MAGNETIC RESONANCE IMAGING OF THE INTERVERTEBRAL DISC
Post-traumatic findings and the value of diffusion-weighted MR imaging

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Post-traumatic findings and the value of diffusion-weighted MR imaging

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2001
Oulu, Finland

Abstract
Magnetic resonance imaging (MRI) provides important information about structural and biochemical changes in organs. MRI is also an effective imaging method for the evaluation of spinal disorders. However, many of its potential applications - particularly diffusion imaging - have not yet been thoroughly explored.

The purpose of this study was to determine the MRI-detectable changes in the intervertebral disc after trauma and to test the feasibility of diffusion-weighted MR imaging of the intervertebral discs.

A minipig model was used in the experimental study to determine the MRI changes in the intervertebral disc after peripheral annular lesions in different time frames. Three of eight discs with experimental annular lesions had a normal annular appearance in MRI. Annular lesions, when detectable, were manifested as a bulging of the disc or as a high-intensity zone (HIZ) inside the annulus. Either the signal intensity or the area of bright signal intensity in the nucleus had nearly always decreased after one month, but they were still detectable even in cases where no signs of annular trauma could be seen in the MR images. The histology of HIZ is presented for the first time: clusters of nuclear cells and disorganized granulation tissue with capillaries were detected in the HIZ area.

Fourteen patients 8 to 21 years of age with histories of vertebral fracture at least one year previously and 14 asymptomatic healthy control subjects 8 to 22 years of age were studied by MRI. In these young people a vertebral fracture, especially with end-plate injury, proved to be a notable risk factor for initiating disc degeneration.

The apparent diffusion coefficients (ADCs) of the thoracolumbar intervertebral discs were determined in three orthogonal directions in 18 healthy young volunteers aged 8-22 years. The ADCs were also determined in 10 young patients with previous vertebral fractures, and clear decreases were found in the ADC_x and ADC_y directions, but in the ADC_z direction values had not changed significantly as compared to the values in the controls. The most marked changes were observed in the degenerated discs, followed by those in the discs with a normal signal intensity adjacent to the primary trauma area. Diffusion-weighted MR imaging affords a useful tool for evaluating disc diseases in the early phases.

Additionally, 37 adult volunteers without back symptoms were studied by MRI and by magnetic resonance angiography (MRA) and it was found that the status of the lumbar arteries significantly explained the diffusion values in the lumbar intervertebral discs. The correlation between disc degeneration and diffusion was mostly linear, but not significant.

Keywords: diffusion-weighted MRI, intervertebral disc, magnetic resonance imaging, trauma
Acknowledgments

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Helsinki, August 2001

Liisa Kerttula
## Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ADC</td>
<td>apparent diffusion coefficient</td>
</tr>
<tr>
<td>CNR</td>
<td>contrast-to-noise ratio</td>
</tr>
<tr>
<td>CSF</td>
<td>cerebrospinal fluid</td>
</tr>
<tr>
<td>CT</td>
<td>computed tomography</td>
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<tr>
<td>DWI</td>
<td>diffusion-weighted magnetic resonance imaging</td>
</tr>
<tr>
<td>EPI</td>
<td>echo-planar imaging</td>
</tr>
<tr>
<td>FSE</td>
<td>fast spin echo</td>
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<tr>
<td>GE</td>
<td>gradient echo</td>
</tr>
<tr>
<td>HIZ</td>
<td>high intensity zone</td>
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<tr>
<td>IVIM</td>
<td>intravoxel incoherent motion</td>
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<tr>
<td>MIP</td>
<td>maximum intensity projection</td>
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<tr>
<td>MRI</td>
<td>magnetic resonance imaging</td>
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<td>MRA</td>
<td>magnetic resonance angiography</td>
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<td>MT</td>
<td>magnetization transfer</td>
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<tr>
<td>NMR</td>
<td>nuclear magnetic resonance</td>
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<tr>
<td>PG</td>
<td>proteoglycan</td>
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<tr>
<td>RF</td>
<td>radiofrequency</td>
</tr>
<tr>
<td>ROI</td>
<td>region-of-interest</td>
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<tr>
<td>SE</td>
<td>spin echo</td>
</tr>
<tr>
<td>SNR</td>
<td>signal-to-noise ratio</td>
</tr>
<tr>
<td>T</td>
<td>tesla</td>
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<tr>
<td>T1</td>
<td>longitudinal relaxation time</td>
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<tr>
<td>T2</td>
<td>transverse relaxation time</td>
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<tr>
<td>TE</td>
<td>echo time</td>
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<tr>
<td>TR</td>
<td>repetition time</td>
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<tr>
<td>US</td>
<td>ultrasound</td>
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List of original publications

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References
1 Introduction

Low back disorders have a major impact on health care in Western countries; about 75–80% of people are affected at some time during their lives (Kelsey & White 1980, White & Gordon 1982, Heliövaara et al 1989). The cumulative lifetime prevalence of low back pain lasting at least 2 weeks has been detected to be 13.8% (Deyo & Tsui-Wu 1987). In Finland, 17% of people are disabled for long periods because of low back pain (Heliövaara et al 1989). Mostly, however, the period of acute back pain is short and the remission rate is high. Nevertheless, recurrences are very common and the consequent disability readily becomes chronic.

The etiology of low back pain is multifactorial. Degenerative changes in the back and the intervertebral discs are very common and are also found in asymptomatic persons, so their responsibility for back pain has been considered controversial (Wiltse 1971). On the other hand, no clear distinction can be made between normal age-related disc changes and pathologic disc changes. Nevertheless, individuals in whom disc degeneration occurs soon after the phase of rapid physical growth have not only an increased risk of recurrent low back pain at this age but also a long-term risk of recurrent pain up to early adulthood (Salminen et al 1999). Inadequate nutrition has been suggested as a cause of disc degeneration (Nachemson et al 1970). Trauma has been regarded as one of the major causes initiating a degenerative process of the disc (Crock 1986, Osti et al 1990), although this matter is controversial (Oner et al 1998).

The lumbar intervertebral disc is the largest avascular tissue in the human body. Thus, the mechanism that transports nutrients into the disc is diffusion (Urban et al 1977, Holm et al 1981). In non-specific low back pain syndromes, intradiscal pathology has been detected to play a key role (Vanharanta et al 1988).

Magnetic resonance imaging (MRI) is the most sensitive method for evaluation of diseases of the spine, including disc degeneration. It is noninvasive and safe, as it does not involve irradiation and is thus ideal for studying young people. However, MRI is still quite a new imaging method and the value and significance of the various findings, such as a high intensity zone (HIZ) in the annulus, have not been fully determined. Apart from imaging, MRI provides a tool for functional measurements of such variables as diffusion. So far, MR-based diffusion imaging has not been utilized in intervertebral discs.
The purpose of this study was first to determine the MRI changes associated with experimental annular disruption in different time frames, and the histologic changes in the lesion areas were also studied. Secondly, the likelihood that a vertebral fracture in children would initiate disc degeneration was investigated. Thirdly, whether the apparent diffusion coefficients (ADCs) of intervertebral discs can be measured by diffusion-weighted imaging was studied. This method was also tested with discs that were exposed to trauma in order to detect any changes in ADC values in already degenerated discs and in discs with normal signal intensity located in the trauma area. Additionally, the correlation between blood flow in the lumbar arteries and the ADC values of the intervertebral discs was examined.
2 Review of the literature

2.1 The spine

2.1.1 Anatomy and arterial supply

The adult vertebral column normally consists of 33 vertebrae, but only 24 of them (7 cervical, 12 thoracic, 5 lumbar vertebrae) are mobile. The five sacral vertebrae are fused to form the sacrum and the four coccygeal vertebrae are fused to form the coccyx (Moore 1985). The vertebral column is stabilized by ligaments which somewhat limit the movements produced by the back muscles. Furthermore, stability is provided by muscles, intervertebral discs, and the shape of the vertebrae (Moore 1985). The spinal cord and the spinal nerve roots are located within the vertebral canal. The end of the spinal cord, the conus, usually is situated at the level of the first lumbar vertebra (Moore 1985). The spinal nerves and their branches are located outside the vertebral canal. A spinal (motion) segment consists of two vertebral bodies connected by an intervertebral disc, facet joints, and ligaments (Lorenz 1996, Dwyer 1996); the intervertebral disc forms the largest part of this three-jointed complex. There are usually 23 complete motion segments (Dwyer 1996).

The upper four lumbar segments are supplied by four pairs of lumbar arteries arising from the posterior wall of the aorta. The fifth lumbar segment is supplied by branches of the middle sacral artery, which typically originates proximally to the aortic bifurcation (Warwick & Williams 1973, Crock & Yoshizava 1976, Moore 1985) and by branches arising from the iliolumbar arteries (Warwick & Williams 1973). There is some anatomical variation in the blood supply to the lower part of the lumbar spine (Crock & Yoshizava 1976) and anastomoses are seen between arteries at different levels. The dorsal branches of the posterior intercostal arteries provide the arterial supply to the thoracic spine (Warwick & Williams 1973).
2.1.2 Function

The spinal (motion) segment acts as a unit of the osseoligamentous spine in transmitting loads imparted to the trunk (Lorentz & Patwardhan 1996). The main movements of the spine are flexion, extension, lateral bending, and rotation. In addition, some circumduction, a combination of flexion-extension and lateral bending, also occurs (Moore 1985). The most mobile sites in the spine are the cervical and lumbar regions (Moore 1985). The normal functioning of the spine depends greatly on the intervertebral discs (Adams & Hutton 1988), and alterations in disc structure may cause pain and impairment. The spine should be considered as an integrated unit, for damage sustained by one part frequently injures other structures in the spinal column (Harris & MacNab 1954, Roberts et al 1989). One such part is the cartilaginous end-plate (Roberts et al 1989).

2.2 The intervertebral discs

2.2.1 General

The intervertebral discs not only stabilize the spine, but also allow movement between the vertebrae, which gives the spine its flexibility (Adams & Hutton 1988, Buckwalter 1995). As a result of their positions in the spine, the intervertebral discs absorb and distribute the complex mechanical stresses to which they are subjected. In man, the intervertebral discs are always under a physical load. During the aging process, the gross and microscopic appearance, cell content, and matrix composition of the disc tissues change more than any other tissues in musculoskeletal system (Buckwalter 1999) and the distinction between normal aging and pathologic degenerative processes is difficult because of their great similarity (Coventry et al 1945b and c, Eyring 1969). No definite criteria between full maturation and degeneration have been found. Pathologic degeneration can be defined as a premature and accelerated course of degenerative changes in a disc.

2.2.2 Anatomy

The adult human intervertebral disc can be considered to consist of three distinct parts: the hyaline cartilage end-plate, the annulus fibrosus, and the nucleus pulposus (Fig. 1) (Coventry et al 1945a and 1969, Brown 1971, Moore 2000). Although there has been some discussion as to whether the end-plates are part of the disc or not (Moore 2000), the key role of these plates, to maintain the health of the intervertebral disc, is well known and recognized (Pritzker 1977, Roberts et al 1996, Moore 2000). The primary structural...
components of the disc are collagens and proteoglycans (PGs) (Eyre et al 1989). The collagens supply its tensile strength and the PGs, through their interactions with water, give the tissue stiffness and resilience to compression (Eyre et al 1989).

![Diagram of intervertebral disc structure](image)

**Fig. 1.** Sagittal (a) and transverse (b) illustrations of the structure of the intervertebral disc. NP = nucleus pulposus, AF = annulus fibrosus, VB = vertebral body, EP = end-plate, PLL = posterior longitudinal ligament.

The central part of the disc, the nucleus pulposus, consists of a highly hydrated gel of PGs containing collagen, mainly of type II (Eyre & Muir 1976), and other proteins. The cells of the annulus fibrosus and the end-plate are derived from the mesenchyme and the cells of the nucleus pulposus from the notochord (Holm & Urban 1987). There are gradual transitions in cell morphology and in the composition of the matrix of the intervertebral discs. With growth and aging, the notochordal cells gradually disappear, and the cells in the nucleus pulposus and in the inner annulus assume morphologic features similar to those of chondrocytes, whereas the cells in the outer layer of the annulus resemble fibrocytes (Postacchini et al 1984, Buckwalter 1999). The cells of the cartilaginous end-plate are typical chondrocytes (Pritzker 1977). The disc comprises only a sparse population of cells, discs mainly consist of connective tissue (Buckwalter 1995). Nevertheless, the cells maintain the disc structure and the health of the tissue ultimately depends on the activity of the cells. The periphery of the nucleus pulposus is called the transitional zone. It is considered to represent the growth plate of the nucleus pulposus. Remodelling occurs in the transitional zone, which is sensitive to physical forces and chemical and hormonal modulation during growth (Taylor et al 1981).

The annulus fibrosus, which surrounds the nucleus pulposus, consists of concentric lamellae. Anteriorly, in the lumbar and cervical spine, the annulus fibrosus is generally thicker (Coventry 1969). In these areas the lamellae are most numerous in the anterior annulus and furthermore are thicker anteriorly (Bell 1996). The most important component of the annulus fibrosus is collagen. The annulus fibrosus resists the radial tension induced by axial loading of the disc as well as the stresses from torsion and flexion (Coventry et al 1945a and b). Collagen type I predominates in the outer annulus providing the greater tensile strength, and type II in the inner annulus (Eyre & Muir 1989).
The annulus fibrosus has been shown to consist of regularly oriented sheets of collagen fibers (Horton 1958). The peripheral lamellae (Sharpey fibers) are attached to the vertebral end-plates and bony vertebral body (Coventry et al 1945a).

The outermost parts of the intervertebral disc are the end-plates, which cover the inferior and superior vertebral body surfaces central to the site of the epiphyseal ring (Coventry et al 1945a) and are composed of hyaline cartilage similar to the articular cartilage in the synovial joints (Pritzker 1977, Roberts et al 1989). The function of the cartilaginous end-plate is to prevent the nucleus, with its high water content, from bulging into the adjacent vertebral bone, while simultaneously absorbing hydrostatic pressure that results from mechanical loading of the spine (Moore 2000). The end-plate is approximately 0.6–0.8 mm thick, being thickest close to the posterior annulus and becoming slightly thinner centrally over the nucleus pulposus (Roberts et al 1989). The maintenance of the nucleus pulposus matrix in the adult human disc is dependent on the functional integrity of the cartilage end-plate cells (Pritzker 1977, Moore 2000).

A healthy adult intervertebral disc has no blood vessels and the disc between the L 4 and L 5 vertebrae is the largest avascular tissue in the human body. The posterior part of the disc is innervated by the sinuvertebral nerves, the posterolateral part by the adjacent ventral primary rami and by branches from the gray rami communicantes and the lateral part by branches from the gray rami communicantes and direct branches from the ventral rami (Bogduk et al 1981). No nerves have been found in the nucleus pulposus of the disc or in the inner annulus (Yoshizawa et al 1980, Grönblad et al 1991), but the outermost layer of the annulus fibrosus is innervated (Jackson et al 1966, Yoshizawa et al 1980, Bogduk et al 1981, Grönblad et al 1991).

### 2.2.2.1 Age-related intradiscal changes

With age the intervertebral disc undergoes striking alterations both in structure (Buckwalter 1995, Coventry 1969) and in composition (Buckwalter 1995).

In a neonatal human disc, the annulus fibrosus is just a thin layer at the periphery of the disc and is fully distinguishable from the hydrated, gel-like nucleus that occupies the greater part of the disc (Taylor & Twomey 1988). The nucleus pulposus is notochordal in prenatal and infant life (Taylor & Twomey 1988), but during the first decade of life the notochordal remnants tend to disappear (Coventry et al 1945b). By the end of the first decade, the annulus has developed into a compact structure. The strands of the lamellae are arranged mostly circularly and their attachment to ligaments has started. During the early years, there are numerous vascular channels perforating the end-plate, but these have greatly diminished by the age of 10 (Coventry et al 1945a and b).

