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**On the effect of repetitive loading
on the spine of young elite athletes**

Clinical and experimental studies

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On the effect of repetitive loading on the
spine of young elite athletes

- Clinical and experimental studies

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abstract

Introduction: The human spine is exposed to many different loads during daily activities and especially during sporting activities. The spine has different biomechanical properties during the lifetime and thereby responds differently to repetitive and sudden loads. The correlation of different motions and load exposures to spine and back problems have not yet been fully clarified

Aim: To investigate the effect of repetitive loading of different magnitude and motion on the spine with both clinical and experimental studies. To investigate the prevalence of LBP and the amount and type of spinal abnormalities on MRI in the spine that young elite athletes in mogul skiing and long distance running are subjected to due to the repetitive loading in their sports compared to non-athletic controls. To investigate the failure and fatigue responses in young porcine Functional Spinal Units (FSU) due to repetitive loading.

Methods and results: The prevalence of LBP and spinal abnormalities were investigated in two cross sectional studies, with young long distance runners and mogul skiers compared to matched control groups with questionnaires and MRI assessment. The results displayed significantly higher lifetime LBP in runners

(45%) than the corresponding controls (12%) while no significance was seen between the skiers (50%) and their control group (42%). The mogul skiers had significantly more MRI abnormalities in mean than the control group (7.3 vs 3.8, $p < 0.023$) and no significant difference was seen between the runners and controls (5.6 vs 9.2).

The fatigue and failure response of young porcine FSUs were investigated in two experimental motion settings. The results displayed that the FSUs were resilient towards the induced fatigue loading in both axial and flexion-extension motions. The endplate and the growth zone displayed corresponding histological and MRI changes and fractures as fatigue and failure responses.

Conclusion: LBP is common among young athletes and the frequency of spinal abnormalities seem to increase with greater spinal load magnitude. Repetitive loading of the young porcine spine cause fatigue and failure responses mainly localized in the growth zone and the endplate.

Keywords: spine, intervertebral disc, athlete, young adult, low back pain, magnetic resonance imaging, porcine, repetitive loading, failure, fatigue

Sammanfattning på svenska

Ryggbesvär är ett mycket vanligt problem bland alla befolkningar och brukar bli vanligare ju äldre man blir. Orsaken till ryggproblemen är oftast svår att med säkerhet förklara. Det finns många orsaker till att få ryggsmärta och en vanlig anledning är skador och förändringar i ryggraden vilka normalt ökar i mängd med ökad ålder. Dessa kan man undersöka med olika radiologiska tekniker där Magnetisk resonans tomografi (MRT) är vanlig. Tidigare studier har påvisat att ryggproblem ofta drabbar idrottare vid ung ålder vilket kan bero på den höga och återkommande belastning som de utsätts för i sina idrotter.

För att utreda och försöka förstå utvecklandet av skadliga ryggförändringar och ryggbesvär på grund av återkommande belastningar, utfördes fyra olika delstudier där två var observationsstudier på idrottare och två var experimentella grisförsök.

Observationsstudierna genomfördes med MRT och enkäter om förekomsten av ryggsmärta hos puckelpiståkare, långdistanslöpare och två kontrollgrupper som inte idrottade. Resultatet visade att löparna (45%), skidåkarna (50%) och en kon-

trollgrupp (42%) hade ungefär samma förekomst av ryggsmärta under deras livstid, medan en kontrollgrupp (12%) låg betydligt lägre. Puckelpiståkare (7,2) hade betydligt fler ryggförändringar i medeltal än kontrollpersoner (3,8) i samma ålder medan det inte noterades någon säker skillnad mellan löpare (5,6) och kontroller (9,2).

De experimentella studierna visade att ryggsegmenten inte blev försvagade av den repetitiva hoptryckningsbelastning som de blev utsatta för vid utmattningstest och att de skador som till slut skedde var lokaliserade i tillväxtzonen och ändplattan. Upprepad framåt och bakåt böjning av griskotor visade tecken till påverkan i tillväxtzonen och ändplattan i både MRT och histologi med förändring av vätskemängd, intracellulärt och extracellulär matrix men inga frakturer.

Sammanfattningsvis är ländryggsmärta vanligt bland unga idrottare och antalet ryggförändringar verkar öka med idrottens belastningsnivå. Repetitiv belastning på unga grisryggar ger framförallt påverkan på ändplattan och tillväxtzonen.

list of papers

This thesis is based on the following studies, referred to in the text by their Roman numerals.

I. Olof Thoreson MD, Adad Baranto MD, PhD, Lars Ekström BS, Sten Holm PhD, Mikael Hellström MD, PhD, and Leif Swärd MD, PhD.

The immediate effect of repeated loading on the compressive strength of young porcine lumbar spine.

Knee Surg Sports Traumatol Arthrosc (2010) 18:694-701.]

II. Olof Thoreson MD, Lars Ekström Bs, Hans-Arne Hansson MD, PhD, Carl Todd MSc, DO, Wisam Witwit MD, Anna Swärd MD, Pall Jonasson MD, PhD and Adad Baranto MD, PhD.

The effect of repetitive flexion and extension fatigue loading on the young porcine lumbar spine. MRI and histological analyzes.

Submitted May 2016.

III. Olof Thoreson MD, Karin Svensson, Pall Jonasson MD, Peter Kovac MD, Leif Swärd MD PhD, Adad Baranto MD, PhD.

Back pain and MRI abnormalities in the thoraco-lumbar spine of elite long distance runners. A cross sectional study.

Medical Research Archives (2015): Vol.2 Issue 4, 22-28.

IV. Olof Thoreson MD, Peter Kovac MD, Anna Swärd MD, Cecilia Agnvall PT, Carl Todd MSc, DO and Adad Baranto MD, PhD.

Back pain and MRI changes in the thoraco-lumbar spine of young elite Mogul skiers.

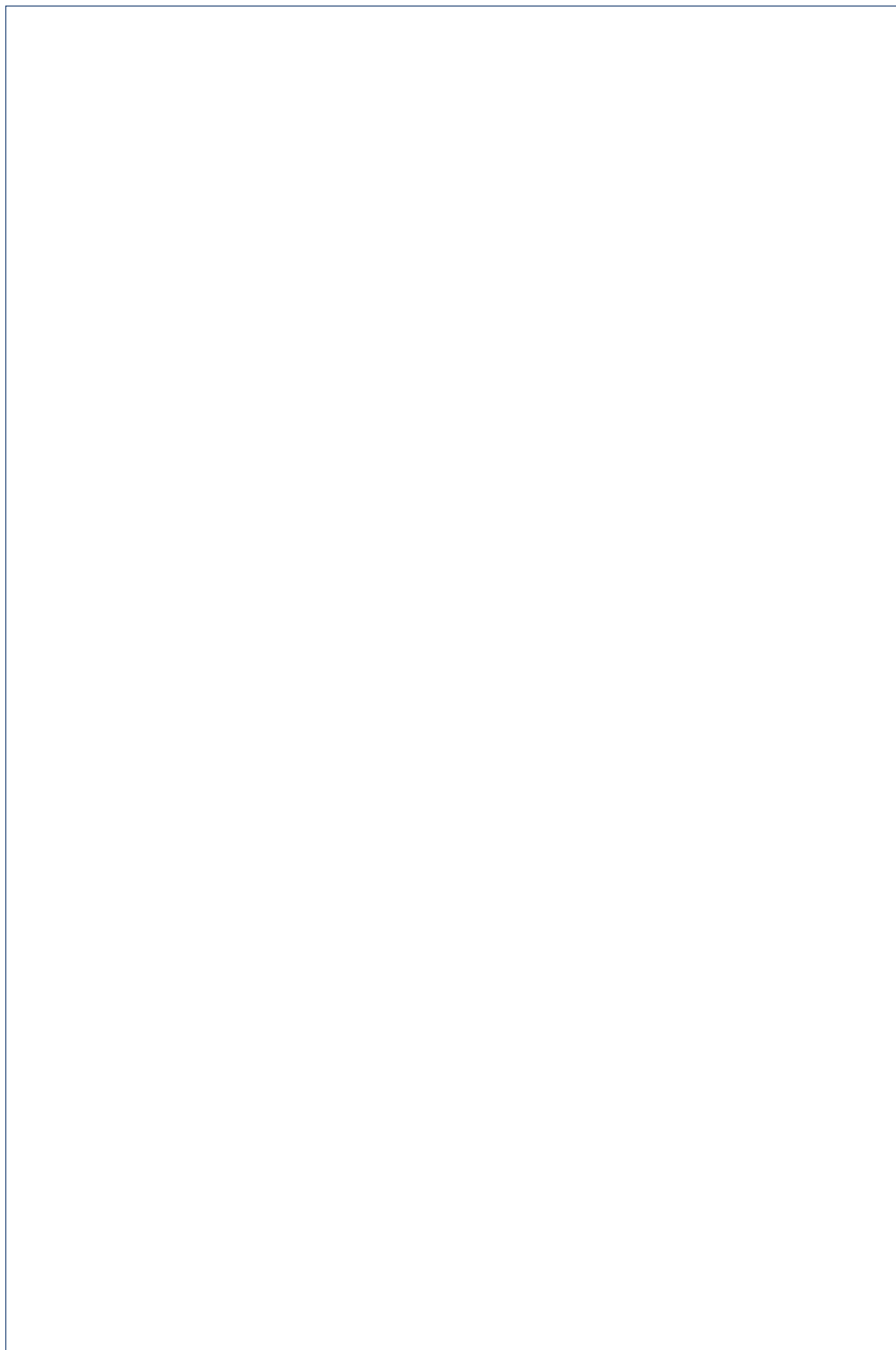
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abbreviation

NP	Nucleus Pulposus	SN	Schmorls Node
AF	Annulus fibrosus	DD	Degenerative Disc
EP	Endplate	DDD	Degenerative Disc Disease
FSU	Functional Spinal Unit	MRI	Magnetic Resonance Imaging
ALL	Anterior Longitudinal Ligament	CT	Computer Tomography
PLL	Posterior Longitudinal Ligament	SPECT	Single Photon Emission Computer Tomography
N	Newton (load)	ICC	Intraclass correlation
Pa	Pascal (pressure)	LBP	Low Back Pain
ROM	Range of motion	CLBP	Chronic Low Back Pain
CTF	Combined task force	ALBP	Adolescent Low Back Pain
ASSR	American Society of Spine Radiology	PROM	Patient Reported Outcome Measures
ASNR	American Society of Neuroradiology	EQ-5D	EuroQoL questionnaire
NASS	North American Spine Society	ODI	Oswestry disability Index
DH	Disc Hernia		

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introduction

The human spine

The development

The normal development of the human spine is mainly during three time intervals. The embryogenic period, the pediatric period and the growth spurt period. The basic spinal structure and anatomy develops during the embryogenic period. During the pediatric period further growth and development occur, such as the uniting of the pedicles to the vertebral body [1]. The vertebral growth is dependent on multiple factors but is mainly done through periosteal ossification, growth plate ossification progression and the addition of new bone tissue [2-6]

The ring apophysis is a bony ring on the vertebra that is the attachment area for the endplate of the disc. The ring apophysis develops and calcify at about 6 years of age, ossify at roughly 13 years of age and fuse with the vertebral body at approximately 17 to 21 years of age [1, 2, 7]. The endplates are the cranial and caudal parts of the vertebral body and the growth plates are located adjacent to the endplates. At the early part of the growth spurt, the central parts of the endplate grow thicker while the growth zone diminishes. A subchondral bone plate is progressively developed and forms the vertebral connection to the disc and endplate at the latter part of the growth spurt [8]. All tissues have internal changes due to ageing and the endplate change during its lifetime with a gradual transformation from hyaline cartilage to fibrocartilage [7].

The anatomy

The following summary of the lumbar spine is based upon the descriptions provided by Bogduk [9] and Baranto [10]. The normal human spine consists of seven cervical vertebrae, twelve thoracic vertebrae and five lumbar vertebrae. The sacrum is composed of five fused vertebrae, which connects to four fused vertebrae forming the coccyx. The size of the vertebral bodies increase from cervical to lumbar spine. The normal sagittal shape of the spine is a slight cervical lordosis, moderate thoracic kyphosis and a moderate lumbar lordosis [9, 11].

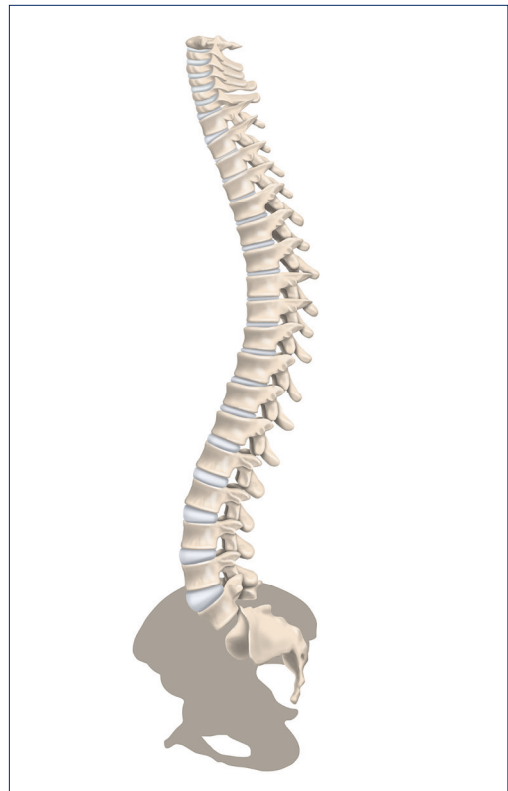


Figure 1. The gross anatomy of the human spine.

The vertebra

The adult vertebral body is the largest part of a vertebra and consists of cancellous bone in the center that is surrounded by stronger cortical bone. The upper and lower surfaces of the body connects to the hyaline endplates of the discs and are surrounded by the ring apophysis, which is an elevated bony rim or ring in young individuals. The vertebra is connected pos-

teriorly with the paired pedicles, laminae, transverse processes and a midline dorsal spinal process. Each vertebra connects to the corresponding vertebra through the disc and the two facet joints. A functional spinal unit (FSU) and motion segment are terms often used in research and refers to the two adjacent vertebrae including the corresponding disc in between [9, 10, 12].

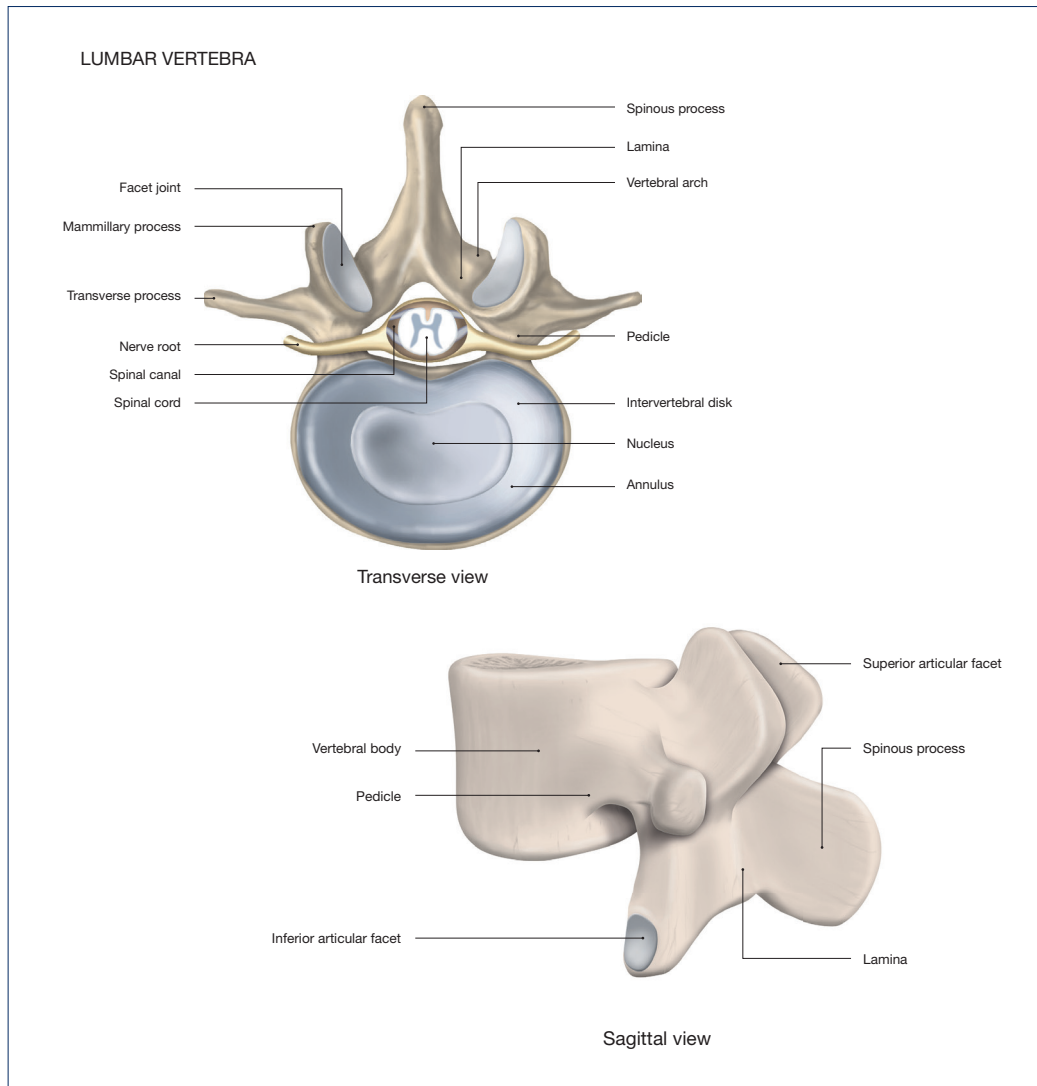


Figure 2. The anatomy of the vertebra, transverse and sagittal view.

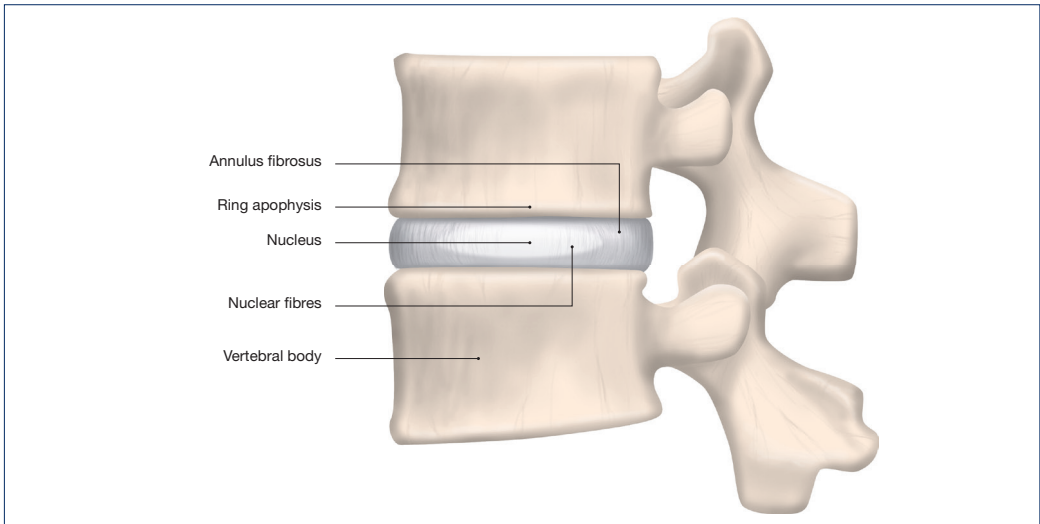


Figure 3. A Functional spinal unit.

