The Intervertebral Disc: Overview of Disc Mechanics

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Contents

2.1 Introduction

The vertebral column is the main structural element of the spine and is composed of the vertebrae and the intervertebral discs. The function of the vertebral column is to provide rigidity to the axial skeleton while allowing limited rotation and bending. The vertebrae are the osseous elements of the vertebral column and the spine. Each vertebra is composed of a vertebral body and posterior elements. The vertebral bodies resemble boxes of cortical bone filled with trabecular bone. They are separated by the intervertebral discs, which are attached to the relatively flat surfaces at the top and bottom of the vertebral body. On the posterior side of the vertebral bodies, a bony structure composed of pedicles and processes, known as the posterior elements, serves as anchor points for tendons and ligaments. Anatomical details of each of the vertebrae that comprise the spine are presented in Chap. 1. Definition of technical terms can be found in Box 2.1.

The zygapophysial joint is an articular joint between the inferior and posterior articular processes of adjacent vertebrae. Like most articular joints, the zygapophysial joint comprises a capsule filled with synovial fluid. Inside this capsule, the bones are covered by a thin layer of articular cartilage separated by the fibroadipose meniscoids. The zygapophysial joints play an important role in the mechanics of the spine. These joints prevent excessive axial rotation between the vertebral bodies, resist forward sliding of the superior vertebra, limit the amount of extension by the contact of the inferior articular process and the lamina of the vertebra below, and contribute to the transmission of a fraction of the load. The ligaments and the joints connecting the vertebral bodies provide some passive stability; the muscles surrounding the vertebral column, through an active mechanism, provide most of the stability of the spine during physical activity. A detailed description of spine muscle anatomy, forces, and lines of action is outside of the scope of this chapter, but can be found in Adams et al. (2006).

The intervertebral disc is the soft tissue in between the vertebral bodies. It is composed of three distinct tissues: nucleus pulposus, annulus fibrosus, and the cartilaginous

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Box 2.1 Glossary of Mechanical Terms

Stress Stress is the force intensity and is calculated as applied load divided by area over which it is applied. Stress is classified into normal (perpendicular to the surface) and shear (along the surface) stresses.

Strain Strain is a measurement of deformation. Similar to stress, there are normal and shear strains. Normal strain is defined as change in length divided by original length. Shear strains are related to the change in angle.

Poisson's ratio When a sample is stretched it contracts in the lateral direction. The Poisson's ratio is the lateral contraction divided by the longitudinal stretch. This mechanical property is related to the compressibility of the material. A material with a Poisson's ratio of 0.0 does not exhibit any lateral contraction, while a material with a Poisson's ratio of 0.5 is incompressible.

Stiffness The stiffness is a measure of the resistance to deformation. It is defined as force divided elongation. The stiffness depends not only on the material itself, but also on the size of the object.

Modulus The modulus is related to the stiffness, except that the effects of object size are eliminated, therefore, the modulus is a material property. Modulus is calculated as stress divided by strain.

Anisotropy A material is anisotropic if its mechanical properties are different depending on direction of load. For instance, in the annulus fibrosus or other fibrous tissues, collagen fibers create direction-dependent anisotropy.

Viscoelasticity A material is viscoelastic when its mechanical behavior changes over time or as a function of the speed at which the loads are applied. The viscoelastic properties of a material are usually measured using *creep* or *stress relaxation tests*. In a creep test, a load is applied to the material and the deformation increases over time. In a stress relaxation test, a deformation is applied and the stress decreases over time.

endplates. Each of these tissues has a characteristic composition and structure which provide them with special mechanical properties to perform their function. Their interaction enables the intervertebral disc to transmit loads while allowing a constrained flexibility between vertebral bodies. In a healthy disc, the nucleus pulposus is a highly hydrated gel-like material which is surrounded by the annulus fibrosus and the cartilaginous endplates (Fig. 2.1). The main function of the nucleus pulposus is to support mechanical loads through hydraulic and osmotic pressure. The cartilaginous endplates are thin layers of cartilage that cover the central area of the vertebral body (Fig. 2.1a). At the periphery of the vertebral body, not covered by the cartilaginous endplate, is the ring apophysis. The cartilaginous endplates have an important role on the exchange of nutrients, waste products, and other metabolites between the nucleus and the blood vessels in the vertebral bodies. The annulus fibrosus is composed of series of concentric layers with collagen fibers in alternating orientations (Fig. 2.1b). The outer lamellae of the collagen fibers attach directly to the vertebral bodies while the inner lamellae attach to the cartilaginous endplates. The annulus fibrosus provides a lateral confinement of the nucleus pulposus, supports vertical loads, and limits the amount of motion between the vertebral bodies.

The intervertebral disc undergoes biochemical and structural changes due to aging and degeneration. Biochemical changes include a decrease of proteoglycan content, an increase in protein cross-linking, and changes in the collagen type and distribution. The biochemical changes during degeneration are similar to those of aging; they are characterized by occurring in a faster rate and accompanied by structural changes that impair disc function. Structural changes observed during degeneration include a decrease in disc height, inward and outward bulging of the annulus fibrosus, and loss of its lamellar organization. The objective of this chapter is to describe the mechanical behavior of the individual tissues of the intervertebral disc and then analyze how they work together in different loading scenarios. In addition, the effects of degeneration on the mechanics at the tissue and disc levels are described.
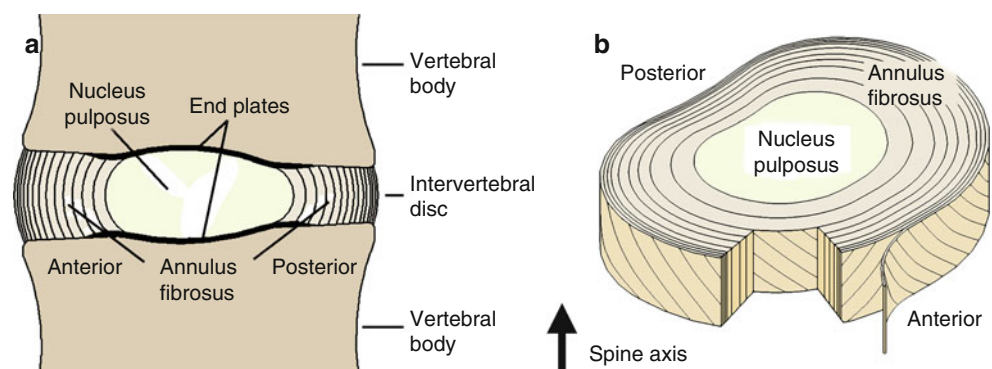

Fig. 2.1 Schematic representations of the adult intervertebral disc. (**a**) Midsagittal cross section showing anatomical regions. (**b**) Three-dimensional view illustrating AF lamellar structure (Adapted from Smith et al. 2011)

2.2   Structure–Function of Intervertebral Disc Tissues

Although many studies have shed light on the structure–function relationships for the tissues that form the intervertebral disc, this is still an ongoing research topic, the aim of which is to describe the mechanical behavior of healthy tissues, the effects of degeneration, and the implications of disc mechanics on the cell biology. Recent findings on the structure–function relationships of the tissues of the intervertebral disc are presented in the following sections.

2.2.1   Osmotic Effects

The tissues of the intervertebral disc are mainly composed of water, proteoglycans, and collagen (Eyre 1979). The relative content of each of these components differs from tissue to tissue. For instance, the nucleus pulposus has the highest proteoglycan content, while the annulus fibrosus has the highest collagen content (see Chaps. 3 and 4) (Eyre and Muir 1976). The differences in relative content of these individual components and their organization provide these disc tissues with their special mechanical properties. For example, it is well known that due to its higher collagen content and fiber organization, the annulus fibrosus has a superior tensile loading capacity. In a similar way, the high proteoglycan content of the nucleus pulposus provides the tissue with high compressive properties. However, since the tissues in the disc have similar components, they also share some mechanical behaviors, specifically, the osmotic effects which reflect the proteoglycan high negative charge density (Urban and Maroudas 1981). The osmotic effects have important implications on the mechanics of the disc. For instance, the osmotic pressure causes a deformation of the tissue usually known as osmotic swelling. This swelling pressure induces tensile stresses and increases the stiffness of the tissue. This osmotic swelling also draws water into these tissues keeping the disc hydrated. Since the osmotic effects play an important role in the mechanics of all disc tissues, this section provides a brief description of the relationship between composition and osmotic effects.

The osmotic effects are mediated by the proteoglycan content of the tissue (Maroudas and Bannon 1981; Urban et al. 1979). Proteoglycans are large molecules composed of many glycosaminoglycan units attached to a long core protein. Glycosaminoglycans are chains of polysaccharides that at a physiological pH present an excess of negatively charged ions (Comper and Laurent 1978). The molecular structure of proteoglycans and glycosaminoglycans is discussed in great detail in Chap. 4. Due to their large size, proteoglycans are trapped in the network of collagen fibers. Therefore, collagen and proteoglycans form a charged, porous, deformable solid material which is embedded in a solution of water and ions (Urban and Maroudas 1981). The amount of negative charges attached to the solid is quantified by the fixed charge density. At equilibrium, the balance of chemical potentials results in an increase of osmotic pressure (p), which is a function of the fixed charge density and the ionic strength of the surrounding fluid (Overbeek 1956). Assuming an ideal solution for the interstitial fluid and external solution, the osmotic pressure can be expressed as

$$p = RT \left(\sqrt{c_{\mathrm{fc}}^2 + 4c_{\mathrm{b}}^2} - 2c_{\mathrm{b}} \right) \qquad (1)$$

where R is the universal gas constant, T is the absolute temperature, c_{fc} is the fixed charge density, and c_{b} is osmolarity of the surrounding fluid bath.

