Anatomy and Biomechanics of the Intervertebral Disc

1

Sumeet Kumar and Vivek Pai

Walking. Running. Jumping. Bending. Climbing. The human spine has evolved beyond supporting an upright posture to permit a wide range of motions. The unique upright position along with the flexibility of the human spine is due to the presence of the paired facet joints and the intervertebral discs, which work together as a three-joint complex. The facet or zygapophyseal joints are synovial joints between the superior and inferior articular processes of adjacent vertebrae [1]. The zygapophyseal joints share the transmission of the mechanical load on the spine, limit excessive axial rotation of the vertebrae and provide passive stability [2]. The bony posterior elements of the vertebrae allow attachment of muscles which provide active stability during motion.

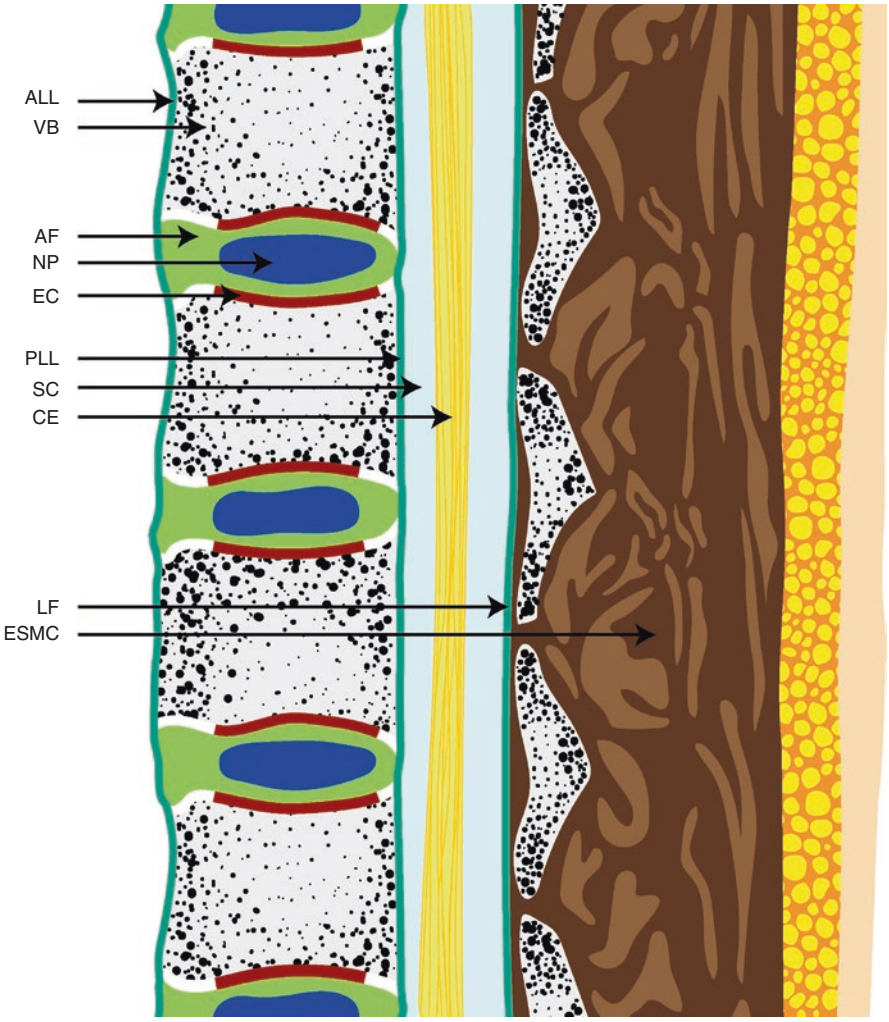
The intervertebral disc is sandwiched between the superior and inferior vertebral body endplates and together they constitute a spinal motion segment [3]. The spine can be viewed as consisting of 23 individual spinal motion segments, across the cervical, thoracic and lumbar regions. The sacral and coccygeal vertebrae being fused, lack intervening discs and thus spinal motion segments. The vertebral endplates are thin cartilaginous layers in the central portion of the superior and inferior surfaces of the vertebrae that allow the exchange of nutrients and metabolites between the disc and the capillaries in the vertebrae. The intervertebral discs are held in place between the vertebrae by the longitudinal ligaments continuous with the outer fibres of the disc. A schematic drawing of the spine is shown in Fig. 1.1. The function of the spinal motion segment is to provide axial stability, absorb shock and allow mobility of the segment in three dimensions. Each segment is subject to static and dynamic mechanical forces of varying kinds—compression, shear, bending and torsional forces.

S. Kumar (✉)
Neuroradiology, National Neuroscience Institute, Singapore, Singapore

Duke-NUS Medical School, Singapore, Singapore
e-mail: sumeet.kumar@singhealth.com.sg

V. Pai
Neuroradiology, National Neuroscience Institute, Singapore, Singapore

L. Manfrè, J. Van Goethem (eds.), *The Disc and Degenerative Disc Disease*,
New Procedures in Spinal Interventional Neuroradiology,
https://doi.org/10.1007/978-3-030-03715-4_1



ALL: Anterior Longitudinal Ligament
VB: Vertebral Body
AF: Annulus Fibrosus
NP: Nucleus Pulposus
EC: Endplate Cartilage
PLL: Posterior Longitudinal Ligament
SC: Spinal Canal
CE: Cauda Equina
LF: Ligamentum Flavum
ESMC: Erector Spinae - Multifidus Complex

Fig. 1.1 Sagittal illustration of the spine showing the relationship of the vertebrae, the cartilaginous endplates and the intervertebral discs

In this chapter, the focus is on the intervertebral disc; we will discuss the structure and anatomy of the disc and elaborate on the biomechanical responses of the intervertebral disc when subjected to various forces.

1.1 Anatomy of the Intervertebral Disc

Intervertebral discs are present in the cervical, thoracic and lumbar regions, varying in shape and volume at different anatomical levels. On gross morphology, the height of the discs in the lumbar region is the largest, measuring about 9–17 mm in adults. The height in the thoracic region is lesser, about 5 mm and it is the least, about 3 mm in the cervical region [4]. In the cervical region, the discs are thicker anteriorly than posteriorly to form the normal cervical lordotic curvature [5]. Similarly, they are thicker in the anterior portions in the lumbar region to form the lumbar lordosis. In the thoracic region, the discs are of uniform thickness from front to back [6].

