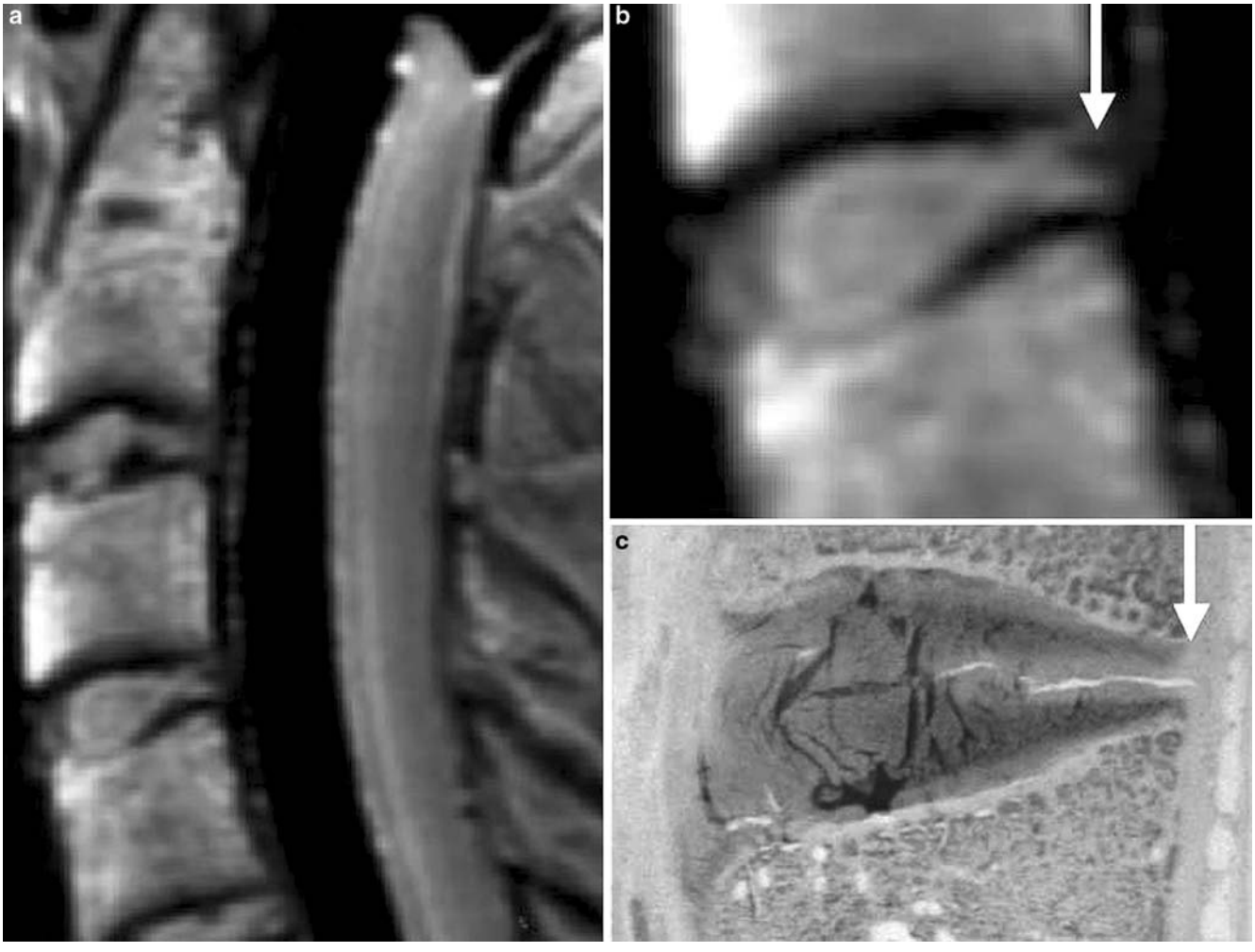

Fig. 1a–c Annular tear at C3/C4 level. In this case the MRI shows irregularity of the posterior part of the disc (*arrow*). This is also seen on the histological HE section (*arrow*)