The osmotic pressure and the external applied forces result in deformation of the solid component of the tissue, which in turn alter the fixed charge density (c_{fc}). That change can be quantified by

$$C_{\mathrm{fc}} = \frac{c_{\mathrm{fc0}} \phi_{\mathrm{f}}^0}{\left(J - 1 + \phi_{\mathrm{f}}^0 \right)} \qquad (2)$$

where c_{fc0} and ϕ_{f}^0 are the fixed charge density and the water content at the reference configuration, respectively, and J is the ratio between the volume at the deformed and reference configurations. The reference configuration, usually defined as the configuration where stresses are zero, plays an important role in the calculation of the osmotic pressure.

2.2.2   Nucleus Pulposus

The nucleus pulposus is the gelatinous core of the intervertebral disc and it is composed of water (70–85 % of total weight), proteoglycans (30–50 % of dry weight), collagen (20 % of dry weight), and other minor proteins (Adams and Muir 1976; Eyre 1979). Aggrecan is the most abundant proteoglycan in the nucleus pulposus, followed by other proteoglycans such as decorin (Melrose et al. 2001). Aggrecan contains keratan and chondroitin sulfate chains which interact with hyaluronic acid filaments forming large molecules that are trapped in the collagen network (Kiani et al. 2002). These side chains are negatively charged; consequently, positively charged Na$^+$ ions bind to these chains creating an accumulation of cations inside the nucleus pulposus. Since the glycosaminoglycans are not able to diffuse out of the nucleus pulposus, there is a permanent difference of the concentration of cations compared to the surrounding environment. This unbalance of cations is the cause of the osmotic pressure in the disc.

Collagen II is the most abundant type of collagen in the nucleus pulposus and other compression-bearing tissues such as articular cartilage (Eyre and Muir 1976). Unlike articular cartilage, collagen II forms an unorganized fiber network in the nucleus pulposus. A recent study showed that long fibers in the nucleus pulposus continuously connect both endplates (Wade et al. 2011). In an intact disc, these fibers are much longer than the disc height; they fold in a rather arbitrary configuration and can withstand substantial tension when unfolded. Experimentally, however, since it was necessary to cut the annulus fibrosus to separate the endplates, it is unlikely that the nucleus pulposus fibers experience high levels of tension under physiological conditions. This is different from articular cartilage, where fibers are highly organized and experience substantial tension due to the osmotic swelling (Ateshian et al. 2009; Cavalcante et al. 2005). In the case of the nucleus pulposus, the osmotic and hydrostatic pressure is supported axially by the endplates and radially by tensile (hoop) stresses in the annulus fibrosus. Consequently, fibers are not required to hold the nucleus pulposus in place as is the case in articular cartilage.

Due to its high levels of hydration and gelatinous consistency, the mechanical behavior of the nucleus pulposus has characteristics of both a fluid and a solid (Iatridis et al. 1996). Consequently, the nucleus pulposus is usually treated as a viscoelastic material. The mechanical properties of the nucleus pulposus have been investigated mainly through torsion and compression tests (Heneghan and Riches 2008a, b; Iatridis et al. 1997a, b; Johannessen and Elliott 2005; Perie et al. 2005). Confined compression has been typically used to measure several mechanical properties of the nucleus pulposus such as aggregate modulus and permeability coefficients (Johannessen and Elliott 2005). It is measured by axially compressing a cylindrical sample in a chamber that prevents lateral expansion. Although physiologically the nucleus pulposus is not fully confined or fully unconfined, confined compression tests have been generally accepted to characterize its compressive behavior. For small deformations (around 5 %), the nucleus pulposus can be considered to have a constant permeability and exhibits a linear relationship between stresses and strains (Johannessen and Elliott 2005). However, the properties are strain dependent (i.e., nonlinear) for moderate and large strains (Heneghan and Riches 2008a). Table 2.1 presents a summary of nucleus pulposus values obtained using confined compression.

The elastic behavior of the nucleus pulposus can be apportioned in terms of the contribution of osmotic (ionic) and solid tissue (nonionic) effects. The contribution of the osmotic effects to the compressive properties has been measured by eliminating the osmotic effects using a surrounding medium with high osmolarity or by reducing the proteoglycan content via enzymatic digestion (Heneghan and Riches 2008a; Perie et al. 2006b). When a high ionic concentration medium was used, the compressive properties of the bovine nucleus pulposus were reduced to 20–30 % of the value measured in isotonic (physiological) medium concentrations. Therefore, the contribution of the osmotic effects to the stiffness and load support of the nucleus pulposus is approximately 70–80 %. The contribution of the osmotic effects was almost constant through a wide range of applied deformations (0–70 % compressive strains). If the proteoglycans are removed by enzymatic digestion, a reduction of 20- to 30-fold was observed in the compressive properties of the nucleus pulposus (Perie et al. 2006b). This suggests that the proteoglycans also have a nonionic contribution to the mechanics of the nucleus pulposus. Evidence of the nonionic contribution of the proteoglycans has been reported for other tissues such as articular cartilage (Canal Guterl et al. 2010).

Viscoelastic or frequency-dependent properties of the nucleus pulposus have been analyzed using torsion tests (Iatridis et al. 1997a, b). Stress relaxation tests measured an instantaneous shear modulus around 11 kPa. However, the shear stress rapidly relaxed to near-zero values suggesting a fluid-like behavior. In dynamic torsion tests, a shear modulus of ~20 kPa and a phase shift (the delay between strain and stress measured in terms of degrees) of ~30° were measured. For comparison, the dynamic modulus of articular cartilage is 600–1,000 kPa, the modulus for the meniscus is 540 kPa, while proteoglycan solutions are 0.01 kPa (Hardingham et al. 1987; Zhu et al. 1993, 1994). Values of phase shift of 13° for cartilage, 22° for meniscus, and 65° for proteoglycan solutions have been reported. Since the phase shift for the nucleus is lower than 45°, it suggests a more solid-like dynamic behavior.

The studies discussed above illustrate the complexity of the mechanical behavior and structure–function relationships of the nucleus pulposus. The contribution of osmotic pressure

Table 2.1 Aggregate modulus (H_A) as a function of the stretch ratio (λ) and glycosaminoglycan content for the nucleus pulposus

Study	H_A (kPa)	λ	NP tissue	s-GAG (% dry wt.)
Heneghan and Riches (2008a)	69–1,650	1.0–0.3	Bovine tail	24
Perie et al. (2005)	350–520	1.0–0.8	Bovine tail	
Perie et al. (2006a)	~600	1.0–0.6	Bovine tail	~35
Perie et al. (2006b)	~400–510	1.0–0.8	Bovine tail	~42
Johannessen and Elliott (2005)	1,010	0.95	Human	44

and the blend between exhibiting characteristics of fluid and solid mechanics pose a difficult challenge to model and also complicate the prediction of deformations during physiological loading. Nonetheless, it is important to understand and characterize the mechanics of the nucleus pulposus as it influences cell function and impacts predictions related to mechanically induced injuries and regeneration.

2.2.3 Annulus Fibrosus

Similar to the nucleus pulposus, the annulus fibrosus is composed mainly of proteoglycans and collagen, although the relative content and organization of its components are substantially different. In the healthy human annulus fibrosus, the water content is 50 %, collagen is approximately 70 % of the dry weight, and proteoglycans make up to 10 % of the dry weight (Eyre and Muir 1976; Eyre 1979). The annulus fibrosus is subjected to both tensile and compressive stresses during physiological loading. Consequently, it has high collagen content similar to other tension-bearing tissues such as tendon and ligaments. Proceeding from the outer to the inner annulus, there is an decrease in the ratio of collagens I to II, and the amount of proteoglycan rises. This profile reflects a change in the loading environment from more tension in the outer annulus fibrosus to more compression towards the nucleus pulposus (Eyre and Muir 1976). In a similar way, in the outer annulus fibrosus, collagen fibers insert directly to the cortical bone of the vertebrae and not to the endplate as in the case of inner annulus fibrosus, again probably reflecting the higher tensile loads present in the outer annulus fibrosus (Nachemson 1963; Wu and Yao 1976).

Noteworthy, in the annulus, collagen fibers are arranged in concentric lamellae with alternating orientations (Fig. 2.1b). The angle between fiber directions of adjacent lamellae changes from ~60° to the spinal axis in the outer annulus fibrosus to ~90° in the inner annulus fibrosus (Cassidy et al. 1989; Guerin and Elliott 2006a; Hickey and Hukins 1980). This arrangement provides the annulus with a series of important mechanical properties, including anisotropy (direction dependence). Since the fibers play such an important role in the mechanics of the annulus fibrosus, this tissue can be analyzed as a combination of fibers and an isotropic material known as extrafibrillar matrix (Spencer 1984). As its name indicates, the extrafibrillar matrix represents all the solid components of the annulus fibrosus, except fibers.

One of the more important characteristics of the mechanics of collagenous tissues is nonlinearity. The nonlinearity of the fibers is characterized by a low stiffness region for small deformations, known as toe region, followed by a transition (heel) region and a much stiffer linear region (Guerin and Elliott 2007; Wu and Yao 1976). Collagen fibers, in most tension-bearing tissues, have a hierarchical organization from

fibrils to large collagen bundles or fascicles (Kastelic et al. 1978). Collagen fibers in these tissues have a wavy or zigzag shape commonly known as crimp (Diamant et al. 1972; Kastelic and Baer 1980). When the fibers are stretched, the fibers progressively straighten with minimal resistance; i.e., a negligible force is required to uncrimp the fibers. The amount of stretch required to straighten the fiber is known as uncrimping stretch. Once a fiber is straight, it starts taking load (Fig. 2.2). The uncrimping stretch is not same for all fibers in a tissue. For small deformations, few fibers with a small uncrimping stretch are straightened as they accommodate the load. Consequently, the stiffness of the tissue is low. Progressively, all the fibers stretch and contribute to load support resulting in high tissue stiffness (Fig. 2.2). If the tissue is further stretched, fibers will fail by several possible mechanisms including breakage and fiber pullout.