On an axial cross section, the disc comprises three zones; the inner most nucleus pulposus surrounded by the inner fibres of the annulus fibrosus and the outer most zone being the outer fibres of the annulus fibrosus [7]. The inner fibres of annulus fibrosus are also sometimes referred to as the transitional zone. The nucleus pulposus is the soft and gelatinous core of the intervertebral disc, occupying about 40% of the cross sectional area in a young healthy adult. The nucleus pulposus has a high water content (about 70–90%), which varies through the time of the day and with activity [8, 9]. The remainder of the matrix of the nucleus pulposus consists of proteoglycans and collagen—primarily type II collagen [4]. The water is held within the domains of the proteoglycans, most abundant of which is aggrecan. The aggrecans attract water molecules and maintain the hydrostatic pressure of the disc [10]. This bound water is responsible for the dynamic viscoelastic properties of the disc that allow it to deform under pressure, sustain and transmit the load in all directions. The type II collagen fibres are fine interconnected fibres that form a meshwork in the matrix and connect with the inner annulus fibres and with the vertebral endplates. Histologically, the nucleus pulposus contains few chondrocyte-like cells which secrete and maintain the abundant extracellular matrix, the predominant component of which is the proteoglycans [11].

Surrounding the nucleus pulposus circumferentially is the ring-shaped annulus fibrosus, which limits the nucleus pulposus forming its outer boundary [12]. The annulus fibrosus is a fibrous structure, consisting of concentric series of collagenous lamellae [13]. Collagen forms about 70% of the dry weight of the annulus fibrosus. Interspersed between the collagen fibrils are proteoglycans, glycoproteins, elastic fibres and fibroblast-like connective tissue cells that secrete these products [14]. The peripheral or outer annulus fibrosus is a more collagenous region than the inner annulus, which forms a transitional layer and lies in contact with the nucleus pulposus. Type I collagen predominates the structure of the outer annulus fibrosus, while type II collagen is abundant in the inner annulus fibrosus [15]. The architecture and composition of the annulus fibrosus change gradually from the outer to the inner layers, being more organised in the outer layers.

The outer annulus is a highly organised lamellated structure made of about 15–25 concentric, densely packed, lamellae of collagen. The number of lamellae is highest in the lumbar discs, up to 25 lamellae [16]. Each lamella varies in thickness from 200 to 400 μm, being thicker towards the periphery [17]. The collagen fibres within each lamella are uniformly oriented in a plane but differ in orientation to the adjacent lamella by about 60° [12]. This alignment leads to the parallel orientation of alternate lamella, referred to as "radial-ply" formation, which provides exceptional strength to the annulus. This arrangement is illustrated in the schematic drawing, Fig. 1.2. The deformation characteristics of the annulus fibrosus are believed to be related to the difference in the angles between adjacent lamella [18, 19]. The lamellae are interconnected through translamellar bridges. The number of translamellar bridges per unit area determines the balance between strength and flexibility. A greater number of bridges provide greater resistance to compressive forces but limit flexibility [12]. In the lumbar discs, the annulus is thicker anteriorly than posteriorly, the lamellae being more numerous anteriorly and spreading out in the peripheral aspects of the disc [20]. The peripheral lamellae connect with the fibres of the longitudinal ligaments, more intimately with the anterior longitudinal ligament than with the posterior longitudinal ligament [21]. The lamellae in the peripheral annulus also attach to the bony edges of the vertebrae by Sharpey's fibres, and the lamellae in the inner annulus are continuous with the cartilaginous endplates [21, 22].

In adults, the intervertebral disc is an avascular structure. It receives its nutrition through diffusion of nutrients through the endplates from the bone vasculature. The vertebral endplates are thin cartilaginous plates composed of hyaline cartilage, about 1 mm thick, at the interface of the vertebral bone and the intervertebral disc. The collagen fibres in the endplates are continuous with the collagen fibres in the disc [23].

Embryologically, the disc originates from two distinct entities. The central nucleus pulposus arises from remnants of the notochord which eventually disappear by the age of 10 years and are replaced by cells which closely resemble chondrocytes [12, 24]. The annulus fibrosus arises from the sclerotome as "annular" condensation of mesenchymal cells between the primordial vertebral bodies [12, 24]. The cells of outer annulus have an oblong, fibroblast-like appearance.

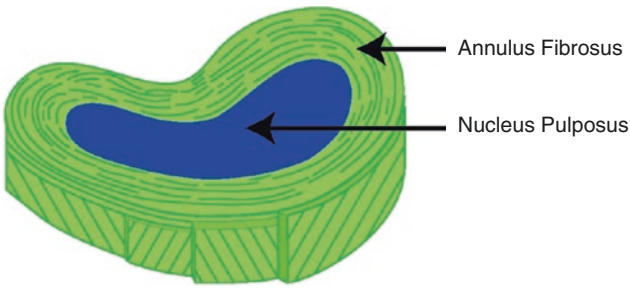


Fig. 1.2 Diagrammatic representation of the intervertebral disc showing the central nucleus pulposus (blue) surrounded circumferentially by the multilayered annulus pulposus (green)

In adulthood, there is a sharp fall in the number of viable cells within the intervertebral disc and with it, the onset of disc degeneration [25]. The nucleus hardens, loses its gel-like consistency and translucent appearance due to a reduction of its proteoglycan and water content and an increase in the density and size of the collagen fibrils within it [26]. Consequent to these structural alterations within the nucleus, there is an overall reduction of the size of the nucleus pulposus and expansion of the inner layer of the annulus. The outer layer of the annulus remains stable in size [26]. The composition of the annulus remains unchanged in adulthood, but areas of myxomatous degeneration occur which eventually progress to fissuring [26, 27]. With degeneration, the collagen fibrils are thinned and their arrangement loses its regularity [28]. With advancing degeneration, the intervertebral disc is no more than a hard fibrocartilage. The volume of the disc reduces markedly with multiple fissures extending to the centre of the disc. The nucleus may be imperceptible from the rest of the annulus.