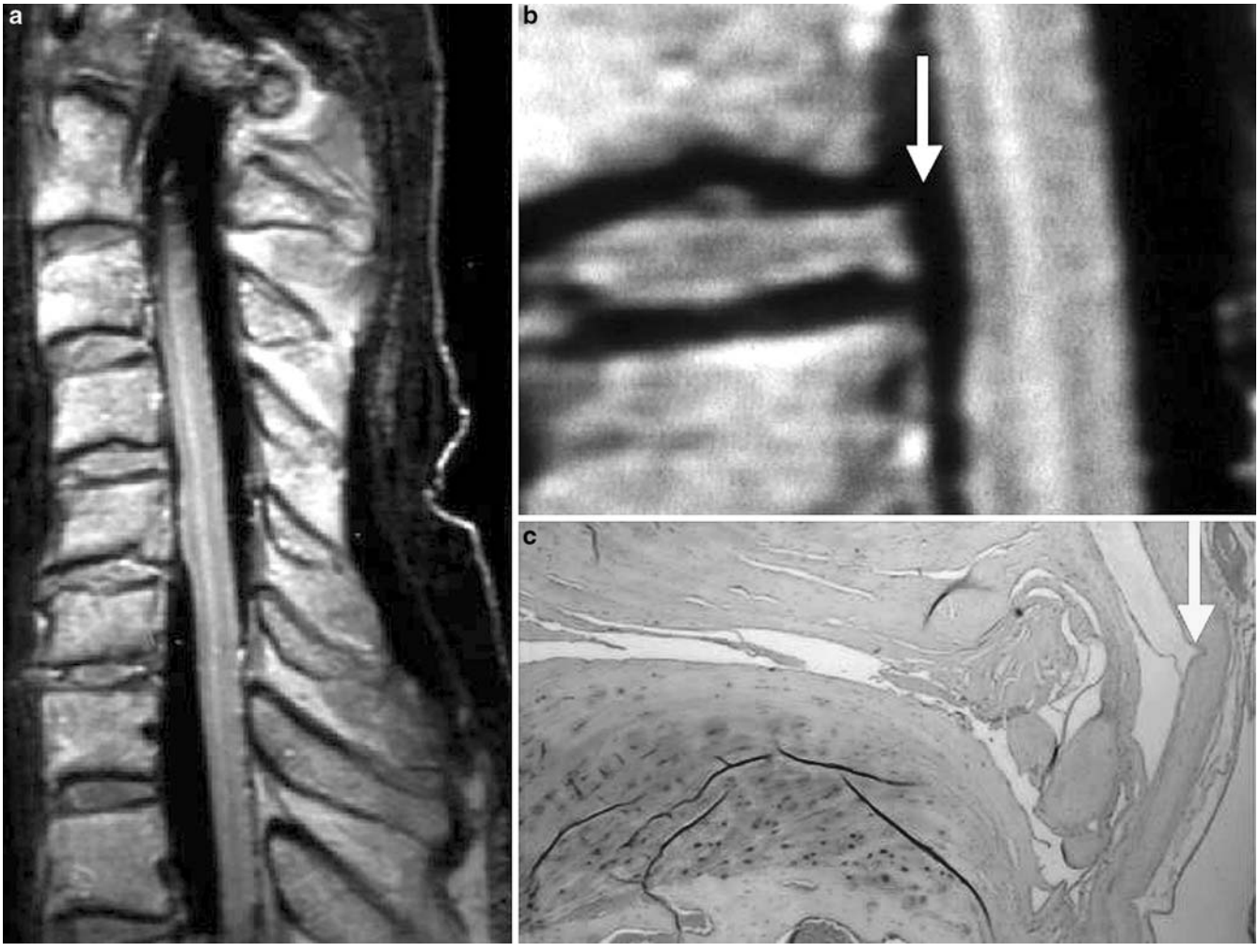

Fig. 2a–c Disc prolapse at C4/5 level only seen on histological HE section (*arrow*) but not on MRI

common and in most cases extended to the peripheral one-third of the discs (64%, 34/52). Lesions were more common in the posterior annulus (12 discs) than in the anterior annulus (three discs), but tears extending from the front to the back of the discs were most common (27 discs). We observed rim lesions of the annulus in 64% (34/52) of the discs, and half of the cases were accompanied by some vascularised granulation tissue. Anterior rim lesions were more common (20 discs) than posterior lesions (nine discs). We found some prolapse of nucleus material either anterior (four discs), posterior (12 discs) or anterior and posterior simultaneously (22 discs) in 74% (38/52) of the discs. In four cases there was disc material between the posterior anulus and the ligament, but without rupture of the annulus. In 52% (28/52) of the discs, remodelling of the bony margins resulted in the formation of osteophytes, approximately half of which were graded as large and extended across at least half of the disc space.