All the other components of the annulus fibrosus (except the fibers) are usually treated as a single material known as extrafibrillar matrix. Since the fibers contribute to the mechanics of the annulus fibrosus when they are in tension, the matrix characterizes the compressive properties of the annulus fibrosus. Other properties, including permeability and diffusivity of solutes, are also attributed to matrix. For simplicity, the elasticity of the matrix has been considered isotropic, which means that the elastic properties (i.e., Young modulus and Poisson's ratio) are same in all directions. Although the matrix includes some fibrillar components such as elastin and protein cross bridges, their content
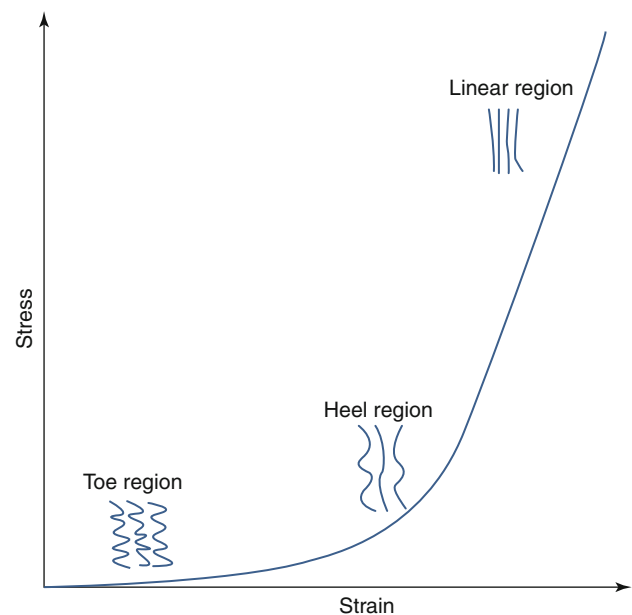

Fig. 2.2 The tensile stress–strain response of collagenous tissues, such as annulus fibrosus, can be divided into several regions, corresponding to different mechanisms. In the toe region, the contribution of fibers is small due to fiber crimping. In the heel region, the increase in stiffness is due to fiber straightening. In the linear region, most of the fibers are straight and contributing to the high tensile stiffness

is small and unlikely to significantly alter the assumption of isotropy. However, transport properties such as permeability and diffusivities have been shown to be anisotropic (Gu et al. 1999; Travascio and Gu 2011), which means that there are directions where the fluid and solutes can flow or move with less resistance.

The tensile properties of the annulus fibrosus have been characterized using uniaxial and biaxial tension tests (Jacobs et al. 2013; Nerurkar et al. 2010). In uniaxial tests, a strip of tissue is cut from the annulus fibrosus in a given orientation (circumferential, axial, radial, or along the fibers), and the force required to stretch the sample is recorded as a function of the applied strain. The Poisson's ratio can be measured by recording the lateral contraction of the sample during the test. The Young modulus is calculated from the slope of the stress–strain response. A summary of these properties is presented in Table 2.2. The Young modulus is higher in the disc's circumferential direction than the axial. This is expected since the fibers are oriented closer in the circumferential direction; therefore, fibers are not stretched during axial loading so that modulus is primarily due to the matrix.

Biaxial loading is another tensile test used to quantify annulus fibrosus mechanics. It is thought that biaxial loading more closely resembles multiaxial physiological load-ing of the annulus fibrosus (Bass et al. 2004; Gregory and Callaghan 2011; Huyghe 2010; Jacobs et al. 2013; O'Connell et al. 2012). For this test, a rectangular thin sample is gripped on all four sides and loads are applied in two directions (Fig. 2.3). Two-dimensional deformations are optically recorded during the test. Unlike a uniaxial test, there is not a direct relationship between the slope of these curves and the elastic properties of the annulus fibrosus; the forces (or stress) in one direction are affected by the deformation applied to the other direction (O'Connell et al. 2012). Consequently, the data from biaxial tests are analyzed through the use of a model. The advantage of using biaxial experiments to characterize the mechanics of the fibers is that the values obtained through these types of tests can be used to predict the response of the annulus fibrosus in uniaxial tests and with other biaxial strain ratios (O'Connell et al. 2012).

Since the collagen fibers only contribute to the mechanics of the annulus fibrosus in tension, the elastic properties of the extrafibrillar matrix can be measured through confined compression tests (Cortes and Elliott 2012; Drost et al. 1995; Klisch and Lotz 2000; Perie et al. 2005). This test provides the aggregate modulus, measured as a function of strain. Similar to the nucleus pulposus, the mechanical behavior of the matrix depends on contributions from the osmotic pressure and the nonionic extrafibrillar matrix (Cortes and Elliott 2012). In this manner, the mechanical properties of this extrafibrillar matrix can be measured in tension and compression by applying osmotic swelling and confined compression simultaneously. The nonionic extrafibrillar matrix is nonlinear with a higher stiffness in compression (~50 kPa) than in tension (~10 kPa), and the contribution of the osmotic pressure in the support of the applied loads is high (~70 % of total) when the EFM is in compression and low (~25 %) when in tension.

Table 2.2 Linear region moduli of nongenerated (ND) and degenerated (D) annulus fibrosus tissue (Elliott and Setton 2001; Guerin and Elliott 2006b)

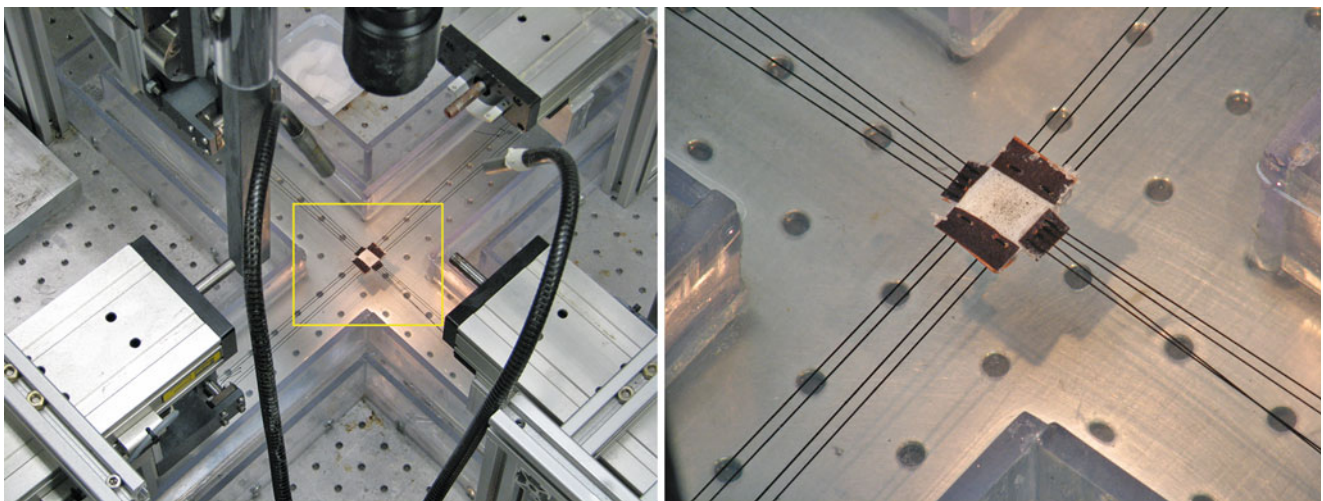|	Circumferential		Axial		Radial	
	ND	D	ND	D	ND	D
Inner anterior	5.6–10.0	5.0	1.0	–	–	–
Outer anterior	17.0–29.0	22.0–29.0	0.8	–	0.4–0.5	0.4
Inner posterior	2.0–6.0	4.0	–	–	0.5	–
Outer posterior	13.0–19.0	8.0	–	–	–	–

Fig. 2.3 In a biaxial test of annulus fibrosus, a sample is loaded simultaneously in the axial and circumferential direction

Table 2.3 Shear modulus (kPa) of human annulus fibrosus: effects of sample orientations and location and type of test

| | | Orientation | | |
Type of test	Location	Circ-radial	Circ-axial	Radial-axial
Simple shear – compressive preload	Anterior	28.92	58.56	40.16
Simple shear – compressive preload	Posterolateral	22.2	53.6	25.1
Simple shear – tensile preload	Anterior	–	193.6	–
Torsion shear – equilibrium	Anterior	20–100	–	–
Torsion shear – dynamic	Anterior	100–280	–	–

Shear tests have been used to determine elastic and viscoelastic properties of the annulus fibrosus. Elastic shear properties have been measured by applying simple shear tests (Fujita et al. 2000; Hollingsworth and Wagner 2011; Iatridis et al. 1999; Jacobs et al. 2011). Since the fibers have a contribution during this test, the shear modulus is anisotropic with a higher modulus in the circumferential–axial plane where the fibers experience stretches (Table 2.3). On the other hand, torsion tests have been used to measure viscoelastic properties of the annulus fibrosus (Iatridis et al. 1999). The dynamic modulus increases with frequency. Both equilibrium and dynamic modulus decrease with shear strain amplitude. The highly viscoelastic nature of the annulus fibrosus is evidenced by the threefold increase of the dynamic modulus over the equilibrium modulus.

Although separating the mechanics of the annulus fibrosus into fibers and matrix is very convenient and describes much of the mechanical behavior of annulus fibrosus, there are interactions between these components. Specifically, the stiffness of the matrix increases with the stretch of the fibers (Guo et al. 2012). To account for these effects, several fiber–matrix and fiber–fiber interactions have been formulated in terms of the strain perpendicular and along the fibers (Guerin and Elliott 2007; O'Connell et al. 2009, 2012; Wagner and Lotz 2004). These interactions have more accurately described the mechanical behavior of the annulus fibrosus. It has also been suggested that shear interactions are essential to obtain a good simultaneous prediction of uniaxial, biaxial, and shear experimental data (Hollingsworth and Wagner 2011; O'Connell et al. 2012).