The intervertebral disc

The disc is a very complex and heterogeneous tissue that connects the vertebral bodies [13, 14]. The disc is traditionally divided into the central nucleus pulposus (NP), the circumferential annulus fibrosus (AF) and two hyaline cartilage endplates (EP). The disc is a strong tissue and can withstand and transfer heavy loads and accommodate movement of the spine. The disc supports heavy loads through

hydrostatic pressure that causes bulging of the NP towards the EP and the AF (figure 6). The different tensile properties of the disc components makes it capable of bearing the loads on the spine [15]. The disc components differ in many ways such as different proportions of collagen, where the AF consists of Collagen I, which has strong tensile properties while collagen II mainly, binds water and is more dominant in the NP [9, 10].

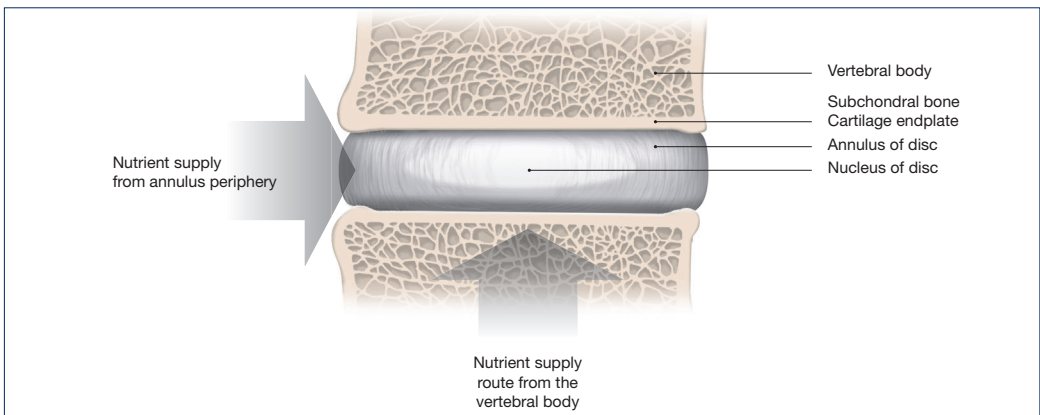


Figure 4. The intervertebral disc.

Annulus Fibrosus

The AF is attached to the vertebra mainly at the ring apophysis [1, 2, 16] but is also embedded in the cartilaginous endplate. The AF is thicker anteriorly and more finely posteriorly [17, 18]. The AF consists of highly organized collagen fibers called lamellae [9], which intricate, concentric and cross-over integration makes it possible to withstand great strain from the NP

during physiological loads [14]. The lamellae is surrounded and embedded among the intra and inter-lamellar matrixes that are connective tissue containing proteoglycans, elastin and collagen [19-21]. The intra-lamellar matrix connects the collagen fiber bundles within each lamellae and the inter-lamellar matrix lies between the different layers of annulus [21].

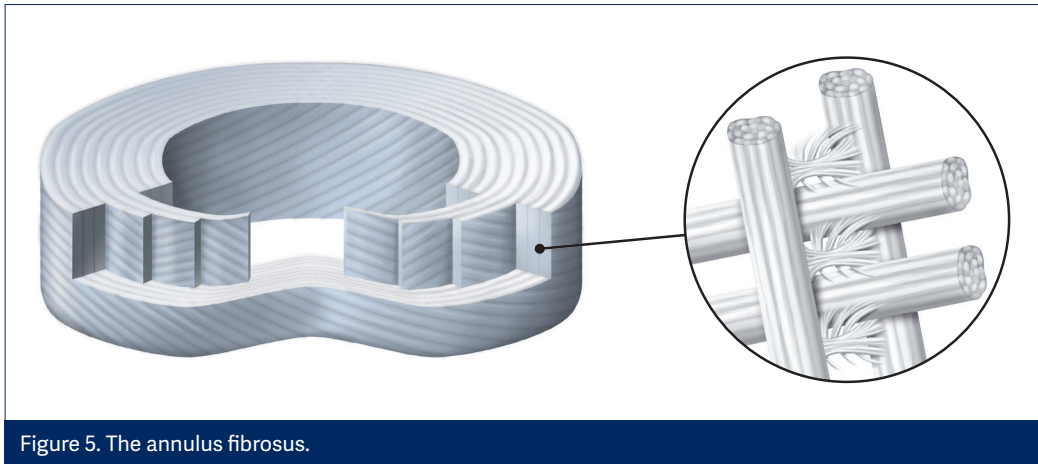


Figure 5. The annulus fibrosus.

Nucleus Pulposus

The NP contains up to 80-90% of water which accounts for the majority of disc volume [22, 23], but also of glycosaminoglycan, collagens and non-collagenous proteins that contribute to NPs hydrostatic and viscoelastic properties [24, 25]. The nucleus contains a structured network of fibers, which is believed to integrate with both the AF and the EPs and thereby support physiological functions [21, 26, 27].

The vertebral endplate

The EP is a 0.6-1 mm thick layer of hyaline- and fibrocartilage that alters by age and covers the superior and inferior surface

of the vertebra [28, 29]. The endplate integration into the disc is through a three-dimensional branched morphology of the annular fibres creating a very tensile and shear stress strong tissue connecting the annulus with the calcified cartilage of the endplate [30]. The area of the EP is the load bearing structure and is thereby important, and the adult fourth lumbar vertebra area is around 1500 mm² [31].

Nutrition and innervation

The disc is largely avascular but small branches from the metaphyseal arteries connect to the outer parts of the AF. [7, 24, 32]. The central part of the disc is nour-

ished by diffusion through the EP and the outer margins of the AF. Innervation of the intervertebral disc is primarily from the meningeal or sinuvertebral nerves that also innervate the posterior longitudinal ligament [33].

Ligaments

The spine is surrounded by muscles and ligaments that regulate the spinal posture. The anterior longitudinal ligament (ALL) extends along the anterior and lateral parts of the whole spine and stabilize the spine by resisting hyperextension. The posterior longitudinal ligament (PLL) extends within the vertebral canal in the spine and connects laterally to the posterior parts of the discs. The PLL gives the spinal cord a mechanical protection and resists hyperflexion of the spine. The elastic ligament flavum connects the corresponding lamina and helps the spine to return to resting posture after movement or loading. The interspinous ligament, connects the adjacent spinous processes and the posteriorly located supraspinous ligament bridges the interspinous spaces. The flavum, interspinous and supraspinous ligaments limit mainly flexion of the spine together with ALL [9, 10].

Biomechanics of the human lumbar spine

Biomechanical evaluation can be used to quantify loading and movement acting on a biological structure and to analyze load distributions and correlate these to injury mechanisms and thereby give evidence to potential therapeutic interventions [34, 35].

Tissue properties and material functions

All biological materials have mechanical properties related to their inherent properties. Deformable bodies, such as all human tissues, have elastic, plastic and often viscoelastic properties. The elastic properties of a material are the capacity to recover to the original form after a load that caused the deformity has been removed. Plasticity is the phase where load is applied beyond the elastic limits and even if the structures ability to withstand a load is maintained, the structure is altered and permanent shape deformation remains. Viscoelasticity reflects a time dependent property and is best exemplified by constant load acting over time on a material containing fluids, causing a flow of fluid potentially resulting in deformation in relation to the materials resistance capacity in a complex process [34]. Viscoelasticity is exemplified by the diurnal changes in disc height, due to load and positional changes [35].

Stiffness is a materials capacity to withstand an applied force without deformation and is the inverse of compliance, which is the ratio of strain to stress. The stiffer an object is the less elastic it is. Stiff-

ness is the property of a structure and dependent on the material and the shape of the structure. The property of a material is the E-modulus, which is derived by the stress-strain relation within the linear region in the stress-strain data diagram and is not altered by shape [36]. Many tissues are complex and do not display linear stress-strain relationship and thereby do not display a constant E-modulus which generates approximated E-modulus in the literature, and the same tissue can in different settings display different E-modulus [34].

Load, pressure, strain and hysteresis

Load is a force that has a magnitude and direction and is best described by vector mathematics. The load mode is usually described as in compression, tension or shear dependent to its direction in relation to the structure. When load is applied to a specific area, a stress is created. Stress is defined as the amount of load divided by the area that it is loaded upon and is described as force / cross sectional area, N/m² or in the case of a fluid or a gas, pressure Pascal (Pa) [34]. Strain is the amount of deformation change of a tissue in relation to its original shape, due to an applied load or stress [34].

Materials can exhibit different load capacities dependent on stiffness, elastic deformation, plastic deformation and ultimate strength properties. In general all materials have an initial elastic phase followed by a plastic phase during increased load until the material strength is exceeded and ultimately failure occurs [34]. Materials that are loaded within their elastic capability

can return to their original format given sufficient unloading. The restoration process have often a different rate compared to the stress-strain curve and is referred to as hysteresis [35].

Properties of the spine

The biomechanical properties of the spine are derived from experimental studies of its macro-structural and micro-cellular anatomy and physiology. The vertebra is a complex viscoelastic material, consisting of different kinds of tissues and each have specific mechanical properties, depending on several variables such as internal location in the spine and external loads. Load magnitude, angle, duration and velocity all affect the biomechanical properties of the spine [34].

One of the main functions of the intervertebral discs is to distribute the axial

loading stress to the vertebral bodies. The annulus fibrosus is mainly subjected to tensile stress from the pressurized nucleus pulposus but can also withstand rotation and some compression when the nucleus is reduced due to injuries or age. The discs are also subject to extension, flexion and rotational movements but these movements are mainly reduced and regulated by other structures such as the facet/apophyseal joints [35].

The biomechanical properties of the spine is influenced by many factors such as genetic, gender, loading exposure, d-vitamin levels and it seems that the genetic factor is probably the most dominant. The stiffness of the spine depends mainly on the area and size of the endplates but also of individual factors, such as bone mineral content (BMC) and earlier tissue changes and injuries [35, 37].

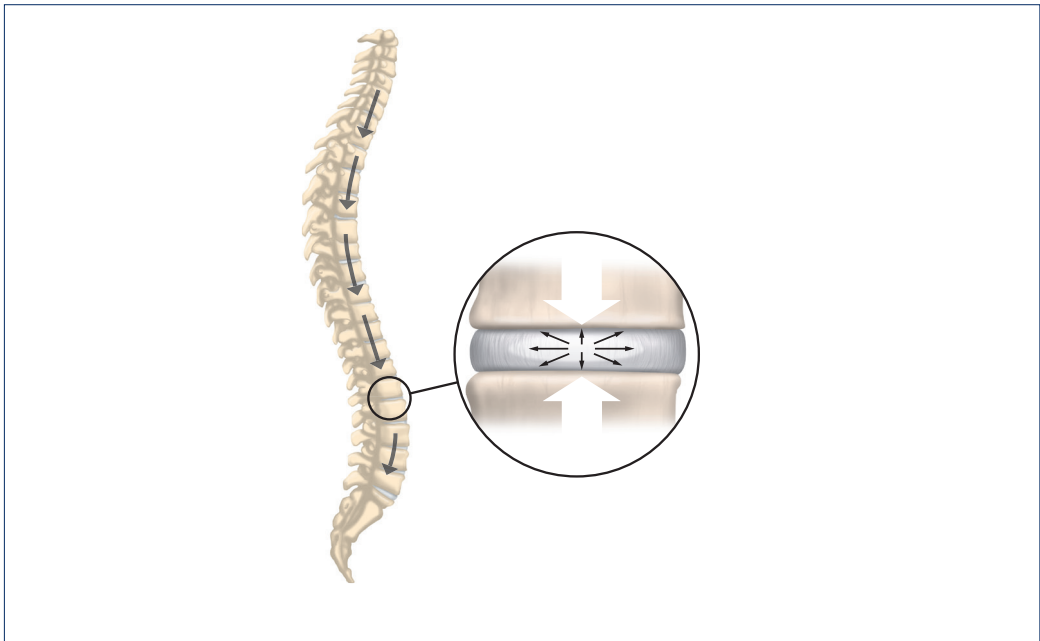


Figure 6. The axial load distribution in the spine.

Ageing and spinal biomechanics

Ageing affect may decrease many of the biomechanical properties of both the vertebrae and the intervertebral disc. Reduction and destruction of proteoglycans lowers the water binding capacity of the nucleus and increases stiffness in the disc. Cartilage and tendons are at higher risks of injury due to a reduction in the collagen cross-linking. The cartilage is also affected by mechanical weakening where the cell density is lowered thereby reducing the load capacity of the disc [35]. Ageing also affects the skeleton, especially among women, with a reduction of bone density [38], reduced ultimate strength and also stiffness changes [39]. The facet joints are affected by age with an increased risk of arthritis and tropism affecting both the load bearing potential as well as the ROM. The ageing effect on the disc is very much similar to the result of disc degeneration and it is difficult to differentiate between these two conditions. The increased stiffness in the disc is correlated to an initial increase of compressive ultimate strength [40] and an increased vulnerability towards shear stress, with a continuous decline of capacity during further age deterioration of the spine [41].

Loading and spinal biomechanics

Loading of the spine is vital to maintain and strengthen the biomechanical properties. The nucleus and inner parts of the annulus are affected by loading and adapts accordingly through proteoglycan and collagen differentiation that regulates the inner matrix stiffness [42]. However, several studies have shown that aggravated levels of loading causes a risk of fatigue and failure injuries in the disc and vertebrae [43]

and insufficient loading cause the bone, muscles and cartilage to successively deteriorate [35, 34].

Spinal Failure load

Failure load is the load that is required to cause failure of a structure to withstand further load. Failure strength is the structure's maximum capacity to withstand the load and in compression loading sometimes referred as ultimate compressive strength [34]. The ultimate compressive strength of FSUs has displayed a great variability in the results of human cadaveric failure force studies and values in the range of 3-10 kN have been reported with even a wider range among porcine studies [45-53].

The failure load is dependent on tissue size and properties and altered by load magnitude, velocity, frequency and total load duration [35]. Different predictors have been used as determination of failure load such as loss of disc height, deformation of the disc, and disc pressure reduction.

The majority of all in vitro tests are done through axial compression and the most common place for failure stress are fractures located through the endplate or the vertebral body [54-59]. When the disc is subjected to more complex loading patterns, different failure location patterns are seen that can also vary dependent on internal factors such as age. By inducing compression together with repetitive flexion and extension loading, the number of disc hernias (DH) as failure patterns are increased among adult FSUs [60] while growth zone fractures have been seen among younger FSUs [61].

Fatigue

Fatigue is the weakening of a structure due to repetitive applied loads. This reduces the ultimate strength and may alter the material properties. Fatigue strength is a structure's capacity to withstand load at a spe-

cific number of load cycles [34]. In FSUs it is believed that the biomechanical fatigue is associated with plastic deformation that usually is displayed as annular separation, endplate micro-cracks and also an alteration of the ultimate strength [41, 51].

Experimental models

Animals and cadaveric FSUs have been used in many different experimental models in spinal research. Common animals are pig, sheep, deer, dog, calf and goat despite the fact that none of them exhibit human bipedal locomotion. The obvious differences in body composition does not necessarily relate to differences in spinal loading due to high muscle contraction in order to stabilize the spine in the quadruped position [62, 63]. When comparing segmental range of motion (ROM) most animal lumbar spine models have less rotation, extension and flexion compared to the human lumbar spine, which is also seen in pig models. The facet joints are steeper in the lower lumbar region of the pig and thereby reduce any rotation and translational motions [64, 65].

The pig spine

The porcine lumbar spine and the human lumbar spine have many similarities regarding biomechanical behavior and structures. The porcine spine has similar stiffness regarding both compression and shear as the human spine. The similarities are at most for young pigs and decrease with age [66-71]. A review of the spinal morphological properties showed that no specific animal model is ideal, but thoracic and lumbar porcine spinal models are considered suitable

animal models [72].

Among the anatomical differences are that the porcine lumbar vertebrae are higher but the EP area is smaller [73], and has bony EP in contrast to the human cartilaginous EP. The posterior structures (transversal, dorsal processes and muscles) of the porcine spine is of a larger dimension compared to the human structures due to the quadruped position of the pig. The adolescent porcine have more growth zones than the human vertebra, with two sagittal growth zones and one also located between the bony endplate and the vertebral body (Figure 7). An important difference is that the porcine spine does not have ring apophyses but instead an epiphyseal plate covering the growth plate. The pig vertebra is generally denser in bone and therefore the fracture location in young human FSUs and porcine may differ, even if similar fracture and failure patterns have been reported between human and porcine spines [71, 74]. The porcine disc is a common experimental model for disc degeneration studies [65, 75] due to the fact that it responds to axial loading [76] and torsion [77] in the same way as the human discs. The porcine lumbar discs have many similarities to the human disc [71] such as content of water [78], proteoglycans [76] and collagen [77] but differ in size [64].

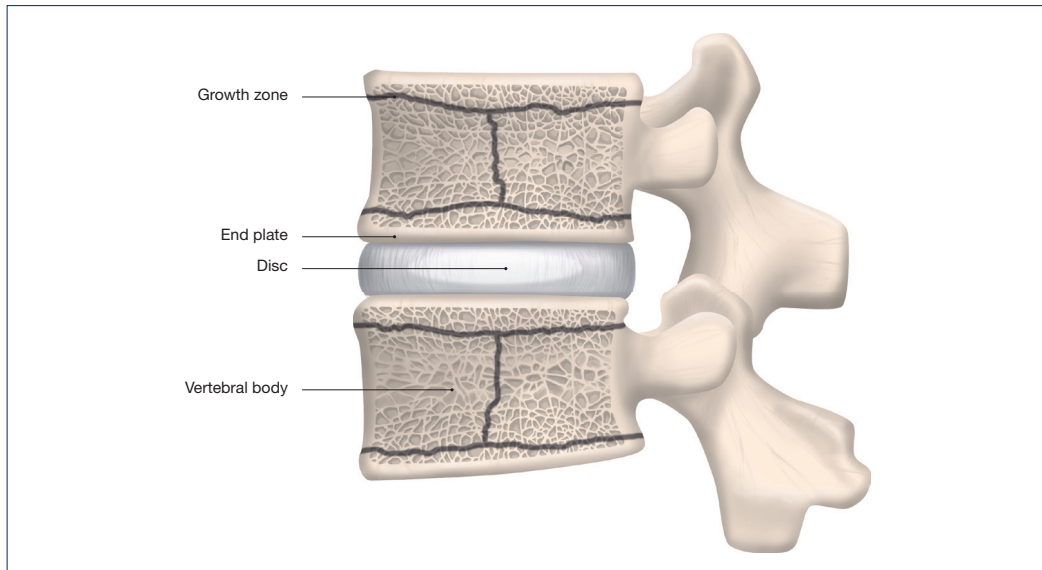


Figure 7. The growth zones of a porcine FSU.

Load magnitude

The Gold standard of the human in-vivo disc loading magnitude, was established by Nachemson et al. (1981) by results from a pressure sensitive needle inserted in the nucleus pulposus in healthy volunteers [79]. Further studies have displayed in general similar results [80, 81]. The Human

lumbar intradiscal pressure in an upright position is around 500 kPa that equals 0.5 MN/m² [81]. The pressure does not change much between standing and sitting but increases when more complex movements, such as flexion, are performed and when external loads are attributed [79-82].