In the second decade, development is progressive and toward the end of the second decade, the disc reaches its adult appearance. Vascular channels may disappear by the age of 8–12 yrs (Resnick 1985) but usually more gradually by the age of 20, although some are occasionally found in the third decade (Coventry et al 1945a and b). In the annulus, the gaps intervening between the lamellae disappear and attachment to the end-plates, the ossified epiphyseal rims, and the ligaments progresses (Coventry et al 1945b). Toward the
end of the second decade, the epiphyseal ring has fused with the vertebral body (Coventry et al. 1945b). The fluid content increases in the nucleus pulposus because the nucleus responds to its increased functional role (Coventry et al. 1945b).

In the elderly, during the sixth decade and later, the nucleus has become fibrotic and macroscopically is difficult to distinguish from the annulus fibrosus (Brown 1971).

The disc cells also change with age (Buckwalter 1999). In the human disc, the absolute cell number increases with age, but the proportion of viable cells decreases. In adults, few if any notochordal cells remain and the percentage of necrotic cells in the nucleus increases from about 2% in the fetus to about 50% in adults (Buckwalter 1999).

Although all the disc tissue components change from birth through old age, the most extensive changes occur in the nucleus pulposus (Buckwalter 1995). Age-related changes can vary in rate and extent within the same person (Buckwalter 1995) and these vary especially much between persons.

### 2.2.3 Biochemistry

The extracellular matrix consists mostly of water, which accounts for approximately 90% of the tissue wet weight of the young human nucleus (Gower & Pedrini 1969), but with increasing age the water content decreases and, by the age of 60, is less than 70% (Holm 1996). The annulus fibrosus contains less water (60–70%), and this content does not diminish significantly with age (Gower & Pedrini 1969).

PGs and collagens constitute the two major classes of macromolecules in the nucleus pulposus, annulus fibrosus, and cartilaginous end-plate of the intervertebral disc. The other molecules in the disc are other glycoproteins, serum proteins, lipids, and inorganic salts, but they are present only in minor quantities.

Collagen fibers provide the framework of the disc and are responsible for its strength. Collagen accounts for about 20% of the dry weight in the nucleus pulposus (Eyre et al. 1989, Buckwalter 1995), being mainly of type II (Eyre et al. 1989). In the annulus, collagen is the most important component. The collagen in the outermost annulus is type I (92–100%). The proportion of type I collagen decreases gradually from the outer to the inner annulus (Eyre & Muir 1976, Buckwalter 1995). Type I collagen is typical of tendons and type II of articular cartilage, thus it is supposed that the tensile strength of the annulus fibrosus is provided by type I collagen, while the compressive component involves type II collagen. The disc also contains minor amounts of other collagens, primarily types III, V, VI, IX, and XI (Eyre et al. 1989, Buckwalter 1995). A variety of noncollagenous proteins and small amounts of elastin are present throughout the disc tissues (Eyre 1979 and 1989). The contribution of elastin to the mechanical properties of the disc remains uncertain, but, because of its low concentration, it is considered to have minor role (Buckwalter 1995). The concentration of noncollagenous disc proteins increases with age; this may be due to accumulation of degraded molecules (Buckwalter 1999). However the total disc collagen remains relatively constant (Eyre et al. 1989).
The PGs, which are embedded in this fibrous framework, have a critical role in the load-bearing capacity of the disc, because they are mainly responsible for the maintenance of disc hydration (Holm 1996). An especially important role has been detected for the PGs in the cartilaginous end-plate, because these appear to regulate the transport of essential solutes into and out of the disc, to the extent that loss of PGs from the end-plate ultimately leads to loss of PGs from the nucleus pulposus (Roberts et al 1996). Changes in their quantity or quality will compromise the shock absorption function of a tissue (McDevitt 1988). PGs are a family of macromolecules that vary greatly in size and composition. The PGs in the intervertebral disc are similar to those in the articular cartilage (Hukins 1988). All the PGs in the intervertebral disc contain one or more glycosaminoglycan chains and oligosaccharides attached to a core protein of variable length. The major components of the glycosaminoglycans in the disc are chondroitin sulfate and keratan sulfate, which both have charged acidic groups (sulfate and carbonate) and the disc has fixed negative charges in the matrix (Holm 1996). Most of the water is bound to negatively charged polysaccharides, which keep the fibrous framework of the nucleus pulposus hydrated (Eyring 1969). The PGs interpenetrate and divide the spaces between the collagen fibers into small pores through which water and small solutes can move. The pore size and the swelling pressure depend on the PG concentration. The more PGs that exist, the more water the disc can attract and the better it can resist a mechanical load. The mechanisms responsible for the extracellular processing of mature nucleus PGs are unknown (McDevitt 1988), but it is known that maintenance of the nucleus pulposus matrix in the adult human disc is dependent on the functional integrity of the cartilage end-plate cells (Pritzker 1977). PGs are the most important constituents of the nucleus pulposus; they account for at least 50% of the dry weight (Eyre 1979). The turnover time of PGs varies with their position in the disc, it is fastest in the periphery of the annulus, which has the lowest glycosaminoglycan concentration, and slowest in the nucleus, which has the highest (Urban et al 1978).

The fluid content of the intervertebral disc is important in determining its mechanical response and also its transport and its biologic properties (Urban& McMullin 1988). However, the hydration of the disc is a dynamic variable, not a stable property of the tissue. A normal diurnal variation in the water content of the intervertebral disc occurs with influx of water overnight and gradual reduction during the day. This produces a measurable change in the hydration, height and volume of the disc (Adams & Hutton 1983, Paajanen et al 1994b). Change in the signal intensity can also be measured although it is not visible in MRI (Boos et al 1993, Paajanen et al 1994b, Silcox et al 1995). Under physical loads, the water content diminishes by up to 5–20% in the nucleus pulposus and the inner annulus (Adams & Hutton 1983, Urban & McMullin 1988). In the study by Boos et al (1993) the diurnal variation was significantly less pronounced in degenerated than in healthy discs. This diurnal variation is suggested to be of clinical significance in spinal mechanics (Adams et al 1990). The relationship between the change in water content and the swelling pressure has been found to depend on the composition of the disc rather than on age or the degree of degeneration (Urban & McMullin 1988).
2.2.4 Nutrition and metabolism

The complex mechanisms of disc nutrition and metabolism have been studied extensively. The intervertebral disc of an adult is avascular. Penetration of the solutes into the disc has been shown to occur from the edge of the annulus and from the vertebral bodies through the end-plates (Brodin 1955, Nachemson et al. 1970, Eyre 1979, Holm et al. 1981), so these are also the possible routes for nutrition of the disc. Nutrients are received by flow and diffusion (Maroudas 1988) and both of these transport mechanisms are affected by spinal movements and posture (Ohshima et al. 1989, Adams & Hutton 1983). The relative importance of the two supply routes into the disc is different for different solutes (Hukins 1988). It has been demonstrated experimentally that the metabolism of the nucleus pulposus is mainly anaerobic (Holm et al. 1981). The oxygen concentrations have been found to vary considerably, being lowest in the central part of the nucleus pulposus and in the inner annulus (Holm et al. 1981). High lactate levels lower the pH and possibly lead to activation of the matrix-degrading enzymes. It has also been shown that the rate of PG synthesis in the human and bovine nucleus pulposus diminishes concomitantly with any decrease in pH (Ohshima & Urban 1992). The well-being of the disc is highly dependent on its cells (Maroudas 1988) and the cell density in the disc is controlled by nutritional factors (Stairmand et al. 1991). Insufficient nutrition has often been thought to be the primary cause of degenerative processes in the disc (Nachemson et al. 1970, Maroudas 1988, Buckwalter 1995). The arterial supply of the discs in the lumbar spine is provided by pairs of lumbar arteries, the middle sacral artery and the branches arising from the iliolumbar arteries. Each artery crosses its related intervertebral foramen and three sets of branches enter the spinal canal (Crock & Yoshizava 1976). The dorsal branches of the posterior intercostal arteries provide the arterial supply in the thoracic spine (Warwick & Williams 1973, Moore 1985). Blood flow in the end-plate is not entirely passive, because muscarinic receptors are present which can influence disc nutrition under altered physiologic conditions (Wallace et al. 1994).

2.2.4.1 Diffusion

Diffusion can be described as the ability of molecules to move randomly in relation to their thermal energy (Gray & MacFall 1998). Molecular motion is a random translational movement that occurs at the microscopic level. Diffusion is the main mechanism for the transport of small solutes into the intervertebral disc (Urban et al. 1978, Holm et al. 1981), because the overall direction of fluid flow, for about 16 hours daily, is mainly out of the disc (Holm 1996). Almost twice as much of small, negatively charged ion, such as sulfate, will diffuse through the periphery of the annulus as through the end-plates. For a small uncharged solute, such as glucose, these two routes are of equal importance, whereas, for positively charged ions the end-plate route is more effective (Urban et al. 1978). Large uncharged solutes tend to be totally excluded from the normal disc (Moore 2000). Proton diffusion in tissues is restricted by both permeable and impermeable barriers due to cellular and fibrous structures. The parameters that mostly influence rates
of nutrient concentration are transport of metabolites to and from the cells through the disc, nutrient consumption and production, disc thickness, and the exchange area (Maroudas 1988, Stairmand et al 1991). Distances for diffusion are large; in adult human discs, some cells may be as much as 20 mm from the blood supply (Moore 2000).

Diffusion in the disc has been studied in vitro (Brodin 1955, Nachemson et al 1970, Holm et al 1981) and in vivo (Urban et al 1977 and 1978). Difficulties in studies in vitro arose in measuring the diffusion coefficients using steady-state or desorption techniques, because the disc samples swelled quickly and lost proteoglycans (Maroudas 1988). The diffusion coefficients of certain solutions in the disc have been measured by placing a spot of a radioactive tracer at one end of a thin strip of disc material (Urban et al 1977). More physiologic in vivo measurements have been made by injecting radioactive tracers into the veins of dogs, which were then sacrificed at different time intervals (Urban et al 1978).

2.3 Disc degeneration

2.3.1 Morphologic features

Degeneration of the intervertebral disc begins early in life and is a consequence of a variety of environmental factors, as well as normal aging. The hydration of the intervertebral disc decreases remarkably with aging and degeneration (Keyes & Compere 1932, Brown 1971). Degenerative changes in the disc, due either to aging or to pathologic process, may appear already in the second decade (Coventry et al 1945b, Miller et al 1988, Tertti et al 1991b).

Intervertebral disc degeneration can be defined as loss of the normal architecture of the disc due to progressive fibrosis. This includes loss of the gelatinous nucleus pulposus by desiccation and fraying (Osti & Cullum 1994), disappearance of the border between the nucleus and the annulus fibrosus (Coventry et al 1945b, Pritzker 1977), coarsening of the annular lamellae, and progressive fibrosis and fissuring of the annulus (Osti & Cullum 1994) with deposition of aging pigment (Coventry et al 1945b and c, Harris & MacNab 1954, Holm 1993). Degenerative splits and clefts can appear in the peripheral part of disc and may extend from there to the central regions (Osti & Cullum 1994, Buckwalter 1995). Degenerative fissures also occur in the center of the disc, and may later enlarge and spread to the annulus and the end-plate (Friberg & Hirsch 1949, Vernon-Roberts 1988). Finally, cavities are formed within the disc (Vernon-Roberts 1988). Ingrowth of blood vessels with nerve fibers appears to take place around the margins of the clefts (Vernon-Roberts 1988). Three usual types of annular defect have been described (Osti et al 1992b, Fraser et al 1993): 1) rim lesions, which are defined as discrete defects of the outer annulus fibrosus; 2) circumferential tears, more commonly seen in the lateral and posterior layers, 3) radiating clefts, which are commonly detected in degenerating discs (Hirsch & Schajowicz 1953) extending from the nucleus pulposus parallel with or oblique to the plane of the end-plates. Rim lesions may occur in otherwise normal discs, and histology has suggested that these are due to trauma rather than to biochemical
degradation (Osti et al. 1992b), but they may precede degenerative changes in the motion unit of the spine (Osti & Cullum 1994). The cartilaginous end-plates become thinner, several microfractures are seen to penetrate through the thinned end-plates (Coventry et al. 1945b), and subchondral bone will replace them during degeneration (Pritzker 1977). As long ago as 1970, Nachemson et al. suggested that the impermeability of the central region of end-plate was positively correlated to degeneration. As a consequence of advanced degeneration, the height of the disc decreases and reactive sclerosis develops in the adjacent vertebral bodies (Keyes & Compere 1932). The connection of end-plate osteophytosis with degenerative disc disease is unclear, because the former may occur without any loss of disc height (Resnick 1985).

### 2.3.2 Biochemical features

Biochemically, degenerative changes in a disc are associated with loss of proteoglycans in the nucleus (Eyre 1979, Lyons et al. 1981, Tertti et al. 1991a, Kääpä et al. 1994b) and this, in turn, leads to a decrease in the ability of the nucleus to remain hydrated (Lorentz & Patwardhan 1996). The ratio of chondroitin to keratan sulfate has also been noticed to diminish significantly during aging and degeneration (Lyons et al. 1981). Both a decrease in proteoglycan synthesis and an increase in the release of proteoglycans occur with aging and degeneration. With immunoassays it has been possible to detect changes in the turnover of the extracellular matrix at different ages (Antoniou et al. 1996); the degenerative phase is illustrated not only by evidence of lack of increased synthesis of aggrecan and type II procollagen, but also by an increase in denaturation of collagen type II and synthesis of type I procollagen (Antoniou et al. 1996). Dehydration of the disc alters the normal mechanics of a motion segment significantly, and disc degeneration may lead to segmental instability (Lorentz & Patwardhan 1996). A slight increase in the collagen content of the nucleus (Lyons et al. 1981, Kääpä et al. 1994a) and a decrease in the collagen content of the annulus have been detected (Lyons et al. 1981).

The collagen X, mainly located in the central region of the cartilage end-plate (Moore 2000), is a marker of hypertrophic chondrocytes and is suggested to be involved in cartilage calcification (Aigner et al. 1998).

### 2.3.3 Etiology

The etiopathogenesis of the degenerative findings in the disc and their relation to pain are poorly understood. Degeneration of the disc is connected with impaired nutrition (Holm & Urban 1987, Kauppila et al. 1997). The risk factors primarily suspected to lead to degenerative spinal changes, apart from age, are traumatic events (Smith & Walmsley 1951, Osti et al. 1990) and heavy physical occupational loading (Riihimäki et al. 1990, Luoma et al. 1998). Additionally, occupation has been noticed to correlate with back pain (Frymoyer et al. 1983, Luoma et al. 2000a). Inactivity and postural stress are also
suspected to have a role in accelerating the degeneration process (Videman & Battie 1996). The role of vibration in accelerating disc degeneration has been called in question (Videman et al 2000). The influence of smoking has also been discussed (Battie et al 1991), but evidence of this has not been demonstrated (Battie et al 1995, Videman & Battie 1996), although a connection with the low back pain has been detected (Frymoyer et al 1983, Deyo & Bass 1989). All these factors appear to explain only a minority of the individual variations in the degeneration of the disc (Videman & Battie 1996). Several studies indicate that end-plate irregularities, such as Scheuermann disease and Schmorl’s nodes, precede nuclear disc degeneration (Hilton et al 1976, Paajanen et al 1989). Some evidence suggests that, besides nutritional and traumato-mechanical factors, genetic (Battie et al 1995, Annunen S et al 1999) and as yet largely undefined systemic factors may also be involved in the etiology of disc degeneration (Battie et al 1995). At most ages, disc degeneration is more common in men (Miller et al 1988), and this has been suggested to be due to longer avascular nutritional pathways and greater compressive loading (Miller et al 1988).