Correlations

Subjective assessment of disc narrowing on plain radiographs was confirmed by the FI of relative disc height ($P < 0.001$). The FI also correlated with histological grade ($P = 0.013$), MRI grade ($P = 0.02$) and radiological grade ($P < 0.001$) of degeneration. Radiological and histological grade of degeneration showed a weak correlation ($r = 0.3$, $P = 0.033$) (Fig. 4). The sensitivity of the radiography to detect osteophytes was 95% for anterior and 92% for posterior osteophytes. The specificity was 100%. In 39% (14/34) of the cases where we observed some prolapse of nucleus material, disc space narrowing was detected in the radiography. There was no correlation between prolapse of nucleus material and the FI. MRI correlated with overall histological grade ($r = 0.41$, $P = 0.015$, $n = 34$). MRI detected 62% (18/28) of the osteophytes, 38% (10/27) of nucleus

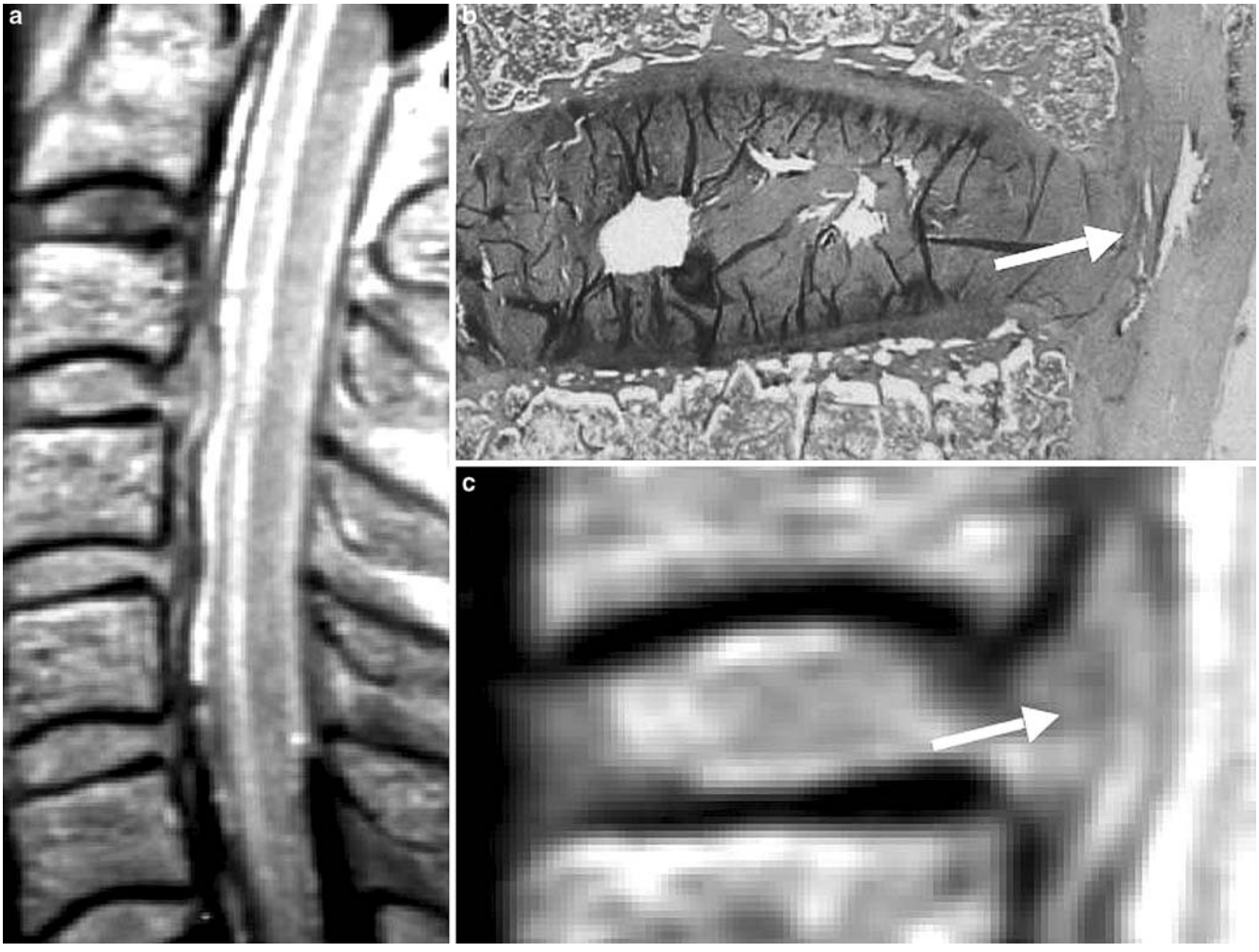

Fig. 3a–c Disc prolapse at C3/4 level only seen on histological HE section (*arrow*) and on MRI

prolapse and 37% (8/22) of the radiating tears. MRI grade of degeneration correlated with radiologic grade of degeneration ($r = 0.43$, $P = 0.01$, $n = 34$). Table 4 shows the correlation between histological and MRI