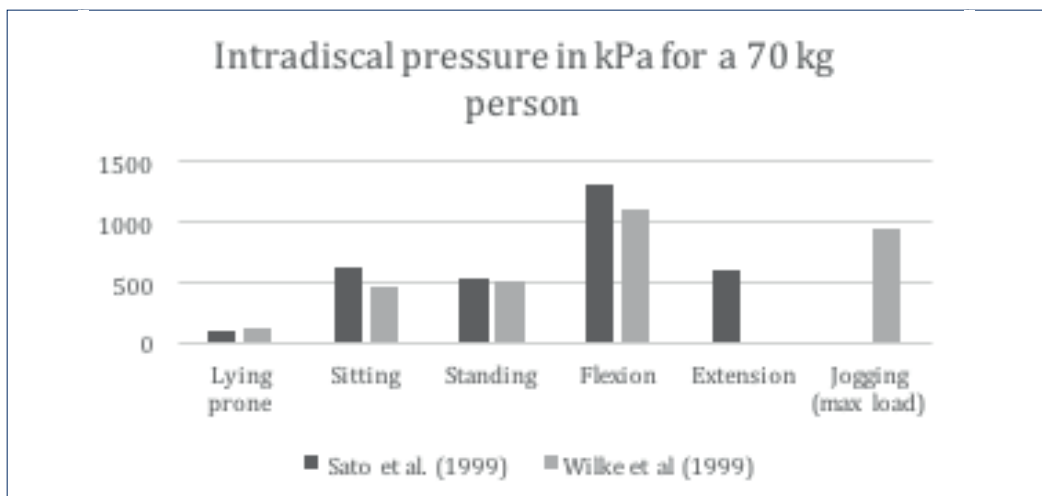


Figure 8. Intradiscal pressure in kPa.

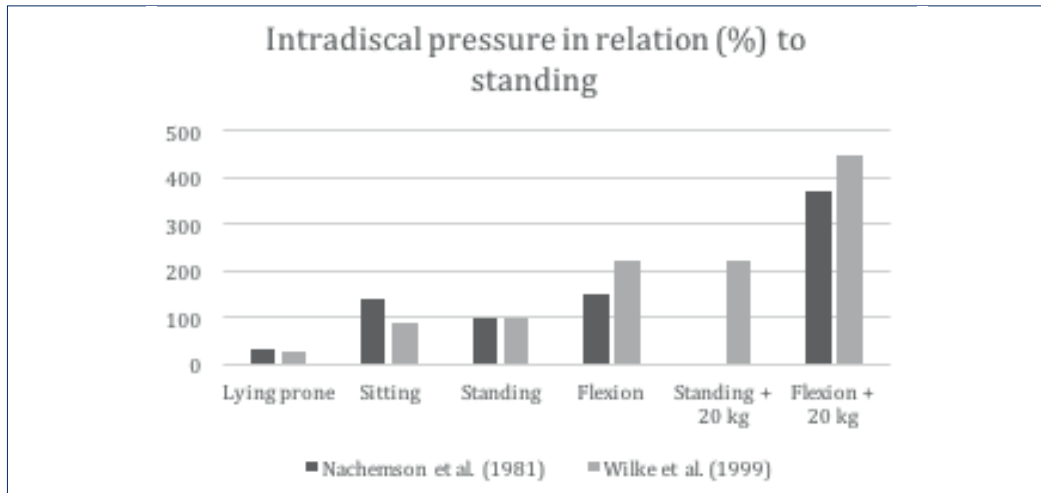


Figure 9. Intradiscal pressure in relation to standing.

The basic erect position has been estimated and correlated to an axial loading of around 500 N in many experimental study designs [51]. In studies of repetitive loading many different magnitudes are used but a widely used magnitude is 1500 N that is correlated to the lift of a 10 kg load. Experimental studies concerning axial loading have displayed high variations of spinal ultimate load in both human and porcine FSUs and typically range between 2-14 kN [45-53].

Load frequency

Load frequency refers to the number of a load cycles per second expressed as Hertz (Hz). The most normal repetitive load is the walk, and a normal walking frequency is around 2 Hz [83]. A normal stride frequency during running is around 1.4 Hz [84, 85]. In other daily activities, the load frequency differs due to external impact, such as among drivers in Sweden and USA where the mean frequency in a study was 4.5 Hz [86]. Work conditions with substan-

tial lifting implementation seldom consists of more than 15 lifts a minute [87] and the American industrial guidelines for lifting consider more than 6 lifts a minute as high frequency lifting.

The load frequency affects the viscoelastic properties in the spine, especially the discs which are affected by the rate of applied loads and can contribute to both fatigue and failure injuries [34]. Fatigue strength studies reported in the literature show the axial loading frequency in the cadaveric spine to range between 0.25 - 5 Hz. This high heterogeneity among the experimental studies yields different study endpoints [88].

Load duration

The spine is always under load since the muscle contraction of the spine is always active [79]. Other internal and external load patterns are though variable and different due to load exposure. The cumulative load time is the combination of the

load frequency and total exposure time. A normal distance covered in soccer and Australian football is around 10 km but at different speeds, loads and stride frequencies during 90 minutes correlating to a high variation of load duration among the players in the same game [89, 90]. In experimental tests with axial compressive fatigue loading the general duration has been shown to be between 1000 to 1,290,000 cycles with a mean of around 10,000 cycles [88].

Load rate

Load rate is the magnitude and the direction of a load movement divided by loaded time and affects the viscoelastic properties of the spine [34]. Load rate can affect the stiffness and the failure pattern of FSUs where higher compressive load rate correlates to increased stiffness and a change of failure characteristics. Studies have displayed increased failure strength with an increased rate and a change from intervertebral disc failure to vertebral failure [91, 92] while other have displayed that the AF or the AF-EP junction are the primary failure locations of sudden impact at a high rate [47].

Post load rest and remodelling

The spine is in normal daily living subjected to a variety of different loading and has the capacity to remodel in response to loading according to Wolff's law. This is a procedure dependent on the previous load and duration but with normal daily load the remodel process needs several hours of reduced loading to achieve adequate remodeling [93]. In clinical tests the total rest is crucial for the risk assessment

of successive low back function reduction [94].

Load direction and motion

The load can be applied in an almost infinite number of positions/directions, however an axial compressive loading is the most common due to its neutral position in normal standing. This loading mode can be complemented by flexion, extension, lateral bending, axial rotation and a combination of these [95]. The interpretation of a more complex loading pattern is somehow challenging and clear conclusions might not be feasible [34]. Different loading regimes and directions give rise to different stress-strain reactions. The loading of the spine causes several adaptations in the spine such as nucleus flow and central location migration in the disc in relation to load regime, where extension causes forward migration and lateral flexion causes migration of NP to the opposite side [96, 97].

The main movement of the spine is located at the cervical and lumbar area. The lumbar facet joints permit flexion, extension and lateral bending, but resist rotation due to both size and facet orientation. The thoracic vertebrae articulate with the heads of the ribs and have reduced range of motion in flexion, extension and lateral bending but allows some rotation. Many studies have discussed the range of motion (ROM) in the spine and results imply that the ROM is generally higher among females and varies between spinal levels for flexion-extension, lateral bending and axial rotation [98].

Axial loading

Axial compression is the axial loading of the spine. The normal static axial compression is the upright position and the normal repetitive axial compression is in walking. Different loading regimes correlate to different loads and different intradiscal pressures [79]. A healthy nucleus is the dominant factor in axial loading where the loading patterns change with disc height reduction such as in degenerated and ageing discs. The diurnal changes in the disc can cause up to around 2 mm decrease in height and 16% of disc volume in the lumbar discs that also alter the loading patterns accordingly and could correlate to diurnal symptom patterns of LBP [99-102]. Other structures that contribute to bear the axial load are the AF in degenerated discs, and the facet joints in the lordotic position [103]. When subjected to compression the FSU may be injured if the ultimate strength is exceeded. The failure injury is dependent on the status and age of the FSU. Experimental studies have displayed that the endplate and growth zone are the weakest part among young FSUs [40, 104] and DH and vertebral fractures are more common with increasing age [59].

Flexion

The normal flexion of the spine has been investigated by Adams et al. [105] through 27 healthy volunteers. The maximum lumbar flexion has been evaluated for 27 healthy adult males by plain radiographs and was in mean L1-2 8.3° (± 2.6), L3-4 11.7° (± 2.2) and L5-S1 10.1° (± 4.9) but displayed great diversity in both the same subject as in between subjects. The flexion-extension ROM seem to in general increase with

lower lumbar segmental levels [98].

Flexion can when combined to a load give rise to high intra-discal pressure and causes failure injuries such as DH [105, 106], EP and growth zone injuries [61] dependent on age. Hyperflexion can also cause injury of the dorsal structures and the facet joints [35]. The collective effect of repetitive flexion is believed to cause DHs even at low load magnitudes but the risk increases with higher load magnitudes [60]. Gallagher et al. (2005) displayed that different flexion angles give rise to different failure responses due to changes in stiffness [58]. The age of the FSU seem to be of great importance where young FSU subjected to flexion and compression are more likely to be injured in the anterior growth zone [61].

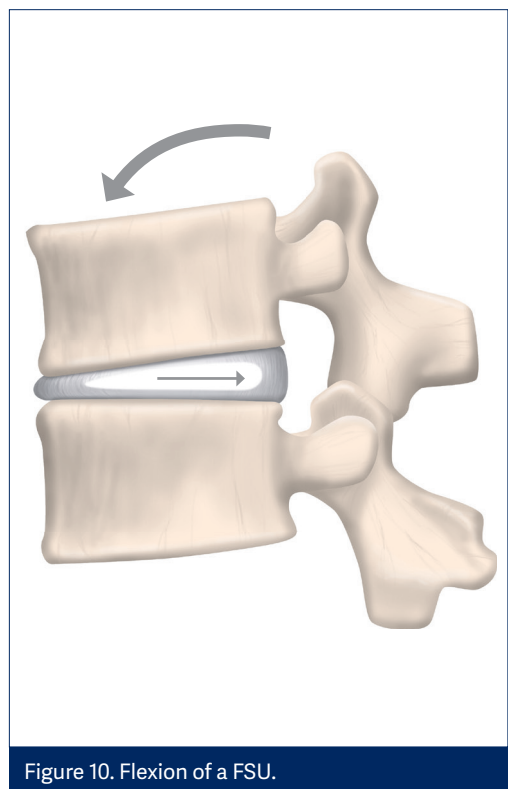


Figure 10. Flexion of a FSU.

Extension

Extension of the spine is limited due to anatomical reasons. The disc and the dorsal spinal anatomy including the posterior processes, mainly the facet joints all may influence extension motion and can in turn be affected and injured by repetitive or extreme extension movements [107]. Extension can cause high intra-discal pressures, where the maximum intra-discal pressure for healthy discs were measured at 2° extension but varied due to disc condition and level of extensions [108]. Extension and compression have been displayed to cause posterior growth zone fractures in young FSUs [61].

Repetitive extension has been used as a treatment for low back pain [109]. Potential positive treatment response could be due to increased disc height [110] and anterior relocation of the nucleus in the disc [111]. An experimental study have also displayed the possibility to relocate flexion-compression induced DH back into the disc [112].

Lateral bending

Lateral bending is the lateral flexion of the spine. In experimental models the flexion and lateral bending alters the disc failure process by changing the direction where the nucleus tracks through the annulus, influencing the development of lateral DH [113]. The ROM of lateral bending has been presented to be around 10° and is generally spread throughout the lumbar spine [98].

Rotation

Rotation is created by a sophisticated ar-

ray of muscle activation and relaxation, which provides a total axial trunk rotation of up to 70° to each side [114, 115]. Trunk rotation has been shown to alter when in combination of different levels of flexion and extension. The spinal rotation for each lumbar segment has a maximum rotation around 3-4° [116, 117] with the highest ROM in the L3-5 segments [98]. The rotation is dependent and altered by the disc and the facet joints where the load distribution is reliant on body and spinal posture and movement [118, 119]. Rotation has in many studies been suggested to be a risk factor for both vertebral and disc injuries and LBP but has also been suggested to reduce both vertebral and disc load [46, 97, 118, 120].

Experimental models have displayed that axial rotation has been correlated to alteration in fatigue and failure responses that reduce the compressive strength of porcine FSUs [113] and increase the risk of intervertebral disc injuries and facet joint injuries when accompanied by flexion movement [46].

Combination of movements

The spine has in many studies been the most at risk for failure injuries when induced by a combination of complex movements and loads. It has been suggested that the weakest part of the adolescent spine are the growth zone and endplate that are at the highest risk of injury failure due to both compression and flexion-extension motions but also to combinations of motions [10]. In the adult spine the endplate and vertebrae are at risk of compressive loading as the annulus and nucle-

us are more affected by combinations of movements and fatigue generated injuries [35].

Repetitive loading

Repetitive loading can be altered in frequency, magnitude, duration and mode of movement. The spine is subject to many repetitive loads during each day that give rise to different stress-strain effects of the vertebrae, disc and annulus and may cause fatigue and failure differentiation [34]. The basic repetitive load effect is the diurnal changes such as the diurnal disc height reduction [102, 121]. This and other biomechanical adjustments cause changes in the elastic properties that can be seen clinically such as the disc becoming more flexible after 3 hours of walking. Moreover, this has been shown to correlate with disc height reduction, higher compressive stiffness and flexion elasticity [99, 101]. Flexion loading affects the nucleus location in the disc, fatigue and failure of the disc and the orientation of the DH. Repetitive loading in the neutral or static flexed position seem to mainly affect the endplate or vertebral body as failure location [51] and can transmit small cracks within the vertebral bone [43]. Repetitive flexion and compression is suggested to cause DH [35, 60].

Repetitive loading and nucleus fatigue

Repetitive loading on the nucleus affects the viscoelastic properties of the nucleus and creates a flow that alters the water content in the nucleus, which correlates to diminished disc height and volume but increased stiffness. If the loaded magnitude is sufficient the pressure within the disc overcomes the tensile properties of the an-

nulus a potential failure can occur such as DH or endplate fracture. Repetitive bending or flexion movements cause the nucleus to move within the disc, which also alters the loading properties of the spine [96, 97, 111].

Experimental studies have displayed that the compressive strength of an FSU is dominated by the nucleus rather than the annulus. Degenerated or injured discs have in studies shown to have less resistance towards repetitive loading [57] but other studies have displayed higher failure strength among degenerated discs [40].

Repetitive loading and annulus fatigue

Repetitive compression has been linked to a more tensile annulus, potentially through destruction of the elastin, and the same study group could also display a causal correlation between repetitive compression and the occurrence of DH [122, 123]. Repetitive cyclic loading of the annulus has been described to increase the risk of flexion fatigue injury to the dorsal parts of the annulus through a process that starts with bone and cartilage separation and ends with the peripheral annular fibers pulling out of the matrix, and is correlated to the load magnitude [19].

Experimental biomechanical studies

Experimental studies regarding biomechanical properties and injuries have been studied throughout many decades [124]. There is great diversity among the study protocols mainly due to different study settings but the majority of the protocols relate to fatigue and failure properties of the spine. Experimental studies are in general either done with cadaveric FSUs [48, 51, 54, 57, 59, 92, 125-138] or with animal FSUs where porcine is a common model [40, 46, 47, 49, 50, 52, 53, 61, 69, 139]. There is a wide diversity in both cadaveric and porcine studies regarding what level of the spine that the FSUs are generated from and age differences among the specimens that both increase the diversity of the ki-

nematic and biomechanical properties as well as the fatigue and failure responses. Other facts that need to be considered are gender, size and loading orientation of the spine especially with regards to the loading axis according to the spinal sagittal alignment [134, 135].

Load Protocols

The different load protocols addresses different fatigue and failure mechanisms and are in general either compressed with static or repetitive load to failure in different motion, frequency, magnitude, duration and velocity settings. The most common set ups are compression and flexion motions, but lateral bending, rotation and different combinations have also been evaluated.

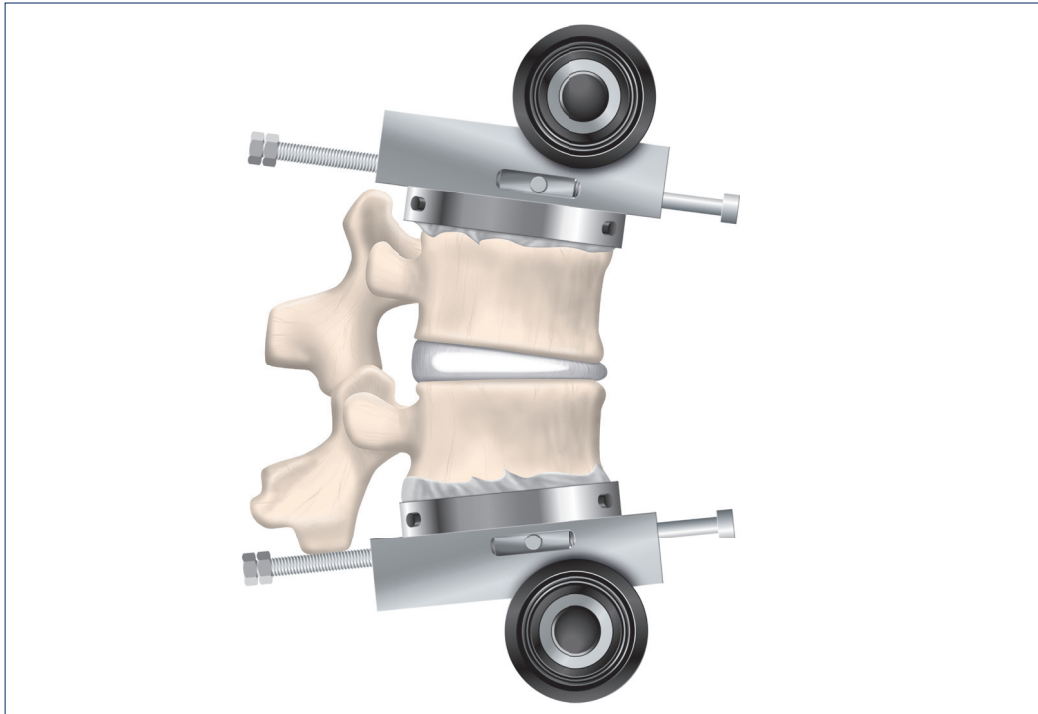


Figure 11. An experimental flexion set-up.

Preload

Preload is used in many studies to resemble the basic load the spine is subjected to due to posture and muscle contraction, where the relaxed supine position gives rise to 0-500 N [79]. The preload can also be adjusted to theoretically resemble other desired loaded starting situations of the experimental study. The normal internal spinal muscle contraction and torso weight is in many studies set to 300 N, which is then often chosen as preload [46, 50].

FSU failure sites

There are several FSU failure sites where endplate fractures, vertebral fractures, annulus injuries and DH are most common. Endplate, ring apophysis and vertebral fractures

Endplate, ring apophysis and vertebral fractures

The endplates and growth zones of young human and porcine vertebra appear to be the weakest aspects for high compression load and pressure in the nucleus. Experimental models [104, 140] have shown an increase in disc pressure transfers to the endplate, which cannot withstand the load and therefore a fracture develops as failure response [140]. The annulus fibers are connected to the endplates through calcified cartilage and not the underlying bone that could be the reason why this is the weak link especially for adolescents where the calcifying is not thorough [30]. Among the fully grown and elderly, reduced bone structure of the apical vertebra may be a reason for an increased risk of EP injury in the apical vertebra in relation to the affected disc [128].