While many aspects of the mechanical behavior of the annulus fibrosus have been well described, this is still an active area of research. Special attention needs be given to relations between interactions and composition of the annulus fibrosus and the contribution of these interactions to mechanics of the disc. Additionally, these interactions between components should be replicated in engineered tissues that are currently being investigated as therapeutic alternatives (Mauck et al. 2009; Nerurkar et al. 2010).

2.2.4 Cartilaginous Endplate

The biomechanics of the cartilaginous endplate has been far less studied than other disc tissues. The endplate is the interface between the nucleus pulposus and inner annulus fibrosus with the vertebral bodies (Fig. 2.1a). It covers most of the vertebral endplate except for a small ring in the periphery called the ring apophysis. The thickness of the cartilaginous endplate varies: it is thinnest in the center (~0.2 mm) and thickest in the periphery (~0.9 mm) (Moon et al. 2013). The composition of the cartilaginous endplate is similar to that of hyaline cartilage, which is characterized by a high proteoglycan and collagen II content. The water content of human endplate is 58 % of the wet weight, the s-GAG content is 17 % of the dry weight, and the total collagen content is 60–80 % of dry weight (Setton et al. 1993). The cartilaginous endplate plays an important role in the transport of nutrients and other metabolites into the nucleus pulposus and the inner portion of the annulus fibrosus.

The mechanics of the cartilaginous endplate has been measured using confined compression tests (Setton et al. 1993). The aggregate modulus of the baboon endplate is 0.44 MPa. The hydraulic permeability (14.3×10^{-14} m⁴/Ns) is considerably higher than values of 0.09×10^{-14} m⁴/Ns and 0.153×10^{-14} m⁴/Ns for the human annulus fibrosus and nucleus pulposus, respectively. The high permeability value suggests that its main function is to allow the transport of fluids, nutrients, and waste products to the cells in the nucleus pulposus and part of the annulus fibrosus.

2.3 Intervertebral Disc Mechanics

In the previous sections, the mechanics of individual disc tissues were described separately. However, these tissues interact with each other providing the disc with a special mechanical behavior. In a similar way, a disruption or a change in mechanical properties of one of these tissues causes an impairment of the mechanical function of the overall disc. In this section, disc mechanics are presented as the contribution of individual tissues during a given loading scenario. First, the residual stresses in the unloaded disc are briefly described. Then, the mechanics of the intervertebral disc are analyzed for three of the most important loads: axial compression, bending, and torsion.

2.3.1 Stress and Strain in the Unloaded Disc

Before analyzing the mechanics of the disc under different types of loading scenarios, it is important to understand the

impact of internal stresses and strains on the unloaded disc. As described above, at the tissue level, the osmotic pressure is balanced by tensile or "residual" stresses. In a similar way, at the disc level, there are residual stresses and strains due to osmotic effects caused by tissue proteoglycans, are present even in the absence of applied loads. When external loads are applied to the disc, additional stress builds up above that of the residual stress. There are several mechanisms, at different scales, contributing to residual stress (Lanir 2009). At the micro-level, the interaction between proteoglycans, ions, water, and the collagen network produces an osmotic pressure that contributes to the total stress of the tissue. At the meso-level, residual stress arises from inhomogeneities within the tissues, e.g., the gradient of proteoglycan and collagen content from inner and outer annulus. Residual stress at meso-level has been recently measured in terms of the opening angle after a radial cut in bovine annulus fibrosus rings (Michalek et al. 2012). This effect is similar to that observed in aortic arteries, where differences in proteoglycan content between the media and the adventitia contribute to this component of the residual stress (Azeloglu et al. 2008; Chuong and Fung 1986). At the disc level, residual stress is also generated by the interaction between different tissues (nucleus pulposus, annulus fibrosus, endplates, and vertebral bodies). The high proteoglycan content of the nucleus pulposus results in a significant osmotic pressure. This pressure has been measured in vitro and in vivo using a needle pressure gauge (Nachemson 1981; Panjabi et al. 1988; Wilke et al. 1996, 1999). The radial expansion of the nucleus is constrained by the annulus fibrosus through tensile stresses in the circumferential direction (hoop stress) and compression stress in the radial direction. Similarly, the osmotic pressure in the nucleus tends to vertically separate the vertebral bodies, which are held in place by tensile stresses in the annulus fibrosus in the axial direction. All these contributions to the residual stress of the disc create a multidirectional and inhomogeneous initial state of stresses and strains that must be considered for the analysis of disc mechanics.

2.3.2 Compression Mechanics

Axial compression loading of the spine is of major physiological importance and arises from the weight of the upper body and by forces exerted by the muscles in the trunk during common daily activities. Compression loads are transmitted from vertebra to vertebra through the intervertebral disc and the zygapophysial joints in proportion to body posture. For instance, 84 % of the compressive load is transmitted through the intervertebral disc in the erect standing posture, whereas 100 % of the load is transmitted through the disc in the erect sitting posture (Adams and Hutton 1980). Although the compressive load to the intervertebral disc

changes with posture and activity, the mechanism by which the different tissues of the intervertebral disc interact to support this load is the same. In this section, the interaction between disc tissues is described for compressive loads over short and long periods of time.

After a compression load is applied to the disc, the immediate mechanics are different from that measured at longer time intervals. Immediately after the load has been applied, the tissues in the disc can be considered to be incompressible materials; due to the low permeability of the disc tissues, there is insufficient time for interstitial fluid flow (Ateshian et al. 2007). In this loading state, the interstitial fluid in the nucleus pulposus pressurizes, supporting a fraction of the load. Since the nucleus pulposus behaves as an incompressible material, it tends to expand radially. However, since it is contained by the annulus fibrosus, there is a large tensile strain in the circumferential direction and outward bulging of the annulus (Tsantrizos et al. 2005). The applied load is supported by the lamellae through compressive stress in the axial direction. As a result, the compressive load causes the lamellae in the inner annulus fibrosus to buckle towards the nucleus pulposus; of course, this is opposed by the outward pressure exerted by the nucleus pulposus. Inward buckling of the inner annulus fibrosus is evident in the degenerate disc due to a decrease in the internal pressure of the nucleus pulposus associated with altered osmotic pressure and permeability changes (Sasaki et al. 2001; Sato et al. 1999; Wang et al. 2010). From this perspective, pressurization of the nucleus pulposus is of critical importance not only to carry part of the compressive load but also to provide stability to the lamellae in the radial direction.

During the diurnal loading cycle, the disc is subjected to a prolonged period of compression followed by a period of low-load recovery. If the load on the disc is maintained for some hours, the pressurized interstitial fluid will flow to regions of lower pressure through the annulus fibrosus and the endplate (van der Veen et al. 2007). During this process, the disc height decreases while the outward bulging of the annulus fibrosus increases (O'Connell et al. 2007). In addition, the nucleus pulposus depressurizes, reducing its contribution to load and increasing the axial compression of the annulus fibrosus (O'Connell et al. 2007). In this "relaxed" state, the tissues in the disc interact, as described above for instantaneous loading; however, the relative contribution of each of the tissues changes. After relaxation, the osmotic pressure in the healthy nucleus pulposus does not vanish completely. In fact, due to osmotic effects the remaining intradiscal pressure is largely responsible for hydration recovery and mechanics during the resting period of the diurnal cycle (O'Connell et al. 2011; van der Veen et al. 2007).

Nutrient and metabolite exchange during loading and unloading is essential for disc cell viability. In this process, nutrients and metabolites are brought to, and waste byproducts

expelled from, the disc by diffusion and convection (Das et al. 2009; Ferguson et al. 2004; Holm et al. 1981; Shirazi-Adl et al. 2010; Soukane et al. 2007; Urban et al. 1978, 1982, 2004). The rate at which fluid leaves the disc depends on the hydraulic permeability and diffusivity of its component tissues. Since the hydraulic permeability of the endplate is higher than the annulus fibrosus, it should enhance aqueous flow through the endplate (Setton et al. 1993). Moreover, from the periphery (endplates and outer annulus) to the center of the disc, there is a change in metabolite concentration. Numerical simulations have also shown that the concentrations of glucose and oxygen are low close to the center of the disc, whereas lactic acid, which is the major metabolite, has a reverse distribution (Jackson et al. 2011; Soukane et al. 2007). Recent studies are aimed at improving the accuracy of the numerical models by considering anisotropy and nonlinearity of elastic, flow, and diffusion properties (Chuang et al. 2010; Jackson et al. 2008).

2.3.3 Flexion/Extension and Lateral Bending

Flexion/extension and lateral bending are spine movements required for many daily activities. Flexion and extension are terms used when the trunk bends forward and backward, respectively. In a well-aligned spine, a neutral position is observed when standing upright. However, the natural curvature of the spine changes during daily activities such as sitting or lifting a weight. This curvature change is the sum of the relative rotations between each of the vertebral bodies, each of which produce internal strains and stresses in the disc. To quantify the mechanics of the disc under this type of motion, the forces and moments can be estimated by monitoring muscle activity. However, this approach has been shown to be inconsistent (Potvin et al. 1991). A better approach to estimating forces and bending moments consists of determining the correlation between in vivo and in vitro measurements (Adams and Dolan 1991).

A common kinematic characteristic of flexion/extension and lateral bending is that the axis of rotation is perpendicular to the axis of spine. Therefore, flexion, extension, and lateral bending produce a similar pattern of internal deformations to the disc. During flexion, the axial compression in the anterior portion of the annulus fibrosus is increased. Consequently, there is an increase in the bulging of the outer region of the annulus and buckling of the lamellae in the inner portion of the anterior annulus fibrosus. On the other hand, the posterior region experiences tension in the axial direction. Additionally, the nucleus pulposus is shifted to the opposite side of bending, and there is an increase in intradiscal pressure (Nachemson 1981; Wilke et al. 1999). When the spine is in extension, the reverse effects are observed: tension in the anterior annulus fibrosus, compression of the posterior annulus, and shifting of the nucleus in the anterior direction. Lateral bending produces

a similar pattern of strains in the disc; however, the compression and tension regions are located in the lateral annulus fibrosus (Costi et al. 2007; Tsantrizos et al. 2005).