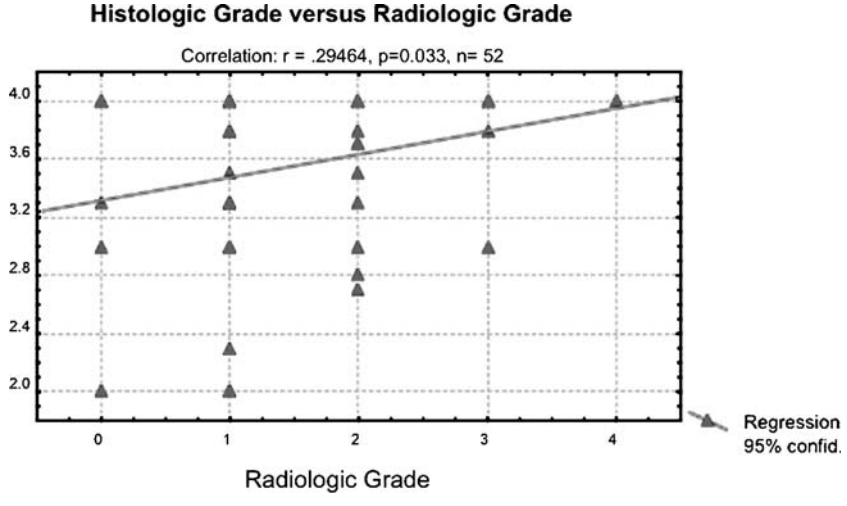

Fig. 4 Correlation between radiological findings and histopathology

Table 4 A comparison of MRI and histologic findings

MRI appearance of disc on T2 images	
Histologic finding	Correlation coefficient (r)
Annular tears	−0.14
Osteophytes	0.46*
Nucleus prolapse	0.14

*Significant correlation, $P < 0.05$

findings (Fig. 5). Age did not correlate with the grade of disc degeneration.

Discussion

In this study we have shown that discs from patients over 50 years of age are histologically severely degenerated; however, these changes may not be detected by conventional radiography and MRI.

This represents a problem, since MRI is typically the method of choice for non-invasive investigation of the spine and spinal canal in patients with pain. Histology is a reliable and sensitive method that has been used to show the natural sequence of degeneration in the human spine. While histology may be the best method to see the structural detail of the spine components, it is obviously not applicable to clinical investigations. For this reason, non-invasive imaging techniques such as plain radiography and MRI are used for initial investigation of patients with spinal disorders. In light of recent knowledge it is appropriate to investigate the ability of these techniques to detect reliably the structural changes to spinal components.

The key question is whether these changes can be seen or predicted radiologically. Indeed, we found correlations between the histologic grade of degeneration and radiography, FI and MRI. However, we did not find a significant correlation between MRI signs of annular tears and histologic annular tears, indicating that MRI is not reliably able to detect this lesion. MRI could not demonstrate full thickness radiating annular tears in any of the discs. These tears are associated with nuclear prolapse and might be expected to elicit pain symptoms from the release of inflammatory mediators [12–14]. Overall, the sensitivity of the MRI to detect tears and nucleus prolapse was less than 40%; thus, our study did not confirm the results from Yu et al. [15], which suggested that MR imaging was an accurate diagnostic tool for investigating tears of the anulus. Two previous studies which compared MRI with discography in the lumbar spine also found that significant annular tears are often missed by MRI [16–18]. In our study, the discs showed no significant loss of T2-weighted signal, and there was no significant loss of disc height, which may be a feature that is peculiar to cervical discs. In addition, the correlation in our study of histology with the FI and radiography demonstrates this. However, when comparing previous studies to our series, it should be noted that degenerated lumbar discs are significantly narrower than cervical discs [11, 19, 20]. In half of the cases we observed anterior nucleus prolapse, a feature which is rarely noted in routine MRI examinations, although it could result in an irritation of nerve endings in the ligamentum longitudinale anterior or anulus fibrosus and thus elicit pain [21–24].