1.2 Biomechanical Properties of the Intervertebral Disc

The extracellular matrix of the intervertebral disc, consisting predominantly of three macromolecules—collagen, proteoglycans and glycoproteins, is responsible for many of the biomechanical properties of the disc. The relative proportion of water and the macromolecules varies in different regions of the disc, imparting distinct mechanical properties to the nucleus pulposus, inner and outer annulus fibrosus. For instance, the proteoglycans are most abundant in the nucleus pulposus. This gives the nucleus pulposus higher hydrostatic and osmotic pressures and thus more compressive properties. Highly organised collagen fibres are more abundant in the annulus, giving the annulus a higher tensile loading capacity. During axial loading (axial force is a force applied along the long axis of the spine) compression is experienced by both the nucleus pulposus and the annulus fibrosus. However, their responses vary due to the relative differences in their composition. The relative composition and architectural arrangement not only vary in different regions, but they also vary with the anatomical level (i.e. cervical versus thoracic versus lumbar level) and with age [29–32]. For example the lumbar intervertebral discs have the highest proteoglycan content in the nucleus pulposus, whereas the nucleus pulposus in the cervical discs show the highest collagen content [30]. Some of the important properties of the disc that influence biomechanical behaviour are discussed below.

1.2.1 Hydrostatic Pressure

The proteoglycans, being hydrophilic, attract water molecules and this maintains the hydrostatic pressure of the nucleus pulposus. The hydrostatic pressure is responsible for maintaining the height of the disc which separates the adjacent vertebrae and expands the annulus fibrosus outwards. The magnitude of hydrostatic pressure varies diurnally depending on the spinal alignment and physical activity, being in

the magnitude range of 0.1 MPa at sleep to 0.5 MPa in quiet standing to more than 3 MPa, with increased loading [31–34]. With advancing age, lower proteoglycan and thus lower water content of the disc result in reduced hydrostatic pressure. This is accompanied by a decrease in the height of the disc along with altered mechanical properties of the disc.

1.2.2 Osmotic Pressure

Osmotic pressure in the disc is due to the differences in the concentration of macromolecules and ions in the extracellular matrix [35]. The presence of charged ions in the disc creates an osmotic pressure, which pulls water into the tissue and keeps the disc hydrated. The proteoglycans in the disc are composed of long chains of glycosamine attached to protein and are responsible for the negative charge. Within the nucleus pulposus, the most abundant proteoglycan is aggrecan, which is composed of negatively charged side chains of chondroitin sulphate and keratan attached to filaments of hyaluronic acid. These large molecules are trapped inside the collagen fibres and cannot diffuse out [36–38]. The negative charge attracts the positively charged Na+ ions creating an imbalance of cations. This draws in water that maintains the osmotic turgor of the nucleus pulposus, causes swelling of the disc and increases the stiffness of the tissue. The osmotic pressure within the disc shows diurnal variation, with changes in standing and supine positions and variations due to posture and activity with about 20–25% water exchange in every diurnal cycle [39].

1.2.3 Permeability

Permeability refers to the ability of fluid to flow in and out of the disc and is a key mechanical property of the nucleus pulposus. During axial loading, fluid flows out of the disc into the plasma. Inward movement of water into the disc is through passive diffusion on removal of the applied forces, for example on lying down. The movement of water into the disc and efflux of water out of the disc is thought to occur through two routes, predominantly through the vertebral endplate. The vertebral endplate is a hyaline cartilage similar to that found in the joints. It is perforated by vascular buds from the bone marrow at the bone endplate interfaces [40]. The other, probably less important route is through the annulus into the blood vessels adjacent to the annulus [40]. The permeability of the disc has been tested using confined compression techniques in which harvested nucleus pulposus tissue is compressed axially with methods to prevent lateral expansion. It has been observed that when subjected to small deformations, the nucleus pulposus demonstrates a constant permeability with a linear relationship between stress and strain. (Stress is a measure of force intensity, that is, force or load per unit area. Strain is a measure of deformation, that is, change in length divided by the original length.) This relation however is non-linear for moderate and large strain.

The hydrostatic and osmotic pressures are related to the permeability of the disc and are mediated by the binding and releasing of water molecules by the aggrecans in the nucleus pulposus [41]. This diurnal and load responsive alteration in the water content of the disc is also referred to as the poroelastic behaviour of the disc [41].

1.2.4 Viscoelasticity

The nucleus pulposus is highly hydrated and has a gelatinous consistency. This makes it a classic example of a biological viscoelastic material, i.e. it demonstrates the properties of both fluid and solid. A fluid is defined as a substance that constantly deforms when subjected to a shear stress (shear stress is a force applied tangential to a surface), irrespective of magnitude of the applied force. Solids, on the other hand, resist shear stress (though minimal initial deformation is possible) and do not continue to deform like fluids, reaching a state of equilibrium with the applied stress. In experimental conditions, it has been found that nucleus pulposus shows a fluid-like behaviour under slow deformation rates and solid-like behaviour under dynamic conditions; its behaviour varying as a function of the rate of loading [42]. The viscoelasticity of the nucleus pulposus is attributed to ionic or osmotic effects and non-ionic or solid effects related to the proteoglycans [43].

1.2.5 Nonlinearity

Non-linear response of the annulus fibrosus to stress refers to a response that is not proportional to the applied loading force. In other words, the stiffness of annulus fibrosus varies with the magnitude of the applied load and is a property imparted by the collagen fibres. The annulus shows low stiffness for smaller deformations and higher stiffness for larger deformations [44–46]. This is related to the zigzag shape or "crimp" of the collagen fibres in the annulus and the gradual "uncrimping" with increasing stretch [47, 48]. On application of a stretching force "crimp" of the collagen fibres is straightened, and the stiffness and load-bearing capacity of the annulus increase with increasing stretch. Progressively further stretching after all the fibres are straightened can disrupt and break the collagen fibres. This important feature allows the annulus to restrain the swelling pressure in the nucleus pulposus.

1.2.6 Elasticity

The elastic properties of the annulus are related to its extra-fibrillary matrix, that is, the material excluding the collagen fibres. The elastic properties have been described in ex vivo studies using shear and compression tests (which may be uniaxial or biaxial), obtaining the Young's modulus (from the slope of stress and strain response) and using mechanical models.