2.3.3.1 Trauma and disc degeneration

In several studies, trauma has been found to initiate a degenerative process in the disc (Smith & Walmsley 1951, Swärd et al 1990, Osti et al 1990, Kääpä et al 1994, Natarajan et al 1994). Nevertheless, in a study of 63 adult patients, vertebral fracture did not cause changes in the signal intensity of the intervertebral discs (Oner et al 1998). In a cross-sectional study examined with plain radiographs, facet arthrosis was more severe in patients with low back pain and a history of trauma than in nontrauma patients with low back pain; however, discal degeneration was not more severe than in the patients without a history of trauma (Peterson et al 2000). Failure of the human lumbar intervertebral discs appears more frequently in the part of the spine subjected to the greatest mechanical stress. Under axial compression stress (Brown et al 1957), postmortem specimens of discs had burst superiorly and inferiorly, i.e. in the cartilaginous end-plate, while radial rupture of the annulus fibrosus was uncommon. Torsion and flexion stresses have been shown to be more injurious to the annulus fibrosus (Brown et al 1957). The extent of damage during compression has been shown to be determined the integrity of the end-plate and the subchondral bone, rather than by the degree of disc degeneration (Holmes et al 1993). The end-plate appears to be susceptible to mechanical failure, for this is a weak link in the structure of the disc (Natarajan et al 1994, Moore 2000). Most vertebral fractures in children are located at the T4-L2 level (Hegenbarth & Ebel 1976); as many as 25% of injuries in children are assumed to be situated in thoracic spine.

Following experimental trauma to the disc, the end-plate has been shown to become vascularized (Resnick 1985, Moore et al 1992). Moreover, after an experimental peripheral tear, granular tissue repair has also been demonstrated perianularly (Osti et al 1990). This has been claimed to mean that, under unusual physiologic circumstances vascular channels can proliferate after maturity, probably to maintain adequate nutrition.
of the disc (Moore 2000). The new vascularity in the end-plate is facilitated by the activation of enzymes such as matrix metalloproteinases and their tissue inhibitors (Crean et al 1997, Goupille et al 1998).

2.3.4 Disc degeneration and back pain

Despite increasing knowledge of the morphologic and biochemical features of intervertebral discs, the relationship between pathologic changes and the production of pain remains obscure (Osti & Cullum 1994). Studies suggesting a positive correlation (Vanharanta et al 1988a, Parkkola et al 1993, Erkintalo et al 1995, Luoma et al 2000a and 2000b) or no correlation (Boden et al 1990, Jensen et al 1994, Wood et al 1995) between disc degeneration and back pain have been published. In the recent study by Weishaupt et al (2001), disc degeneration showed a weak positive predictive value and low specificity for a painful disc.

The majority of episodes of back pain occur in adulthood, mostly in middle age. Nevertheless, low back pain has been found to be a common complaint in adolescence (Salminen et al 1992, Taimela et al 1997). In studies covering populations of 300 adolescents and more, the lifetime prevalence of low back pain varies between 30% and 51% (Balague et al 1999). A significant proportion of the back pains are recurrent or chronic already in 14-year-olds (Salminen et al 1992, Taimela et al 1997). Additionally, a subpopulation representing 2% to 3% of the target population has reported recurrent low back pain up to early adulthood (Salminen et al 1999). In MRI disc degeneration can already be noticed in the second decade (Tertti et al 1991b). According to the some MRI studies (Modic et al 1984, Powell et al 1986, Boden et al 1990) and a cadaver study (Miller et al 1988) the prevalence of disc degeneration has shown to increase rapidly from about 30% in the third decade to 60–97% by the age of 50. Significant low back pain is detected in 5–7.6% of 7 to 17 -year-old children (Salminen 1984). In studies of young adults, 6–26 % of those without symptoms had disc degeneration, whereas 13–38% of those with symptoms had disc degeneration in MRI (Powell et al 1986, Tertti et al 1991b, Salo et al 1995).

In an immunohistochemical study, nerve fibers growing into the end-plate and subchondral bone along with blood vessels have been identified in degenerative discs (Brown et al 1997). The back pain is probably connected to nerve ingrowth (Osti & Cullum 1994, Brown et al 1997). Because only the outermost part of the annulus fibrosus is innervated, the peripheral tears are assumed to be painful (Ost et al 1992b, Fraser et al 1993); they are also suggested to accelerate the degenerative process (Ost et al 1990, Fraser et al 1993).
2.4 Imaging of the intervertebral disc

2.4.1 Conventional imaging studies

2.4.1.1 Plain radiography

Plain radiography is capable of defining only the gross morphologic changes in the intervertebral disc and vertebral bodies; only secondary degenerative changes such as disc space narrowing, sclerosis on the end-plates with osteophytes, and the vacuum disc phenomenon can be detected on plain radiographs (Knutsson, 1942, Resnick 1985, Modic et al 1988a). The validity of disc height as an indicator of early disc degeneration is questionable (Luoma K 2000 b). Calcification of the disc may also be detected (White & Gordon 1982). Nevertheless, because of the good anatomical detail of the bone structure, conventional plain radiography provides an anatomical map (Korman1989). A normal healthy intervertebral disc has no apparent density on plain radiographs. The argument for performing plain radiography in back pain is the need to rule out tumors, infections, instability and other anatomical defects.

2.4.1.2 Contrast myelography

Contrast myelography is another indirect method for assessing the disc. Historically, the role of myelography has been delineation of the thecal sac, the spinal cord, and the exiting nerve roots, and their possible compromise by disc bulging, herniation, and spinal stenosis (Wright et al 1971, Modic et al 1988a). The first myelographic findings in intervertebral disc herniation were described in 1936 by Hampton & Robinson. Surgical correlations with myelographic findings have been 80–90% at L4-5 and lowest at L5-S1 (Modic et al 1988a). However, myelography is less sensitive for the detection of lateral disease (Haughton et al 1982, Daniels et al 1984, Schipper et al 1987, Modic et al 1988a). Myelography is an invasive procedure that adds little if anything to the evaluation of degenerative disc disease compared with CT or MR imaging (Modic et al 1988a) and involves a moderate gonadal radiation dose (Ilkko et al 1987). Despite of the considerable radiation dose CT-myelography is used especially in cases with previous spine surgery (Schönström & Willen 2001).

2.4.1.3 Discography

The technique and the idea of an image of the intervertebral disc with a contrast agent were described by Lindblom in 1948. With the advance of imaging methods and contrast agents, discography has developed as a diagnostic method. Usually, discography has been
combined with computed tomography (CT), as that provides better possibilities for the exact location of fissures and defects in the annulus fibrosus as well as herniations (Vanharanta et al 1988, Guyer & Ohnmeiss 1995, Tehranzadeh 1998). Pain provocation during discography has been considered to be an important part of the examination (Moneta et al 1994, Tehranzadeh 1998); when a disruption of the outer annulus fibrosus is present, the patient’s pain may be reproduced or aggravated by injection of a contrast agent into the nucleus (Moneta et al 1994). Nevertheless, the value of discography has been under lively discussion (Yasuma et al 1988, Walsh et al 1990, Guyer & Ohnmeiss 1995, Bogduk & Modic 1996, Modic 2000). Discography is invasive, rather time-consuming, and moreover includes a potential risk of infection and a moderate dose of radiation when combined with CT. Subjects with significant emotional and chronic pain problems may especially have long-term back symptoms after this procedure (Carragee et al 2000). Nowadays CT and MRI imaging are available and particularly the development of MRI techniques has increased the information obtainable about the internal parts of the disc. Therefore discography has fallen out of favor. It is not recommendable as a screening technique (Guyer & Ohnmeiss 1995, Tehranzadeh 1998). Nevertheless, only a few authors have considered MR imaging to be as good as discography (Gibson et al 1986, Schneiderman et al 1987); others have shown abnormal findings in discography of patients with normal MR imaging (Zucherman et al 1988, Osti & Fraser 1992a) and some have pointed out the value of pain provocation (Zucherman et al 1988, Horton & Daftari 1992). However, some consider that it is still a complementary test in the preoperative investigation of the intervertebral disc as a pain source (Zucherman et al 1988, Lam et al 2000).

2.4.1.4 Computed tomography

Despite the advanced MR imaging, computed tomography (CT) is still an important method for evaluating patients suspected to have disc disease (Tallroth 1998). During recent years, a new helical technology has revolutionized CT scanning; study times have become shorter and costs have lessened (Tallroth 1998). Although the main interest in the interpretation of CT is mostly to search for possible nerve entrapment caused either by intervertebral disc extrusion or by spinal stenosis, degenerative changes in disc may also be detected. Bulging of the disc has been found to be a sign of intradiscal damage (Yu et al 1988a, Tervonen et al 1990). However, CT is relatively insensitive to the early phases of a degenerative process in the disc, especially when the configuration of the disc itself has not altered (Williams et al 1982, Modic et al 1988a). In cadaver studies, it has been shown that discoloration and fissuring within the nucleus may be considerable, and yet the disc may appear normal in configuration and density on CT images (Williams et al 1982). With disc herniation, local hypodensity in the posterior part of disc is usually seen in CT (Jahnke 1983) and has proved to be a specific but insensitive sign of annular disruption (Tervonen et al 1990). Usually, a bulging disc with an intact annulus can be accurately distinguished from a herniated nucleus pulposus by CT (Williams et al 1982). Other reactive or secondary signs of degeneration reliably detected with CT are
calcification, the vacuum phenomenon, and sclerosis of the adjacent intervertebral body (Modic et al 1988a). CT represented a major advance in the evaluation of disc diseases, distinguishing soft tissues from bone changes (Modic et al 1988a). Additional advantages of CT compared with myelography include three-dimensional reformatting, which allows multiple planes to be reconstructed (Modic et al 1988a). However, the contrast sensitivity between various soft tissues is limited in CT especially when compared with MRI (Modic et al 1988a, Gundry & Fritts 1997a). The advantages of CT, as compared with MRI, include imaging of claustrophobic patients and patients with underlying contraindications to MRI, such as those with pacemakers, cochlear implants, or intracerebral aneurysm clips.

2.4.1.5 Ultrasound imaging

Ultrasound (US) is widely used for imaging the soft tissues of the human body. Measurement of the lumbar spinal canal by ultrasound was described by Porter et al in 1978. Transabdominal US examination of the lumbar discs was presented later (von Tölly 1984, Portela 1985). Pathologic changes in the discs were detected by transabdominal ultrasound with a specificity of 0.86 and a sensitivity of 0.84 compared with CT and myelography (von Tölly 1984). At the level of single discs, a sensitivity of 0.92 and a specificity of 0.95 have been reported when comparing the US finding with CT, myelography, or surgery (Tervonen 1988). In a cadaver study, a good correlation was also detected between the intradiscal degenerative changes and the discographic findings (Tervonen & Videman 1988). In that study, disc degeneration caused an increase in echogenicity and a local hyperechoic lesion with acoustic shadowing was a specific sign of moderate-to-severe degenerative changes. However, in US, examination of the diseased discs may be restricted by intervening abdominal tissues and bowel gas (Tervonen & Videman 1988). In addition, the narrowing of the disc space because of disc degeneration may limit the visibility (von Tölly 1984). A combined test of vibration pain provocation and US has been described as a promising method for evaluating back pain (Yrjämä et al 1996). Nevertheless, despite this method’s noninvasiveness and the lack of ionizing radiation, the development of MRI has decreased the potential interest in US.

2.4.1.6 Radionuclide imaging

Degenerative changes in the spine may also be detected by scintigraphy, primarily using technetium-99m-labeled diphosphonates (Modic et al 1988a). This method is sensitive to degenerative changes that increase bone turnover, e.g. in osteophytes or in discogenic sclerosis, but it has no role in the evaluation of disc degeneration, because of its lack of specificity and poor spatial resolution (Gundry & Fritts 1997a).
2.4.2 Magnetic resonance imaging

2.4.2.1 Imaging techniques and normal MRI findings

MRI is based on the magnetic properties of the nuclei of tissues, which are mainly water, in the human body. The first magnetic resonance imaging scans of the human body were made in 1977 (Mansfield & Maudsly 1977). Since then the method and the imaging instrument have been enormously developed. The superior soft tissue contrast and multiplanar imaging capability make MRI as the procedure of choice for a host of spinal disorders, including intervertebral disc diseases (Modic et al 1988a, Gundry & Fritts 1997b). The magnetic field strengths generally used vary between 0.5 and 1.5 T. In experimental studies, the relative tissue contrast has been considered better at low fields because of the increased T1 dispersion (Koenig & Brown 1984). T2 has been found to be practically independent of field strength, while T1 increases toward higher field strengths.

The parameters used in spinal MR imaging depend both on the portion of the spine that is studied and the clinical problem involved (Gundry & Fritts 1997a). The epidural fat is more prominent in the lumbar spine than elsewhere, which helps to distinguish the thecal sac from the other epidural tissues. Surface coils are used in spine imaging, because they provide a relatively high signal-to-noise ratio (SNR) (Axel 1984) and limit the amount of the artefact related to respiratory motion (Ruggieri 1999).

Fast spin echo imaging is a variation of the rapid relaxation enhancement technique, in which all phase encoding data were collected within a single TR interval (Jones et al 1992, Georgy & Hesselink 1994). The pulse sequence begins with a 90° RF pulse and this is followed by the acquisition of two to 16 refocused echoes. The middle lines of the K-space, which have the highest signals and the greatest impact on contrast, are acquired around the TE for the desired image contrast. This technique provides shorter acquisition times, while at the same time permitting long repetition times and long echo times for obtaining heavily T2-weighted images. With FSE sequences, imaging times decrease and resolution improves (Georgy & Hesselink 1994) and on T2-weighted images SNR improves (Constable et al 1992). The contrast-to-noise ratio (CNR) has also been shown to be better in FSE than in conventional SE images (Chappell et al 1995). So FSE sequence has been considered to replace the conventional T2-weighted SE images in the sagittal planes for evaluation of disc degeneration (Jones et al 1992, Ross et al 1993, Ruggieri 1999). FSE images provide a better myelographic effect with reduced magnetic susceptibility as compared with gradient echo (GE) sequences. However, the routine evaluation has become quite standardized. Recent developments are shortening the examination time and improvement of the sensitivity of existing techniques (Ruggieri 1999). In the cervical and thoracic spine, cerebrospinal fluid (CSF) flow creates problems, including signal loss, spurious signals and blurred interfaces. Because of CSF pulsation and respiratory motion, the routine use of true T2-weighted images in the cervical and thoracic spine is prevented (Gundry & Fritts 1997a). In the lumbar spine, CSF pulsation is considerably dampened and therefore MR imaging in this area is distinctly easier (Ruggieri 1999).
Many different pulse sequences have been applied to MR imaging of the spine (Murayama et al 1990, Georgy & Hesselink 1994). The lumbar spine is commonly imaged using T1-weighted spin echo (SE) and T2-weighted fast spin echo (FSE) images (Morgan & Saifuddin 1999), supplemented T1-weighted SE and/or T2-weighted FSE axial images at selected levels (Gundry & Fritts 1997a). GE imaging has also been performed on the spine, especially in the cervical region (Enzmann & Rubin 1988). The problems with respiratory motion can be decreased by using rephasing gradients (Haacke & Lenz 1987); this may be helpful in the thoracic spine. Although the anatomy of the annulus in GE sequences is usually poorly visualized, these sequences may help to distinguish disc herniations from hypointense spondylophytes (Wasenko et al 1994). In the lumbar region, GE sequences are not used as frequently as elsewhere in the spine (Ruggieri 1999). Fat suppression techniques are used in conjunction with gadolinium-based contrast material to improve visualization of inflammatory and neoplastic diseases. T2-weighted fat suppression technique is used in the assessment of traumatic involvement of the spine (Young & Petersilge 1999). Routine thoracic spine studies consist of T1-weighted and T2* (GE) or T2 FSE sagittal images. If disc abnormalities are seen in sagittal images T2* axial images are obtained (Gundry & Fritts 1997a).