In this study, MR was a moderate indicator of advanced disc pathology (grade 4) only and poor at detecting lesser degrees of pathology that were confirmed by microscopy. This is also supported by a macroanatomic study by Vikarii et al. [25], who reported that MRI correlated weakly with macroanatomy of disc degeneration and that nuclear intensity changes tended to underestimate such changes. In our study, four were classified by MRI as healthy discs (grade 0), which

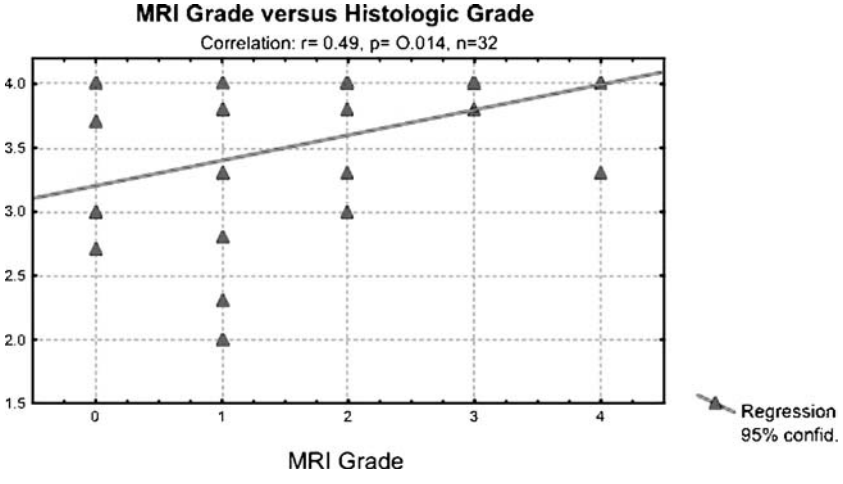

Fig. 5 Correlation between MRI findings and histopathology

corresponded to two out of 16 discs that were graded histologically as normal.

Typically, grade 4 discs were severely degenerated with extensive annular tearing, with either partial or complete nuclear prolapse. MRI would not be a critical investigation in such cases as patients would generally present with symptoms that would be detected during careful clinical examination. And, as our study revealed, disc protrusion (bulging) on MRI is in most cases histologically a prolapse, since MRI cannot recognise earlier stages of disease. A previous study showed that the interobserver reliability for the diagnosis of a disc protrusion was only moderate [26]. Previous studies have also shown that reduced T2-weighted signals on MRI correlate with decreased water content and proteoglycan concentration in lumbar discs, as well as general radiologic indicators of disc degeneration [27–31]. As in our study, these studies found that there was no correlation between MRI and histologic features of early degeneration. In terms of the treatment of degenerative spinal disorders, it is probably more important for MRI to detect these early changes. The failure of MRI in this study to detect early changes probably reflects the inherent limitations of the technique and may be overcome with improved resolution of newer devices.

Our results call into question the study of Dai [31], which confirms cervical segmental instability as an indicator for early degeneration; importantly, we may have to redefine the expression "early" since MRI may not be able to recognise histologically confirmed early degeneration [32]. Indeed, Dai et al. found a correlation between MRI findings on T2-weighted images with disc degeneration and findings on cervical spine flexion radiographs, indicating that MRI could detect early changes. However, they did not perform any histological studies, as we did, and, therefore, did not have pathological confirmation. In our study, MRI was often unable to demonstrate early histologic changes.

To our knowledge, no other studies comparing histology to radiology of the cervical spine have been performed as extensively as those concerning the lumbar spine. We have extrapolated our findings to those from lumbar spine studies; this represents one of the weaknesses of this paper, since there are well-know biomechanical differences between these two spinal segments.

Spinal degeneration is an inevitable consequence of aging. While it is not possible to stop this degenerative process, understanding the basis for such changes may provide options for the treatment of the pain and disability associated with aging. If it is possible to demonstrate reliably particular morphologic features that are associated with painful discs and facet joints, it may increase therapeutic options for the clinical treatment of degenerative spinal disorders. Clinicians have to be careful when interpreting X-ray and MRI, because discs which seem to be normal on X-ray and MRI can have degenerative changes which could induce pain (false negative results). Conversely, there is no proof that highly degenerated discs are a source of pain (false positive results) [27]. Although one of the aims of this study was to provide data on the normal processes involved with cervical motion segment degeneration, we were only able to provide data on specimens that were well advanced in the degenerative process due to difficulties in specimen collection.

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