1.2.7 Anisotropy

Anisotropic behaviour of the disc is a property of the annulus. It means that the stress in the annulus fibrosus varies in different axes. This is a function of the collagen fibre orientation with respect to the applied stress [20, 49].

1.3 Biomechanics of the Intervertebral Disc

1.3.1 Unloaded Disc

There are baseline forces at work within the intervertebral disc even in the absence of external loading. These forces arise mainly due to the internal tissue inhomogeneities within the disc. The higher proteoglycan concentration in the nucleus causes a higher hydrostatic and osmotic pressure within it. This is resisted in the axial plane by the vertebral endplates and in the radial plane by the tensile stress of the annulus, also referred to as the "hoop stress" (tensile stress tends to pull and elongate the material in the direction of applied force). These multidirectional "residual" stresses are present in the unloaded state within the disc and have been studied by measuring the opening angle after an incision on the annulus fibrosus of an animal disc and by needle pressure gauge studies [50–52]. When an external load is applied, it creates additional stresses on top of the baseline "residual" stress.

1.3.2 Response to Compression

Compression is a force that has the action of shortening the material in the direction of the applied force. The direction of axial compression on the disc is depicted schematically in Fig. 1.3. The key function of the intervertebral disc is transmission of compression load in the spinal column, together with facet joints. The discs and facet joints work synergistically, the disc supports the compressive forces anteriorly and the facet joints posteriorly. To maintain spinal stability, the net load vector passes through the centre of rotation of each adjacent spinal motion segment in the sagittal axis, also described as follower load path [53]. Using this strategy, the spine can support static loading for physical tasks more than physiological demands while maintaining flexibility [54–56]. Muscle activation occurs in vivo so that during static conditions, the primary loading of the disc is axial compression.

The amount of compression loading force on the disc depends on the weight of the upper body, action of the muscles and posture of the spine. For example in erect standing position and erect sitting position, the intervertebral disc transmits 84% and 100% of the compression load, respectively. The response of the disc depends on the duration of the loading, the frequency of change of loading and on the spinal level (cervical vs. lumbar).

The water content of the disc and movement of water inside and out of the disc are major determinants to the biodynamic mechanical behaviour of the disc to

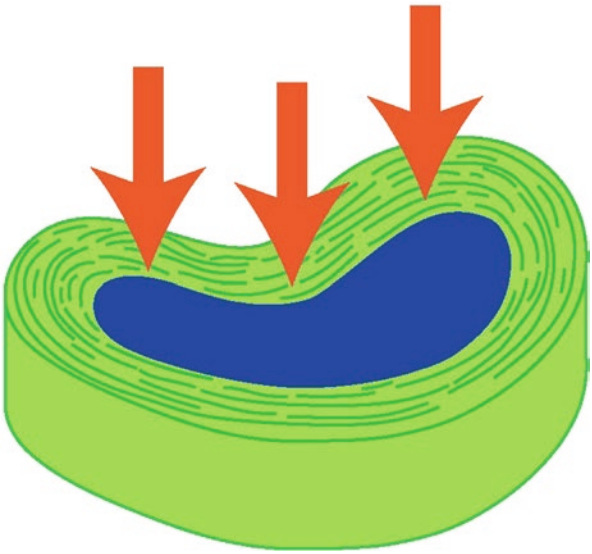


Fig. 1.3 Illustration of the direction of axial compressive force on the disc

compression loading [57–60]. The disc tends to maintain an equilibrium with respect to the external loading and internal disc swelling [61]. Upon application of a compressive load, the initial changes in the disc are different from the later changes. Initially, the hydrostatic pressure rapidly rises within the disc, more specifically, within its core, the nucleus pulposus. The nucleus pulposus behaves as an incompressible material and dissipates the pressure radially outwards to the annulus fibrosus and axially to the vertebral endplates—both of which restrain the nucleus pulposus. The hydrostatic pressure transferred to the outer fibres of the annulus causes them to experience a radial stretch or tensile stress and bulge outwards [62, 63]. This outward tensile force on the annulus is schematically represented in Fig. 1.4. The lamellae of the annulus fibrosus also experience axial compressive stress, which causes the inner lamellae to buckle inwards. The inward buckling of these lamellae is counteracted by the circumferentially outwardly directed hydrostatic pressure from the nucleus pulposus, thus stabilising these lamellae. This mechanism fails in the degenerating disc, which allows the inner lamellae of annulus to buckle inwards. The axial compression experienced by the inner fibres of annulus fibrosus is eventually transferred to adjacent vertebrae [63]. During prolonged external compressive loading, interstitial fluid is forced out of the nucleus pulposus towards the annulus and the endplates [64]. This causes a decrease in the disc height and increased outward bulging of the annulus. During this state, the nucleus pulposus bears less of the axial compression, and the contribution of the annulus fibrosus towards bearing the compression load increases [65].

As the fluid is expressed out from the nucleus pulposus, the concentration of the proteoglycans and fixed charge density within it increases. This causes a build-up of

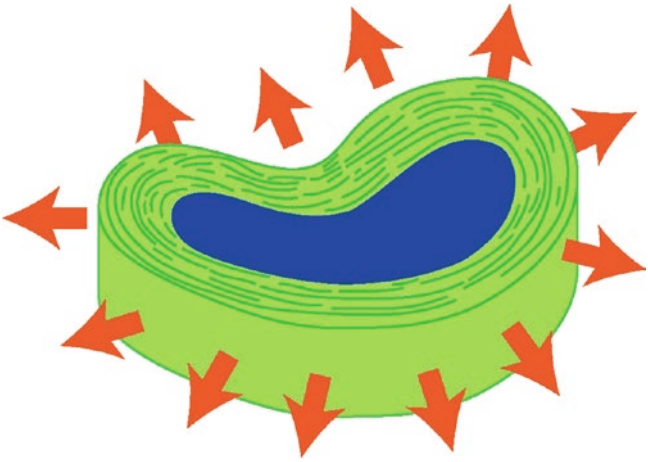


Fig. 1.4 Illustration of the outwardly directed tensile stress on the annulus fibrosus

osmotic pressure within the disc which tries to recover equilibrium [61]. The direction of water movement is reversed during rest, restoring the mechanical properties of the disc [66]. The water content is re-imbibed into the disc when the loading pressure is released, for example in supine position [67–70]. Sleeping or supine position is a low loading state that facilitates re-entry of fluid into the disc and decrease in disc osmolality. Correspondingly, the height of the disc (or its axial stiffness) changes, showing reduction in height during the loading cycle (during the day) and increase in height in the recovery (sleeping) phase. In vivo MRI studies have shown an increase in the water content of the discs and increase in height of the discs after a night of rest [66, 71, 72].