The stiffness and range of motion of disc segments can be obtained by applying a known force and/or bending moment. The range of motion is defined as the relative rotation of the vertebral bodies when a pure moment is applied in the sagittal or coronal plane. On the other hand, the stiffness can be calculated as the slope of the moment–rotation curve at the end of the range of motion. Due to the asymmetric shape of the disc and the effect of the posterior elements, measurements of the range of motion and stiffness are different in flexion and extension. For instance, an increase of the compression strain from 2.7 to 6.7 % for an applied force of 500 N was reported for human L2/L3 spine segments when the posterior elements were removed (Heuer et al. 2008). In a similar way, the range of motion increased from 5.2° to 6.9° in flexion and from 3.4° to 8.2° in extension for a pure applied moment of 7.5 Nm (Heuer et al. 2008). The stiffness of disc segments has been measured on the principal axes of the disc and on multidirectional axes (Spenciner et al. 2006). It was concluded that the experimentally measured stiffness along the multidirectional axes do not match with the analytical predictions from the stiffness along principal axes (Spenciner et al. 2006).

2.3.4 Torsion

During a twisting motion of the trunk, torsion becomes another important component of the loading of intervertebral discs. Similar to flexion/extension, torsion is defined as the relative rotation of consecutive vertebral bodies; however, the axis of rotation is parallel to the axis of the spine. Consequently, the strains in the disc are substantially different. During physical activity, the rotation between vertebral bodies is about 1°–3° which is very small compared to the rotations observed during flexion or extension (Pearcy et al. 1984). The torsion range of motion is constrained by contact of the zygapophysial joints, which also increases the stiffness of intact spine segments (Adams and Hutton 1981). In vitro and numerical studies have reported a range of motion of 4°–8° for intact spinal segments. The removal of the posterior elements of the spine increases the range of motion twofold (Shirazi-Adl et al. 1986).

Shear strains are the main component of deformation during torsion. Deformation results in tensile stretch of one of the fiber populations, and while not contributing to torsion support due to fiber buckling, the other experiences compression. The tensile stretch on the fibers increases radially; consequently, the maximum fiber stretch is found in the outermost lamella. Removing the posterior elements of the spine resulted in an increase in the maximum fiber stretch from 3.1 to 11.4 % for

an applied torque of 7.5 Nm (Heuer et al. 2008). From in vitro experiments, there is a reduction of the outward bulging of the annulus fibrosus and an increase of disc height and intradiscal pressure (Heuer et al. 2008; van Deursen et al. 2001a, b). The decrease of outward bulging can be directly linked to the high tensile fiber stresses in the outer lamellae. The decrease of lateral bulging also explains the increase of disc height and intradiscal pressure. Although the strains observed in torsion may be too small to cause significant damage to the disc, a decrease in the failure loads have been observed when torsion is combined with compression and flexion/extension.

2.4 Effect of Degeneration on Disc Mechanics

Intervertebral disc degeneration can be defined as a post-traumatic cell-mediated cascade of biochemical, mechanical, and structural changes that affect the function of the disc (Adams and Roughley 2006) (Fig. 2.4). Compositional changes during disc degeneration are mainly loss of proteoglycans, increased cross-linking, and an increase in the amount of collagen I over collagen II. These changes are first noticeable in the nucleus pulposus and later spread outwards to the annulus fibrosus. Although the causes remain largely unclear, factors that include structural injury, genetic heritance, age, inadequate metabolite transport, and loading history have been associated with the onset and progression of disc degeneration (Adams and Roughley 2006; Battié et al. 2008; Buckwalter 1995; Hsu et al. 1990; Pye et al. 2007; Rannou et al. 2004). In this section we limit our discussion to the effect of degeneration on the mechanics at the tissue and disc levels. A brief review of total disc replacements, which is of the treatments for disc degeneration, is presented in Box 2.2.

Numerous studies have measured the changes in the mechanical behavior of the disc tissues at several stages of degeneration. The compositional changes in the nucleus pulposus include a decrease in proteoglycan content and an increase in collagen I cross-links. These changes exert contradictory effects on the mechanics of the nucleus pulposus. On one hand, the loss of proteoglycans causes a decrease in the osmotic pressure and consequently a reduction in tissue stiffness. On the other hand, the increase in cross-linking and collagen content causes tissue stiffening. Experimentally, it has been noted that there is an overall decrease in the compression properties of nucleus pulposus (Johannessen and Elliott 2005). This observation is in accord with other studies that show that proteoglycans contribute approximately 80 % to the compressive properties of the nucleus pulposus with degeneration (Heneghan and Riches 2008a; Perie et al. 2006b). However, there is also a significant increase in the shear modulus (Iatridis et al. 1997b). Transport properties of the nucleus pulposus are also affected by degeneration as there
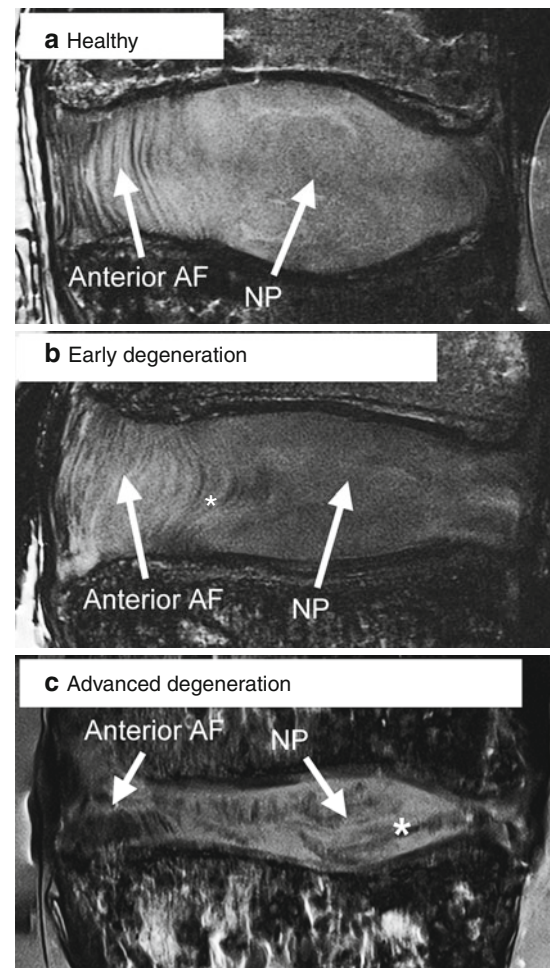

Fig. 2.4 Magnetic resonance images illustrating different stages of human lumbar disc degeneration. (**a**) Healthy disc exhibiting distinct AF lamellae (*AF*) and central NP region (*NP*). (**b**) Disc exhibiting early stages of degeneration, including moderate height reduction, decreased NP signal intensity, and inward bulging of AF lamellae (*). (**c**) Disc exhibiting advanced stages of degeneration, including severely reduced height, large fissure (*), and generalized structural deterioration. Images obtained using 7T Siemens scanner and a turbo spin echo sequence at 200 μm isotropic voxel resolution (Adapted from Smith et al. 2011)

is an increase in the hydraulic permeability (Johannessen and Elliott 2005).

The annulus fibrosus undergoes mechanical changes with degeneration. The modulus at the toe region increases with degeneration, probably due to changes in the water content and the increase in collagen I levels (Guerin and Elliott 2006a).The Poisson's ratio decreases about 50 % with degeneration (Acaroglu et al. 1995; Elliott and Setton 2001; Guerin and Elliott 2006a), as does the shear modulus (Iatridis et al. 1999). Additionally, fiber reorientation decreases, while interaction between fibers and extrafibrillar matrix increases with degeneration (Guerin and Elliott 2006a; O'Connell et al. 2009). That fiber–matrix interactions increase with

Box 2.2 Total Disc Replacements

Total disc replacement (TDR) is a relatively new treatment for discogenic pain that may be used instead of fusion in some patients. In a TDR, a mechanical device replaces the disc and aims to permit motion between the vertebrae, as opposed to fusion where there is no motion. Rational for TDR are related to perceived advantages over fusion for reduced surgical time, improved patient recovery, and long-term improved mechanics to prevent degeneration at other sites in the disc. An ideal artificial disc should have the same range of motion and mechanical properties as a healthy disc. However, this is generally not the case. Metallic spheres were the first intervertebral disc replacements and were implanted in patients in the early 1960s. The most common complication was subsidence, or penetration of the ball into the endplate and vertebral body, and this device was abandoned. The Acroflex, from the 1970s, consists of two porous plates separated by a hyperelastic polymer. The design was revolutionary in the sense that the porous plate allowed integration with the bone and the polymer provided controlled flexibility. Unfortunately short-term failure of the polymeric material stopped wide clinical use. The Charite, introduced in the 1980s, has two metallic endplates articulating against a polymeric core similar to a ball-and-socket articulation. Although this device has been very popular in Europe, long-term studies have reported several complications including migration, subsidence, ejection, and wear of the core. Recent designs similar to the Charite include the ProDisc and FlexiCore. These devices all permit motion, but generally do not mimic normal disc mechanics in terms of have axial compression motion, energy absorption, and resistance to torsion. While the FDA has approved some models for use, they are not widely used in patients. Total disc replacement in the cervical spine, which requires more motion and less axial load, appears to be more widely applied and successful. A more detailed review of total disc replacements and other devices can be found in "*Intervertebral disc properties: challenges for biodevices*" by Costi et al. (2011).

degeneration is evident from biaxial tests (O'Connell et al. 2012).