Age-related changes are also detected in MRI (Yu et al 1989). Immature, transitional, and adult nuclei pulposi are associated with an intact annulus fibrosus (Yu et al 1989). The outer annulus is visualized as hypointense on all pulse sequences and is optimally demonstrated on T2-weighted FSE images (Morgan & Saifuddin 1999). The normal nucleus pulposus is bright on T2-weighted FSE images and the inner annulus is indistinguishable from the nucleus pulposus (Schiebler et al 1991). The intranuclear cleft, reflecting a fibrous transformation of the gelatinous matrix of the nucleus pulposus (Schiebler et al 1991) is visualized as a dark band in T2-weighted sagittal images and is a normal finding in the nuclei of subjects over 30 years old (Aguila et al 1985). In T1-weighted SE images the nucleus pulposus is relatively hypointense compared to normal bone marrow (Morgan & Saifuddin 1999). The end-plates and the ligamentous structures as well as the outer annulus fibrosus have low signal intensities on both T1- and T2-weighted images. Sagittal T1-weighted images are needed for the anatomy (Ross et al 1993) and sagittal T2-weighted images demonstrate the degree of hydration of the discs.

### 2.4.2.2 Traumatic and degenerative findings

MR is considered to be the most sensitive imaging method for evaluating the intervertebral disc (Modic et al 1984). The structural status of the intervertebral disc is accurately demonstrated with modern MR scanners and imaging methods (Cassar-Pullicino 1998). However, as yet MRI does not differentiate abnormal asymptomatic disc levels from symptomatic painful discs. Moreover, abnormal discs are frequently detected in asymptomatic subjects (Boden et al 1990, Jensen et al 1994, Wood et al 1995).

Biochemical and structural changes associated with disc degeneration will be depicted as significant signal loss on T2-weighted images and diminished disc height. The first sign of early disc degeneration is infolding of the fibers in the outer annulus and this is
sometimes associated with the low signal intensity area in the anterior part of the nucleus, the central dot (Schiebler et al 1991). In the early phase of a degenerative process, fibrotic changes associated with decreased water content cause loss of the high T2 signal from the nucleus pulposus. In the advancing phase, the hyaline cartilage end-plate is separated from the inner annulus and the nucleus (Schiebler et al 1991) and fluid-filled fissures may be generated, which can be seen as high signals on the T2-weighted sequences, commonly with loss of disc height (Yu et al 1988b and 1989, Cassar-Pullicino 1998). Radial annular tears are considered an important hallmark of disc degeneration (Yu et al 1989). The inner annulus inverts and becomes concave, departing from its normal convex contour (Cassar-Pullicino 1998), especially anteriorly. These early degenerative changes affect the mechanical properties of annulus and thus lead to general bulging with loss of disc height (Cassar-Pullicino 1998).

Disc herniation is considered to be one of the sequels and complications of disc degeneration. It is a focal displacement of the nuclear, annular, or end-plate material beyond the normal peripheral margins of the disc delimited by the margins of the vertebral bony end-plates (Herzog 1996, Milette 2000). Bulging is described as an annular phenomenon that does not require operation (Cassar-Pullicino 1998). On the other hand, bulging can be defined as a disk in which the contour of the outer annulus extends in the horizontal plane beyond the edges of the disc space, normally greater than 50% of the disc circumferentially (Milette 2000). Herniations are subdivided into protrusions and extrusions, depending on the extent of the base of herniation compared with other diameters of the herniation (Milette 2000). Extrusions can further be described as sub- or transligamentous, depending on the integrity of the posterior longitudinal ligament. Nevertheless, the terminology in clinical use for evaluating the different kinds of herniation is confusing (Cassar-Pullicino 1998, Morgan & Saifuddin 1999, Milette 2000). Sequestered fragments of the disc are reliably demonstrated with MRI (Masaryk et al 1990). These usually have a slightly higher signal intensity on T2-weighted images than the parent disc in the early phase and may enhance peripherally after an injection of intravenous gadolinium. The configuration of the sequesters varies, depending their location (Masaryk et al 1990). Discs can also herniate intraosseously in the vertical direction, these have been named Schmorl node’s. Any process which weakens the vertebral end-plate or the subchondral bone can cause these nodes. Commonly, they are incidental findings, but some are assumed to be traumatic in origin and also symptomatic (Walters et al 1991). Schmorl’s nodes are strongly associated with Scheuermanns disease and latter is associated with an accelerated degenerative process in the disc (Paajanen et al 1989, Terti et al 1991b, Swischuk et al 1998). Intraosseus herniations, which occur peripherally and undermine the ring epiphysis, separating it from the body of the vertebra, will lead to limbus vertebrae (Swischuk et al 1998).

In addition to radial tears, transverse tears may also be detected in MRI (Yu et al 1988b). Transversal tears are ruptures in the peripheral part of the annulus in Sharpey’s fibers near the apophysis and according to current knowledge, they are assumed to be clinically insignificant (Morgan & Saifuddin 1999). Radial tears in the annulus, when extending from the nucleus to the outer third of the annulus circumferentially by more than 30°, representing a grade 4 fissure in the Dallas discogram scale, are seen in MRI as the high intensity zone (HIZ) (Aprill & Bogduk 1992). The HIz is defined as a focal area of high signal intensity within the posterior annulus surrounded by areas of low signal
intensity on all sides and thus clearly separated from the nucleus (Aprill & Bogduk 1992). The signal of the HIZ often is brighter than that of the nucleus pulposus (Aprill & Bogduk 1992). After discovery, the HIZ was suggested to be highly correlated with pain (Aprill & Bogduk 1992, Schellhas et al 1996). Recently it has also been demonstrated in asymptomatic subjects (Stadnik et al 1998, Weishaupt et al 1998), and its sensitivity and positive predictive value have been shown to be poor (Weishaupt et al 2001). The presence of annular tears is often followed by fibrovascular proliferation (Osti et al 1990). The distinction between the fluid within the injured annulus and the hydrated fibrovascular repair tissue within the annulus is not clear (Cassar-Pullicino 1998), since both may increase the signal in T2-weighted images. Annular tears can also be demonstrated also with gadolinium-DTPA-enhanced T1-weighted images, because of their vascularized granulation tissue (Ross et al 1990, Cassar-Pullicino 1998). In the normal low-signal intensity annulus on T2-weighted images the enhancement of posterior annular tears has been found to be more common than the presence of an increased signal intensity (Ross et al 1990). In clinical practice, it is not known whether a high signal in the posterior annulus is associated with an acute or an already recuperating phase.

Degenerative disc disease is frequently associated with changes in the vertebral end-plate (Modic et al 1988a and 1988b). These are also called Modic changes and were at first subdivided into two types (Modic et al 1988 a and b). Type 1 changes include decreased signal intensity on T1-weighted and increased signal intensity on T2-weighted images. In type 2, the signal intensity is increased in both T1- and T2-weighted sequences. Type 1 changes are caused by fibrovascular replacement of the subchondral bone and type 2 changes are accompanied by fatty replacement of subchondral bone and are considered to be chronic (Modic et al 1988a and b). In plain radiographs, these two classes cannot be separated. If bone sclerosis is extensive in plain radiographs, signal intensities are decreased in both T1- and T2-weighted images and this change in end-plate is called type 3 change (Modic et al 1988a). In a longitudinal study it has been demonstrated that type 1 changes often convert to type 2 (Modic et al 1988a and b). A mixture of types has also been demonstrated, accompanied by disc degeneration (Braithwaite et al 1998). These degenerative end-plate changes are shown to be associated with back pain (Weishaupt et al 2001); they are most commonly type 1 changes (Toyone et al 1994, Braithwaite et al 1998). Type 1 changes are nonspecific; similar signal intensity changes are associated with malignancy, trauma, intraosseus herniation (Schmorl’s nodes), and infection (Morgan & Saifuddin 1999).

The site most commonly injured in the vertebral column is the thoracolumbar junction. Injury to the intervertebral disc is quite commonly associated with fractures (Young & Petersilge 1999). Damage can be detected as increased signal intensity of the disc on T2-weighted images (Flanders et al 1990). Protrusions and herniations may also be traumatic in origin, particularly when the posterior longitudinal ligament is affected (Flanders et al 1990, Young & Petersilge 1999).
2.4.2.3 Quantitative MR studies

Because it is influenced by the organization of biological systems at the molecular level, MRI can also noninvasively provide information about the biochemical features of tissue in addition to high-resolution anatomical images. Two relaxation times are defined: T1 (longitudinal or spin-lattice relaxation time) and T2 (transverse or spin-spin relaxation time). T2 relaxation times have been used for rough estimations of water content (Boos & Boesch 1995). The motional freedom of the molecule and the water content have major roles influencing the T1 and T2 relaxation times (Bottomley et al 1984, Boos & Boesch 1995). It is obvious that the major sources of relaxation time variations among the different tissue types are not only the water content but also the differences in the macromolecular composition and structure, which could affect the amount and motion of absorbed water molecules (Bottomley et al 1984). Magnetization transfer (MT) imaging is a quantitative method which provides information on the interactions between macromolecules and water. There are few studies applying MT imaging to intervertebral discs (Paajanen et al 1994a, Antoniou et al 1998).

Relaxation times provide a quantitative analysis of images which is independent of the observer (Boos et al 1994) and T1 and T2 relaxation time measurements have also been performed on the intervertebral disc (Jenkins et al 1985, Bobest et al 1986, Hickey et al 1986, Chatani et al 1993, Boos et al 1993 and 1994). Although the reproducibility in vitro has been modest, in vivo it has been less satisfactory; the major reasons for the worse reproducibility in vivo than in vitro have been assumed to be motion artefacts and involuntary displacement of the patient during the study (Boos et al 1994). Several other factors, such as temperature, has also in fluenced the relaxation times (Boos & Boesch 1995). The variation in relaxation values has been large (Boos et al 1994) and quantitative MRI studies of discs have not proved sufficiently reliable for monitoring the biochemical alterations associated with lumbar disc pathology in vivo (Boos & Boesch 1995). However, such studies can provide a sufficiently accurate estimation of the variation in diurnal hydration at the cohort level (Boos et al 1993). Proton density measurements have been suggested to be influenced by the machine parameters (Boos et al 1994) and proton density has been suggested to be one of the most difficult parameters to measure accurately (Boos & Boesch 1995). For the reasons mentioned above, quantitative analyses of proton density and T1 and T2 relaxation times in vivo, in vitro, and ex vivo have to be considered separately (Boos & Boesch 1995).

Quantitatively, disc degeneration occurs as a decrease in relaxation time (Tertti et al 1991a, Boos et al 1994), which is also detected with advancing age (Jenkins et al 1985). In a study by Paajanen et al (1994a), the transfer rate of magnetization between free water and macromolecular-bound protons was higher in degenerated than in healthy discs, but MT imaging did not prove more sensitive in depicting incipient disc degeneration than conventional T2-weighted images. MT has been shown to increase significantly with increasing degeneration of the nucleus and is not much applied in clinical practice nowadays. A combination of MT and T1 and T2 values has been considered to reflect information about the structural integrity of the disc matrix (Antoniou et al 1998).
2.5 Diffusion imaging

2.5.1 Diffusion imaging of the intervertebral disc

Using paramagnetic contrast media, diffusion into the intervertebral disc has been demonstrated in animals (Ibrahim et al. 1994b) and humans (Akansel et al. 1997) in MRI. Measurements of the signal intensities of intervertebral discs after intravenous gadolinium have shown significant differences between healthy and degenerated discs (Nguyen-minh et al. 1998). The diffusion rate is slower with ionic than with nonionic contrast media (Ibrahim et al. 1994a) and in mature than in immature intervertebral discs (Ibrahim et al. 1995). A decreased diffusion rate has been suggested to be a marker for early disc degeneration (Nguyen-minh et al. 1997 and 1998). However, this method needs moderate amounts of contrast medium intravenously (Akansel et al. 1997, Nguyen-minh et al. 1998) and so far this method has not been utilized clinically.

Recently, a study of diffusion tensor microscopy in the annulus fibrosus of excised porcine intervertebral disc has been presented (Hsu & Setton 1999). In that study, the diffusion anisotropy of water and the lamellar structure of the annulus fibrosus were detected with high spatial resolution.

2.5.2 Diffusion-weighted MR imaging

2.5.2.1 Principles

Diffusion-weighted MR imaging (DWI) characterizes tissues at the microscopic level; molecular diffusion is described as general, thermal, and random displacement of molecules. Water molecules diffuse for distances of a few micrometers in a second, and thus DWI is a very suitable method for examining the structure of biological tissues at the microscopic level — well beyond the typical resolution of MR images (Le Bihan 1998). Diffusion is translational motion and, unless restricted, it occurs in all directions, i.e. isotropically (Gray & MacFall 1998). The term intravoxel incoherent motion (IVIM) refers to microscopic translations occurring in voxels on MR images (Le Bihan et al. 1986). Small motions in biologic tissues are caused by molecular diffusion and microcirculation of the blood in the capillary network. IVIMs are quantified by a parameter termed the apparent diffusion coefficient (ADC). The ADC is equal to the true diffusion coefficient D when diffusion is the only type of motion. Because perfusion contributes to the ADCs, the reported ADC values are commonly higher than expected (Le Bihan et al. 1986). On the other hand, in cases in which the ADC is higher than the diffusion coefficient of pure water, separation of diffusion and perfusion is not essential (Le Bihan et al 1988) since the high value is then the result of perfusion. Other factors contributing to ADCs are CSF flow, cardiac pulsations, restriction of possible cellular membranes, and fiber packing and orientation (Gray & MacFall 1998). In the abdominal organs, a wide scatter of ADCs among subjects has been demonstrated (Muller et al
This has been suggested to be due to the contribution of perfusion (Yamada et al 1999). Diffusion in tissue is always anisotropic to some extent. The anisotropy can be mathematically modelled using the so called diffusion tensor formalism. Diffusion tensor imaging has been suggested to characterize diffusion imaging more accurately, especially in heterogeneous and anisotropic tissues (Pierpaoli et al 1996, Gray & MacFall 1998). Diffusion is measured in each voxel in each of the three directions (x, y, z) and the measurements are averaged to generate a Trace D, which is a measure of the average of the three independent scalar elements of the diffusion tensor. The sum of the three scalar elements is known as the trace and is independent of direction and location. However, a full diffusion tensor measurement requires measurements in at least six directions and is therefore quite time-consuming because of the increased data acquisition and postprocessing. In the assessment of stroke, a diffusion image acquired with a gradient applied in one direction only may be adequate (Gray & MacFall 1998). When diffusion coefficients are measured, multiple images are acquired by applying different gradient strengths with their particular b-values. The diffusion coefficient is plotted as the natural log of the signal intensities versus the b value.

DWI is very sensitive to motion, and therefore strong gradients of short duration are preferable to reduce nondiffusion-related motion (Le Bihan 1991, Le Bihan et al 1992). The initial technique, which was based on SE two-dimensional Fourier transform (2DFT) imaging, was slow and therefore very sensitive to motion artefacts (Le Bihan et al 1986). On conventional MR images, diffusion effects are extremely small and invisible. In practice, DWI is performed by incorporating strong magnetic field gradient pulses within any imaging pulse sequence and the degree of diffusion weighting is based on the strength and duration of the gradient pulses (gradient factor). Quantitative diffusion images can also be performed from a series of diffusion-weighted images by using adequate software (Le Bihan et al 1992). Calculated diffusion images are often noisier than diffusion-weighted images; anyway, they only provide quantitative information (Le Bihan et al 1992). The echo-planar imaging (EPI) is the fastest clinically useful imaging technique (Edelman et al 1994) and is considered the best method for quantifying diffusion (Le Bihan 1998).