The response of the disc to loading depends on the type of compression loading, whether it is static or dynamic, duration of the loading and the frequency of the loading. The responses to various loading and recovery protocols have been studied extensively in many animal models [64, 66, 73–75]. Since most of these properties have been studied by application of loads in cadaveric animal intervertebral disc experiments, it is worth keeping in mind that the biological properties of the discs studied in vitro may not precisely simulate the in vivo behaviour of discs in humans.

The healthy disc remains soft under low compression loads but stiffens under high compression loads, to increase the stability [76]. A degenerated disc is less hydrated than a disc in health and is unable to generate enough hydrostatic pressure, and the pressure transfer mechanisms fail [76]. As a consequence, the load is transferred predominantly to the annulus rather than the vertebrae. In other words, in a degenerating disc, the annulus is subjected to a larger tensile stress [63].

While the compressive load is absorbed by the healthy nucleus pulposus, tensile force is resisted by the healthy annulus fibrosus. As mentioned previously, due to its unique structure, the annulus fibrosus is able to resist the tensile stress transmitted to it by the nucleus pulposus [77]. The alignment of the fibres within the annulus is responsible for absorbing a high magnitude of the tensile stress [63].

1.3.3 Response to Bending and Torsion

Much of the stress exerted on the spine is due to changes in posture. Bending and torsional movements are common movements of the spine associated with activity. These result in a combination of shear, compression and tensile forces on the spine [59, 63, 78]. Bending forward (spinal flexion), backward (spinal extension) or lateral bending are movements that result in rotation of the segments perpendicular to the axis of the spine. This causes a tensile stress on the annulus on the convex aspect of the spine and a compressive stress on the annulus on the concave aspect of the spine. For example on forward bending of the torso, the anterior annulus fibrosus experiences most of the compression. The outer fibres of the anterior annulus bulge outwards and the inner fibres of the anterior annulus buckle inwards. The posterior annulus on the other hand does not contribute to compression loading. It is subjected instead to a tensile or stretching stress in the axial direction. The nucleus pulposus pressurises and shifts backwards (opposite to the direction of bending) [43]. Effectively, there is asymmetric distribution of forces in different aspects of the annulus, the one side under the tensile stress stretching and the other side bulging under the weight of the body [59, 63, 78].

Torsion of the spine along its long axis is resisted by the zygapophyseal joints and is limited to 1–3° during physical activities [79]. It causes a combination of tensile and shear stresses in the annulus. Shear stress occurs in the horizontal plane in relation to the axis of rotation and perpendicular to the annulus fibres. Shear stress on the disc is schematically shown in Fig. 1.5. The oblique orientation of the lamellae of annulus results in tensile stress being generated within the fibres resisting the rotation [63] but not in the other fibres. When subjected to torsion, the peripheral or outer portion of the annulus is subjected to the largest stresses, thus developing the greatest strains. The strain on the annulus being directly proportional to the distance between the axis of rotation and the peripheral fibres [80, 81]. In the lumbar disc, this stress is maximum at the posterolateral portions of the annulus.

Therefore, bending and twisting movements of the spine when performed individually or in combination, especially when superimposed with a compressive load, result in increased stress and strain on the intervertebral disc. The effects of these

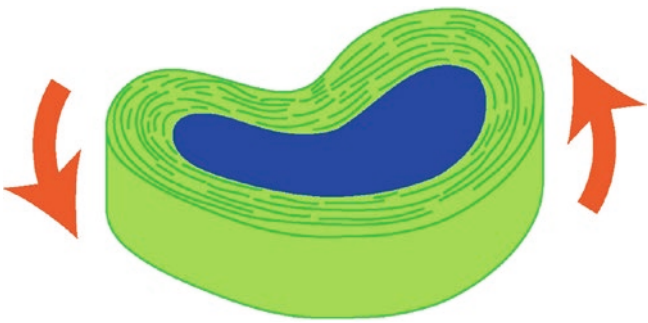


Fig. 1.5 Illustration of the shear stress acting on the disc in torsion

movements are magnified when applied to an already degenerating disc and account for disc injury.

The physical forces acting on the disc are translated into chemical signals which induce a cellular response. The cellular responses influence the biomechanical properties of the disc. This is dealt within the subsequent section of mechanotransduction.

1.4 Mechanotransduction in Intervertebral Disc

Three-dimensional mechanical forces acting on the disc cause biological responses at a cellular level within the disc through the phenomenon of mechanotransduction. For example on application of a compressive load, there is a physical deformation or a decrease in height of the nucleus pulposus. This results in a series of important intracellular changes, such as gene expression, protein synthesis and proliferation in response to this mechanical stress.

The mechanical stimuli are received by receptors, the mechanoreceptors, located in the nerve endings that begin the biological response by firing an action potential. In the spine, mechanoreceptors have been found in the peripheral lamellae of the annulus fibrosus and the longitudinal ligaments, most populous of which are the Golgi tendon organs [77]. The others are Pacinian corpuscles and Ruffini endings [77]. The Golgi tendon organs are primarily related to pain stimuli while the others are related to posture [77, 82]. On stimulation by mechanical stress, the mechanoreceptors activate various pathways which depend on the type and magnitude of the load, the duration, frequency and the anatomical zone where it is applied. These pathways induce biological effects by altering the gene expression that affects intracellular processes such as enzyme synthesis and apoptosis via signalling pathways [77]. The cellular pathways are different in a healthy disc versus a degenerated intervertebral disc, for example mechanosensing in healthy disc cells is via the arginine-glycine-aspartic acid (RGD) integrin protein whereas in the degenerated discs it is shown to trigger a different pathway that involves calcium [83, 84] and nitric oxide [84, 85].