All the degenerative changes observed at the tissue level have an effect on the mechanics at the disc level. Of all of the tissues in the intervertebral disc, the most mechanically affected with degeneration is the nucleus pulposus. The loss of osmotic pressure and hydration in the center of disc leads

to a reduction of the disc height and an increase in instability of the disc measured by an increase in the range of motion and neutral zone (Mimura et al. 1994; O'Connell et al. 2007). The decrease of disc height causes an increase in the compression load in the axial direction which in turn results in buckling of the lamellae, increase of outward and inner bulging of the annulus fibrosus, and loss of organization of the lamellae structure (O'Connell et al. 2007, 2010). The decrease in osmotic pressure also causes a reduction in fluid exchange during the diurnal cycle (Massey et al. 2011). The fluid exchange reduction affects the transport of metabolites such as glucose and lactic acid, thereby influencing cellular function.

2.5 Mechanically Induced Injury of the Intervertebral Disc

In a healthy person, the loads applied to the intervertebral disc are not likely to exceed its strength limits. However, in some cases such as trauma, a single high-magnitude load causes a mechanical disruption of the structure of the spine. Usually, in such events, the posterior elements of the spine such as the zygapophysial joints are damaged before the disc is affected. However, under certain conditions, damage to the intervertebral disc in the form of disc prolapse, fracture of the vertebral endplate, or tears in the annulus fibrosus or nucleus pulposus can be observed. Such catastrophic changes can cause a permanent change on the internal distribution of stresses and strains, thereby affecting the normal functioning of disc. In addition, such changes in the mechanical environment trigger a cell mediate cascade of biochemical, structural, and morphological changes known as degenerative disc disease that further impairs disc function. Another case of abnormal loading occurs when a low-magnitude load is applied a great number of times. This repeating loading event, known as fatigue, is believed to be linked to the onset and propagation of tears in the disc and is a cause of herniation. In this section, recent studies analyzing the relationship between abnormal loading and injury of the intervertebral disc are discussed.

2.5.1 Herniation

Herniation is characterized by the prolapse of the nucleus pulposus through the annulus fibrosus. In vitro, herniation can be produced by a single high-intensity load or the repetitive application of forces with lower intensity (Callaghan and McGill 2001; Iencean 2000). Herniation has been induced mechanically by applying a compressive force in the order of 5.4 kN to the disc in an anterolateral flexion position. This results in extrusion of the nucleus pulposus

in a posterolateral radial direction (Aultman et al. 2005). The internal strains developed during flexion/extension and lateral bending show tensile strains in the axial direction and thinning of the annulus fibrosus at the opposite direction of bending (Costi et al. 2008; Tsantrizos et al. 2005). Therefore, a radial protrusion in posterolateral direction occurs when there is anterolateral flexion. Non-degenerated, highly hydrated discs have higher risk of herniation than severely degenerated discs (Gallagher 2002; Simunic et al. 2001). This is probably due to the reduction of intradiscal pressure in the nucleus pulposus with degeneration. However, when mechanical disruption is caused by artificially increasing the nucleus pressure (instead of applying a compressive load), degenerated discs fails at a lower rupture pressure (Iencean 2000).

Herniation has also been induced in vitro when cyclic flexion/extension motion is applied to the disc (Callaghan and McGill 2001). In this case, the herniation pathway is in a posterolateral radial direction. Increasing the compression load decreases the number of cycles required to cause disc damage. Similarly, the application of a static torque moment shortens the disc cycle life (Drake et al. 2005). The increase in intradiscal pressure due to the applied torque may accelerate the susceptibility of intervertebral discs to injury. The shape of the disc has also been found to influence the herniation pathway in repetitive flexion/extension bending (Yates et al. 2010). Specifically, limacon-shaped discs had a defined posterolateral herniation pathway, whereas oval-shaped discs had a more diffuse herniation pathway.

2.5.2 Endplate Fracture

Another mechanically driven injury is the fracture of the vertebral endplate. The endplate is the cortical bone on the superior and inferior (cranial and caudal sides, respectively) aspects of the vertebral body. On one side, the vertebral endplate is in contact with the intervertebral disc through the cartilaginous endplate; on the other side, it is supported by the trabecular bone inside the vertebral body. The main component of the load applied to the vertebral endplate comes from the intradiscal pressure. However, tension and shear forces are also applied by traction of the annulus fibrosus (Baranto et al. 2005). Fracture of the vertebral endplate occurs when the strains exceed the strength of the vertebral endplate (Fields et al. 2010). Endplate strength has been correlated with the density of the supporting trabecular bone (Adams and Dolan 2011; Ordway et al. 2007; Zhao et al. 2009). In fact, due to lower density of the cranial trabecular bone, there is a greater incidence of fractures in this endplate. The degree of degeneration of the intervertebral disc also affects the loads at which endplate fracture occurs: a higher force is required to cause endplate fracture in degenerated

discs (Baranto et al. 2005). The rationale behind this observation is that healthy, hydrated discs have a higher intradiscal pressure; in degenerated discs there is a lower compression stress in the center of the disc, while the posterior elements transmit a larger portion of the compressive load (Adams and Dolan 2011).

2.6 Summary of Critical Concepts Discussed in the Chapter

- The mechanics of the intervertebral disc is determined by the interaction between the annulus fibrosus, nucleus pulposus, and endplates in different loading scenarios.
- The osmotic pressure plays an important role in the transmission of forces through the spine as well as in the stability of the intervertebral disc structure.
- Nonlinearity is an important mechanical characteristic of disc tissues. Nonlinearity is evident in the spine's relatively lax neutral zone mechanics and stiffer linear region response in motion segment tests. Nonlinearity is important to permit both disc motion and stability.
- Anisotropy (see Box 2.1) is an important mechanical characteristic of the annulus fibrosus and comes from the structural organization of collagen fibers.
- The viscoelastic behavior of the disc can be explained in part by the interstitial fluid flow during loading and unloading and the intrinsic viscoelasticity of disc tissues.
- Degeneration affects the mechanics of disc tissues, which is then reflected on the mechanics of the entire disc. One major effect of degeneration is an increase of the range of motion.
- Several modes of injury, such as herniation and endplate fracture, are closely related to the pressure in the nucleus pulposus and are more frequent in healthy discs.

References

Acaroglu ER, Iatridis JC, Setton LA, Foster RJ, Mow VC, Weidenbaum M (1995) Degeneration and aging affect the tensile behavior of human lumbar anulus fibrosus. Spine (Phila Pa 1976) 20(24):2690–2701

Adams MA, Dolan P (1991) A technique for quantifying the bending moment acting on the lumbar spine in vivo. J Biomech 24(2):117–126

Adams MA, Dolan P (2011) Biomechanics of vertebral compression fractures and clinical application. Arch Orthop Trauma Surg 131(12):1703–1710

Adams MA, Hutton WC (1980) The effect of posture on the role of the apophysial joints in resisting intervertebral compressive forces. J Bone Joint Surg Br 62(3):358–362

Adams MA, Hutton WC (1981) The relevance of torsion to the mechanical derangement of the lumbar spine. Spine (Phila Pa 1976) 6(3):241–248

Adams P, Muir H (1976) Qualitative changes with age of proteoglycans of human lumbar discs. Ann Rheum Dis 35(4):289–296

Adams MA, Roughley PJ (2006) What is intervertebral disc degeneration, and what causes it? Spine (Phila Pa 1976) 31(18):2151–2161

Adams MA, Bogduk N, Burton K, Dolan P (2006) The biomechanics of back pain, 2nd edn. Churchill Livingstone Elsevier, London, pp 29–48

Ateshian GA, Ellis BJ, Weiss JA (2007) Equivalence between short-time biphasic and incompressible elastic material responses. J Biomech Eng 129(3):405–412

Ateshian GA, Rajan V, Chahine NO, Canal CE, Hung CT (2009) Modeling the matrix of articular cartilage using a continuous fiber angular distribution predicts many observed phenomena. J Biomech Eng 131(6):061003

Aultman CD, Scannell J, McGill SM (2005) The direction of progressive herniation in porcine spine motion segments is influenced by the orientation of the bending axis. Clin Biomech (Bristol, Avon) 20(2):126–129

Azeloglu EU, Albro MB, Thimmappa VA, Ateshian GA, Costa KD (2008) Heterogeneous transmural proteoglycan distribution provides a mechanism for regulating residual stresses in the aorta. Am J Physiol Heart Circ Physiol 294(3):H1197–H1205

Baranto A, Ekstrom L, Hellstrom M, Lundin O, Holm S, Sward L (2005) Fracture patterns of the adolescent porcine spine: an experimental loading study in bending-compression. Spine (Phila Pa 1976) 30(1):75–82

Bass EC, Ashford FA, Segal MR, Lotz JC (2004) Biaxial testing of human annulus fibrosus and its implications for a constitutive formulation. Ann Biomed Eng 32(9):1231–1242

Battié MC, Videman T, Levälahti E, Gill K, Kaprio J (2008) Genetic and environmental effects on disc degeneration by phenotype and spinal level: a multivariate twin study. Spine (Phila Pa 1976) 33(25):2801–8. doi: 10.1097/BRS.0b013e31818043b7

Buckwalter JA (1995) Aging and degeneration of the human intervertebral disc. Spine (Phila Pa 1976) 20(11):1307–1314

Callaghan JP, McGill SM (2001) Intervertebral disc herniation: studies on a porcine model exposed to highly repetitive flexion/extension motion with compressive force. Clin Biomech (Bristol, Avon) 16(1):28–37

Canal Guterl C, Hung CT, Ateshian GA (2010) Electrostatic and non-electrostatic contributions of proteoglycans to the compressive equilibrium modulus of bovine articular cartilage. J Biomech 43(7):1343–1350

Cassidy JJ, Hiltner A, Baer E (1989) Hierarchical structure of the intervertebral disc. Connect Tissue Res 23(1):75–88

Cavalcante FS, Ito S, Brewer K, Sakai H, Alencar AM, Almeida MP et al (2005) Mechanical interactions between collagen and proteoglycans: implications for the stability of lung tissue. J Appl Physiol 98(2):672–679