Apophyseal injuries are common among adolescents and especially adolescent athletes who are subject to high loads that increase the pressure in the NP and subsequently cause injury [141]. This has also been displayed in experimental settings with young porcine FSUs [40, 61]. The high load causes the NP to penetrate the endplate and fracture through the growth zone of the vertebrae and releasing the unfused apophyseal ring that is still attached to the AF through Sharpeys fibers and the PLL [12, 140].

Experimental studies have also displayed that vertebral fractures are common as failure location mainly when compressed in the neutral location or in static flexion [51]. The growth zone has earlier been displayed as the weakest part of the vertebrae which could correlate to the increased prevalence among younger individuals [61]. In an elderly population, the vertebra may be the weakest link of the spine due to a reduction of BMC and increased stiffness in the disc due to DD [127, 130].

Disc hernias

Disc hernias are due to many factors but have been displayed as failure due to the cumulative load of complex motions in primarily adult FSUs experimental studies. Flexion, extension, rotation, compression, lateral bending and combinations of these movements all contribute to disc failure [46, 50, 60]. Flexion and compression simultaneously seem to be the most important load to create DH [106] where the flexion axis may also can alter the direction of the hernia [142].

When repetitive loading of adequate mag-

nitude is induced upon the spine, fatigue reactions are developed in the vertebrae, annulus and the nucleus. The annulus turn more elastic and damage occurs between the annulus and the bone [19]. High intra-discal pressure increases the tension in the weakened annulus which makes it possible for the nucleus to advance through clefts in the annulus lamellae and if favorable loading motion and magnitude continue, DH will protrude [49, 60]. The DH cascade and other disc changes may sometimes be preceded by endplate failure which can be seen in apophyseal injuries [125, 126]. DH reduces the disc height and alters the biomechanics of the disc causing increased range of motion and reduced stiffness [143].

An impact load can also create DH where the failure response is dependent on the rate of the impact. A high load rate in an impact load, which is thought to give rise to high stress in the AF-EP junction, especially in flexion, where micromechanical imbalance occurs between the soft tissue of the AF and the more bony tissue of the EP. This may become a cause of potential injury as a rupture of the AF and DH may

occur [47].

Cadaveric studies

Experimental studies with cadaveric FSUs are common, and well established [124-128, 131, 133-135, 137, 138]. The use of cadaveric FSUs have the advantage of human tissue but are usually older specimens with DD and thereby correlating to the biomechanical properties of adult or elderly degenerated FSUs where not only size is important but also BMC. The failure strength in cadaveric studies range generally between 1,5-10 kN [51, 92] but quite many studies display results between 3 - 6 kN [54, 127-132] dependent on loading protocols and individual factors of the FSUs where age seem to be the most important factor. The most common fatigue protocols with repetitive loading have a frequency between 0.25 - 5 Hz in different motion settings. The fatigue limits and correlation of total accumulation of load to failure and failure location have been investigated in different settings and experiments but no general rule or equation has been established. Different study protocols of cadaveric FSU studies are displayed in table 1.

table 1 Overview of examples of experimental cadaveric study protocols.

Study	Year	Age mean (range)	Level of FSUs	Load	Angle	Hz	Duration/cycles	Magnitude	Pre-load	Result
Perey [124]	1957	(20-90)	T12 to L5	Sudden compression	0	167	1	12 000N	250 N	Failure, location.
Brown et al. [132]	1957	NA	NA	Static compression	0	-	10-30 min	4450 - 5780 N failure	-	Creep is sustained before failure
Evans and Lissner [131]	1959	(37-85)	NA	Static compression / flexion / lateral bending	0	-	NA	3514 N failure	-	Highest failure stress among compression.
Kazarian [138]	1975	(0-65)	-	Static compression	0	-	1	-	-	FSU creep

Hansson et al. [130]	1980	(31-79)	T12 to S1	Compression	0	-	5mm / min	1520 – 11000 failure	-	BMC correlate to failure load.
Hutton and Adams [92]	1982	33 (22-73)	L1 to S1	Static compression + flexion	(4-10°)	-	3000 N/sec	3698 -12981 failure	1000 N, 5min	FSUs of young men are strong.
Panjabi et al. [137]	1984	(25-73)	T12 to L5	Sudden compression	-	-	1	150 N / 7,5 Nm	-	Changed motion mechanics due to DD
Koeller et al. [134, 135]	1984	(5-84)	L5 to S1	Dynamic and static compression	0	-	5 min – 6 hours	250 – 1490 N	10	Creep biomechanics
Adams et al. [68]	1985	8-54	L1 to L5	Compression in flexion	13°	0,67	2500-19 000	500 – <7000N	-	Gradual disc prolapse in young discs.
Keller et al. [129]	1987	65 (37-82)	T11 to L5	Static compression	0	-	30 min	Body weight	-	Creep variety, due to DD
Hansson et al. [74]	1987	65 (37-82)	T11 to L5	Cyclic compression	0	0.5	1-950 cycles	60-100 % of calculated ultimate strength	Body weight, 30 min	Failure location correlate to fatigue strength
Brinckmann et al. [71]	1988	51 (19-87)	NA	Cyclic compression	0	0.25	1-5000 cycles	30-70% of ultimate strength	-	Fatigue and failure risk increase with load.
Gordon et al. [144]	1991	57, (18-65)	L1 to L5	Cyclic compression / rotation / flexion	0/<3/7°	1.5 Hz	3-13 hours	1334 N	226 N, 30 min	Fatigue acts through AF inj. before DH
Brinckmann and Porter [145]	1994	20-52	T12 to L5	Compression / flexion / extension	0-5°	0.25	1000 cycles	1000 / 2000 N	-	DH secondary to DD
Adams et al. [125]	2000	51 (19-87)	T12 to L5	Dynamic – static – dynamic.	-2/8°	1.5	4 hours (8000-1000)	50-3000 N	300 N, 15 min	EP damage leads to structural disc changes
Frei et al. [136]	2002	52 (37-67)	T12 to L2	compression and Extension / flexion / lateral bending	-	0.03	1	500 N	-	Differences of shear and axial loading
Adams et al. [133]	2006	79 (62-94)	T9 to S1	Static compression / flexion	5°	-	1	1500 N	300N	Posterior load bearing due to DD
Przybyla et al. [126]	2006	61 (49-79)	T12 to L5	Static compression / flexion / extension	-2/6°	-	20 sec	200 / 2000 N	-	EP inj cause more disc changes than AF inj.
Skrzypiec et al. [127]	2007	75 (48-91)	T8 to S1	Static compression in slight flexion	2-6°	-	1 mm/ sec	3130 N failure	1.5 kN, 2h	Age reduce vertebral strength.
Zhao et al. [128]	2009	81 (48-92)	T8 to L5	Static compression in slight flexion	2-6°	-	2 mm/ sec	3121 N failure	300N, 15 min	EP fracture cranial due to less bone.
Huber et al. [76]	2010	20-60	L4-5	Dynamic compression , neutral / flexion	0/10°	5	300 000	0-1000 / 2000 N	0-2 kN, 90 min	Fatigue failure due to age not motion.
Showalter et al. [143]	2014	50 (22 – 75)	L5-S1	compression	0	2	10 000	1467 N	-	Reduced effect of cyclic loading on DD
Alkalay et al. [65]	2015	(62-85)	L1-3	Sudden compression	0	3000	1	10 000 N	112N	Failure, biomechanical properties

Porcine studies

Porcine experimental models are common among experimental studies regarding both fatigue and failure mechanisms and are considered appropriate for both vertebral and disc experimental models [71, 72, 74]. The biomechanical and anatomical

differences in comparison to human FSUs are mainly size dependent among adult specimens [64] but among younger FSUs there are also differences in the growth zone location and in the EP tissue [71, 72, 74]. Examples of experimental porcine study protocols are described in table 2.

table 2 Overview of examples of experimental porcine study protocols.

Name	Year	Level	Load	Angle mean	Hz	Duration / cycles	Magnitude	Pre-load	Result
Lundin et al. [41, 104]	1998 and 2001	L2 to L5	Compression	0	1mm/sec	1	To failure (9400 – 23500 N)	-	Growth zone + apophyseal failure
Marshal and McGill [67]	2001	C5-6	Flexion + extension / rotation	12-5°	1 Hz / 0,5 Hz	6000 / 2000-4000	1500 N / 12-17 Nm	300 N	AF fatigue, radial delamination.
Callaghan and McGill [77]	2001	C3-4	Cyclic compression,	0	1	0-86400	260 / 867 / 1472 N	260 N, 15 min	Increased load creates failure, mainly DH.
Drake et al. [70]	2005	C5-6	Constant compression + Flexion - extension / rotation	15,5°/5°	-	10 000	1500 N / 12-17 Nm	300 N, 15 min	Complex motion, Increased risk of failure
Drake et al. [63]	2005	C 3-4	Compression + flexion - extension / rotation	20-3°	1	1000-6000 cycles	1472 N / 5 Nm	300 N, 15 min	Complex motion, Increased risk of failure
Baranto et al. [78]	2005	L2 to L5	Flexion + compression / Extension + compression	12-19°	1mm/sec	1	To failure (1158-3138 N)	-	Growth zone + apophyseal failure
Baranto et al. [57]	2005	L2 to L5, DD	Compression / Flexion + compression / Extension + compression	12-19°	1mm/sec	1	21-79 Nm (3600 -15100 N)	-	DD FSU higher ultimate strength.
Tampier et al. [66]	2007	C3-4	Flexion - extension	15-2°	1 Hz	4400-14 400	1472 N	260 N, 15 min	50% DH failure, between AF.
Scannel and McGill [112]	2009	C3-4	Flexion – extension / compression + extension	10°	1 Hz	1800-14 400	1472 N	260 N, 15 min	DH failure.
Balkovec and McGill [69]	2012	C3-4	Flexion / flexion - extension	15 / 16-4°	1 Hz	10 000	1500 N	300 N, 15 min	Risk of DH failure, ext+flex>flex

Spinal load exposure in daily activities

The clinical exposure to spinal load is determined by several factors such as load magnitude, velocity, frequency, duration, cumulative load and movement type. Individual factors such as BMC, lifting tech-

nique, muscle fatigue and earlier injuries to the spine are also very important and make clinical exposure and effect determination difficult to assess and correlate [146-148].

There are several study methods regarding clinical exposure where spinal load-

ing can be quantified by external devices such as EMG but needs to relate to individual muscle factors [149]. Other common study designs are objective studies in different settings. A study by Coenen et al. (2013) assessed load through direct load measurement and videotape monitoring of study participants during their workday and assessed LBP through the Nordic questionnaire. The results displayed a correlation between LBP and total cumulative load, increased lifting frequency, flexed position and load magnitude [150].

The clinical exposure to repetitive motions and loads are often in machine related work but also participation in sports where increased exercise hours and earlier specialization generates increased exposure to repetitive load and to increased risk of fatigue and failure injuries.

Work exposure limitation

Vibration, repetitive lifting and impact loads with or without trunk movement may be a risk factor for spinal pathologies such as disc degeneration, endplate failure [54, 151] and LBP [152, 153]. Guidelines have been developed to decrease vibration exposure in mechanical work conditions through the ISO regulations 2631-1 (1997) and 2631-5 (2004) Other regulations consider the conditions such as the lifting frequency and maximum load magnitude [154].

Whole body vibration

Whole body vibration is a heterogeneous factor dependent on frequency, magnitude and duration and is a common exposure among drivers and industrial workers.

Studies have displayed a correlation between career exposures of vibration to low back pain among different study groups [86, 155, 156]. The correlation have not been consistent and whole body vibration has also been suggested as a treatment for LBP even if clear evidence is lacking [157]. Whole body vibration have also been investigated among athletes and substantial exposure has been seen among athletes in sports as alpine skiing, snowboarding, cycling and kite surfing [158].

Athletic exposure

Participation in sports generates increased exposure to repetitive and high magnitude forces and several studies have displayed high prevalence of both fatigue and failure generated injuries among athletes [159-166]. The prevalence of LBP and spinal abnormalities seem to differ to age and the specific loading demands of each sport [167, 168]. Early participation in athletics during adolescence increases the risk of both LBP and the development of spinal abnormalities such as disc degeneration and ring apophyseal injuries [160, 162, 167-171]. The number of spinal abnormalities increases during and after the growth spurt indicating that the spine is more vulnerable during that time [164, 172-175]. Follow up studies have also concluded that the increased prevalence of spinal abnormalities among athletes maintains sustained a very long time after the athlete's active sport participation retirement, compared to non-athletes [159, 160].

Running

Running is a very common sport at leisure level where up to 28 million Americans

run every week. Running related injuries are common and the injury development is believed to be generated through the repetitive load generating properties that causes overuse injuries [176-178]. The load of each stride is usually under 1 MPa [81] but is dependent on both internal and external properties such as body weight, velocity, course inclination but also to stride length and frequency where increased length correlate to increased load [179, 180]. Stride length and frequency are related to individual length and running speed but a study concluded that stride frequency around 1,4 Hz as the optimal frequency regarding metabolic and fatigue factors for a one hour race [85]. A systematic review regarding stride, frequency and body mechanics displayed few studies that met the inclusion criteria and most of the studies were low in sample size. The results showed that a reduced stride length and increased stride frequency relate to reduced risk of injury development biomechanically [176].

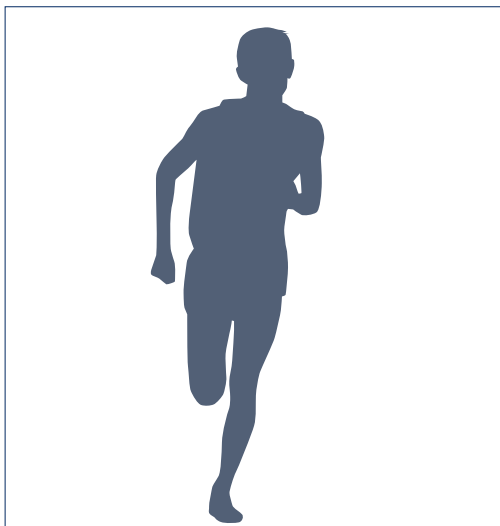


Figure 12. A long distance runner.

The basic biomechanical properties of running are focused on spine, pelvic and hip parameters. The normal stride is usually described in gait cycles that start when the loading of one foot initiates and ends when the same foot will be loaded again and consists thereby of two load moments [181, 182]. The spinal movement consists of a combination of all motion angles, where the lumbar spine contributes with lateral bending to counteract the hip and pelvic motions but also with flexion-extension and rotation [183]. The spinal flexion-extension range of motion increases with speed and is greatly altered by course inclination [184].

The spine is subjected to many repetitive loads during a run and 30 minutes of treadmill jogging cause disc height decrease in both the lumbar and thoracic spine [185] meanwhile a one hour run decreases the disc height significantly and may cause significant strain that can be visualized by MRI [186]. How and if spinal overuse injuries relate to long distance running have not been clarified. Runners had in a cross sectional study less disc degeneration compared to other athletes (soccer, baseball, basketball, swimming and kendo) and non-athletes [167]. An objective study of orienteers involving a small study sample highlighted a high prevalence of Schmorls nodes [14].

The correlation between running and LBP is unclear where some studies have displayed generally low LBP prevalence [187-189] while other studies have displayed a positive correlation to LBP that has increased with the number of hours jogging

[190]. Orienteers are subjected to variable terrain and no clear correlation has been confirmed to LBP in this group [159, 191, 192] moreover, it has been theorized that orienteering could even be protective towards future LBP [191].

Mogul Skiing

Mogul skiing is a freestyle skiing sport that is performed on a heavily moguled course including two jumps that in optimum should create around 2-4 m of jump distance [193]. The mogul skiers are objected to repeat spinal loading of different magnitude and movement types subjecting the participant to high amounts of heavy loading.



Figure 13. A mogul skier.

Mogul skiing is an alpine skiing competition but differs in technique compared to traditional alpine skiing, mainly due to the jumping and turning techniques. The events have many similarities in the basic skiing position where the athletes have flexed knees and hips and the spine is objected to different combinations of flexion, lateral bending and rotation motions [194-196]. During a Giant slalom turn the back of a world cup skier can have a flexion up to 44° , a lateral bending of up to 16° and a rotation of 10° and a force almost up to 3 times the body weight [196]. Kinematics and loading properties during a mogul ski race is still mainly unknown but the spine is generally in a straight position subjecting it primarily to compression loads. A minor study evaluated the basic kinematics and the body posture that differs during a mogul ski run with a lateral bend upon the spine and compared it to a more neutral spine position with flexed knee and hip position at the turn [195].

Traumatic injuries are common in both alpine and mogul skiing and the majority of the injuries affect the knee. Around 10% of all traumatic injuries among world cup freestyle skiers affect the lower back meanwhile the back injury prevalence is less among younger alpine skiers [197-201]. Ski jump landings are highly risky in relation to injuries and cause high load impacts on the body of the skier [202]. The location of the trunk at the landing has been evaluated as the most important factor regarding force to the knee and risk of ACL injury [194] where another study measured a peak force of 1350 N acting on the ACL in the landing of downhill jumps generated mainly by external forces [203].

Overuse injuries are most common in the back of alpine skiers and this is believed to be correlated to the repetitive loading in different motions that the skiers are subjected to [196]. Skiers and ski jumpers have been displayed to have an increased prevalence of anterior endplate injuries and the authors correlated the injuries to the fatigue due to the excessive loading and trauma occurrences that were imposed upon the athletes during their sport participation [204]. Endplate injuries have also been suggested to increase the risk of LBP among skiers [205].

Correlation between alpine skiing and LBP is not established and even less regarding mogul skiing. Objective studies have displayed normal LBP prevalence among Alpine ski instructors and protective factors that have been suggested relate to Whole body vibration [206] and the flexed position in the knee, hips and back that have an absorbent effect and reduce the load impact on the spine and back [194, 195]. Alpine skiing has also been proposed to increase muscle mass and lumbar bone density among young skiers [207].

Spinal injuries and abnormalities

Basic definitions of nomenclature are taken from Fardon et al. (2014) that established the consensus recommendations of contemporary combined task forces (CTF) of the American Society of Spine Radiology (ASSR), American Society of Neuroradiology (ASNR), and North American Spine Society (NASS) [12]. The etiology and pathogenesis regarding the possible correlation of spinal injuries and MRI abnormalities to LBP are still unclear. It is well known that all conditions stated below can cause LBP but also can be asymptomatic [12, 208-210].

Normal Disc aging

The normal disc demonstrates various effects due to aging, which is also called disc degeneration (DD) or degenerative disc disease (DDD) dependent on symptoms. Normal effects in the disc is loss of water content due to proteoglycan changes [211],

followed by collagen changes [212] and an increase of fibrous tissue which may affect the disc color, disc properties and function with increased stiffness [12, 213]. Ageing changes occur in all the disc tissues including the NP, AF, EP and matrixes. The cellular changes include proteinopolysaccharides changes such as glucosamine, galactosamine, hexosamine and a protein increase due to age in the NP, AF and the EP [214]. The mediation of the cellular changes occur through different pathways were the upgrading and inhibition of several metalloproteinases are vital steps [215]. Structural changes such as annular fissures are also common in ageing discs and increase the risk of the disc to be dehydrated [12].