On application of compressive stress, different responses are seen in distinct parts of the intervertebral disc. Most responses of the inner annulus fibrosus and the nucleus pulposus are similar, while the outer annulus fibrosus is not equally responsive to low-to-moderate magnitudes of load [34]. The compressive stress also regulates transport of nutrients and cell receptor signalling. Dynamic compression stress increases the oxygen concentration and consumption in the disc and reduces the accumulation of lactate [86]. On the other hand, static compression inhibits transport and metabolism of oxygen and lactate [86]. When exposed to in vivo static compression, changes in the biosynthesis and gene expression for molecules such as collagen, proteoglycans and protease activation are reported in some studies [34]. Most studies have found that dynamic loading largely leads to an anabolic effect, while static loading leads to catabolism [34, 87]. Short periods of loading elevate gene expression of collagens I and II as well as proteoglycans (e.g. aggrecan,

decorin and biglycan) in isolated annulus fibrosus cells and long duration of loading disrupt the transport of oxygen and nutrients [34, 88]. The age of the cells also plays a role in the response to dynamic compression, the younger cells maintaining the homeostasis better than the mature cells [89].

These studies give a glimpse of how the mechanical forces of the three-dimensional environments of the cells regulate the cells and their most fundamental cellular processes through complex pathways.

1.5 Summary

To summarise, the structure of the intervertebral disc is closely coupled with its biomechanical properties, allowing the spine to sustain load and maintain flexibility. The biomechanics vary at different levels of the spine, there being more rotation, less compression in the cervical segments and more compression, less rotation in the lumbar segments. The constitution of the intervertebral discs and the morphology of the facet joints are adapted for these mechanically different forces.

The composition of the central core of the intervertebral disc—the nucleus pulposus is geared towards retaining hydration through its proteoglycan rich matrix, which bequeaths it with hydrostatic properties. The annulus fibrosus or the outer restraining ring of the intervertebral disc, on the other hand, is rich in type I collagen and has a unique cross-ply design so that it can withstand high tensile forces.

Mechanical and cellular responses to loads through alterations in gene expression, enzyme synthesis and signalling pathways maintain a complex homeostasis to preserve disc structure and execute repair pathways. Failure of these mechanisms to cope with the applied loads leads to injury and initiates degeneration of the disc. The understanding of the anatomy and the biomechanics of load transfer in the intervertebral disc is important in understanding how we perform our day-to-day activities in health.

References

1. Singh V. General anatomy. 2nd ed. Gurgaon: Elsevier; 2015. p. 108.
2. Jaumard N, Welch W, Winkelstein B. Spinal facet joint biomechanics and mechanotransduction in Normal, injury and degenerative conditions. J Biomech Eng. 2011;133(7):071010. https://doi.org/10.1115/1.4004493.
3. Dennison C, Wild P, Wilson D, Cripton P. A minimally invasive in-fiber Bragg grating sensor for intervertebral disc pressure measurements. Meas Sci Technol. 2008;19(8):085201.
4. White T, Malone T. Effects of running on intervertebral disc height. J Orthop Sports Phys Ther. 1990;12(4):139–46.
5. Cifu D. Braddom's physical medicine & rehabilitation. 5th ed. Amsterdam: Elsevier; 2015. p. 688.
6. Mirab SMH, Barbarestani M, Tabatabaei SM, et al. Measuring dimensions of lumbar intervertebral discs in normal subjects. Anat Sci. 2017;14(1):3–8.
7. McCann M, Séguin C. Notochord cells in intervertebral disc development and degeneration. J Dev Biol. 2016;4(1):3.

8. DePalma AF, Rothman RH. The intervertebral disc. Philadelphia, PA: W.B. Saunders Company; 1970.
9. Bogduk N. Clinical anatomy of the lumbar spine and sacrum. 3rd ed. Churchull Livingstone: New York, NY; 1997.
10. Gawri R, Moir J, Ouellet J, et al. Physiological loading can restore the proteoglycan content in a model of early IVD degeneration. PLoS One. 2014;9(7):e101233.
11. Yoon S, Patel N. Molecular therapy of the intervertebral disc. Eur Spine J. 2006;15(S3):379–88.
12. Waxenbaum J, Reddy V, Futterman B. Anatomy, back, intervertebral discs. Ncbi.nlm.nih.gov. https://www.ncbi.nlm.nih.gov/books/NBK470583/.
13. Beadle OA. The intervertebral discs: observations on their normal and morbid anatomy in relation to certain spinal deformities. Issued by the Medical Research Council. Royal 8vo. Pp. 79, with 47 illustrations. 1931. London: His Majesty's stationery office. 2s. Net. Br J Surg. 1932;19(76):667.
14. Adams M. Intervertebral disc tissues. Eng Mater Process. 2014;2014:7–35.
15. Hayes A, Isaacs M, Hughes C, et al. Collagen fibrillogenesis in the development of the annulus fibrosus of the intervertebral disc. Eur Cells Mater. 2011;22:226–41.
16. Roberts S. Disc morphology in health and disease. Biochem Soc Trans. 2002;30(Pt 6):864–9.
17. Inoue H. Three-dimensional observation of collagen framework of intervertebral discs in rats, dogs and humans. Arch Histol Jpn. 1973;36:39–56.
18. Horton W. Further observations on the elastic mechanism of the intervertebral disc. J Bone Joint Surg Br. 1958;40-B(3):552–7.
19. Naylor A. The biophysical and biochemical aspects of intervertebral disc herniation and degeneration. Ann R Coll Surg Engl. 1962;31(2):91–114.
20. Galante J. Tensile properties of the human lumbar annulus fibrosus. Acta Orthop Scand. 1967;38(Sup100):1–91.
21. Hirsch C, Schajowicz F. Studies on structural changes in the lumbar annulus fibrosus. Acta Orthop Scand. 1952;22(1–4):184–231.
22. Tandon P, Ramamurthi R. Ramamurthi and Tandon's textbook of neurosurgery. New Delhi: Jaypee Brothers Medical Publishers; 2012.
23. Scott JE, Bosworth TR, Cribb AM, Taylor JR. The chemical morphology of age-related changes in human intervertebral disc glycosaminoglycans from cervical, thoracic and lumbar nucleus pulposus and annulus fibrosus. J Anat. 1994 Feb;184(Pt 1):73–82.
24. Subhadra DV. Inderbir Singh's human embryology. New Delhi: Jaypee Brothers Medical Publishers; 2016.
25. Buckwalter JA, Pedrini-Mille A, Pedrini V, Tudisco C. Proteoglycans of human infant intervertebral disc. Electron microscopic and biochemical studies. J Bone Jt Surg. 1985;67(2):284–94.
26. Buckwalter JA. Aging and degeneration of the human intervertebral disc. Spine (Phila Pa 1976). 1995;20(11):1307–14.
27. Buckwalter JA, Smith K, Kazarien L, et al. Articular cartilage and intervertebral disc proteoglycans differ in structure: an electron microscopic study. J Orthop Res. 1989;7(1):146–51.
28. Coventry MB, Ghormley RK, Kernohan JW. The intervertebral disc: its microscopic anatomy and pathology. Part III Pathological changes in the intervertebral disc. J Bone Jt Surg. 1945;27:460.
29. Antoniou J, Steffen T, Nelson F, et al. The human lumbar intervertebral disc: evidence for changes in the biosynthesis and denaturation of the extracellular matrix with growth, maturation, ageing, and degeneration. J Clin Invest. 1996;98:996–1003.
30. Scott JE, Bosworth TR, Cribb AM, Taylor JR. The chemical morphology of age-related changes in human intervertebral disc glycosaminoglycans from cervical, thoracic and lumbar nucleus pulposus and annulus fibrosus. J Anat. 1994;184(Pt 1):73–82.
31. Demers CN, Antoniou J, Mwale F. Value and limitations of using the bovine tail as a model for the human lumbar spine. Spine (Phila Pa 1976). 2004;29(24):2793–9.
32. Wilke HJ, Neef P, Caimi M, et al. New in vivo measurements of pressures in the intervertebral disc in daily life. Spine (Phila Pa 1976). 1999;24(8):755–62.