Chuang SY, Popovich JM Jr, Lin LC, Hedman TP (2010) The effects of exogenous crosslinking on hydration and fluid flow in the intervertebral disc subjected to compressive creep loading and unloading. Spine (Phila Pa 1976) 35(24):E1362–E1366

Chuong CJ, Fung YC (1986) On residual stresses in arteries. J Biomech Eng 108(2):189–192

Comper WD, Laurent TC (1978) Physiological function of connective tissue polysaccharides. Physiol Rev 58(1):255–315

Cortes DH, Elliott DM (2012) Extra-fibrillar matrix mechanics of annulus fibrosus in tension and compression. Biomech Model Mechanobiol 11(6):781–790

Costi JJ, Stokes IA, Gardner-Morse M, Laible JP, Scoffone HM, Iatridis JC (2007) Direct measurement of intervertebral disc maximum shear strain in six degrees of freedom: motions that place disc tissue at risk of injury. J Biomech 40(11):2457–66

Costi JJ, Stokes IA, Gardner-Morse M, Laible JP, Scoffone HM, Iatridis JC (2008) Direct measurement of intervertebral disc maximum shear strain in six degrees of freedom: motions that place disc tissue at risk of injury. J Biomech 40(11):2457–66

Costi JJ et al (2011) Intervertebral disc properties: challenges for biodevices. Expert Rev Med Devices 8(3):357–376

Das DB, Welling A, Urban JP, Boubriak OA (2009) Solute transport in intervertebral disc: experiments and finite element modeling. Ann N Y Acad Sci 1161:44–61

Diamant J, Keller A, Baer E, Litt M, Arridge RG (1972) Collagen; ultrastructure and its relation to mechanical properties as a function of ageing. Proc R Soc Lond B Biol Sci 180(60):293–315

Drake JD, Aultman CD, McGill SM, Callaghan JP (2005) The influence of static axial torque in combined loading on intervertebral joint failure mechanics using a porcine model. Clin Biomech (Bristol, Avon) 20(10):1038–1045

Drost MR, Willems P, Snijders H, Huyghe JM, Janssen JD, Huson A (1995) Confined compression of canine annulus fibrosus under chemical and mechanical loading. J Biomech Eng 117(4):390–396

Elliott DM, Setton LA (2001) Anisotropic and inhomogeneous tensile behavior of the human anulus fibrosus: experimental measurement and material model predictions. J Biomech Eng 123(3):256–263

Eyre DR (1979) Biochemistry of the intervertebral disc. Int Rev Connect Tissue Res 8:227–291

Eyre DR, Muir H (1976) Types I and II collagens in intervertebral disc. Interchanging radial distributions in annulus fibrosus. Biochem J 157(1):267–270

Ferguson SJ, Ito K, Nolte LP (2004) Fluid flow and convective transport of solutes within the intervertebral disc. J Biomech 37(2):213–221

Fields AJ, Lee GL, Keaveny TM (2010) Mechanisms of initial endplate failure in the human vertebral body. J Biomech 43(16): 3126–3131

Fujita Y, Wagner DR, Biviji AA, Duncan NA, Lotz JC (2000) Anisotropic shear behavior of the annulus fibrosus: effect of harvest site and tissue prestrain. Med Eng Phys 22(5):349–357

Gallagher S (2002) Letters. Spine (Phila Pa 1976) 27(12):1378

Gregory DE, Callaghan JP (2011) A comparison of uniaxial and biaxial mechanical properties of the annulus fibrosus: a porcine model. J Biomech Eng 133(2):024503

Gu WY, Mao XG, Foster RJ, Weidenbaum M, Mow VC, Rawlins BA (1999) The anisotropic hydraulic permeability of human lumbar anulus fibrosus. Influence of age, degeneration, direction, and water content. Spine (Phila Pa 1976) 24(23):2449–2455

Guerin HA, Elliott DM (2006a) Degeneration affects the fiber reorientation of human annulus fibrosus under tensile load. J Biomech 39(8):1410–1418

Guerin HA, Elliott DM (2006b) Structure and properties of soft tissues in the spine. In: Kurtz SM, Edidin AA (eds) SPINE: technology handbook. Elsevier Academic Press, Amsterdam/Boston

Guerin HL, Elliott DM (2007) Quantifying the contributions of structure to annulus fibrosus mechanical function using a nonlinear, anisotropic, hyperelastic model. J Orthop Res 25(4): 508–516

Guo Z, Shi X, Peng X, Caner F (2012) Fibre-matrix interaction in the human annulus fibrosus. J Mech Behav Biomed Mater 5(1): 193–205

Hardingham TE, Muir H, Kwan MK, Lai WM, Mow VC (1987) Viscoelastic properties of proteoglycan solutions with varying proportions present as aggregates. J Orthop Res 5(1):36–46

Heneghan P, Riches PE (2008a) The strain-dependent osmotic pressure and stiffness of the bovine nucleus pulposus apportioned into ionic and non-ionic contributors. J Biomech 41(11):2411–2416

Heneghan P, Riches PE (2008b) Determination of the strain-dependent hydraulic permeability of the compressed bovine nucleus pulposus. J Biomech 41(4):903–906

Heuer F, Schmidt H, Wilke HJ (2008) The relation between intervertebral disc bulging and annular fiber associated strains for simple and complex loading. J Biomech 41(5):1086–1094

Hickey DS, Hukins DW (1980) Relation between the structure of the annulus fibrosus and the function and failure of the intervertebral disc. Spine (Phila Pa 1976) 5(2):106–116

Hollingsworth NT, Wagner DR (2011) Modeling shear behavior of the annulus fibrosus. J Mech Behav Biomed Mater 4(7):1103–1114

Holm S, Maroudas A, Urban JP, Selstam G, Nachemson A (1981) Nutrition of the intervertebral disc: solute transport and metabolism. Connect Tissue Res 8(2):101–119

Hsu K, Zucherman J, Shea W, Kaiser J, White A, Schofferman J et al (1990) High lumbar disc degeneration. Incidence and etiology. Spine (Phila Pa 1976) 15(7):679–682

Huyghe JM (2010) Biaxial testing of canine annulus fibrosus tissue under changing salt concentrations. An Acad Bras Cienc 82(1):145–151

Iatridis JC, Weidenbaum M, Setton LA, Mow VC (1996) Is the nucleus pulposus a solid or a fluid? Mechanical behaviors of the nucleus pulposus of the human intervertebral disc. Spine (Phila Pa 1976) 21(10):1174–1184

Iatridis JC, Setton LA, Weidenbaum M, Mow VC (1997a) The viscoelastic behavior of the non-degenerate human lumbar nucleus pulposus in shear. J Biomech 30(10):1005–1013

Iatridis JC, Setton LA, Weidenbaum M, Mow VC (1997b) Alterations in the mechanical behavior of the human lumbar nucleus pulposus with degeneration and aging. J Orthop Res 15(2):318–322

Iatridis JC, Kumar S, Foster RJ, Weidenbaum M, Mow VC (1999) Shear mechanical properties of human lumbar annulus fibrosus. J Orthop Res 17(5):732–737

Iencean SM (2000) Lumbar intervertebral disc herniation following experimental intradiscal pressure increase. Acta Neurochir (Wien) 142(6):669–676

Jackson AR, Yuan TY, Huang CY, Travascio F, Yong Gu W (2008) Effect of compression and anisotropy on the diffusion of glucose in annulus fibrosus. Spine (Phila Pa 1976) 33(1):1–7

Jackson AR, Huang CY, Gu WY (2011) Effect of endplate calcification and mechanical deformation on the distribution of glucose in intervertebral disc: a 3D finite element study. Comput Methods Biomech Biomed Engin 14(2):195–204

Jacobs NT, Smith LJ, Han WM, Morelli J, Yoder JH, Elliott DM (2011) Effect of orientation and targeted extracellular matrix degradation on the shear mechanical properties of the annulus fibrosus. J Mech Behav Biomed Mater 4(8):1611–1619

Jacobs NT, Cortes DH, Vresilovic EJ, Elliott DM (2013) Biaxial tension of fibrous tissue: using finite element methods to address experimental challenges arising from boundary conditions and anisotropy. J Biomech Eng 135(2):021004. doi:10.1115/1.4023503

Johannessen W, Elliott DM (2005) Effects of degeneration on the biphasic material properties of human nucleus pulposus in confined compression. Spine (Phila Pa 1976) 30(24):E724–E729

Kastelic J, Baer E (1980) Deformation in tendon collagen. Symp Soc Exp Biol 34:397–435

Kastelic J, Galeski A, Baer E (1978) The multicomposite structure of tendon. Connect Tissue Res 6(1):11–23

Kiani C, Chen L, Wu YJ, Yee AJ, Yang BB (2002) Structure and function of aggrecan. Cell Res 12(1):19–32

Klisch SM, Lotz JC (2000) A special theory of biphasic mixtures and experimental results for human annulus fibrosus tested in confined compression. J Biomech Eng 122(2):180–188

Lanir Y (2009) Mechanisms of residual stress in soft tissues. J Biomech Eng 131(4):044506

Maroudas A, Bannon C (1981) Measurement of swelling pressure in cartilage and comparison with the osmotic pressure of constituent proteoglycans. Biorheology 18(3–6):619–632

Massey CJ, van Donkelaar CC, Vresilovic E, Zavaliangos A, Marcolongo M (2011) Effects of aging and degeneration on the human intervertebral disc during the diurnal cycle: a finite element study. J Orthop Res 30(1):122–128

Mauck RL, Baker BM, Nerurkar NL, Burdick JA, Li WJ, Tuan RS et al (2009) Engineering on the straight and narrow: the mechanics of nanofibrous assemblies for fiber-reinforced tissue regeneration. Tissue Eng Part B Rev 15(2):171–193

Melrose J, Ghosh P, Taylor TK (2001) A comparative analysis of the differential spatial and temporal distributions of the large (aggrecan, versican) and small (decorin, biglycan, fibromodulin) proteoglycans of the intervertebral disc. J Anat 198(Pt 1):3–15