Disc Degeneration and Degenerative Disc Disease

Disc degeneration refers to changes in the disc that can occur due to age but may also be aggravated by other causes [12]. The etiology and pathogenesis are not ful-

ly described but mechanical, cellular, traumatic, nutritional, and genetic factors are all believed to interact in the process of the progressive structural failure that is mediated through several different pathways and mechanisms [12, 211-216]. The definition of disc degeneration is one or more degenerative changes in either the NP, AF, EP or vertebral apophyses. Degenerative changes can be such as desiccation; mucinous degradation, cleft formation, fibrosis, and gaseous (usually nitrogen) degradation of the nucleus; mucinous degradation, fissuring, and loss of integrity of the annulus; defects in and/or sclerosis of the endplates; and osteophytes at the vertebral apophyses) [12]. The presence of physical disruptions due to mechanical pressure, like a fissure in the annulus, DH or endplate fracture, are signs of pathological disc degeneration rather than normal ageing [217]. Disc degeneration is mainly evaluated through MRI and there are many proposed classifications but no Gold standard [213, 216]. The prevalence of disk degeneration in the normal population increases with age and presented examples of prevalence are 6% in individuals younger than 20 years, 30% in 21-30 years old and 79% in people older than 60 years [218]

Degenerative disc disease is when symptoms can be clearly be correlated and attributed to the degenerated disc. The symptoms of disc degeneration are generally believed to be impaired range of motion due to a stiffer and less elastic disc, and pain due to different effects such as discogenic pain [12, 216, 217].

Disc degeneration can be seen as early as adolescence and the prevalence increases with age [219, 220] with prevalence of up to 90 % among the adult population as a whole [221, 222]. Since DD is less common among adolescents than adults, it is believed that early DD correlates stronger to DDD [223, 224].

Disc height

Disc height is defined as the central distance between the vertebral bodies cranial and caudal to the disc [12]. Disc height is correlated to fluid volume and pressure, which can be affected by age and several pathological disc conditions [12, 225]. The disc height is normally altered by normal living and loading and has a diurnal response where it is rehydrated, during reduced loading, to baseline without plastic remodeling [99, 226]. Disc height reduction can also be seen during compressive intense settings such as exercise.

Disc bulging

Disc bulging is a generalized disc extension beyond its normal borders of the apophyseal rim without AF disruption and is not defined as a herniated disc. There are no distinct correlation to symptomatic pathology or described etiologies or pathogenesis but relate to various causes and is in general correlated to disc aging or degeneration [12].

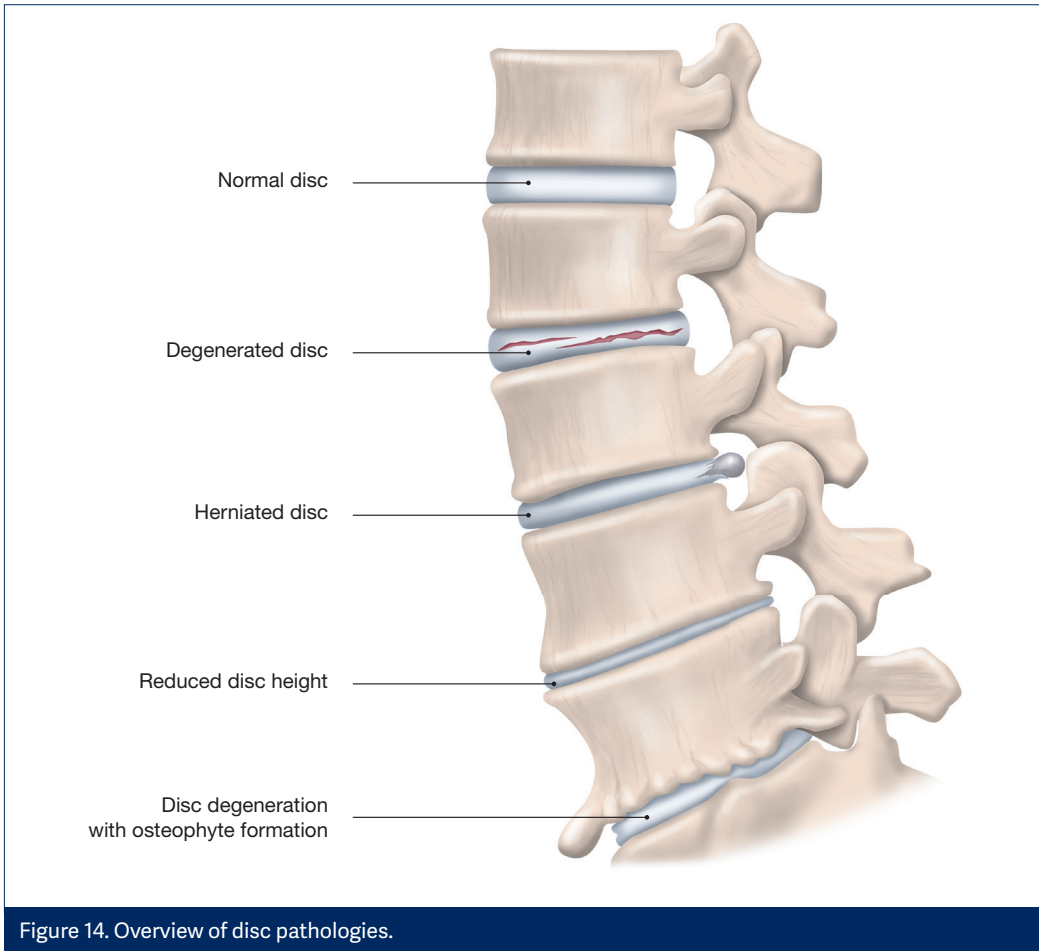
Disc herniation

Disc herniation (DH) is the state whereas the AF disrupts and disc material herniates beyond its normal borders, especially posteriorly into the spinal canal. Further morphological classification includes pro-

trusion, extrusion, containment and migration definitions [12].

The etiology and pathogenesis of DH are not fully understood but there are several theories and some established causes. DH is strongly correlated to the biomechanical properties of the nucleus, annulus, and both the inter- and intra-lamellar matrices. Recent studies have implied that the risk of DH increase when the disc is exposed to a combination of high compression and flexion loading [106] and could also be affected by repetitive loading [122]. The correlation between disc degeneration and DH is debated but a potential pathway is that the disc needs to be degenerated before herniation can occur due to the increased load on the annulus when the nucleus is dehydrated and disc height reduced [217]. Another suggested pathogenesis is that the disc needs to be well hydrated to be able to produce the hydrostatic pressure needed for the nucleus to protrude through the annulus [49]. Risk factors to DH is mainly correlated to disc degeneration such as participation in athleticism and age but a straight sagittal alignment of the spine is also a potential risk factor [227]. Symptomatic DH is uncommon among adolescents and children but increases with age to a suggested lifetime prevalence level of around 1-5% [228, 229]. Asymptomatic DH is though much more common and has been detected as high around 30% among adult persons [230] and around 40% among people older than 60 years of age [231]. DH is most common at the lower lumbar level [232].

Lumbar DH can cause both back and radiating pain as well as sensory or motoric neurological symptoms, but can sometimes display more subtle symptoms without radiating pain especially among adolescents [106]. Hospitalization due to DH has been investigated and increases with age but most rapidly around the late teenage years [233] that could be due to the ossification and increased stability of the endplate and thereby shifting the failure location to the NP and AF. Treatments differs between operative to conservative treatment. Open discectomy, microscopic discectomy, tubular discectomy or endoscopic discectomy are common surgical techniques but no significant clinical differences between them have yet been displayed [234, 235]. Early operative treatment has a high effect on immediate pain reduction but appears to be equivalent with conservative treatment long-term [236, 237]. Lumbar DH, especially of the extruding kind, can regress and even disappear spontaneously in time without surgical intervention [238].



Endplate lesions and Schmorls nodes

Disc displacement in the cranio-caudal (vertical) direction through a defect in the vertebral body and endplate are referred to as an intravertebral DH /Schmorls node (SN), which is believed to cause pain in certain cases [12, 209]. An accepted consensus of SN is still not defined and a Gold standard examination is not fully validated and gives rise to a highly different prevalence in different studies [239, 240]. The pathogenesis, etiology, epidemiology and clinical significance such as

pain correlation are not yet fully described either [239] but both axial compression and spinal movement during growth are believed to effect the development of SN [209, 240]. This is supported by a clinical study where SN has been noted at a high frequency among Orienteers [159]. There are no established specific treatments for symptomatic Schmorls nodes [209]. Other lesion such as fractures, calcification and erodations can affect the EP and are suggested to be associated with both back pain and disc degeneration [241, 242].

Endplate signal is determined by MRI exams and classified according to the Modic classification [243]. Several studies correlate Modic signal changes to LBP but it can also be seen among asymptomatic individuals [244, 245]. The endplate has been investigated extensively in different experimental settings, describing the EP to be a sensitive tissue in the young spine where endplate injuries are also believed to increase the risk of DH [125, 126].

Internal disc disruption

Internal disc disruption is a condition when no DH appears but damage and tear in the AF occur, and can cause discogenic pain, and is suggested to be a cause of chronic back pain [208]. The term discogenic pain is often used in both clinic and research but is lacking clear diagnostic criteria, terminology and treatment [246].

Spondylolysis

Spondylolysis represents a defect of the pars interarticularis of the neural arch, which can cause a sagittal movement (listhes) of a vertebra in relation to the spine. The defect can originate by a stress fracture or repetitive stress. The anatomical and biomechanical causes are elongated facet joint, vertical shaped pars, hyperlordosis and repetitive hyperextension loading. Spondylolysis occurs more often among adolescent athletes and are due to the not matured skeleton [247, 248]. Individual factors such as the sagittal alignment of the spine are potentially a risk factor for both generating spondylolysis that further evolves into spondylolisthesis and the most common location of the defect occurs at the L5 level [248-250].

Spondylolysis can cause spine instability, back pain, and radiculopathy or be asymptomatic [251]. Lifetime prevalence in the normal population vary between 4-6% with an increased risk for athletes where increased prevalence have been shown among Swedish elite gymnasts (15%) and weightlifters (50%) [161] as well as among Japanese judo (20%), wrestlers (20%), soccer players and baseball players (30%) [252]. MRI should be used as the primary clinical investigation for diagnosing the first steps of spondylolysis especially among adolescents while CT-scan is a better method for detecting manifest spondylolysis [251]. Other techniques available are scintigraphy and single emission photon computer tomography (SPECT) that provides highly sensitive results [253].

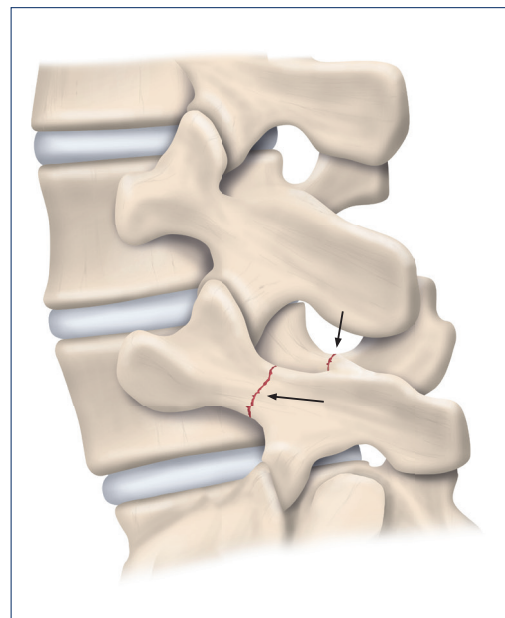


Figure 15. Spondylolysis.

Spondylolisthesis

Spondylolisthesis is the slip of a vertebra in relationship to the corresponding inferior vertebrae, and the slip can be either anteriorly or posteriorly. The pathogenesis and etiology is not defined but seem multifactorial and in many cases associated with spondylolysis [254]. Spondylolisthe-

sis is most common at the L5-S1 level and the prevalence in children is about 1-5% and increases slightly towards adulthood due to the majority of the slip progression occurs during the growth spurt [255]. The potential treatment is operative fusion dependent on slippage and symptoms level [250].

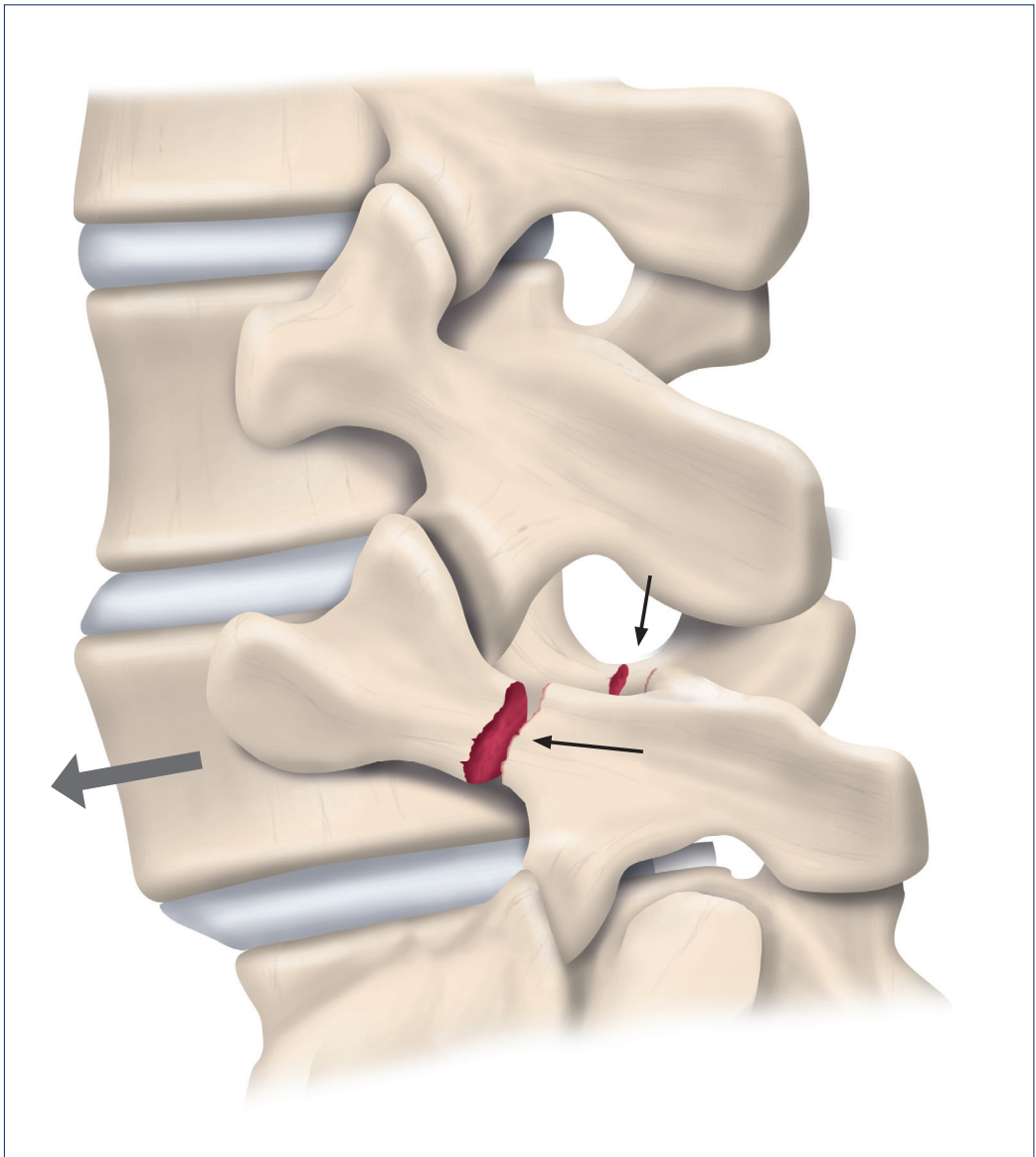


Figure 16. Spondylolisthesis.

Disc signal

The disc signal is different according to the discs internal water composition, where the main difference is between the NP and AF. Disc signal reduction is seen as gradual darkening in the T2 MRI examinations and generally considered as a sign of disc degeneration and is assessed in different classification such as the Decandido [256] and the Pfirman DD classifications [257].

High intensity zones

High intensity zones (HIZ) are localized fluid and or granulation tissue within the AF and are evaluated in T2-weighted MRI scans. The cause of HIZ are annular fissures which can be of radial, concentric and transverse types and are typically caused by normal ageing and are not correlated to traumatic origin [12]. HIZ is considered as a sign of disc degeneration and is evaluated by the Dallas classification [258].

Fractures of the vertebral body

Vertebral body fractures are common among osteoporotic patients but uncommon among the normal population. Vertebral fractures are though seen in high-energy sports and are often correlated to a fall or traffic related trauma [210]. The vertebral fractures cause acute and chronic back pain, decreases in quality of life, and diminished lifespan among the elderly [210].

Apophyseal injury

Apophyseal injuries are manifested during adolescence due to injuries in unfused apophyseal rings. Limbus vertebrae apophyseal ring fracture is the separation or avulsion of a segment from the vertebral

ring apophysis in the growth zone from the vertebral body. Apophyseal injuries are generated through either a developmental abnormality, chronic intervertebral herniation that causes a bony displacement, or due to a fracture through the apophyseal ring accompanied by DH [12]. Apophyseal injuries are more common among adolescent athletes who are at higher risk of high compressive loads to the spine especially where the spine is vulnerable due to the young EP, existing growth zones and the unfused apophyseal ring [140]. CT is the Gold standard examination of apophyseal injuries.

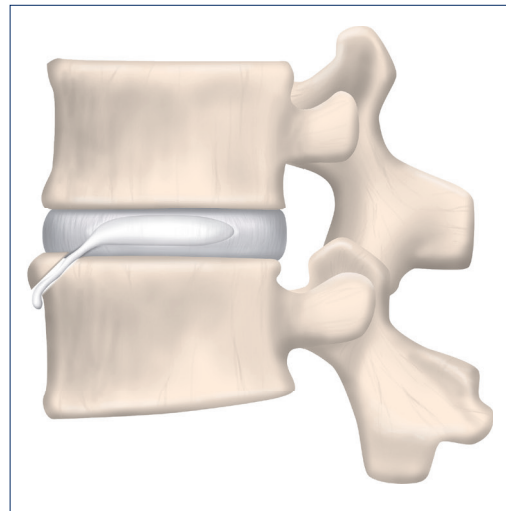


Figure 17. Apophyseal injury.

Shape of vertebra

The shape of a vertebra can differ due to age, genetic, traumatic and degenerative causes. Pediatric vertebral bodies have open growth zones that affect the shape of the end plates especially and can sometimes mimic pathological conditions. Genetic conditions can be the existence of

ventrally shaped vertebral bodies that can be seen in the Scheuermann condition where three consecutive thoracic vertebrae create a thoracic lordosis. Traumatic changes are due to fractures of both traumatic and osteoporotic origin. Degenerative changes like osteophytes and facet joint arthrosis can alter the shape of vertebra. The vertebrae can also be affected by disease such as infections, primary cancer and secondary metastasis [259].

Spinal stenosis

Spinal stenosis is the condition where the spinal canal is partially narrowed causing an obstruction of the neural structures and potential symptoms like neurogenic pseudo claudication of the legs. The origin of spinal stenosis is mainly due to a combination of DH, facet joint arthrosis and thickening of the ligament flavum in the spinal canal but could also be affected by a congenital narrowing of the canal. The investigation and diagnosis is based on MRI imaging of the spine but no Gold standard of assessment has been generally accepted [260].