2.5.2.2 Applications for clinical use

The potential of DWI for evaluating acute brain ischemia was presented more than a decade ago (Le Bihan et al 1986). The measurement of molecular diffusion in the human body has enormous clinical potentialities. So far, diffusion imaging has been used mainly to evaluate cerebral stroke (Le Bihan et al 1986, Moseley et al 1990, Chien et al 1992, Warach et al 1995). Compared to CT and conventional MR methods, DWI offers earlier and more precise detection of the location and extent of an ischemic lesion during the critical first hours after the onset of stroke. Besides, a diffusion study can be performed very rapidly; with single-shot echo-planar imaging it is possible to acquire an image in a few tens of milliseconds and to image the entire brain in less than a second (Edelman et al 1994). Water diffuses more slowly in ischemic regions and DWI can describe cytotoxic
edema associated with acute stroke within minutes after vascular occlusion (Le Bihan 1998). The very significant decrease in ADC in ischemic tissue is presented as regional high signal intensity in DWI. Another significant application of DWI is for studies of brain white matter (Doran et al 1990, Larsson et al 1992, Nomura et al 1994). Diffusion may also be useful for distinguishing the various components of brain tumors (Tsuruda et al 1990, Le Bihan et al 1992). Studies demonstrating the value of DWI for investigating abdominal organs have been presented (Muller et al 1994, Yamada et al 1999) and recently a study was presented differentiating benign from malignant vertebral fractures (Baur et al 1998). Very limited diffusion studies of the spine have been done so far. This is related to susceptibility artefacts and spatial resolution (Ruggieri 1999). Hardware and substantial technical progress may be assumed to provide several potential applications of DWI in clinical use (Gray & MacFall 1998, Le Bihan et al 1992 and 1998).

2.6 Imaging of lumbar arteries

2.6.1 Angiography

In aortography, the aorta and its branches are imaged, and also four pairs of lumbar arteries and the arteria sacralis media are reliably evaluated. Nowadays, angiographies are mostly performed with a subtraction technique, which increases contrast sensitivity as compared with conventional angiographies (Katzen 1995). Angiography is still considered to be the gold standard in imaging vascular structures. However, angiography of the aorta or its branches is an invasive method and requires a moderate radiation dose. Contrast allergy and renal insufficiency are also at least relative contraindications for angiography. Atherosclerotic changes occur frequently in the abdominal aorta; they are located at the orifices of large trunks and at the ostia of the lumbar arteries. One angiographic study has been performed in which atherosclerosis in the lumbar area was associated with low back pain (Kauppila & Tallroth 1993). In spinal angiography, the lumbar arteries may be selectively examined when an AV-malformation is imaged.

2.6.2 CT angiography

The use of volumetric (spiral) CT scanning has provided possibilities for imaging vascular structures multiplanarly by a minimal invasive technique. The images can be reconstructed by various computed rendering techniques to generate two- (2-D) or three-dimensional (3-D) images of the blood vessels (Rubin et al 1995). In a study performed by the electron beam tomography computed tomography angiography technique, visceral branches, renal arteries and lumbar arteries were visualized in all 155 cases (Lehmann et al 1999). CT angiography is already considered to be a promising imaging method for identifying or excluding hemodynamically significant stenoses, but may require
considerable amounts of contrast medium (Rubin et al 1995) and there is also a noticeable radiation dose. Further benefits in speed and resolution are likely to be realized with multislice CT.

### 2.6.3 MR angiography

MR angiography is a term used to describe a variety of MR imaging techniques designed to create angiographic images without the use of invasive techniques, contrast media or ionizing radiation (Sheppard 1995). The first efforts at MR imaging of the aorta included spin echo, time-of-flight (TOF), and phase contrast angiography (PCA) techniques. Recently, advances have occurred in three-dimensional contrast-enhanced imaging and image quality has improved significantly (Smyth & Grist 1998). Nowadays, the MR angiography methods most commonly used are TOF, PC, and contrast-enhanced techniques (Korosec & Mistretta 1998). In the imaging of the abdominal aorta, contrast-enhanced MR angiographic methods have become superior, but 2D TOF is also used, particularly for demonstrating the length of occlusion and the patency of distal vessels, although the mesenteric branches are not usually adequately delineated (Smyth & Grist 1998).

TOF is also known as inflow and flow-related enhancement. PCA and TOF differ from each other fundamentally. TOF achieves a contrast between flowing blood and stationary tissues by manipulating the magnitude of the MR signal from stationary tissues and PCA achieves a contrast between blood and stationary tissues by manipulating the phase of the MR signal. Both TOF and PC angiographies can be performed by a two-dimensional (2D) or a three-dimensional (3D) acquisition scheme (Korosec & Mistretta 1998). In PCA, the signal intensity depends on the blood velocity. The signal from static tissues is obliterated by subtraction (Korosec & Mistretta 1998). TOF is more widely used than PC techniques (Korosec & Mistretta 1998). Contrast-enhancing techniques are based on the T1 shortening effects of gadolinium chelates (Smyth & Grist 1998), which enhance the contrast between the signal from the vessels and the stationary tissues.

TOF maximizes the contrast between flowing blood and stationary tissues. Static tissues are exposed to many radiofrequency pulses (RF) with a repetition time much faster than T1, so these spins in the stationary tissues will be saturated. After saturation, magnetization will be small and there are very few MR signals to detect. The blood, which is constantly flowing to the imaging volume, is not subjected to many RF pulses. So the net magnetization of these unsaturated spins (blood) is much greater than the saturated spins in the static tissues (Sheppard 1995, Korosec & Mistretta 1998). Arterial and venous flows are separated with presaturation slabs, which are placed on one side of the imaging slice (Sheppard 1995). TOF technique is widely used in the study of carotid arteries and the circulus Willis. TOF has limitations being less valuable for imaging tortuous vessels in which the flow is slow (Sheppard 1995). SNR is poorer in 2D TOF compared to 3D TOF (Korosec & Mistretta 1998). In 2D TOF, thin slices oriented perpendicular to the vessels of interest are obtained. The multiple thin slices are
postprocessed and angiographic images are obtained with maximum intensity projection (MIP) or with the data adaptive ray tracing (DART) algorithm (Korosec & Mistretta 1998).
3 Purpose of the study

The purpose of the present study was:

1. to determine the MRI changes in the intervertebral disc after peripheral experimental annular lesion in different time frames and the histology of HIZ.
2. to investigate whether trauma can initiate a degeneration process in the intervertebral disc.
3. to test the feasibility of diffusion-weighted MR imaging of intervertebral discs.
4. to study whether the degree of degeneration or the status of the lumbar arteries has more effect on the measured diffusion in the lumbar intervertebral discs.
4 Materials and methods

4.1 Materials

4.1.1 Experimental material (I)

A total of 8 adult minipigs of both genders were included in the experiment. One lumbar disc in each minipig was carefully incised; the traumatized disc level varied from L 2/3 to L 4/5. The lesions were made in the anterolateral part of the annulus fibrosus with a no.11 scalpel blade through a left-sided retroperitoneal approach without damage to the nucleus pulposus. The minipigs were sacrificed after 1 month, (4 pigs) and 3 months (4 pigs). The lumbar spine was excised as a whole after death and the spines were stored in liquid nitrogen. Each disc was cut into blocks with parallel end-plates, using a butcher`s bandsaw. The upper and lower discs adjacent to the damaged discs as well as other discs of the lumbar and lower thoracic spines were used as controls. The blocks \((n = 57)\) were stored at \(-70^\circ\) C until the MRI examination. At the time of imaging, the blocks were at room temperature.

4.1.2 Young controls (II, III)

A total of 18 healthy young volunteers (10 boys and 8 girls) underwent MRI studies. Four of these were not included in study II; thus their mean age was 15.5 yrs in study II and 15.8 yrs in study III. The age range was 8–22 yrs in both of these studies. These volunteers had no history of back pain or previous spinal injury. Studies were approved by the local ethics committee.
4.1.3 Patients (II, IV)

Altogether 14 (6 female and 8 male) young patients with earlier vertebral fracture in the thoracolumbar spine were studied (table 1). All the fractures were confined to the vertebral body and had been considered stable and treated conservatively. In all the patients, more than one year had elapsed between the accident and the current study. The patients’ mean age was 11.8 yrs (range; 7.1–15.9 yrs) at the time of the accident and 15.5 yrs (range; 8.8 yrs–20.8 yrs) at the time of the MRI and clinical study. The patients had had altogether 42 fractured vertebrae. The number of damaged vertebrae had varied from 1 to 9, the mean being 3 vertebral fractures per patient. Some patients had only upper end-plate fractures and others had wedge-shaped compression fractures; most patients had both of these fracture types. Thus, the patients had 46 discs located in the primary trauma area. The classification into the primary and secondary trauma areas, was made in study IV. A disc was defined as located in the primary trauma area if it was adjacent to a fractured vertebra, and in the secondary trauma area if it was adjacent to an intact vertebra and separated by three discs from the primary trauma area at maximum. The discs of the patients were classified into three groups: 1) degenerated discs in the primary trauma area, 2) discs in the primary trauma area with normal signal intensity in T2-weighted FSE images, and 3) discs in the secondary trauma area with normal signal intensity in T2-weighted FSE images. The nine degenerated discs that were located outside the primary trauma area were excluded from the ADC and T2 relaxation time measurements.

On the basis of the type and force of the trauma, the energy of the trauma was classified as high, medium, or low. Studies II and IV were approved by the local ethics committee.

4.1.4 Adults (V)

Thirty-seven asymptomatic adult volunteers (15 men and 22 women) underwent MR examinations. None of these volunteers had low back pain at the time of the present study, nor had they any relevant history of back pain. The mean age of the volunteers was 38 yrs and the range was 22–68 years. L1/2 – L 4/5 discs and their segmental lumbar pairs were evaluated. Study V was approved by the local ethics committee.
4.2 Methods

4.2.1 Macroscopic and histologic evaluation of the minipig preparations (I)

Macroscopic examination of the minipig blocks was made to verify the level of the incision. Discs showing a clearly distinguishable, reddish area in the anterolateral part of the annulus fibrosus were classified as injured.

Histologic examinations of the injured preparations were also made. The blocks were fixed in phosphate-buffered 10% formalin and decalcified in EDTA-solution for 5 weeks. After fixation, the samples were dehydrated in a graded series of ethanols with xylene and thereafter embedded in paraffin wax. The samples were sectioned at 5 μm with a microtome, fixed, and stained with Ehrlich’s hematoxylin and eosin in order to study the morphology and cell density of the injured annulus fibrosus.

4.2.2 Questionnaires (II–V)

The healthy young volunteers and asymptomatic adults (II, III, V) answered a questionnaire by which any back pain in the medical history or previous back trauma was excluded. In study II, the patients answered a standardized questionnaire concerning any back pain at rest, during leisure time, at school, or in activities and were also asked whether pain medication or physical therapy had been needed. Contacts with a doctor and interruption of leisure time activities on account of back problems were recorded. Descriptions of the traumas in study II were recorded from the case histories.

4.2.3 Clinical examination (II)

A pediatric surgeon performed clinical examinations on the young patients who had previously had vertebral fractures. Possible scoliosis and changes in posture were assessed. Scoliosis was estimated from the reading of a scoliometer; the angle of Cobb was 4.35 x scoliometer reading –12.6. Clinical examinations were performed without knowledge of the lateral radiograph or MR findings.

4.2.4 Radiographic study (II)

A lateral radiograph was taken in 12 patients in the upright posture to evaluate pathologic kyphosis and to check the shape and height of the fractured vertebrae.
4.2.5 Magnetic resonance imaging

4.2.5.1 Protocols for high resolution anatomical imaging (I–II, V)

In study I, MR imaging was performed using either a 1.0 T MR unit (Magnetom Expert, Siemens, Erlangen) or a 1.5 T MR unit (Signa, Echo Speed, General Electric Medical Systems, Milwaukee, Wis). The use of two different MR units was due to an upgrade during the course of the study. In both of these examinations, the imaging was made with a volume send-and-receive knee coil. Imaging consisted of axial and sagittal T1-weighted images, as well as axial and sagittal T2- and proton-density-weighted images. Nine blocks were imaged, using the 1.0 T MR unit. T1-weighted SE images were obtained, using a 20-cm field of view, a 256 x 256 matrix 3.0 mm thick, interleaved slices, a repetition time (TR) of 600 msec and an echo time (TE) of 15 msec. This was followed by T2-weighted SE (TR/TE 2700/90 ms) and proton-density (TR/TE 2700/20 ms) sagittal and axial images, obtained by using a 20-cm field of view, a 256 x 256 matrix, and 3.0 mm thick interleaved slices.

In the examinations made using the 1.5 T MR unit, T1-weighted images were taken, using two different protocols. In one protocol (29 blocks), T1-weighted SE (TR/TE 500/8 ms) sagittal images were obtained by using a 23-cm field of view and a 3-mm slice thickness and (TR/TE 400/14 ms) axial images with a 3-mm slice thickness. In the other protocol (19 blocks), T1-weighted SE (TR/TE 600/9 ms) sagittal images were obtained with a 4-mm slice thickness and T1-weighted SE (TR/TE 500/14 ms) axial slices with a 3-mm slice thickness. In this protocol, the field of view was 20 cm. In both of these protocols, T2-weighted FSE sagittal and axial images had, the same repetition and echo time (3500 ms/98 ms) and proton-density-weighted images had a 14 ms echo time. The field of view was 20 cm x 15 cm and in sagittal PD and T2 images in both protocols the slice thickness was 4 mm. In T2-weighted FSE axial slices, the field of view was 20 x 20 cm and the slice thickness was 3 mm. Matrix size did not vary between these protocols and was always 256 x 224.

In studies II–V, the MR examinations of the spines were performed using a 1.5 T MR unit (Signa, Echo Speed, General Electric Medical Systems, Milwaukee, Wis) with a phased-array surface coil.

In studies II–IV, the imaging consisted of T1-weighted (TR/TE 500/14 ms) sagittal and T2-weighted fast SE (TR/TE 6000/105 ms) sagittal and coronal images, and T2-weighted fast SE axial images were obtained, concentrating on the trauma level. In study V, only T2-weighted fast SE sagittal images (TR/TE 6000/105 ms) were taken for high-resolution anatomic imaging. In all images, the slice thickness/gap was 4 mm/0.5 mm. The field of view was 30 x 30 cm in the sagittal and coronal planes and 20 x 20 cm in the axial plane. The imaging matrix was 512 x 224 in the sagittal images and 256 x 192 in the axial and coronal images.
4.2.5.2 Analyses of anatomic images (I–V)

In study I, discs were classified visually in a double-blind manner from T2-weighted images into one of three categories. In category 1, the signal intensity was bright and was considered normal. In category 2, the signal intensity was moderately decreased, with blurred margins of the nucleus pulposus and/or the area of bright signal was greatly diminished in the nucleus pulposus or in the inner annulus. In category 3, there was severe loss of the signal intensity of the nucleus pulposus. In addition, the presence of an intranuclear cleft in the nucleus was evaluated and a search was made for central dots representing degeneration. The imaging findings analyzed from the annular changes were: signal intensity changes, chiefly the presence of high-signal-intensity areas in the annulus, and bulging of the annulus, which were evaluated from the sagittal slices.