Moon SM, Yoder JH, Wright AC, Smith LJ, Vresilovic EJ, Elliott DM (2013) Evaluation of intervertebral disc cartilaginous endplate structure using magnetic resonance imaging. Eur Spine J doi:10.1007/s00586-013-2798-1

Michalek AJ, Gardner-Mose MG, Iatridis JC (2012). Large residual strains are present in the intervertebral disc annulus fibrosus in the unloaded state. J Biomech 45(7):1227–1231

Mimura M, Panjabi MM, Oxland TR, Crisco JJ, Yamamoto I, Vasavada A (1994) Disc degeneration affects the multidirectional flexibility of the lumbar spine. Spine (Phila Pa 1976) 19(12):1371–1380

Nachemson A (1963) The influence of spinal movements on the lumbar intradiscal pressure and on the tensil stresses in the annulus fibrosus. Acta Orthop Scand 33:183–207

Nachemson AL (1981) Disc pressure measurements. Spine (Phila Pa 1976) 6(1):93–97

Nerurkar NL, Elliott DM, Mauck RL (2010) Mechanical design criteria for intervertebral disc tissue engineering. J Biomech 43(6):1017–1030

O'Connell GD, Johannessen W, Vresilovic EJ, Elliott DM (2007) Human internal disc strains in axial compression measured noninvasively using magnetic resonance imaging. Spine (Phila Pa 1976) 32(25):2860–2868

O'Connell GD, Guerin HL, Elliott DM (2009) Theoretical and uniaxial experimental evaluation of human annulus fibrosus degeneration. J Biomech Eng 131(11)

O'Connell GD, Vresilovic EJ, Elliott DM (2010) Human intervertebral disc internal strain in compression: the effect of disc region, loading position, and degeneration. J Orthop Res 29(4):547–555

O'Connell GD, Jacobs NT, Sen S, Vresilovic EJ, Elliott DM (2011) Axial creep loading and unloaded recovery of the human intervertebral disc and the effect of degeneration. J Mech Behav Biomed Mater 4(7):933–942

O'Connell GD, Sen S, Elliott DM (2012) Human annulus fibrosus material properties from biaxial testing and constitutive modeling are altered with degeneration. Biomech Model Mechanobiol 11(3–4):493–503

Ordway NR, Lu YM, Zhang X, Cheng CC, Fang H, Fayyazi AH (2007) Correlation of cervical endplate strength with CT measured subchondral bone density. Eur Spine J 16(12):2104–2109

Overbeek JT (1956) The Donnan equilibrium. Prog Biophys Biophys Chem 6:57–84

Panjabi M, Brown M, Lindahl S, Irstam L, Hermens M (1988) Intrinsic disc pressure as a measure of integrity of the lumbar spine. Spine (Phila Pa 1976) 13(8):913–917

Pearcy M, Portek I, Shepherd J (1984) Three-dimensional x-ray analysis of normal movement in the lumbar spine. Spine (Phila Pa 1976) 9(3):294–297

Perie D, Korda D, Iatridis JC (2005) Confined compression experiments on bovine nucleus pulposus and annulus fibrosus: sensitivity of the experiment in the determination of compressive modulus and hydraulic permeability. J Biomech 38(11):2164–2171

Perie D, Iatridis JC, Demers CN, Goswami T, Beaudoin G, Mwale F et al (2006a) Assessment of compressive modulus, hydraulic permeability and matrix content of trypsin-treated nucleus pulposus using quantitative MRI. J Biomech 39(8):1392–1400

Perie DS, Maclean JJ, Owen JP, Iatridis JC (2006b) Correlating material properties with tissue composition in enzymatically digested bovine annulus fibrosus and nucleus pulposus tissue. Ann Biomed Eng 34(5):769–777

Potvin JR, McGill SM, Norman RW (1991) Trunk muscle and lumbar ligament contributions to dynamic lifts with varying degrees of trunk flexion. Spine (Phila Pa 1976) 16(9):1099–1107

Pye SR, Reid DM, Lunt M, Adams JE, Silman AJ, O'Neill TW (2007) Lumbar disc degeneration: association between osteophytes, end-plate sclerosis and disc space narrowing. Ann Rheum Dis 66(3):330–333

Rannou F, Lee TS, Zhou RH, Chin J, Lotz JC, Mayoux-Benhamou MA et al (2004) Intervertebral disc degeneration: the role of the mitochondrial pathway in annulus fibrosus cell apoptosis induced by overload. Am J Pathol 164(3):915–924

Sasaki M, Takahashi T, Miyahara K, Hirosea T (2001) Effects of chondroitinase ABC on intradiscal pressure in sheep: an in vivo study. Spine (Phila Pa 1976) 26(5):463–468

Sato K, Kikuchi S, Yonezawa T (1999) In vivo intradiscal pressure measurement in healthy individuals and in patients with ongoing back problems. Spine (Phila Pa 1976) 24(23):2468–2474

Setton LA, Zhu W, Weidenbaum M, Ratcliffe A, Mow VC (1993) Compressive properties of the cartilaginous end-plate of the baboon lumbar spine. J Orthop Res 11(2):228–239

Shirazi-Adl A, Ahmed AM, Shrivastava SC (1986) Mechanical response of a lumbar motion segment in axial torque alone and combined with compression. Spine (Phila Pa 1976) 11(9):914–927

Shirazi-Adl A, Taheri M, Urban JP (2010) Analysis of cell viability in intervertebral disc: effect of endplate permeability on cell population. J Biomech 43(7):1330–1336

Simunic DI, Broom ND, Robertson PA (2001) Biomechanical factors influencing nuclear disruption of the intervertebral disc. Spine 26(11):1223–1230

Smith LJ, Nerurkar NL, Choi KS, Harfe BD, Elliott DM (2011) Degeneration and regeneration of the intervertebral disc: lessons from development. Dis Model Mech 4(1):31–41

Soukane DM, Shirazi-Adl A, Urban JP (2007) Computation of coupled diffusion of oxygen, glucose and lactic acid in an intervertebral disc. J Biomech 40(12):2645–2654

Spencer AJM (1984) Continuum theory of the mechanics of fibre-reinforced composites. Springer, Wien/New York

Spenciner D, Greene D, Paiva J, Palumbo M, Crisco J (2006) The multidirectional bending properties of the human lumbar intervertebral disc. Spine J 6(3):248–257

Travascio F, Gu WY (2011) Simultaneous measurement of anisotropic solute diffusivity and binding reaction rates in biological tissues by FRAP. Ann Biomed Eng 39(1):53–65

Tsantrizos A, Ito K, Aebi M, Steffen T (2005) Internal strains in healthy and degenerated lumbar intervertebral discs. Spine 30(19):2129–2137

Urban JP, Maroudas A (1981) Swelling of the intervertebral disc in vitro. Connect Tissue Res 9(1):1–10

Urban JP, Holm S, Maroudas A (1978) Diffusion of small solutes into the intervertebral disc: as in vivo study. Biorheology 15(3–4):203–221

Urban JP, Maroudas A, Bayliss MT, Dillon J (1979) Swelling pressures of proteoglycans at the concentrations found in cartilaginous tissues. Biorheology 16(6):447–464

Urban JP, Holm S, Maroudas A, Nachemson A (1982) Nutrition of the intervertebral disc: effect of fluid flow on solute transport. Clin Orthop Relat Res 170:296–302

Urban JP, Smith S, Fairbank JC (2004) Nutrition of the intervertebral disc. Spine (Phila Pa 1976) 29(23):2700–2709

van der Veen AJ, van Dieen JH, Nadort A, Stam B, Smit TH (2007) Intervertebral disc recovery after dynamic or static loading in vitro: is there a role for the endplate? J Biomech 40(10):2230–2235

van Deursen DL, Snijders CJ, Kingma I, van Dieen JH (2001a) In vitro torsion-induced stress distribution changes in porcine intervertebral discs. Spine (Phila Pa 1976) 26(23):2582–2586

van Deursen DL, Snijders CJ, van Dieen JH, Kingma I, van Deursen LL (2001b) The effect of passive vertebral rotation on pressure in the nucleus pulposus. J Biomech 34(3):405–408

Wade KR, Robertson PA, Broom ND (2011) A fresh look at the nucleus-endplate region: new evidence for significant structural integration. Eur Spine J 20(8):1225–1232

Wagner DR, Lotz JC (2004) Theoretical model and experimental results for the nonlinear elastic behavior of human annulus fibrosus. J Orthop Res 22(4):901–909

Wang C, Witschey W, Elliott MA, Borthakur A, Reddy R (2010) Measurement of intervertebral disc pressure with T 1rho MRI. Magn Reson Med 64(6):1721–1727

Wilke HJ, Wolf S, Claes LE, Arand M, Wiesend A (1996) Influence of varying muscle forces on lumbar intradiscal pressure: an in vitro study. J Biomech 29(4):549–555

Wilke HJ, Neef P, Caimi M, Hoogland T, Claes LE (1999) New in vivo measurements of pressures in the intervertebral disc in daily life. Spine (Phila Pa 1976) 24(8):755–762

Wu HC, Yao RF (1976) Mechanical behavior of the human annulus fibrosus. J Biomech 9(1):1–7

Yates JP, Giangregorio L, McGill SM (2010) The influence of intervertebral disc shape on the pathway of posterior/posterolateral partial herniation. Spine (Phila Pa 1976) 35(7):734–739

Zhao FD, Pollintine P, Hole BD, Adams MA, Dolan P (2009) Vertebral fractures usually affect the cranial endplate because it is thinner and supported by less-dense trabecular bone. Bone 44(2):372–379

Zhu W, Mow VC, Koob TJ, Eyre DR (1993) Viscoelastic shear properties of articular cartilage and the effects of glycosidase treatments. J Orthop Res 11(6):771–781

Zhu W, Chern KY, Mow VC (1994) Anisotropic viscoelastic shear properties of bovine meniscus. Clin Orthop Relat Res 306:34–45