Micro-injuries of the disc and vertebrae

The spine is subjected to many micro-injuries during loading. The spine is very heterogeneous and the biomechanical properties are dependent on many complex factors. The spine has internal factors such as size, bone mineral density and age that determine the elastic, plastic and viscoelastic properties and abilities to withstand external loads. The successive fatigue micro-injuries are believed to follow a special hierarchy where microstructures

like osteons are important as are the different load patterns with an emphasis on strain [43, 261, 262].

Other potential painful abnormalities

Other potential painful spinal abnormalities are conditions as scoliosis, sacral stress fracture, facet joint syndrome and scoliosis. Scoliosis is an S-shaped curvature in the frontal spinal view. Sacral stress fracture is a fracture in the sacrum and is uncommon among the normal population but has is slightly more common among specific groups like runners [263]. Facet joint syndrome is a debated condition that could be a cause of LBP [264]. Facet joint tropism is the asymmetry between the two facet joints at the same level and is a common condition that is potentially involved in the development of both DH and DD [265]. Other non-spinal diagnoses can also cause pain in the lumbar back such as infections, rheumatic conditions and cancer [266, 267].

Sagittal alignment

Several studies have suggested an association between certain pathologies in the spine, especially the lumbar spine, and an individual's spinal sagittal alignment. This is due to that different spinal alignments having differences in the loading of the distal lumbar segments [227, 268-273]. However, there is a large normal variation in spinal alignments between asymptomatic individuals [274].

Roussouly et al. [11] have established a classification system describing the normal variation in sagittal alignment of the human lumbar spine and pelvis on lateral

radiographs of the whole spine. The classification identifies 4 types of spine curves. Type 1 has a long thoraco-lumbar kyphosis and a short hyperextended lordosis. Type 2 has a flat thoracic kyphosis and a flat lumbar lordosis. Type 3 has what is considered as a normal spine alignment - a moderate thoracic kyphosis and a moderate lumbar lordosis. Type 4 has an increased thoracic kyphosis and an increased lumbar lordosis

Roussouly and Pinheiro-Franco [227] described each of the four Roussouly types to be linked to specific pathologies. The type 1 spine is suggested to have an increased risk of disc degeneration in the thoraco-lumbar kyphosis area. Further, in the kypho-lordotic junction area the discs are tilted with a greater risk of retrolisthesis. Type 2, has a horizontal disc orienta-

tion, which is suggested to cause increased disc pressure with a higher risk of early disc degeneration and central DH. This correlation is supported by several clinical publications [270, 275] indicating that operated patients due to DH had a more flat back compared to controls [276]. According to Roussouly and Pinheiro-Franco [227] the sagittal normal spine in type 3 has not been linked to any certain pathological conditions. The type 4 spine with its hyper-lordotic lumbar curve is believed to cause increased force on either the posterior or anterior elements dependent on disc tilt. High stress on the facet joints increases the risk of dorsal structure injuries and spondylolisthesis while increased load anteriorly is potentially correlated to retrolisthesis [269, 271].

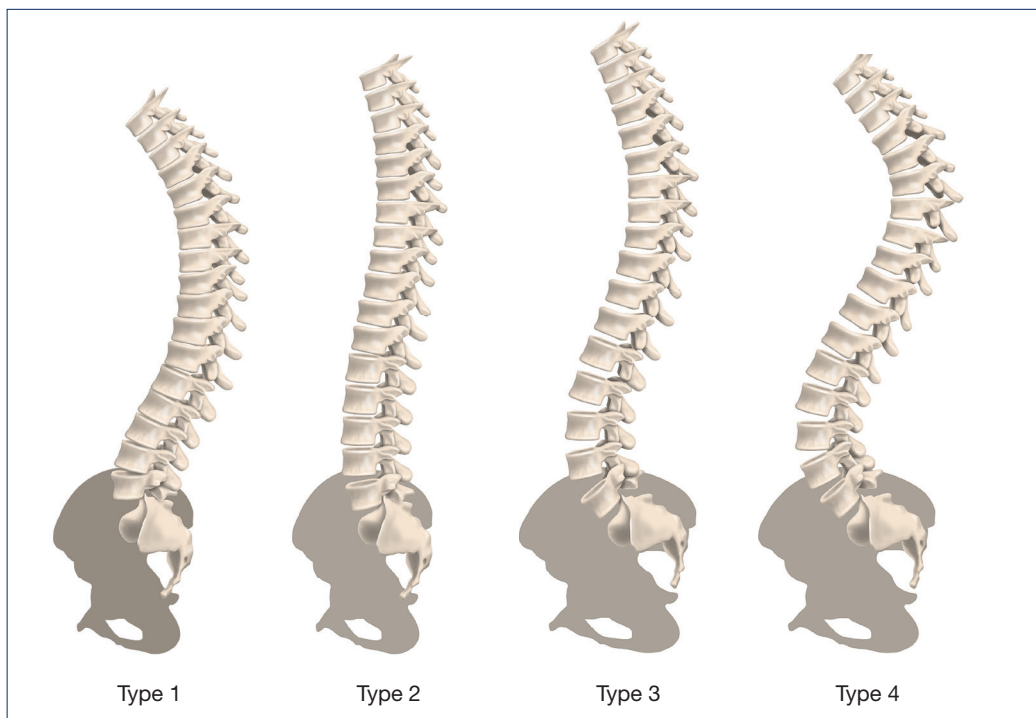


Figure 18. The sagittal alignment types according to Roussouly.

Imaging and examination of the spine

The radiology techniques used for examining the spine in normal clinical situations are Plain radiography, Computer Tomography (CT) and Magnetic Resonance Imaging (MRI). Lumbar imaging does not improve the clinical outcome due to the fact that all examinations have specificity and sensitivity problems in relating the radiological findings to LBP and should thereby not be used as screening methods [266, 277-279]. Technical evolution and progress have made great advances and it is important to consider potential differences between different generations of imaging techniques when evaluating radiological examinations [280].

Validity of radiologic examination

The validity of radiologic imaging is dependent on several factors. The examination itself must be sensitive and specific to the endpoint itself and provide the possibility to identify the endpoint that is wanted without systematic error. Examinations should be stable over time and without response shift. The validation of techniques are generally done by comparing with the Gold standard [281].

The validity of radiologic imaging examination is dependent on the reliability to identify the endpoint that is desired on the radiological images. It is dependent on inter- and intra-rater reliability that is the internal and external consistency to achieve stable decision. The reliability can be measured in several different ways dependent on method; common statistical

measurements are intra-class correlation (ICC) and kappa. All steps are very important to validate as to achieve true results and high external validation without false positive and negative findings [281].

Imaging techniques

Plain radiography is a common and useful examination regarding vertebral conditions such as sagittal alignment, fractures, spondylolisthesis, and scoliosis but have high sensitivity and specificity problems regarding other spinal causes for LBP [266, 277, 278].

CT is a detailed radiology examination capable of high visualization of the spine and nerve root disorders but is also cause for radiation during the exam compared to MRI [266, 277, 278].

In general MRI is considered as the clinical Gold Standard for all disc related conditions and also for vertebral conditions due to higher soft tissue contrast which makes tissues possible to distinguish and separate from each other. The two most used settings in MRI are T1 and T2 weighted sequences where the T1 highlights fatty tissue meanwhile T2 highlight fluid. There are several different kinds of MRI examinations and protocols that can be used dependent on investigations required for diagnosis. MRI should be primarily used when considering radiating pain, neurological deficit or serious spinal disorders, potentially through the help of "red flag" symptoms, due to the high asymptomatic prevalence of spinal disorders [230, 266, 282].

Other examinations used in the evaluation of spinal disorders such as Discography, Scintigraphy, Single Photon Emission Computer Tomography (SPECT) and Myelography. Discography is a diagnostic examination where the disc is examined by contrast injection into the disc often complemented by measurements of disc pressure while examining conditions as annu-

lar fissures. Provocative discography is an assessment of pain response related to the disc such as in discogenic pain [12]. The clinical use of discography has been debated due to lack of supportive evidence [266]. SPECT is a very sensitive examination capable of high contrast images which is sometimes used in the determination of conditions like spondylolysis [253].

Interpretation of imaging techniques

The interpretation of different spinal conditions are subject to high validity and reliability problems due to differences in quality of examination, a lack of Gold standard and the quality of the examiner [283]. Many different studies have analyzed inter- and intra-rater agreement according to different spinal conditions and classification where the results display great variability concerning the Fleiss kappa coefficient and the Landis and Koch score [283-286].

Classification of disc herniation

There are many ways to examine and grade DH such as the CTF classification [287], Michigan State University classification [288] and Jensen's criteria [230] but no specific Gold standard exists. According to a systematic review the CTF classification is the most reliable and defines lumbar discs as normal, focal protrusion, broad based protrusion, or extrusion [285].

When analyzing nerve root compression the van Rijn classification [289] and Pfirrmann classification [290] are generally

used. The van Rijn divides nerve roots into no root compression or root compression and is potentially the most reliable [285].

Classification of disc degeneration

Disc degeneration can be graded in different ways with many different classification systems. A review article revealed several different DD classifications in different modalities including macroscopic, histology, X-ray, CT, MRI and discography but only a few of these were tested for reliability [286]. The Thompson scheme grades the disc's macroscopic morphology [291], the Dallas CT classification [258] observes the anterior integrity of the disc after discography. The Pfirrmann classification [257] evaluates MRI observed changes in the nucleus, the Modic classification [292] assesses MRI verified changes in the vertebral adjacent to the disc while The Decandido classification depends on T2 MRI disc signal [256]. Various modifications of these schemes have been proposed to suit specific clinical and research needs [12]. Other classification systems have been proposed that also include the endplate condition and the state of the posterior column of the spine including the facet joints [293].

The Thompson classification is a six-point macro grading scale of degenerative changes in the human intervertebral disc, from 0 (normal) to 5 (severe degeneration), based on gross pathologic morphology of mid-sagittal sections of the lumbar spine [291].

The Dallas classification is a six-level grading of post-discography discs. Dallas Grade 0 is normal; Grade 1: leakage of contrast into the inner one-third of the annulus; Grade 2: leakage of contrast into the inner two-thirds of the annulus; Grade 3: leakage through the entire thickness of the annulus; Grade 4: contrast extends circumferentially; Grade 5: contrast extravagates into the epidural space [258].

The Pfirrmann classification is a 5-point grading system for the severity of degenerative changes within the nucleus of the intervertebral disc. A Pfirrmann Grade I disc has a uniform high signal in the nucleus on T2-weighted MRI. Grade II shows a central horizontal line of low signal intensity on sagittal images. Grade III shows high intensity in the central part of the nucleus with lower intensity in the peripheral regions of the nucleus. Grade IV shows low signal intensity centrally and blurring of the distinction between the nucleus and the annulus. Grade V shows homogeneous low signal with no distinction between the nucleus and the annulus [257].

The Modic classification is a three-level classification of degenerative changes, involving the vertebral endplates and adjacent vertebral bodies associated with disc inflammation and degenerative disc

disease, as seen on MRIs. Type I refers to decreased signal intensity on T1-weighted spin echo images and increased signal intensity on T2-weighted images, representing penetration of the end plate by fibrovascular tissue, inflammatory changes, and perhaps edema. Type I changes may be chronic or acute. Type II refers to increased signal intensity on T1-weighted images and isointense or increased signal intensity on T2-weighted images, indicating replacement of normal bone marrow by fat. Type III refers to decreased signal intensity on both T1- and T2-weighted images, indicating reactive osteosclerosis [243].

The Decandido classification is a four-level disc degeneration classification system dependent on T2 MRI signal (water signal). Level 1 is the brightest lumbar disc or Th12-L1; 4 is a totally blackened disc and 2 and 3 are intermediate signal intensities between the two extremes [256].

Disc height and volume

Disc height is defined as the central distance between the endplates of the superior and inferior vertebrae to the disc [12]. There are several classification modules that measure disc height and volume but no Gold standard. Examples of disc height programs are the Dabbs method that is the mean of the anterior and posterior disc height [294]. The Pfirrmann disc height measurement that calculates a mean from the anterior, central and posterior height measurements [295] and the Farfan index which is the sum of the anterior and posterior disc heights divided by the disc diameter on plain radiographs [296].

Disc volume can be measured in several ways such as the Cavalieri method which is a point counting method [297]. There are several semi automatized computer programs available that uses either CT or MRI scans to evaluate disc height and / or volume that have displayed high reliability [298, 299].

Sagittal alignment

Roussouly et al. [11] have established a classification system describing the normal variation in sagittal alignment of the human lumbar spine and pelvis on full-spine radiographs of the spine in the lateral plane, extending from the base of the skull to the proximal femora in the erect position. The classification identifies 4 types of spine curves. Similar sagittal measurements have been validated and displayed poor intra- and interrater reliability but computerized programs displayed better results [300].

Spondylolisthesis

There are several classifications regarding spondylolisthesis that asses the severity of spondylolisthesis through different measurements of the amount of slip. The Meyerding classification is the generally most used and is a I-IV level classification of the spondylolisthetic slip on static lateral radiographs [301]. Other classifications include the sagittal alignment or potential vertebral abnormalities in the classifica-

tion. Computerized assessment have lately been more implemented which seem to increase the reliability of measurements [302].

Schmorls nodes

No true Gold standard is established and few studies regarding validity and reliability are available.

Apophyseal injuries

Apophyseal injuries can be seen in both CT and MRI and the Gold standard is dependent on the growth phase of the apophysis that includes calcification and ossification level. Few studies regarding validity and reliability are available.

Scoliosis

Scoliosis can be measured on several different radiologic modalities where the generally accepted Gold standard is the Cobb angle assessments on plain radiographs [303]. The reliability of this method is generally good and is further improved by different digital assessment aids [304].

Abnormal configuration of the vertebral bodies

No true Gold standard is established and few studies regarding validity and reliability of abnormal configuration of the vertebral bodies are available [259]. Fractures of the vertebral bodies are generally assessed according to the AO classification.

Low back pain

Low back pain (LBP) is heterogeneous complex of symptoms all referring to pain in the lumbar back area. The definition of LBP is pain localized under the costal margin and above the gluteal folds with or without leg pain. LBP is often divided into three different groups, LBP with nerve root pain, specific LBP and non-specific LBP [267]. The most common source of LBP is that the underlying cause and pathogenesis of LBP cannot be surely presented and is defined as non-specific LBP [267, 305]. LBP with nerve root affection is radiating pain usually in either leg derived from nerve root affection such as DH or spinal stenosis. The specific LBP are due to both spinal, such as disc and vertebral conditions, and non-spinal, such as abdomen and hip conditions, causes and diagnoses [263]. The need of investigation of each patient with LBP is individual, but so-called “red flag” symptoms increase the potential risk of serious spinal disorders meanwhile “yellow flag” symptoms are linked to personal psychosocial attributes that affect the potential sickness burden to the patient [267].

Acute LBP (ALBP) is LBP that last less than three months compared to chronic LBP (CLBP) that exceeds three months. The term subacute LBP is also common and is LBP lasting between 6-12 weeks [282]. The great majority of all LBP events have a rapid recovery within the first month but minor pain and recurrence is common within the first 12 months [267, 306].

Definition problem with LBP is the lack of

conformity regarding the location, minimum duration and the severity of pain to be defined as LBP that makes meta- and systematic reviews subject to study biases.

Prevalence

Low back pain is a very common symptom in cultures and in populations [305, 307, 308] where both the incidence and prevalence increases with age [309, 310]. Due to definition diversity, the prevalence differs greatly among studies but a lifetime prevalence exceeding 80% appears to be consistent in many reviews [267, 282, 311]. High levels but also high differences of point prevalence in different studies (11-40%) [311-314] also reflect that LBP is very common but also difficult to measure. LBP is common worldwide but the published prevalence appears to be lower in many low-income countries, however this is not fully verified [310, 314]. It has been reported that 10-15% of all acute LBP will develop into chronic LBP [282] which is similar to acute LBP, and has an increased prevalence according to age [310].

Socioeconomics and illness cost

The cost of LBP for the society is very high and is an international health and economic issue [278, 311, 315-317]. The socioeconomic costs or illness costs are the sum of all costs associated with a particular condition, which would otherwise not exist. The illness cost can be divided into direct, indirect and intangible costs. Direct costs are related to medical and non-medical examinations and treatment. Indirect costs relate to consequences of the symptom such as employment and household production losses. Intangible costs are re-

lated to the decrease of value of life due to the illness. Illness costs are complex and can be derived in many ways, where indirect costs are difficult to measure and intangible costs usually are not measured at all in socioeconomic studies [315].

The cost for all socioeconomic consequences in Sweden in 1995 related to LBP was estimated to 29.4 billion Swedish crowns, which was three times higher than all socioeconomic costs for all cancers at the same time. The cost for directly related factors was 8% and the indirect cost dominated with 92% [278]. The illness cost of LBP in United Kingdom in 1998 was estimated to £12.3 billion, with proportions of direct cost at 13% and indirect cost 87%, which was the greatest economic burden on society due to a disease [318]. Similar median proportions have been seen internationally in a systematic review in 2008 with a median proportion of direct costs at 14.5% and indirect cost proportion at 85.5% [315]. An American study in 2006 estimated the annual cost of LBP to exceed \$100 billion per year [317]. An estimation in the Netherlands in 2011 have seen a decline of total socioeconomic costs of back pain between 2002 to 2007, believed to relate to Governmental interventions to lower indirect costs. The total cost was in 2007 estimated to 3.5 billion euros divided in direct costs at 12% and indirect costs at 88% [319].

Risk factors to LBP

Many different risk factors for LBP have been presented in different studies but no clear individual risk factors are established generally in larger systematic re-

views [282, 314, 320-325]. Due to the many etiologies of LBP, homogenous risk factors are unlikely and further definition and subgroup analyzes are important to clarify such risk factors of LBP [326].

Mechanical loading such as physical exercise have been suggested to be a risk factor for LBP and display a U-shaped curve where too little and too much are equally harmful [327]. Repetitive heavy loading, such as manual material handling and lifting, and whole body vibration, as caused by trucks and machines, have been reported to correlate with LBP [267, 277]. Moreover, a strong association to LBP has also been reported with flexion, rotation and endpoint positions of the spine [324]. A systematic review by SBU in 2014 revealed that people that worked with a flexed or twisted back, manual handling as repetitive lifts, were exposed to whole body vibration or had a physical work in general had increased risk of back problems. No difference was seen regarding gender when subjected to the same work conditions [328]. But traditional mechanical loading have also been suggested to not be a risk factor [282, 325] where occupational repetitive body positioning and loading could not be clearly correlated to LBP independently according to multiple systematic reviews with the Bradford Hill causation model [321, 322, 329-333]. Mechanical loading is difficult to measure and also to correlate to LBP but the occurrence of LBP is probably due to the total amount of burden on movement that includes both the nature and intensity of the movements rather than any specific movement type [324].

Other risk factors that are discussed such as physiological factors, heredity, leg flexibility, trunk asymmetry, early onset of LBP, gender, age, weight and smoking [282, 320, 321, 334]. Overweight and obesity have been correlated to radicular pain and sciatica [335] but should be considered as a weak risk indicator for LBP [320, 334]. MRI abnormalities, such as disc degeneration [334], has not at an individual level been correlated to non-specific LBP due to fact that MRI abnormalities are very common in the asymptomatic lumbar back [336].

The main risk factor to develop and to be affected by chronic LBP seem to be of psychological origin [267], like catastrophizing thoughts [305, 337] and maladaptive pain coping behavior [338].