In studies II–IV, when evaluating degeneration from T2-weighted FSE sagittal images, discs were divided into two classes. In class 1, a normal disc was present with bright signal intensity. When there was a decrease in the intensity of nucleus pulposus the disc intensity was categorized as abnormal, i.e. degenerated. Both T1- and T2-weighted images were used to assess disc protrusion, wedging and other structural abnormalities of the vertebral bodies and end-plate changes. End-plate changes were estimated either from an irregularity in the contour, including Schmorl nodes, or from signal intensity changes in the end-plates.

In study V the intervertebral discs were classified independently by two examiners into three groups: 0 = discs with bright signal intensity, or only a slightly blurred intranuclear cleft, 1 = discs with a normal height, but slightly decreased signal intensity, and 2 = discs with a significantly decreased signal intensity and height loss indicating severe degeneration.

The signal intensity in the disc was compared with that in the CSF (Luoma 2000b). If the opinions of the radiologists differed, a consensus was negotiated.

4.2.5.3 T2 relaxation time measurements (III–IV)

In the T2 relaxation time measurements, a phased-array spine coil was used. The coil contained four receivers, which could be applied independently to different parts of the spine. The T2 relaxation time was measured using an axial multiecho SE protocol with TE values of 20, 40, 60, and 80 ms, a 2000 ms repetition time, and a 256x256 matrix size. Slice thickness was 4 mm and spacing 5 mm. The T2 value was determined on a pixel-by-pixel basis by the least-squares fitting routine. Regions of interest (ROI) were then set for the discs to obtain the mean T2 values and their standard deviations.
4.2.5.4 Diffusion-weighted study (III–V)

The diffusion measurements were made using a non-phased-array, general-purpose, receive-only, flexible coil (GPFLEX) with two electronically summed surface coils. The coil could be wrapped around the patient’s back to produce a relatively uniform signal throughout the region of interest. The diffusion-weighted images were obtained using a spin echo single-shot EPI sequence (effective TE about 73 ms, TR 5000 ms, slice thickness 5 mm, spacing 10 mm, FOV 40x20 cm, matrix size 128x128, 1 NEX). This yielded spatial resolutions of about 3.1 mm and 1.6 mm in the readout and phase-encoded directions, respectively. The imaging plane chosen was axial. The diffusion weighting was obtained by adding two diffusion sensitizing gradients, one on either side of the 180° refocusing pulse. The pulse duration was $\delta = 32$ ms, the pulse interval $\Delta = 38.1$ ms, and the maximum gradient strength $G_{\text{max}} = 22$ mT/m. The gradient ramp time was 184 $\mu$s.

The read-out was always in the vertical direction and the phase-encoding in the horizontal direction. Despite the presence of aortic and cerebrospinal fluid pulsations in the field of view, no noticeable phase-encoding ghosts could be seen in either the T2 or the diffusion-weighted axial images. The cerebrospinal fluid flow was found to generate a flow void in some of the images. However, this did not overlap with the intervertebral disc areas. Susceptibility artefacts were not detected in the images. The diffusion-sensitizing gradients were applied sequentially in the $x$, $y$, and $z$ directions ($z$ is the direction of the main magnetic field) using diffusion weighting factors (b values) of 250 and 500 s/mm$^2$. The b-scale was also checked using the apparent diffusion coefficient value $\text{ADC} = 2.0 \times 10^{-3}$ mm$^2$/s of water at a temperature of 23°C.

The ADC values were determined by first calculating the average intensities from a selected region of interest (ROI), separately for image sets taken with the b values 0, 250 and 500 s/mm$^2$. To optimize the SNR, rather low b values were chosen. A least-squares fit was then applied to the resulting three-point attenuation curve.

The ADC values were obtained from the slope of the fitted line, were determined in the three orthogonal directions ($\text{ADC}_x$, $\text{ADC}_y$ and $\text{ADC}_z$). In study III an average $\text{ADC}_{\text{mean}}$ was then calculated from the three ADC values as

$$\text{ADC}_{\text{mean}} = \frac{1}{3} (\text{ADC}_x + \text{ADC}_y + \text{ADC}_z)$$

The imaging area with a sufficient signal covered by the coil was about 20 cm in the slice direction selected. In studies III–IV the diffusion imaging was carried out almost an hour after the anatomic high-resolution imaging and T2 relaxation time measurements. In study V, diffusion imaging was performed after the anatomic imaging and 2 D TOF MRA, thus about 20 minutes after starting the MR study. The time required to perform a diffusion study was about 10 minutes.
4.2.5.5 *D time of flight MRA (V)*

2D TOF MRA was used for evaluating the patency of the lumbar arteries. These arteries were evaluated as segmental pairs, which were categorized as 0 = normal vessels on both sides, 1 = one segmental artery narrowed, 2 = both segmental arteries narrowed or one or both arteries occluded. The diameters of the lumbar arteries were analyzed and the largest diameter was used as a reference. Both MIP and coronal source images were used to determine stenosis of the lumbar arteries. The images were evaluated by two radiologists, using a GE Advantage Windows workstation. In the case of disagreement, a consensus was negotiated. MR images were obtained in the coronal direction to cover the area of the lumbar spine, using a TE of 5.1, a TR of 29, a flip angle of 60°, 256 × 512 matrix, a 30 cm FOV, and a slice thickness 1.5 mm. A spatial presaturation pulse was placed posterior to the imaging slices in order to suppress the signal from the lumbar veins.

4.2.6 *Statistical methods*

In the experimental study (study I) the results were expressed only as percentages. In study II, Fisher’s exact test was performed to evaluate the significance of disc degeneration with adjacent end-plate damage. In study IV, student’s t test was used.

In study V, many tests were used. The associations between the ADC values of the discs, disc degeneration, and the status of the lumbar arteries at the same level were analyzed by analysis of covariance, with age as the covariate (ANOVA) and pairwise between-groups (Scheffe’s Post Hoc multiple comparison) with the SPSS 9.0 software. P values less than 0.01 were considered significant.
5 Results

5.1 Histologic findings in injured discs (I)

Normal lamellar structure was detected in uninjured discs. In injured annuli, where no HIZ could be seen in MRI, disorganized granulation tissue with capillaries was detected in the injured part of the annulus fibrosus. Cell density was also markedly higher than in the normal annulus. In the injured discs with HIZ, intact and partially destroyed islands of notochordal cells originating in the nucleus pulposus were observed. Histologic figures of a normal annulus fibrosus and an injured annulus fibrosus may be seen in the original publication of study I.

5.2 Clinical and radiographic findings in young patients with previous vertebral fractures (II)

Two of the 14 patients were symptomatic (Table 1). One of these had incurred wedged compression fractures in the thoracic spine 5.7 yrs before the present study and still had discomfort when he stretched his back. The other had suffered two vertebral wedged compression fractures in the lumbar spine 1.1 yrs before the current study and still had pain daily in her back at rest. However, despite these symptoms, the patients needed no pain medication.

No significant scoliosis was diagnosed in any patient: the angle of Cobb was 9° at maximum. There was no pathologic angle of kyphosis either in the lateral radiograph or in the clinical study, the angle of kyphosis being less than 35 degrees in the thoracic spine in all patients. Patients who had had fractures in the thoracolumbar or lumbar spine had no abnormal kyphosis in the fracture area.
Table 1. Clinical data of patients with histories of vertebral fracture.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age at study</th>
<th>Interval</th>
<th>Fractures</th>
<th>Pain in back</th>
<th>Type of trauma</th>
<th>Trauma energy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>f</td>
<td>20.8 yrs</td>
<td>4.9 yrs</td>
<td>T10–L1</td>
<td>no</td>
<td>falling from 1 m height</td>
<td>low</td>
</tr>
<tr>
<td>2</td>
<td>m</td>
<td>16.2 yrs</td>
<td>2.5 yrs</td>
<td>T7–9</td>
<td>no</td>
<td>moped accident</td>
<td>medium</td>
</tr>
<tr>
<td>3</td>
<td>m</td>
<td>18.1 yrs</td>
<td>3.4 yrs</td>
<td>L1–L2</td>
<td>no</td>
<td>serious car accident</td>
<td>high</td>
</tr>
<tr>
<td>4</td>
<td>m</td>
<td>17.8 yrs</td>
<td>5.8 yrs</td>
<td>T3–7 and T12–L3</td>
<td>no</td>
<td>falling 6 m through roof</td>
<td>high</td>
</tr>
<tr>
<td>5</td>
<td>f</td>
<td>12.9 yrs</td>
<td>4.2 yrs</td>
<td>T9–12</td>
<td>no</td>
<td>falling from 2 m height</td>
<td>low</td>
</tr>
<tr>
<td>6</td>
<td>f</td>
<td>14.1 yrs</td>
<td>2.7 yrs</td>
<td>L3</td>
<td>no</td>
<td>falling from roof (&gt; 2 m)</td>
<td>medium</td>
</tr>
<tr>
<td>7</td>
<td>m</td>
<td>16.1 yrs</td>
<td>5.7 yrs</td>
<td>T5–7</td>
<td>yes</td>
<td>falling from tree (3–4 m)</td>
<td>medium</td>
</tr>
<tr>
<td>8</td>
<td>m</td>
<td>11.8 yrs</td>
<td>3.3 yrs</td>
<td>T6–7</td>
<td>no</td>
<td>falling from 0.5 m height</td>
<td>low</td>
</tr>
<tr>
<td>9</td>
<td>f</td>
<td>15.0 yrs</td>
<td>6.4 yrs</td>
<td>T6</td>
<td>no</td>
<td>slipped and fell</td>
<td>low</td>
</tr>
<tr>
<td>10</td>
<td>f</td>
<td>16.5 yrs</td>
<td>1.1 yrs</td>
<td>L2 and L4</td>
<td>yes</td>
<td>falling from horseback</td>
<td>low</td>
</tr>
<tr>
<td>11</td>
<td>m</td>
<td>20.5 yrs</td>
<td>5.4 yrs</td>
<td>T6</td>
<td>no</td>
<td>moped accident</td>
<td>high</td>
</tr>
<tr>
<td>12</td>
<td>m</td>
<td>12.6 yrs</td>
<td>1.1 yrs</td>
<td>T5, T6 and T8</td>
<td>no</td>
<td>jumping from 1 m height</td>
<td>low</td>
</tr>
<tr>
<td>13</td>
<td>m</td>
<td>8.8 yrs</td>
<td>1.7 yrs</td>
<td>T5–7</td>
<td>no</td>
<td>falling from 2nd floor</td>
<td>medium</td>
</tr>
<tr>
<td>14</td>
<td>f</td>
<td>15.8 yrs</td>
<td>3.9 yrs</td>
<td>T11–L2</td>
<td>no</td>
<td>falling from 1 m height</td>
<td>low</td>
</tr>
<tr>
<td>Average</td>
<td></td>
<td>15.5 yrs</td>
<td>3.8 yrs</td>
<td></td>
<td></td>
<td>3 fract./pat.</td>
<td></td>
</tr>
</tbody>
</table>

5.3 MRI findings

5.3.1 MRI findings after an experimental annulus lesion (I)

5.3.1.1 Intact discs

The discs that were not injured (n = 49) were used as a reference for normal discs (Table 2). Of these, 96% had a bright signal in the nucleus pulposus. In two pigs, intact presacral discs showed moderate signal loss in the nucleus pulposus and also annular bulging. An intranuclear cleft was detected in 82% of intact discs. No signs of a high intensity zone in the annulus or periannular region or central dots in the nucleus pulposus were observed. Annular bulging was detected in 8% of the reference discs anteriorly. The intact discs adjacent to the injured discs did not differ from the other reference discs in MRI appearance.
Table 2. Findings in experimentally injured and intact discs of minipigs.

<table>
<thead>
<tr>
<th>Discs</th>
<th>Nuclear structures</th>
<th>Annular structures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SI** of nucleus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>bright</td>
<td>moderate loss*</td>
</tr>
<tr>
<td>lesion discs 1 mo n = 4:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>disc 1 ( = n:o 36)</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>disc 2 ( = n:o 49)</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>disc 3 ( = n:o 57)</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>disc 4 ( = n:o 75)</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>posttraumatic period 1 mo n = 4</td>
<td>25%</td>
<td>75%</td>
</tr>
<tr>
<td>lesion discs 3 mo n = 4:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>disc 1 ( = n:o 12)</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>disc 2 ( = n:o 19)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>disc 3 ( = n:o 28)</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>disc 4 ( = n:o 80)</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>posttraumatic period 3 mo n = 4</td>
<td>0%</td>
<td>75%</td>
</tr>
<tr>
<td>Intact discs n = 49</td>
<td>47/49 = 96%</td>
<td>2/49 = 4%</td>
</tr>
</tbody>
</table>

*= the signal intensity was moderately decreased or the area of bright signal intensity was remarkably diminished, **SI = signal intensity

5.3.1.2 Injured discs

In three of the four discs, 1 month after the post-traumatic period the area of bright signal intensity in the nucleus pulposus was moderately decreased (Table 2) and no intranuclear cleft was visible. In two of the four discs 1 month after the post-traumatic period both bulging and HIZ lesions were detected in the anterolateral part of the annulus (Table 2). However, 1 month after the trauma, there were two discs in which the annular lesion had healed without detectable changes in the normal low signal annulus. After this 1 month post-traumatic period, one disc was found to be normal without signal intensity changes in the nucleus pulposus, or a high intensity area in the annulus, or bulging (Table 2).
In all four of the group of 3-month post-traumatic follow-up discs, the area of bright signal intensity in the nucleus pulposus was considerably diminished; in three discs at least moderately and in one disc severely (Table 2). HIZ was detected anterolaterally in two discs (50%) and the frequency of anterior bulging was also 50%.

No central dots were observed, neither were any changes in the vertebrae adjacent to the cartilaginous end-plates observed in the injured discs.

5.3.2 MRI findings in healthy young volunteers (II)

The MRI findings in the volunteers were few. One 15-year-old girl had end-plate changes and disc degeneration in the lower part of the thoracic spine and disc herniation in the T 2/3 disc. One 18-year-old boy had disc protrusion in the presacral disc. One 8-year-old boy had a small cavitation in the thoracic spinal cord, but otherwise his spine findings were normal. The others had normal spine findings.

5.3.3 MRI findings in young patients with earlier vertebral fractures (II)

Disc degeneration and end-plate changes were detected more often in patients than in control subjects; however, in six of the fourteen patients the MRI of the spine was normal. End-plate damage was significantly associated with adjacent disc degeneration (Table 3), p < 0.01 in Fisher’s exact test. The energy of the trauma had no detectable correlation with the occurrence of disc degeneration, which appeared to depend on the age of the patients; none of the patients under 15 years of age had disc degeneration, whereas it was very common (eight of the nine patients) among those who were over 15 years old. Neither traumatic nor other spinal cord changes were detected in the patients.

Table 3. Disc degeneration vs end-plate damage in patients with an earlier vertebral fracture.

<table>
<thead>
<tr>
<th>end-plate damage</th>
<th>disc degeneration +</th>
<th>disc degeneration -</th>
</tr>
</thead>
<tbody>
<tr>
<td>yes</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>no</td>
<td>2</td>
<td>6</td>
</tr>
</tbody>
</table>

Fisher’s exact test p < 0.01

5.3.4 MRI and MRA findings in asymptomatic adults (V)

In the group of asymptomatic adults, there were 39 degenerated discs in the evaluated disc levels of L 1/2 to L 4/5, 25 of which were slightly degenerated (class 1) and 14 severely degenerated (class 2). The other discs (n = 108) had normal signal intensities. Forty-two lumbar artery pairs were graded as normal, 35 as grade 1, and 21 as grade 2.
5.4 The T2 relaxation times of intervertebral discs in young volunteers and in patients (III–IV)

The T2 relaxation times of the normal discs in healthy young volunteers were within normal limits, varying from (73 ± 10) ms to (93 ± 10) ms in the thoracic and lumbar spine. The results of T2 relaxation times in healthy young volunteers and patients are presented in Table 4.