33. Vergroesen P, Kingma I, Emanuel K, et al. Mechanics and biology in intervertebral disc degeneration: a vicious circle. Osteoarthr Cartil. 2015;23(7):1057–70.
34. Fearing B, Hernandez P, Setton L, Chahine N. Mechanotransduction and cell biomechanics of the intervertebral disc. JOR Spine. 2018;1(3):e1026.
35. Urban J. The role of the physicochemical environment in determining disc cell behaviour. Biochem Soc Trans. 2002;30(6):858–63.
36. Urban JP, Maroudas A. Swelling of the intervertebral disc in vitro. Connect Tissue Res. 1981;9(1):1–10.
37. Melrose J, Ghosh P, Taylor TK. 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. 2001;198(Pt 1):3–15.
38. Kiani C, Chen L, Wu YJ, et al. Structure and function of aggrecan. Cell Res. 2002 Mar;12(1):19–32.
39. Chan S, Ferguson S, Gantenbein-Ritter B. The effects of dynamic loading on the intervertebral disc. Eur Spine J. 2011;20(11):1796–812.
40. Ogata K, Whiteside LA. Volvo award winner in basic science. Nutritional pathways of the intervertebral disc. An experimental study using hydrogen washout technique. Spine (Phila Pa 1976). 1981;6(3):211–6.
41. Vergroesen P, van der Veen A, Emanuel K, et al. The poro-elastic behaviour of the intervertebral disc: a new perspective on diurnal fluid flow. J Biomech. 2016;49(6):857–63.
42. Iatridis J, Setton L, Weidenbaum M, Mow V. The viscoelastic behavior of the non-degenerate human lumbar nucleus pulposus in shear. J Biomech. 1997;30(10):1005–13.
43. Cortes D, Elliott D. The intervertebral disc: overview of disc mechanics. New York, NY: Springer; 2013. p. 17–31.
44. McGraw-Hill PS. McGraw-Hill dictionary of scientific and technical terms. New York, NY: McGraw-Hill; 2003.
45. Guerin HL, Elliott DM. Quantifying the contributions of structure to annulus fibrosus mechanical function using a nonlinear, anisotropic, hyperelastic model. J Orthop Res. 2007;25(4):508–16.
46. Wu HC, Yao RF. Mechanical behavior of the human annulus fibrosus. J Biomech. 1976;9(1):1–7.
47. Diamant J, Keller A, Baer E, et al. Collagen; ultrastructure and its relation to mechanical properties as a function of ageing. Proc R Soc Lond B Biol Sci. 1972;180(60):293–315.
48. Kastelic J, Baer E. Deformation in tendon collagen. Symp Soc Exp Biol. 1980;34:397–435.
49. Setton L, Chen J. Cell mechanics and mechanobiology in the intervertebral disc. Spine. 2004;29(23):2710–23.
50. Michalek AJ, Gardner-Mose MG, Iatridis JC. Large residual strains are present in the intervertebral disc annulus fibrosus in the unloaded state. J Biomech. 2012;45(7):1227–31.
51. Nachemson AL. Disc pressure measurements. Spine (Phila Pa 1976). 1981;6(1):93–7.
52. Panjabi M, Brown M, Lindahl S, et al. Intrinsic disc pressure as a measure of integrity of the lumbar spine. Spine (Phila Pa 1976). 1988;13(8):913–7.
53. Patwardhan AG, Havey RM, Meade KP, et al. A follower load increases the load-carrying capacity of the lumbar spine in compression. Spine (Phila Pa 1976). 1999;24(10):1003–9.
54. Rohlmann A, Neller S, Cleas L, et al. Influence of a follower load on intradiscal pressure and intersegmental rotation of the lumbar spine. Spine (Phila Pa 1976). 2001;26(24):E557–61.
55. Patwardhan AG, Havey RM, Ghanayem AJ, et al. Load-carrying capacity of the human cervical spine in compression is increased under a follower load. Spine (Phila Pa 1976). 2000;25(12):1548–54.
56. Patwardhan AG, Havey RM, Carandang G, et al. Effect of compressive follower preload on the flexion-extension response of the human lumbar spine. J Orthop Res. 2003;21(3):540–6.
57. Lanir Y. Mechanisms of residual stress in soft tissues. J Biomech Eng. 2009;131(4):044506.
58. Iatridis JC, Setton LA, Weidenbaum M, Mow VC. Alterations in the mechanical behavior of the human lumbar nucleus pulposus with degeneration and aging. J Orthop Res. 1997;15:318–22.
59. White A, Panjabi M. Clinical biomechanics of the spine. Philadelphia, PA: J.B. Lippincott; 1990. p. 14–5.