Physical exercise and LBP

Regarding preventive and salutogenic factors regarding LBP, there appears to be evidence to support that physical exercise [339] has a good effect however, in general the evidence appears to be lacking [277, 282]. A possible correlation could be that too little and too much exercise are both equally at risk to LBP in a U-shaped curve [327]. The treatment of LBP is mainly focused on limiting disability and recurrence through pain limitation and activity [267]. Worldwide clinical guidelines suggest patients with acute LBP to maintain as high physical activity as possible to minimize the risk of chronicity development [267]. The evidence for this is though slim, due to high heterogeneity and measurement bias, and no real positive or negative predictions could be determined of physical activity [340].

Regarding the management of CLBP is multi variable and needs to be adapted to each person where behavior intervention to maintain or increase physical activity is a key factor [341]. Other management principles include conservative, pharmaceutical and potential invasive treatments [266].

LBP in adolescents

Adolescent LBP (ALBP) has a proposed definition as LBP among persons within 10-19 years of age with pain localized in the lumbar area [342]. The prevalence of LBP increases with age and a meta review displayed high variations in lifetime (34-46%), year (27-41%) and point (9-16%) prevalence [343] but the implication on quality of life is less among adolescents compared to adults [282, 344]. Risk factors among adolescents differ in different studies but increased growth, smoking, gender, high level of physical activity and competitive sports, psychological state of mind and poor leg flexibility due to tight muscles in thigh area have been discussed [309, 345].

LBP in young athletes

Participation in sports have been discussed as a risk factor for LBP but a strong correlation has not been seen in systematic reviews mainly due to lack of clinical studies [282]. Even if some specific spinal movements have been correlated to LBP, it is in general difficult to correlate specific movements to LBP when it is the cumulative effect of all movements and loading that the spine is affected by that is of importance [324]. Excessive exposure to sports have been linked to LBP during youth but seem to differ regarding

the specific demands by each sport [168]. The prevalence of LBP among adolescents seem to follow a U-curve dose relationship where both absence of and excessive amount of physical exercise correlate to LBP [346]. Many different studies have though presented both statistically and clinically significantly higher prevalence of LBP among young athletes in various sports compared to controls [159, 161, 162, 168, 170].

LBP among athletes have a different clinical effect where the absence of play is vital and other clinical effects such as decrease in health or disability appears not have to be affected. There are several definitions regarding the definition of a sport injury in

both America and Europe that correlates mainly to a limitation in sport participation. The severity of a sport injury is linked to the absence of play and is usually defined as minor < 1 week, moderate <3 weeks and severe >3 weeks [347]. It is also important to distinguish between traumatic and overuse injuries where different treatments are potentially suitable [348].

The reason for LBP among young elite athletes may also be different from the general population where structural spinal conditions such as stress fractures, disc degeneration and spondylolysis are more frequent dependent on loading patterns [167, 171, 263, 349, 350].

Patient reported outcome measures (PROMs)

Several different PROMs are common among LBP studies that assess LBP and the general health. The EuroQoL questionnaire and the Oswestry disability index are commonly suggested to be included in LBP research [351].

The EuroQoL questionnaire

The EuroQoL (EQ-5D) questionnaire (©EuroQoL Group 1990) evaluates the quality of life and is scored with 1-3 or 1-5 dependent on version, and relates to movement capacity, hygiene, activity, and pain and anxiety level. A VAS estimation of health is also included in the questionnaire [352].

The Oswestry disability index (ODI)

The ODI (version 1) provides a subjective

performance rating of daily activities. Each question is scored between 0-5 where 5 represents the greatest disability. The ODI is expressed in percentage and thereafter derived to minimal disability 0-19%, moderate 20-39%, severe 40-59%, crippling 60-79%, and bed bound 80-100% [353].

Swärd and Baranto back pain questionnaire

The Swärd and Baranto back pain questionnaire is a three-part questionnaire. In the first part, basic characteristics such as physical activity are evaluated and back pain in the thoraco-lumbar spine area is evaluated as present or previous pain. Further questions evaluate radiating pain, if the pain is/was correlated to exercise and competition, and if any movements aggravated or relieved the pain. The debut, duration and if any medical assessments

or interventions had taken place are investigated. Back pain was self-assessed and graded moderate or severe. Moderate level relates to the daily living, work, training or competition is not affected by back pain. Severe level relates to if the back pain influenced daily living, work, training or competition at any time. Athletic and physical activity is investigated through questions regarding present and previous activity level. The location and type of pain are investigated by using the visual analogue scale including a schematic body picture. Accompanying pain in other joints and body regions is also described through a schematic body picture [161].

Other PROMs

Other PROMS regarding LBP are among others the extended Nordic Musculoskeletal Questionnaire (NMQ-E), Roland Morris back disability score, Back pain index, Quebec back pain disability score (QB-PDS), Pain symptoms frequency (SFI), Pain symptom bother-some-ness (PSB) and the Von Korff back pain grades.

The NMQ-E is a questionnaire including 99 question items, regarding prevalence, severity and impact of musculoskeletal symptom. An adapted version for adolescents is validated to English and is focused on school attendance and participation in sports and leisure time activities and is called the Teen Nordic Musculoskeletal Screening Questionnaire (TNMQ-S) [354].

Assessment of physical activity

The assessment of total cumulative physical activity is important when comparing groups but is difficult due to the many

different methods of physical activities that are possible. There are several questionnaires regarding this matter such as the Tegner activity scale that include both work and sports activities [355] and the International Physical Activity Questionnaire (iPAQ) [356] that estimates the time spent being physically active during a 7-day period [357].

Limitations of questionnaires

The development of questionnaires to different groups is a complicated process, which is well defined and described by the COSMIN standards. There are several factors to be addressed such as validity, responsiveness, and reliability that are further sub-classified such as cultural validity [358]. There are many different PROMs regarding back pain but few are validated towards LBP and none appears to be considered as the Gold Standard regarding LBP. Many of the questionnaires have sensitivity and specificity problems such as floor-ceiling effects.

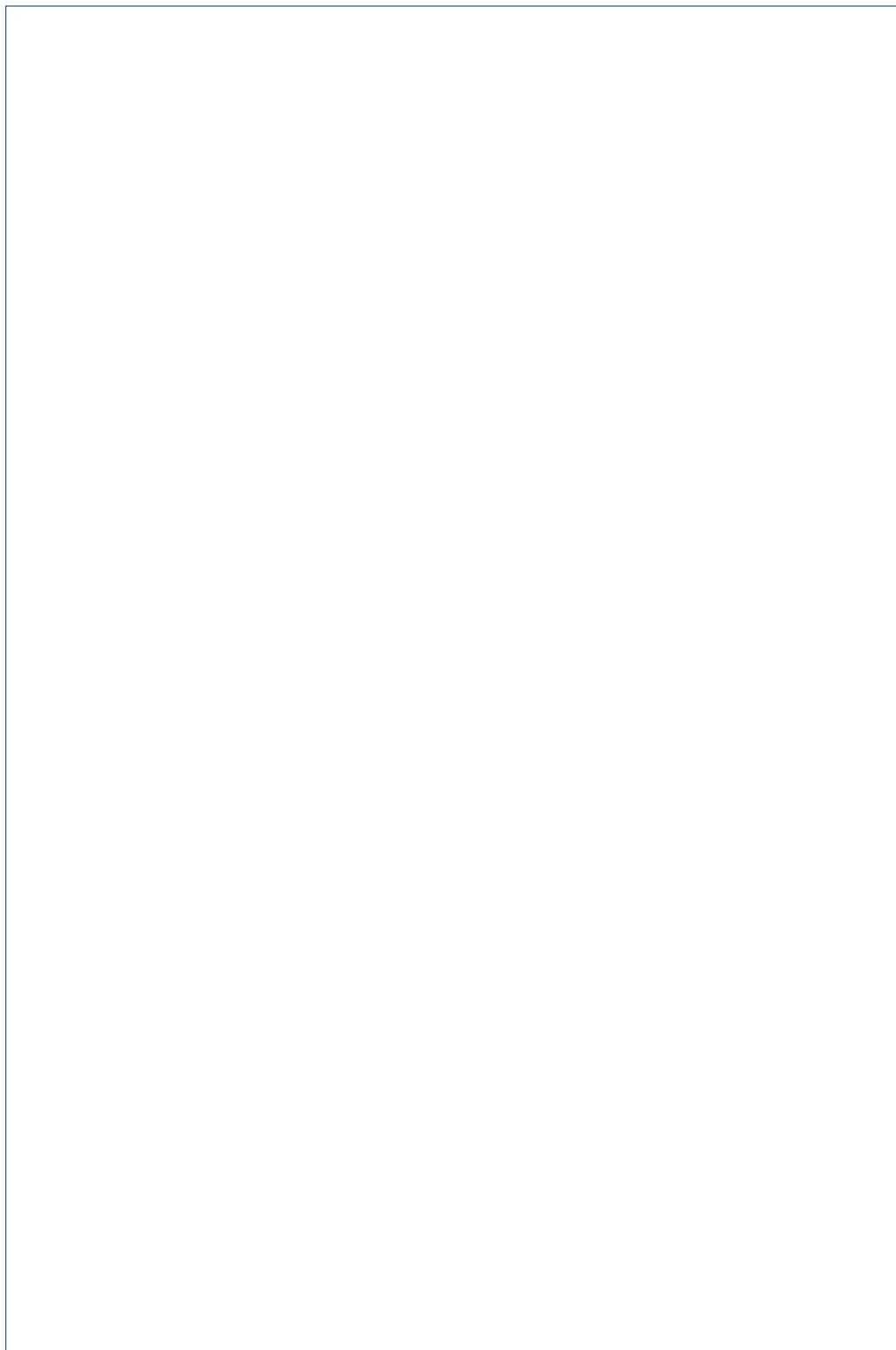
Definition of LBP

There is a great heterogeneity regarding the definition of LBP and ALBP. The main problem is the minimum duration of pain to be considered as an episode of LBP which affect all LBP questionnaire result regarding prevalence and incidence [342].

Re-call bias

Many studies examine the lifetime prevalence of LBP however; there is a risk of not remembering LBP events correctly, which is defined as re-call bias. Re-call bias increases with the shorter time of symptoms and the duration of occurrence where the

severity of symptoms also need to be considered when analyzing results from retrospective and epidemiological studies [359]. In ALBP studies a prevalence duration of one year is suggested to decrease re-call bias [342]. Forward telescoping is also a potential bias where more distant occurrences are wrongly forwarded in time and thereby affecting the results.



Why is this thesis needed?

During sports participation is the spine and the whole body subjected to a wide array of motions and loads dependent on the sport demands. The specific correlation of different motions and load exposure to spine and back problems has not yet been fully clarified even if disc herniation seem to primarily relate to flexion-extension motion while endplate fracture are more linked to compression loads. The many involved factors in the development of potential painful spinal abnormalities seem to be highly linked to different internal and external factors and properties such as bone mineral content and age but also to external load motion and subjected cumulative load.

Experimental studies on both cadaveric and porcine models are well-established study models where extensive research has been made regarding both fatigue and failure injuries in different load and motion settings. However there is still no clear evidence if and how the correlation between load, motion and spinal injuries are developed.

Low back pain is very common condition among athletes and also among the population as a whole with extremely high correlated society costs. The definition in the literature is though not cohesive and needs to be standardized to increase external validity and be able to compare different groups and interventions. There are

several risk factors presented in different studies but no clear causation is established but common risk factors are athletic participation, high levels of physical activity and endpoint movements.

Increased amounts of exercise in early years put the immature spine to great risk for injuries. High cumulative exposure of spinal loads to young athletes increases the risk of both acute back symptoms as well as increased risk of back problems later in life. The need for increased knowledge regarding both the fatigue and failure mechanisms of the spine, the development of different spinal abnormalities and their potential correlation to LBP is vital, to be able to develop prevention interventions to decrease the individuals problems, absence from training and competition and the sickness burden upon society.

The general aim of this thesis was to investigate the effect of different load magnitudes regarding fatigue and failure effect on the spine experimentally, biomechanically and clinically. The groups were chosen due to the different loading properties and motions that they are subjected to during their athletic participation in mogul skiing and long distance running. Experimental studies are essential to address the fatigue and failure pathogenesis that young athletes are subjected to.

Specific aims of the studies

Experimental studies

To investigate the fatigue response of repetitive axial loading on the failure strength and failure location in young porcine FSUs.

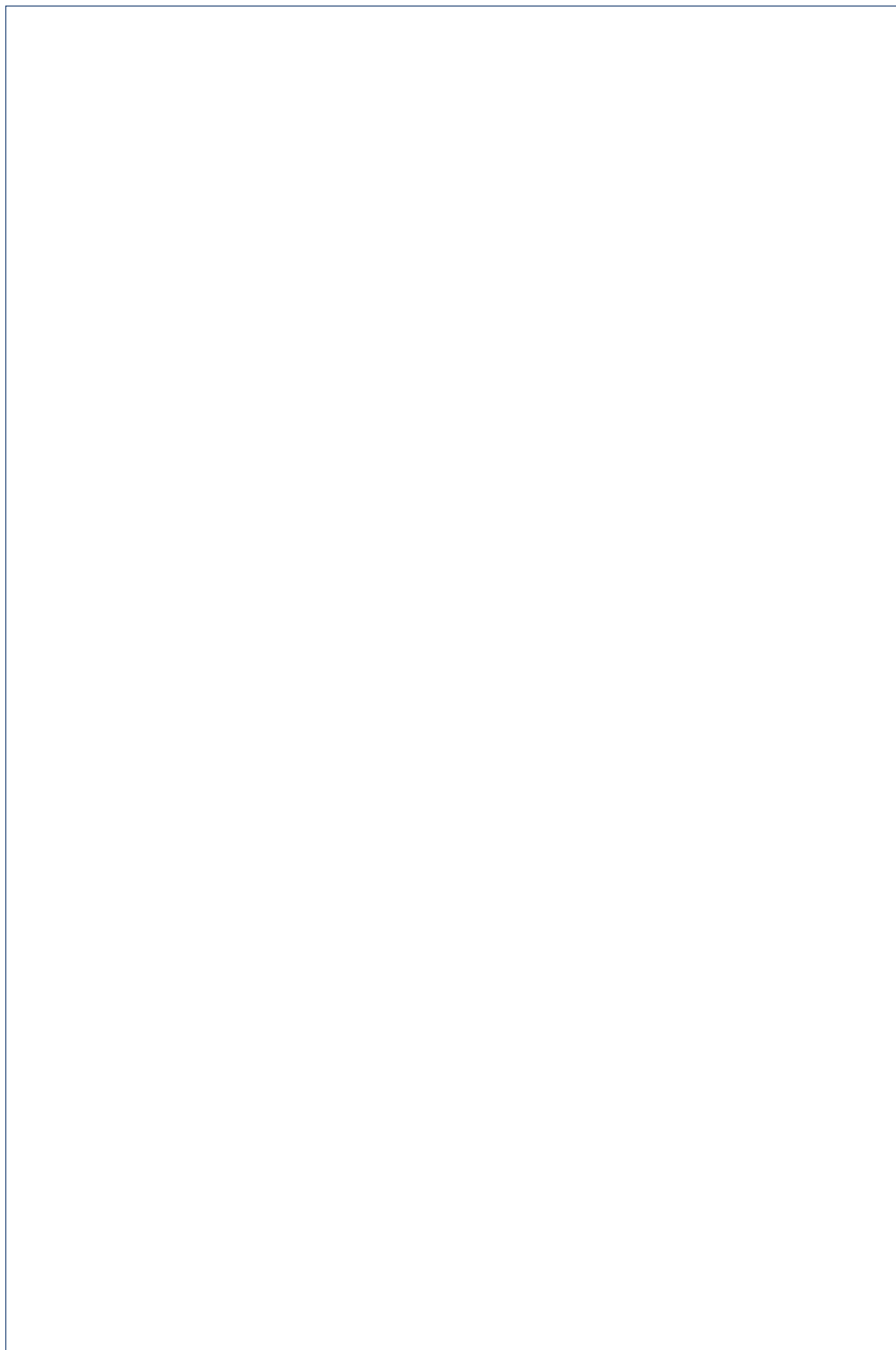
To investigate the fatigue response of repetitive flexion and extension motion in young porcine FSUs and to correlate MRI findings with histological findings.

Clinical studies

To investigate the prevalence of LBP and spinal abnormalities on MRI among young elite distance runners compared to

a non-athletic control group. Runners are exposed to high repetitive loading of low magnitude in a primarily axial loading.

To investigate the prevalence of LBP and of spinal abnormalities on MRI among adolescent Mogul skiers compared to a non-athletic control group. Mogul skiers are exposed to high repetitive loading in complex motion setting with a high number of flexion-extension motions of different load magnitudes.



patients and methods

Study I and II, biomechanical experimental studies

Experimental animals

In study I, a total of eight FSUs were harvested from four young, healthy, male domestic pigs with an age of 6 months and weight between 65-70 kg. The pigs were first sedated and then anaesthetized through intravenous injections. The spines were dissected and the FSUs were harvested and the muscles were removed from the lumbar spines, while the posterior bony elements, capsular structures and ligaments were left intact [360, 361]. Four of the FSUs were at the L2-3 and four at the L4-L5 level. The segment height, anterior-posterior diameter, width and of the disc were measured with a digital caliper.

In study II, seven porcine spines from seven male domestic pigs at an age of 6 months and body weight between 75-80 kg were acquired through a local abattoir. Nineteen FSUs, seven at the L2-L3 level, seven at the L4-L5 level and five at the Th12-L1 level were collected in the same dissection manner as in study 1. The FSUs were divided into the flexion and extension test groups with eight FSUs in each and three were used as unloaded controls.

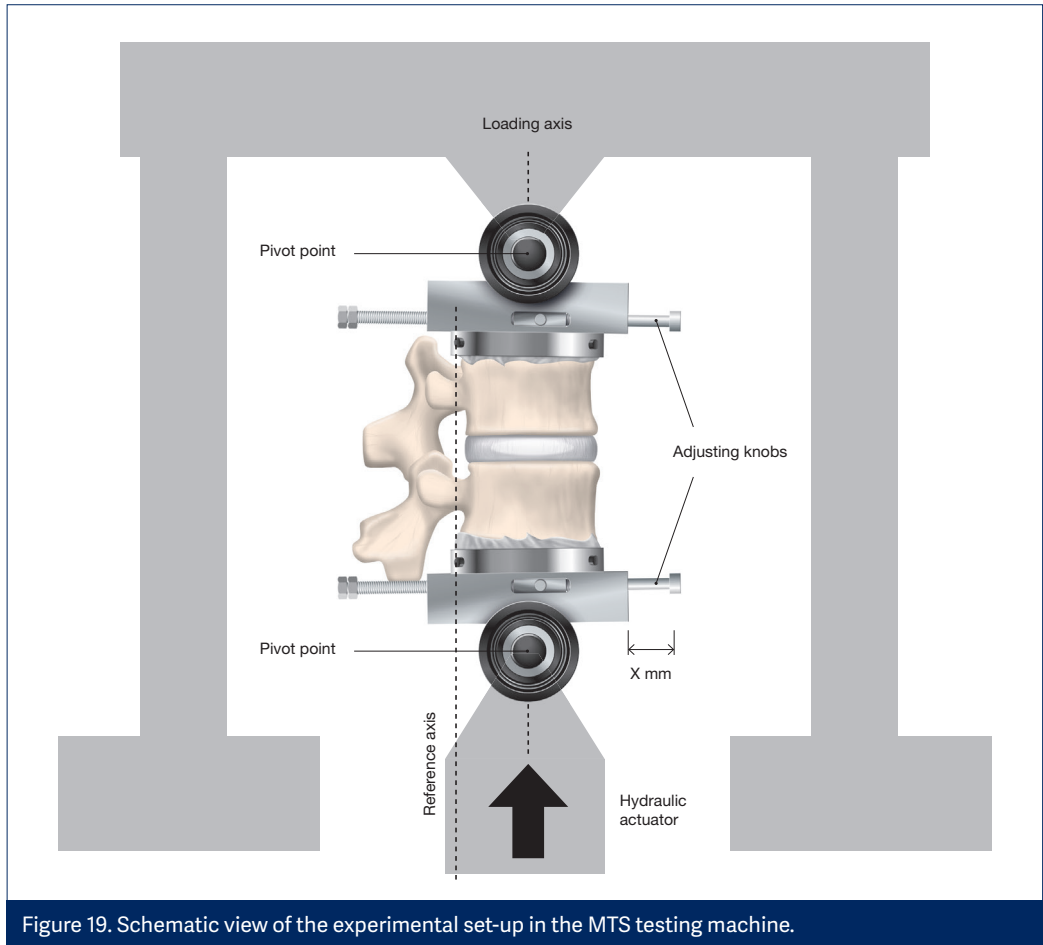
Mechanical test procedures

The FSUs were mounted in special testing cups and stabilized with Polyester putty (Loctite Sweden AB, Gothenburg, Sweden). Each FSU was mounted in a servo-hydraulic universal testing machine

(MTS Test Star, Minneapolis, MN, USA), that allows graded flexion or compression motion and graded frequency. Specimens were wrapped in saline-soaked gauze during the tests to prevent dehydration of the discs.