The degenerated discs had strikingly lower T2 relaxation times (mean 59 ms) compared with the discs of control subjects (mean 80 ms), (p = 0.001). In the discs with a normal signal intensity in the primary trauma area, the mean T2 relaxation times were lower (mean 68 ms, p = 0.002) than in the control group, as was also the case with the discs in the secondary trauma area (mean 70 ms).

Table 4. T2 relaxation times in discs of patients and controls.

<table>
<thead>
<tr>
<th>Group</th>
<th>Discs</th>
<th>Mean T2 (ms)</th>
<th>sd</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls (n = 18)</td>
<td>normal discs * n = 81</td>
<td>80</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>Secondary trauma area (Patients n = 12)</td>
<td>normal discs * n = 29</td>
<td>70</td>
<td>19</td>
<td>0.024</td>
</tr>
<tr>
<td>Primary trauma area (Patients n = 12)</td>
<td>normal discs * n = 28</td>
<td>68</td>
<td>14</td>
<td>0.002</td>
</tr>
<tr>
<td>Primary trauma area (Patients n = 7)</td>
<td>degenerated discs n = 10</td>
<td>59</td>
<td>17</td>
<td>0.001</td>
</tr>
</tbody>
</table>

* discs having normal signal intensity in T2-weighted FSE sagittal images

5.5 The ADC values of intervertebral discs in young volunteers and in patients (III–IV)

The ADC values in the x, y and z directions of the nucleus pulposus in the thoracic and lumbar spines of healthy young volunteers are summarized in Table 5. The ADC_{mean} of all the intervertebral discs was (1.5 ± 0.3) x10^{-3} mm^2/s in the thoracolumbar spine. In the thoracic area, the ADC values were almost identical, where as in the lumbar spine the ADC_z value was clearly higher, (1.9 ± 0.2) x10^{-3} mm^2/s, than the ADC_x (1.49 ± 0.07) x10^{-3} mm^2/s or the ADC_y (1.64 ± 0.08) x10^{-3} mm^2/s. The ADC values tended to increase toward the lower-positioned discs.
Table 5. Mean ADC values and their corresponding error limits for thoracic and lumbar intervertebral discs.

<table>
<thead>
<tr>
<th>Direction of gradient</th>
<th>Thoracic</th>
<th>Lumbar</th>
<th>Thoracic + Lumbar</th>
</tr>
</thead>
<tbody>
<tr>
<td>x</td>
<td>1.27 +/- 0.14</td>
<td>1.49 +/- 0.07</td>
<td>1.38 +/- 0.14</td>
</tr>
<tr>
<td>y</td>
<td>1.4 +/- 0.3</td>
<td>1.64 +/- 0.08</td>
<td>1.5 +/- 0.3</td>
</tr>
<tr>
<td>z</td>
<td>1.3 +/- 0.3</td>
<td>1.9 +/- 0.2</td>
<td>1.6 +/- 0.3</td>
</tr>
<tr>
<td>Mean</td>
<td>1.4 +/- 0.3</td>
<td>1.7 +/- 0.2</td>
<td>1.5 +/- 0.3</td>
</tr>
</tbody>
</table>

The results of the ADC values in 14 patients are presented in Table 6. ADC values were significantly lower in the degenerated discs of the primary trauma area in the x and y directions as compared with the values for the discs in controls ($p = 0.009$ in the x direction, the $p$ value in the y direction was not applicable because of too small $n$). Similarly, ADCs were also lower in the x and y directions in the discs of patients with normal signal intensity in T2-weighted FSE images in primary ($p = 0.037$ in the x direction) and secondary trauma areas for both x and y directions. However, there was no significant difference in the values in the z direction between controls and patients.

Table 6. The ADC values in three orthogonal directions in discs of patients and controls.

<table>
<thead>
<tr>
<th>Group</th>
<th>Discs</th>
<th>$\text{ADC}_x$ mean</th>
<th>$\text{ADC}_x$ sd</th>
<th>$\text{ADC}_y$ mean</th>
<th>$\text{ADC}_y$ sd</th>
<th>$\text{ADC}_y$ mean</th>
<th>$\text{ADC}_y$ sd</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>normal</td>
<td>1.38E-03 1.40E-04</td>
<td>1.60E-03 3.00E-04</td>
<td>1.50E-03 3.00E-04</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n = 18)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sec. trauma area (8 pat.)</td>
<td>normal</td>
<td>1.19E-03 4.01E-04</td>
<td>0.014 1.55E-03 3.20E-04</td>
<td>0.439 1.39E-03 2.88E-04</td>
<td>0.073</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n = 20)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prim. trauma area (5 pat.)</td>
<td>normal</td>
<td>1.19E-03 3.05E-04</td>
<td>0.037 1.49E-03 2.36E-04</td>
<td>0.441 1.09E-03 1.95E-04</td>
<td>**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n = 8)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prim. trauma area (5 pat.)</td>
<td>deg. 1.09E-03 2.56E-04</td>
<td>0.009 1.48E-03 1.44E-04</td>
<td>0.504 1.25E-03 1.26E-04</td>
<td>**</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(n = 5)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* discs have normal signal intensity in T2-weighted FSE sagittal images

** $p$ value was not calculated because, in this group $n$ was too small

$\text{p} \neq$ Result of the $t$ test between the control group and the group indicated by the leftmost column

5.6 The ADC values of intervertebral discs compared with MRI and MRA findings (V)

The mean ADC values ($x 10^{-3} \text{mm}^2/\text{s}$) in normal discs (all levels) in x, y and z directions were 1.38, 1.52, 1.56, in the mildly degenerated discs 1.05, 1.12, 1.21, and in the severely degenerated discs 1.06, 1.10, 1.16, respectively. The mean ADC values (all levels) in the x, y, and z directions in the discs with normal lumbar artery pairs were 1.49, 1.60 and 1.64, in the discs with grade 1 lumbar artery pairs 1.35, 1.52, 1.57, and in the discs with grade 2 lumbar artery pairs 0.63, 0.66, 0.70, respectively.
There was a significant correlation between the status of the lumbar arteries and the ADC values of the lumbar discs in the three orthogonal directions (x, y and z) at levels L1/2, L2/3, L3/4 and for ADC in the x direction at L4/5 (p < 0.001). The correlation was less but still significant (p < 0.01) for ADCs in the y and z directions at the L4/5 level. The results are presented in Table 7. Also, when age was controlled for the association between the ADCs and the lumbar arteries, the correlation between the status of the lumbar arteries and the ADC values remained significant.

Table 7. The association between ADC values (mm²/s) and the status of the lumbar arteries in L1/2-L4/5.

<table>
<thead>
<tr>
<th>Lumbar arteries 2DTOF</th>
<th>L1/2</th>
<th>L2/3</th>
<th>L3/4</th>
<th>L4/5</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADCx</td>
<td>N = 19</td>
<td>N = 28</td>
<td>N = 27</td>
<td>N = 24</td>
</tr>
<tr>
<td>0</td>
<td>1.51*</td>
<td>1.50*</td>
<td>1.54*</td>
<td>1.49*</td>
</tr>
<tr>
<td>1</td>
<td>1.27*</td>
<td>1.29*</td>
<td>1.39*</td>
<td>1.44*</td>
</tr>
<tr>
<td>2</td>
<td>0.44*</td>
<td>0.55*</td>
<td>0.63*</td>
<td>0.69*</td>
</tr>
<tr>
<td>ADCy</td>
<td>N = 24</td>
<td>N = 27</td>
<td>N = 28</td>
<td>N = 19</td>
</tr>
<tr>
<td>0</td>
<td>1.64*</td>
<td>1.55*</td>
<td>1.67*</td>
<td>1.66**</td>
</tr>
<tr>
<td>1</td>
<td>1.54*</td>
<td>1.45*</td>
<td>1.49*</td>
<td>1.59**</td>
</tr>
<tr>
<td>2</td>
<td>0.16*</td>
<td>0.54*</td>
<td>0.55*</td>
<td>0.90**</td>
</tr>
<tr>
<td>ADCz</td>
<td>N = 24</td>
<td>N = 19</td>
<td>N = 27</td>
<td>N = 28</td>
</tr>
<tr>
<td>0</td>
<td>1.64*</td>
<td>1.61*</td>
<td>1.77*</td>
<td>1.80**</td>
</tr>
<tr>
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<td>1.54*</td>
<td>1.51*</td>
<td>1.68*</td>
<td>1.65**</td>
</tr>
<tr>
<td>2</td>
<td>0.16*</td>
<td>0.49*</td>
<td>0.71*</td>
<td>0.92**</td>
</tr>
</tbody>
</table>

The correlation between the mean ADC values (mm²/s) of the discs and the status of the lumbar arteries (2D-tof) is statistically significant (One-Way ANOVA; * p < 0.001; ** p < 0.01).

Although the ADC values for all the orthogonal directions decreased with increasing disc degeneration, there were no statistically significant correlations between the ADC values and the degree of disc degeneration (Table 8).
Table 8. Association between ADC values (mm²/s) and disc degeneration in L1/2-L4/5.

<table>
<thead>
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<tr>
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<td></td>
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<tr>
<td>0</td>
<td>1.35 (0.25/0.06)</td>
<td>1.35+ (0.3/0.07)</td>
<td>1.41 (0.35/0.09)</td>
<td>1.45** (0.13/0.04)</td>
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<tr>
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<td>1.02+ (0.6/0.27)</td>
<td>1.22 (0.4/0.12)</td>
<td>0.90** (0.56/0.19)</td>
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<tr>
<td>2</td>
<td>1.30 (0.07/0.05)</td>
<td>0.98+ (0.36/0.16)</td>
<td>0.63 (0.73/0.52)</td>
<td>1.14** (0.52/0.23)</td>
</tr>
<tr>
<td><strong>ADCy</strong></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<td>1.53 (0.47/0.12)</td>
<td>1.45* (0.32/0.07)</td>
<td>1.53+++ (0.37/0.09)</td>
<td>1.63 (0.16/0.04)</td>
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<tr>
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<td>1.21+++ (0.51/0.16)</td>
<td>1.15 (0.67/0.24)</td>
</tr>
<tr>
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<td>0.87* (0.55/0.24)</td>
<td>1.01+++ (0.93/0.66)</td>
<td>1.23 (0.5/0.23)</td>
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<tr>
<td><strong>ADCz</strong></td>
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<td>1.49++ (0.38/0.09)</td>
<td>1.70 (0.46/0.11)</td>
<td>1.75*** (0.19/0.05)</td>
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<tr>
<td>1</td>
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<td>1.19++ (0.56/0.25)</td>
<td>1.31 (0.41/0.13)</td>
<td>1.13*** (0.64/0.22)</td>
</tr>
<tr>
<td>2</td>
<td>1.57 (0.24/0.17)</td>
<td>0.92++ (0.61/0.27)</td>
<td>1.07 (0.9/0.64)</td>
<td>1.27*** (0.46/0.21)</td>
</tr>
</tbody>
</table>

The correlation between the mean ADC values (mm²/s) of the discs and disc degeneration (One-Way ANOVA)

*p = 0.024; ** p = 0.028; *** p = 0.016; + p = 0.085; ++ p = 0.051; +++ p = 0.072)

The number of severely degenerated discs was small at L1–2 (n = 2) and L3–4 (n = 2), and therefore statistical significance can be reliably assessed only at the L2–3 and L4–5 levels.

Even though the correlation between disc degeneration and the diffusion values was not statistically significant, there was a trend with eight outliers: These eight severely degenerated discs had almost normal diffusion values for all directions (ADCx 1.36, ADCy 1.45, ADCz 1.54) and normal or grade 1 lumbar artery status as compared with all severely degenerated discs (1.06, 1.10, 1.16, respectively).
6 Discussion

In the current study, a diffusion-weighted MRI study of the intervertebral disc is presented for the first time. ADCz values were slightly higher than ADCx or ADCy values in the lumbar spine. The diffusion values were shown to decrease considerably during the degeneration process in the ADCx and ADCy directions. Lumbar artery status and the degree of disc degeneration were compared with the ADC values of the lumbar intervertebral discs in asymptomatic adults. The artery status at the same disc levels explained with statistical significance, the alteration in the ADC values in the discs. The correlation between disc degeneration and the diffusion values was linear, although not statistically significant.

Trauma was significantly associated with disc degeneration in children, particularly when the adjacent end-plate had been injured. In an experimental study, at 1- or 3-month follow-ups after peripheral annular lesions, there were no clear differences in MRI findings. Nevertheless, histologically noticeable findings due to trauma were detected: in the injured discs with HIZ, clusters of nuclear cells originating in the nucleus pulposus were noticed, and also in the injured annuli, where no HIZ could be seen in MRI, disorganized granulation tissue with capillaries was detected in the injured part of the annulus fibrosus.

6.1 Trauma and its effect on disc degeneration

6.1.1 Experimental annular lesions

In this study, the histology of HIZ was presented for the first time: clusters of nuclear cells and disorganized granulation tissue with capillaries were detected in the HIZ area. Intact and partially destroyed islands of notochord cells were seen only in those preparations where HIZ was seen in MRI. In injured discs without HIZ disorganized granulation tissue and capillaries were seen. This histologic finding of HIZ is in accord with the previous agreement that HIZ indicates the presence of an unhealthy peripheral
rim tear progressing to a radial tear (Aprill & Bogduk 1992) and therefore these nucleated cells can be seen in the area of HIZ. The signal intensity of HIZ is same or slightly brighter than the nucleus pulposus. Therefore, it can be assumed that there is fluid in the area of HIZ. On the other hand, nuclear material is hydrated because of its proteoglycan content. Lam et al (2000) have suggested that HIZ represents an area of secondary inflammation resulting from an annular tear. With the used Ehrlich’s hematoxylin and eosin staining the possible inflammatory reaction could not be seen histologically in this study.

Three of eight discs with experimental annular lesions had a normal annular appearance in MRI. Annulus lesions, when detectable, were manifested as a bulging of the disc or as a high-intensity zone inside the annulus. The signal intensity or the area of bright signal intensity in the nucleus had nearly always decreased after as little as one month and was also visible in the cases where no signs of annular trauma could be seen in the MR images. Our result is in agreement with a previous experimental study (Kääpä et al 1994 b), in which a significant decrease in water and in proteoglycans in the nucleus was noticed after annular trauma, even though the nucleus had not been directly damaged. Because the inner annulus and the nucleus pulposus are normally avascular, they are more sensitive to degenerative changes. In an experimental study (Smith & Walmsley 1951), the outermost part of an annular tear in rabbits healed within 3 or 4 weeks after trauma, while the innermost part had failed to heal at 2-year follow-up. There were no clear differences in findings after 1 or 3 months.

Minipigs were used as an experimental model for studying the effect of an annular tear on disc degeneration. The posture and the loading patterns of minipigs are different from those of man, but the quadruped posture is considered to have no significant effect on the distribution of vessels in the end-plates and thus it does not affect the nutrition of the disc either (Moore et al 1992). Considerable difference exists between the injury inflicted on the porcine annulus fibrosus and the damage that occurs in the human situation. However, it is reasonable to suppose that the model used here includes the same mechanism for initiating the degenerative process as natural ruptures of the annulus. Moreover, the annulus cut that was made in this study closely reproduced the finding which is demonstrated in unhealed cases in human spines as a high intensity zone (HIZ). Experimental studies make it possible to obtain images in ideal circumstances — phase misregistration artefacts from the aorta, pulsation artefacts from CSF, and motion artefacts can all be avoided. Moreover, the time of injury can be accurately determined, which is not always unambiguously clarified in human patients.