60. van Dieen JH, Kingma I, Meijer R, et al. Stress distribution changes in bovine vertebrae just below the endplate after sustained loading. Clin Biomech (Bristol, Avon). 2001;16(Suppl 1):S135–42.
61. Urban JP, McMullin JF. Swelling pressure of the lumbar intervertebral discs: influence of age, spinal level, composition, and degeneration. Spine (Phila Pa 1976). 1988;13(2):179–87.
62. Inoue N, Espinoza OA. Biomechanics of intervertebral disk degeneration. Orthop Clin N Am. 2011;42(4):487–99.
63. Jensen G. Biomechanics of the lumbar intervertebral disk: a review. Phys Ther. 1980;60(6):765–73.
64. van der Veen AJ, van Dieen JH, Nadort AETAL. Intervertebral disc recovery after dynamic or static loading in vitro: is there a role for the endplate? J Biomech. 2007;40(10):2230–5.
65. O'Connell GD, Johannessen W, Vresilovic EJ, Elliott DM. Human internal disc strains in axial compression measured noninvasively using magnetic resonance imaging. Spine (Phila Pa 1976). 2007;32(25):2860–8.
66. Malko JA, Hutton WC, Fajman WA. An in vivo MRI study of the changes in volume (and fluid content) of the lumbar intervertebral disc after overnight bed rest and during an 8-hour walking protocol. J Spinal Disord Tech. 2002;15:157–63.
67. Adams MA, Dolan P, Hutton WC, Porter RW. Diurnal changes in spinal mechanics and their clinical significance. J Bone Joint Surg Br. 1990;72(2):266–70.
68. Kraemer J. Dynamic characteristics of the vertebral column, effects of prolonged loading. Ergonomics. 1985;28(1):95–7.
69. MacLean JJ, Lee CR, Grad S, Ito K, Alini M, Iatridis JC. Effects of immobilization and dynamic compression on intervertebral disc cell gene expression in vivo. Spine (Phila Pa 1976). 2003;28(10):973–81.
70. McMillan DW, Garbutt G, Adams MA. Effect of sustained loading on the water content of intervertebral discs: implications for disc metabolism. Ann Rheum Dis. 1996;55(12):880–7.
71. McGill SM, Axler CT. Changes in spine height throughout 32 hours of bedrest. Arch Phys Med Rehabil. 1996;77:1071–3.
72. Reilly T, Tyrrell A, Troup JD. Circadian variation in human stature. Chronobiol Int. 1984;1:121–6.
73. Ayotte DC, Ito K, Perren SM, Tepic S. Direction-dependent constriction flow in a poroelastic solid: the intervertebral disc valve. J Biomech Eng. 2000;122:587–93.
74. Tyrrell AR, Reilly T, Troup JD. Circadian variation in stature and the effects of spinal loading. Spine (Phila Pa 1976). 1985;10:161–4.
75. Johannessen W, Vresilovic E, Wright A, Elliott D. Intervertebral disc mechanics are restored following cyclic loading and unloaded recovery. Ann Biomed Eng. 2004;32(1):70–6.
76. Oktenoglu T, ECE K. Biomechanics of the lumbar spine and lumbar disc. 2019. https://www.turknorosirurji.org.tr/TNDData/Books/426/biomechanics-of-lumbar-spine-and-lumbar-disc.pdf.
77. Tsai T, Cheng C, Chen C, Lai P. Mechanotransduction in intervertebral discs. J Cell Mol Med. 2014;18(12):2351–60.
78. Farfan HF, Farfan H. Mechanical disorders of the low back. Philadelphia, PA: Lea & Febiger; 1973. p. 13–24, 63, 90, 201.
79. Pearcy M, Portek I, Shepherd J. Three-dimensional x-ray analysis of normal movement in the lumbar spine. Spine (Phila Pa 1976). 1984;9(3):294–7.
80. Frankel VH, Burstein AH. Orthopaedic biomechanics. Philadelphia, PA: Lea & Febiger; 1971. p. 40–76.
81. Frost HM. Orthopaedic biomechanics. Springfield, IL: Charles C Thomas; 1973. p. 49–56, 146–163.
82. Roberts S, Eisenstein SM, Menage J, et al. Mechanoreceptors in intervertebral discs. Morphology, distribution, and neuropeptides. Spine (Phila Pa 1976). 1995;20(24):2645–51.
83. Pritchard S, Erickson GR, Guilak F. Hyperosmotically induced volume change and calcium signaling in intervertebral disk cells: the role of the actin cytoskeleton. Biophys J. 2002;83:2502–10.

84. Le Maitre C, Frain J, Millward-Sadler J, Fotheringham A, Freemont A, Hoyland J. Altered integrin mechanotransduction in human nucleus pulposus cells derived from degenerated discs. Arthritis Rheum. 2009;60(2):460–9.
85. Benallaoua M, Richette P, Francois M, Tsagris L, Revel M, Corvol M, et al. Modulation of proteoglycan production by cyclic tensile stretch in intervertebral disc cells through a post-translational mechanism. Biorheology. 2006;43:303–10.
86. Huang C, Gu W. Effects of mechanical compression on metabolism and distribution of oxygen and lactate in intervertebral disc. J Biomech. 2008;41(6):1184–96.
87. Wuertz K, Godburn K, MacLean J, Barbir A, Stinnett Donnelly J, Roughley P, et al. In vivo remodeling of intervertebral discs in response to short- and long-term dynamic compression. J Orthop Res. 2009;27(9):1235–42.
88. Chen J. Static compression induces zonal-specific changes in gene expression for extracellular matrix and cytoskeletal proteins in intervertebral disc cells in vitro. Matrix Biol. 2004;22(7):573–83.
89. Korecki C, Kuo C, Tuan R, Iatridis J. Intervertebral disc cell response to dynamic compression is age and frequency dependent. J Orthop Res. 2009;27(6):800–6.