Annular tears have been postulated to initiate degeneration of the disc (Smith & Walmsley 1951, Osti et al 1990, Osti et al 1992b, Fraser et al 1993, Kääpä et al 1994a and b). On the other hand, in humans, most annular tears are probably secondary to a degenerative process of the disc. The presence of an annular lesion has been found to have a significant influence on the nutritional supply to all of the discs of the lumbar spine and injury of one disc may possibly accelerate the degeneration of the other discs also (Moore et al 1992). In the experimental work, this was not demonstrated in discs adjacent to lesion discs. Probably longer follow up times would have revealed this.

The presence of annular tears is often followed by fibrovascular proliferation; this was seen in the present study also and was detected in previous animal experiments (Osti et al 1990). In cadaver studies, annular tears have been frequently demonstrated (Yu et al
1988b, Osti et al 1992b) and also these have shown evidence of attempted repair with fibrovascular and cartilaginous tissue in the region of the rim (Hilton & Ball 1984). The distinction between fluid within the damaged annulus and hydrated granulation tissue within the annulus is not clear (Cassar-Pullicino 1998), since both may increase the signal in T2-weighted images. Annular tears could thus be demonstrated, with enhancement of gadolinium due to their vascularized granulation tissue, and it has been suggested that more annular tears could be visualized with gadolinium enhancement (Ross et al 1990, Cassar-Pullicino 1998, Jarvik & Deyo 2000). In this study, the preparations were made before the MR imaging studies and thus the enhancement of posterior annular tears could not be investigated.

The outermost part of the annulus fibrosus is innervated and therefore it is logical to suppose that annular tears have been associated with clinical pain (Fraser et al 1993). When HIZ was first discovered, it was considered to be the sign of a painful disc (Aprill & Bogduk 1992, Schellhas et al 1996). Later, HIZ has also been demonstrated in asymptomatic subjects (Stadnik et al 1998, Weishaupt et al 1998). The pain possible associated with disc damage could not be assessed in this study. Recently, in the study by Weishaupt et al (2001), HIZ was shown to be of little value in predicting a painful disc. However, no follow-up study to clarify the appearance of HIZ in the different phases of back pain has been made. Thus, it seems that the cause-and-effect relation between HIZ findings and pain is still poorly understood and it is obvious that this has not yet been sufficiently explored.

6.1.2 Vertebral fractures in children

In children with clinically and radiographically verified fractures, a close association was detected between disc degeneration and earlier trauma in this study. Particularly, a compression fracture in conjunction with end-plate injury correlated significantly with disc degeneration in these young patients. These results are in accord with a previous prospective study in which acute low-back injury during the adolescent growth spurt was associated with degenerative changes in the lumbar spine (Kujala et al 1994). The effect of the normal aging process was minimized in this study, which clarified the causal role of trauma in disc degeneration. In our series, 57% of the young patients with histories of radiographically verified fracture had disc degeneration, which was far more than in our sex- and age-matched control group (7%) or in the previous studies of asymptomatic young adults (6–26%) (Powell et al 1986, Terti et al 1991b, Salo et al 1995).

In contrast, in two studies of adult patient groups (Oner et al 1998 and Peterson et al 2000) no correlations were detected between disc degeneration and previous trauma. In the study by Oner et al (1998), adult patients with a previous vertebral fracture had normal signal intensities in MRI in most discs adjacent to the injured vertebrae. Thus, it seems that spinal trauma is a potential risk factor for degenerative process of the disc only in adolescence.
The most obvious explanation for this finding is the difference between adults and children in the nutrition of the disc. A vascular network supplies blood to the cartilaginous end-plate and the intervertebral disc, but this blood supply generally atrophies by the age of 8–12 years (Resnick 1985). The mean age of the patients was 15.5 years and their mean age at the time of the trauma was 11.8 years, which is the time at which the blood supply disappears.

The differential diagnosis between Scheuermann’s disease and traumatic compression fractures may sometimes be difficult, because the trauma bringing a patient to hospital may be minimal. In our study, none of the patients fulfilled the criteria of Scheuermann’s disease. On the other hand, wedge-shaped vertebral compression fractures can easily be missed in children: the finding in the lateral radiograph may be minimal and obscure. Moreover, it is obvious that not all children with back trauma are examined radiographically, and therefore these fractures may often be overlooked.

Although disc degeneration was frequently detected in young patients, only a minority complained back pain. Thus, in adolescents with previous vertebral fractures, morbidity is low, at least in the short term. Moreover, in our series, back pain did not correlate with the MRI findings.

6.2 Diffusion-weighted MR imaging of the intervertebral disc

6.2.1 Feasibility and limitations of the method

The feasibility of diffusion-weighted MR imaging of the intervertebral disc was tested in this study. ADC values of normal intervertebral discs were determined in the three orthogonal directions with a reasonable correlation in the study of healthy young volunteers (III). ADC values were shown to be higher in the lumbar spine than in the thoracic spine, especially in the z direction.

Although the feasibility and clinical potential of diffusion-weighted imaging (DWI) in neurologic disorders was presented by Le Bihan et al as long ago as 1986, in clinical use this method is still mostly kept for evaluating the central nervous system. DWI evaluates tissues at the microscopic level, which is beyond the typical resolution of MR images (Le Bihan 1998). Water molecules diffuse for distances of a few micrometers in a second. ADCs are also contributed by restriction of possible cellular membranes, fiber packing, and orientation (Gray & MacFall 1998). Echo-planar imaging (EPI) is a very fast imaging method (Edelman et al 1994) and has therefore been considered the best method for quantifying diffusion (Le Bihan 1998). Its feasibility for the spine had not been demonstrated before on account of probable susceptibility artefacts and slightly low spatial resolution (Ruggieri 1999). As a fast imaging technique, the EPI sequence, while minimizing motion artefacts, is very sensitive to susceptibility artifacts. However, susceptibilities have been found to be almost the same in cortical bone, water, and soft tissues (Sumanaweera et al 1993, Schenk 1996). Thus, although various tissue-bone interfaces are located very close to the intervertebral discs, it is probable that they do not
affect the ADC values; at least no susceptibility artefacts were detected in the images. In
the present work, a diffusion-weighted MR study was carried out using a SE single-shot
EPI sequence.

In brain diffusion studies, much higher b values are used. In the present study, low b
values were chosen to optimize the SNR, because, with higher b values, the signal was
too low. The SNR of the diffusion-weighted images was still rather poor. This is
explained at least partly by the coil used and the relatively long echo time needed for
diffusion imaging. The general-purpose surface coil collects signals only from a very
limited source volume and the discs are located relatively deep in the body, where the
signal is already considerably attenuated. Thus, the size of the patient also affects the
signal intensity. The slice thickness of 5 mm used in this study was chosen as a
compromise between the SNR and the reasonably reliable positioning of the slice within
the disc.

The intervertebral disc is a favorable object for a diffusion study; because of its
On the other hand, the spine and particularly the intervertebral discs are challenging
objects for diffusion-weighted MR imaging, because of the pulsations of the aorta, the
heart, and the cerebrospinal fluid and the location of the discs near the bone. However,
DWI studies of vertebral bone with a steady state sequence (Baur et al 1998) and of the
spinal cord with an SE sequence (Clark et al 2000) have recently been successful. In the
lumbar spine, cerebral spinal fluid flow does not cause problems (Ruggieri 1999).

Clear anisotropy of the diffusion values was detectable in the results of studies III–V.
Diffusion values in the z direction were slightly higher than values in the plane of the disc
despite the presumably random microstructure of the disc. Interestingly, anisotropy was
noticed despite degeneration. To quantify diffusion anisotropy accurately, diffusion tensor
imaging should be carried out. Nevertheless, the full diffusion tensor method requires
measurements in at least six directions and is therefore very time-consuming because of
the increased data acquisition and the postprocessing. An experiment was made with
diffusion tensor imaging. It was found to be unreliable due to motion, noise, and magnetic
field inhomogeneities.

Slightly lowered values in the thoracic spine may partly have been explained by axial
imaging planes and thus the possible partial volume effect. An experiment was made (in
study IV) by imaging the lumbar intervertebral discs of the same volunteers in both the
sagittal and the axial planes and it was found that within the limits of experimental error,
the results were almost identical. Thus, it is suggested that, in the lumbar area, both
imaging planes are reliable. With sagittal imaging, there is less possibility of a partial
volume effect, but, imaging in sagittal slices limits the ROI size more than in axial slices.

In a previous study of abdominal organs, large variation in ADC values among
subjects was demonstrated (Muller et al 1994), which has been suggested to be due to the
contribution of perfusion (Yamada et al 1999). In this study, the ADC-values of the discs
are not discordant with the values detected in the abdominal organs (Muller et al 1994,
Yamada et al 1999) and the spinal cord (Clark et al 2000). When diffusion is the only
type of motion, ADC is equal to the true diffusion coefficient D. Because perfusion
contributes to the ADCs, the reported ADC values are commonly higher than expected
(Le Bihan et al 1986). However, quite a large scatter was also detected in the values for the intervertebral discs, although the effect of perfusion in the discs was expected to be negligible because of their avascularity.

ADC values behaved like T2 relaxation times, which were determined in this study to confirm the visual assessment. A significant decrease was detected in the relaxation times of degenerated discs (IV) followed by discs with normal signal intensity adjacent to the primary trauma area and the secondary trauma area compared to the values of the controls (III). These results are in good agreement with the T2 relaxation times presented earlier (Modic et al 1984, Jenkins et al 1985, Boos et al 1994) and it appears likely that no potential sources of error applied to these values.

Relaxation times provide quantitative information about the biochemical content, especially the hydration (Boos & Boesch 1995) and the disc matrix integrity (Antoniou et al 1998). However, direct quantification of the water content by relaxation time measurements is not considered possible (Boos & Boesch 1995). Moreover, quantitative determinations in vivo and in vitro must be considered differently (Boos et al 1994 and 1995). T2 relaxation times are known to decrease during both aging and the degeneration process (Modic et al 1984, Jenkins et al 1985). Thus, measurements of relaxation times are not able to differentiate these phenomena either. For clinical use, T2 relaxation time measurements are rather time-consuming compared to ADC measurements with EPI sequence. Moreover, T2 relaxation time measurements do not offer more valuable information than visual assessments of disc degeneration in practice.

6.2.2 The effects of trauma and degeneration on diffusion values

Study IV was presented as a preliminary study for evaluating possible changes in the ADC values of the discs after vertebral fracture. During the degeneration process, the ADC values in x and y directions became significantly lower (IV,V) while the alteration in the z direction was less significant. The ADC values decreased most in the degenerated discs in the primary trauma area, followed by the discs with normal signal intensities adjacent to the primary and secondary trauma areas. This result indicates that vertebral fracture may also affect other discs near the trauma area, possibly by diminishing their nutrition. In an experimental study, injury to one disc has been suggested to accelerate the degeneration of other lumbar discs (Moore et al 1992).

During the degenerative process, considerable alterations occur in the structure and biochemistry of the intervertebral disc. The effect of altered hydration on solute transport is rather complex (Maroudas 1988), because a decrease in hydration means a lower diffusion coefficient, but, on the other hand, the height of the disc has decreased. Thus, the distances through which metabolites have to move is shorter (Maroudas 1988). This may explain our findings that during the degeneration process seen in study V, the ADC values did not decrease linearly.

The intradiscal water content undergoes a normal diurnal variation, with influx of water overnight and gradual reduction during the day. This produces measurable changes in the hydration, height, and volume of the disc and these changes can also be measured
by quantitative MRI (Boos et al 1993). However, the diurnal variation has been shown to be significantly less pronounced in degenerative than in healthy discs (Boos et al 1993). It has been suggested, that decreased water content as such is not likely to have a significant effect on the balance between cellular requirements and metabolite transport, although the effect on the mechanical properties of the disc is obvious (Maroudas 1988). The relationship between the change in water content and the swelling pressure has been found to depend on the composition of the disc rather than on age or the degree of degeneration (Urban & McMullin 1988). Volunteers and patients were imaged during afternoons, so that, in this respect, the conditions were similar for all the measurements.

These results suggest that decreased ADC values reflect a change in the integrity of the intervertebral disc, and also in the arterial flow to the spine. They suggest that measurement of diffusion coefficients may depict the degradation and disintegration of the nucleus pulposus better and/or at an earlier time point than observational assessment of disc degeneration. This method may offer a sensitive tool for evaluating changes in the disc after trauma associated with lost integrity of the disc and in the early phases of degenerative process. Although there are various technical problems associated with diffusion imaging of the spine, it is worth while to study the future potential of this method — more sensitive methods are needed for detecting early degenerative changes in the intervertebral discs. Even with its present limitations, diffusion spine imaging may become feasible in the near future, when MR scanners with stronger gradients become available.

6.2.3 Correlation with lumbar artery status

The stenoses and occlusions in lumbar arteries were significantly associated with decreased diffusion in the lumbar disc of same level. In previous studies, insufficient nutrition has been suggested as a cause of disc degeneration (Nachemson et al 1970, Maroudas 1988, Buckwalter 1995). Atherosclerotic changes in the lumbar arteries have also been shown to be associated with lumbar disc degeneration (Kauppila et al 1994) and with low back pain (Kauppila & Tallroth 1993, Kurunlahti et al 1999). These studies are in agreement with the finding of study V, in which lumbar artery status explained the diffusion values most significantly; moreover, the correlation between degeneration and the diffusion values was linear. However, it is obvious that the diffusion coefficients obtained by MR imaging will probably differ from “nutritional diffusion” through the end-plates. The strong correlation between lumbar artery occlusion and the decrease of the ADC values may be due to diminished intradiscal osmotic pressure.

The diminished flow through stenosed or occluded lumbar arteries may lead to the creation of collateral vessels, which may also supply nutrients to the intervertebral discs (Kauppila et al 1994). The image resolution of the 2D TOF MRA method did not allow detection of such collaterals. The role of collaterals in intradiscal nutrition is, however, obscure (Kauppila et al 1994). The ostia of the lumbar arteries were not well visualized in
our TOF MRA study, but any significant stenosis of the ostium can be detected as diminished flow in 2D TOF images. Bolus MRA was not considered in the present study because of high cost.

There was moderate variation in the findings regarding lumbar artery status between the disc levels. It was demonstrated earlier that the correlation between atherosclerotic changes and disc degeneration was stronger in the upper levels of the lumbar spine than in the lower levels (Kauppila et al 1994). Surprisingly, eight intervertebral discs were severely degenerated, but the corresponding paired lumbar arteries and the diffusion values were normal. This supports the previous view that the pathogenesis of disc degeneration is multifactorial.
7 Conclusions

1. Annular tears can manifest in MRI as three different findings: These lesions may be detected either as local bright signal intensity within a low signal annulus (HIZ) or as annular bulging, and, the signal intensity or the area of bright signal intensity in the nucleus may be decreased. These changes may already be evident 1 month after the trauma and are still detectable at least 3 months after the injury. Histologically, HIZ contain clusters of nuclear cells originating from the nucleus pulposus.

2. In children and adolescents, a vertebral fracture, especially with end-plate injury, disposes the adjacent disc to undergo degeneration. This is probably because of atrophy of the blood supply to the end-plates, which is of importance in children. Changes in the ADC values of discs with normal signal intensity located in the previous trauma area probably reflect a change in the integrity of these discs.

3. The ADC values can be measured reliably with an EPI sequence. In the lumbar spine, significant differences were between the ADC values of normal and degenerated discs. Lowered ADC values were also found in discs with normal signal intensities adjacent to a previous vertebral fracture. Measurement of the ADC values may offer a more sensitive method than MR imaging to study the integrity or well-being of the intervertebral disc.

4. Narrowed or occluded lumbar arteries were strongly associated with decreased diffusion in the lumbar discs. The correlation between the degree of disc degeneration and the diffusion values was mostly linear; however it was not significant.
References


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