In study I, the FSUs were mounted to achieve axial compression. The FSUs were loaded in axial sinusoidal cyclic compression with a force of 0 - 1000 N at a frequency of 3 Hz for a duration of 20 000 cycles and the testing cups could move freely in the sagittal plane. Immediately after the cyclic loading, the FSUs were exposed to axial compression to failure at a rate of 1 mm/s. Failure was defined as a 5% decline of peak force.

In study II, a procedure according to Baranto et al [61] was used to achieve adequate flexion and extension angles and motion. The flexion test had a mean angle of 12° while the extended test had a mean angle of 9°. The applied force was set to 700N at a frequency of 1 Hz with a duration of 20,000 cycles and the testing cups were free to move around the pivot points during the tests.



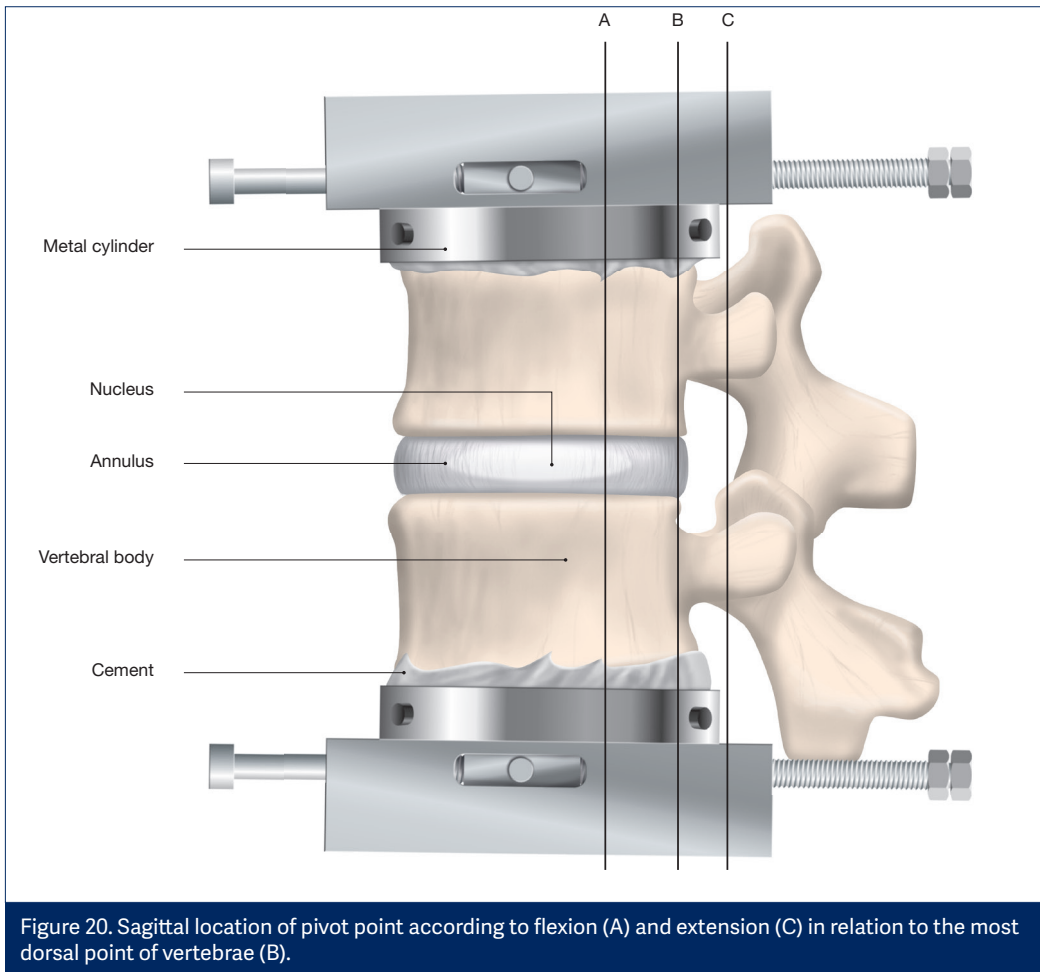


Figure 20. Sagittal location of pivot point according to flexion (A) and extension (C) in relation to the most dorsal point of vertebrae (B).

Biomechanical properties analyses

In study I the biomechanical properties were analyzed. Ultimate strength was calculated by dividing the force at failure by the intervertebral disc area. Disc height was used in the calculation of strain, and E-modulus was derived from data originating from the most linear part of the stress-strain curve. The ultimate strength was compared to that of the control group of age- and weight-matched porcine in the same experimental setting, location and temperature from an earlier study, using

the same loading technique and equipment where the only difference being the absence of cyclic loading in the reference group [69].

Radiologic examinations

In study I the FSUs were examined with plain radiographs, CT and MRI pre- and post-loading. Sagittal and axial T1 and T2 images were obtained by a 1.0 Tesla MRI with an extremity coil. CT was performed with a multidetector CT machine (GE Lightspeed/GE Healthcare) where trans-

verse and sagittal CT reconstructions were used for analysis. The radiographs were assessed by two of the co-authors with long experience of analyzing experimental porcine radiographs independently in a test re-test manner. When assessment was not agreed a new re-test was done together to reach agreement.

In study II, the FSUs were examined with MRI within an extremity coil, field strength of 3.0 Tesla. Study protocol was sagittal and transversal T2 images. The MRI radiographs were examined in a blinded manner by two of the authors independently in a test re-test manner. When assessment was not agreed a second retest was done side by side to reach agreement.

Macroscopic and histological examinations

In both study I and II the FSUs were frozen and sawn into 3-4 mm thick sagittal slices. Each slice was macroscopically examined for injuries in study I but merely checked for iatrogenic damage in study II. The slices were then prepared and stained for histological analysis where a specialist

in histology examined the histological sections from each FSU microscopically in a blinded manner.

Definition of injuries

Fracture of the endplate was defined as a fracture line through the endplate itself. Separation of the endplate was defined as a widening (fracture) of the growth zone with separation of the endplate from the vertebral body [360, 361].

In study II, the MRI exams were examined regarding disc height and the signal according to intensity and location. Disc degeneration was graded according to Pfirman et al. [257].

Statistical analysis

Study I and II are experimental studies where the statistical analyses are mainly described in terms of mean and standard deviation (SD), median and range, or frequencies and percentage when appropriate. In study 1 the comparison of biomechanical properties between the study group and the control group was done using the Mann-Whitney U test.

Study III and IV, clinical studies of athletes

Subjects

In study III, the participants consisted of twenty-two elite male long distance runners and a control group of 25 subjects. All participants received oral and written information before entering the study. The recruitment was done through contact with the coach of the Swedish National

team and coaches of long distance Clubs during 2013-2014. Inclusion criteria for the runners were male gender between 18-28 years of age; to be an elite long distance runner, defined as to practice more than 5 times a week for at least the last 5 years; and not to be active in any other sports. The control group consisted of 25 subjects between 20-25 years of age that were not active in any organized or elite sport activities at present or previously. The control

group was recruited through flyers at the Gothenburg University. The control group participants were offered two cinema tickets as participation compensation. Inclusion criteria for the control group were male gender, maximum 2 exercises/week and 20-25 years of age. Exclusion criteria for both groups were previous surgery in the thoraco-lumbar spine and obesity. The recruitment of both groups occurred simultaneously but due to difficulty to recruit runners the age span of the runner group was increased and therefore the age range was not completely matched.

In study IV, all mogul skiers of both genders at the Åre Ski Academy, Järpen, Sweden, which is a 4 year Swedish elite skiing High School with a total of 16 enrolled Mogul skiers, were offered participation and all of them accepted (N=16). The skiers were between 15-20 years of age. Exclusion criteria were previous surgery in the thoraco-lumbar spine, hip, pelvis or present activity in another sport. No skiers were excluded due to the inclusion or exclusion criteria.

Thirty age matched students at the Östersund and Åre/Järpen High Schools were invited to participate in the present study. Twenty-eight (N=28) of the students accepted to participate. The controls were offered two cinema tickets as participation compensation. Inclusion criteria for the control group were to be a first year High School student and no previous or present participation in any organized sport or training more than 2 hours/week. Exclusion criteria were surgery to the thoraco-lumbar spine, hip or pelvis. All partici-

pants and their parents received oral and written information regarding the study in advance, and signed written consent forms before entering the study.

MRI examinations

In study III, the participants were investigated with either a 1.5 or 3.0 Tesla MRI machine, with T1 and T2 sagittal examinations of the thoraco-lumbar spine, from Th5 to sacrum. The MRI images were evaluated in a blinded manner by an experienced radiologist and a senior spine surgeon.

In study IV, all participants were examined in a 3.0 Tesla machine from Th5 to the sacrum. Sagittal T1 images and T2 images of the thoracic and lumbar spine were taken. The images were evaluated in a blinded manner by a specialized radiologist.

All examinations were anonymous and allocated a random number, the MRI examinations were mixed and evaluated randomly. The images were evaluated according to a standardized protocol [159], including a four level severity assessment of disc signal, disc bulging, disc height, apophyseal injury, disc herniation, Schmorls nodes and shape of vertebrae. Potential fractures, scoliosis and spondylolisthesis were graded as present or not. Disc degeneration was in study III classified according to Pfirrmann et al. (2001) [257] and in study IV according to DeCandido et al. [256].

Back pain questionnaires

In both study III and IV all participants answered a three-part questionnaire according to Swärd et al. [161] and Baranto

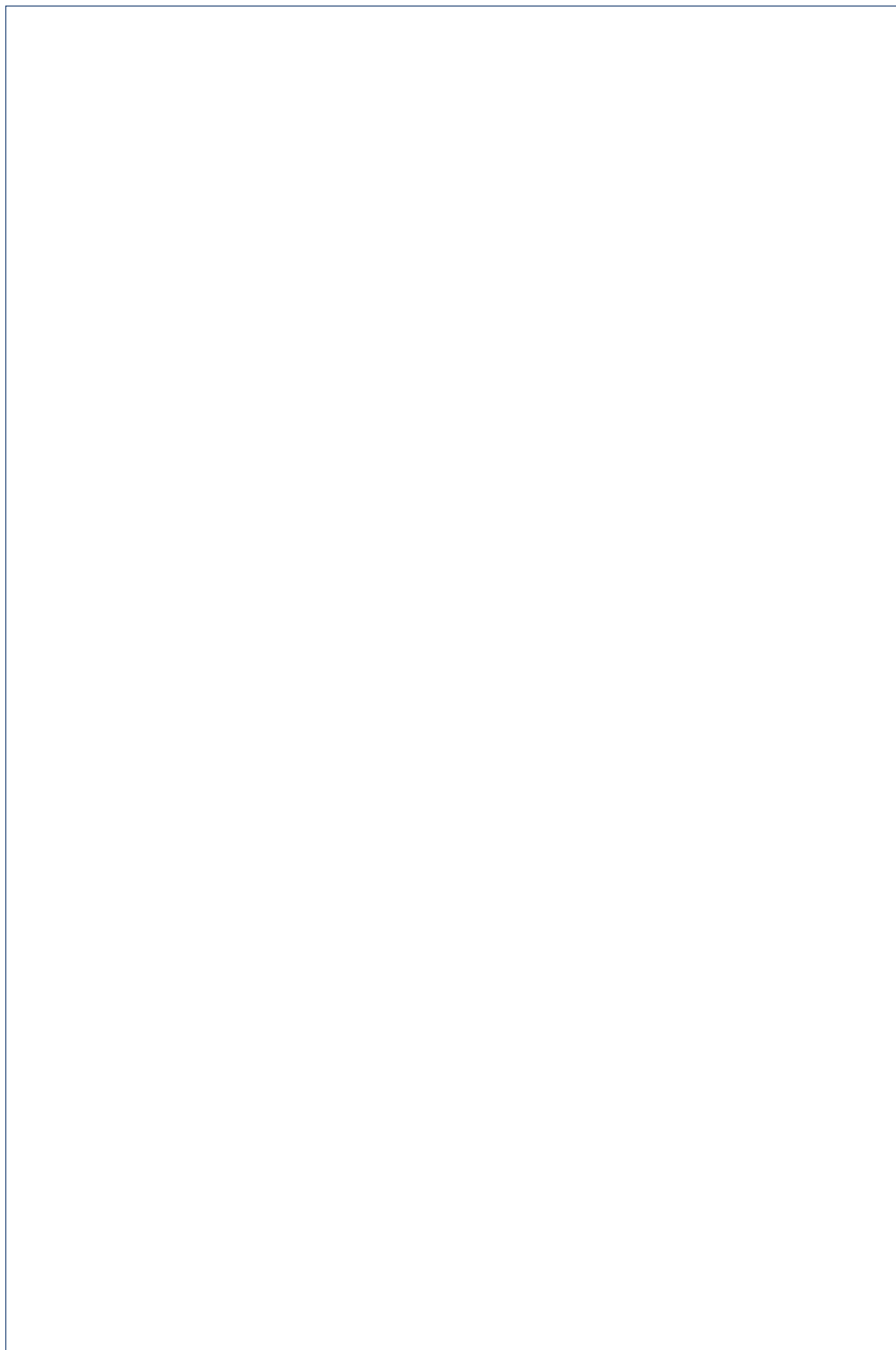
et al. [159]. The questionnaire includes the Swärd-Baranto Questionnaire, the Oswestry questionnaire (ODI) and the Euro-QoL (EQ5D ©EuroQoL Group 1990) questionnaire.

The Swärd-Baranto questionnaire includes two questions regarding the prevalence of back pain. The questionnaire assesses many parameters such as the total duration, occurrences, severity and impact of back pain.

Statistical analysis

In both study III and IV no good data for power analyses were available and therefore power was not calculated. The data in

both studies were statistically described in terms of mean and standard deviation (SD), median and range, or frequencies and percentage when appropriate. Comparison of numerical variables between groups was done using an independent t-test. A nonparametric Mann-Whitney U test was used for ordinal data. For comparing categorical data in two by two tables' a Chi-square test was performed. Fisher's exact test was used when expected cell count was less than 5. All tests were two-sided, and significance was set at $p < 0.05$ for each test. The analyses were carried out using SPSS (IBM SPSS Statistics for Windows, Version 22.0.Armonk, NY: IBM Corp.).



summary of studies

Study I

The failure strength and injury location of young porcine lumbar FSUs after low magnitude repetitive axial compression fatigue loading are similar to FSUs without prior fatigue in an experimental study.

Introduction

The human spine is exposed to vibration or cyclic loading during daily activities and more extremely during sports. Despite this common cause of spinal injury there remains a lack of knowledge regarding the effects on the spine due to this mode of loading. The purpose of the present study was to investigate the biomechanics and fracture patterns of cyclic loading followed by axial compression to failure in functional spinal units (FSU) in an experimental model.

Methods

Eight lumbar FSUs from four young porcine spines were used in the experimental study. The FSUs were axially compressed with 20,000 cycles, at 3 Hz and with a magnitude of 0-1000 N and then axially compressed to failure. The compression load at failure, ultimate stress and viscoelastic parameters were calculated. The FSUs were examined with plain radiography, CT and MRI before and after the load protocol. All FSUs were macroscopically and histologically assessed after the load protocol. The results were compared to earlier study in the same method, settings and conditions with the difference of absence of fatigue

loading before the compression to failure of the FSUs.

Results

The median compression load at failure in this study was 8.35 kN (range 5.6-8.7 kN). The median deformation for all cases was 2.24 mm (range 2.30 - 2.7 mm) and stiffness was 3.45 kN/mm (range 3.5 - 4.5 kN/mm). Failure was seen as endplate fracture in all cases in both the MRI and histological examinations whereas CT detected seven fractures and plain radiography could detect only one fracture of all the FSUs. No disc hernias were detected.

Conclusion

The axially vibrated and fatigued lumbar FSUs in the present study were not more sensitive to axial compression than non-vibrated FSUs from young porcine. The FSUs displayed the same compression failure expression as non-vibrated FSUs where the endplate and the growth zone were the weakest parts in the vibrated FSUs. The induced repetitive loading was either too low in load magnitude or too short in duration to induce failure-moderated fatigue. The E-modulus value found in this study was of the same order of magnitude as found by others using a porcine animal model.

table 3 Functional spinal units (FSU) levels, ultimate force at failure, deformation and stiffness values for all specimens after the load protocol.

Specimen	FSU Level	Ultimate force at failure kN	Deformation mm	Stiffness kN/mm
1	L2 - L3	8.3	1.83	4.5
2	L4 - L5	8.7	2.33	3.7
3	L4 - L5	5.6	1.94	2.9
4	L2 - L3	5.7	2.00	2.8
5	L2 - L3	8.6	2.31	3.7
6	L4 - L5	8.3	2.7	3.0
7	L2 - L3	8.5	2.5	3.4
8	L4 - L5	8.4	2.3	3.6

table 4 Plain radiography, Computed tomography (CT), Magnetic Resonance Imaging (MRI), macroscopic and histological findings for all cases after the load protocol.

FSU	FSU Level	Plain radiography	CT	MRI	Macroscopic examination	Histological examination
1	L2 - L3	-	+	+	+	+
2	L4 - L5	-	+	+	+	+
3	L4 - L5	-	+	+	-	+
4	L2 - L3	-	+	+	+	+
5	L2 - L3	-	+	+	+	+
6	L4 - L5	-	-	+	+	+
7	L2 - L3	-	+	+	+	+
8	L4 - L5	+	+	+	+	+

Described as fracture (+) or not detected (-).

table 5 Endplate fracture location according to Histology.

FSU	FSU Level	Anteriorly	Posteriorly	Superior vertebra	Inferior vertebra
1	L2 - L3	-	+	-	+
2	L4 - L5	+	+	-	+
3	L4 - L5	-	+	-	+
4	L2 - L3	-	+	-	+
5	L2 - L3	+	+	+	+
6	L4 - L5	+	+	-	+
7	L2 - L3	+	+	+	+
8	L4 - L5	+	+	-	+

Described as fracture (+) or not detected (-).

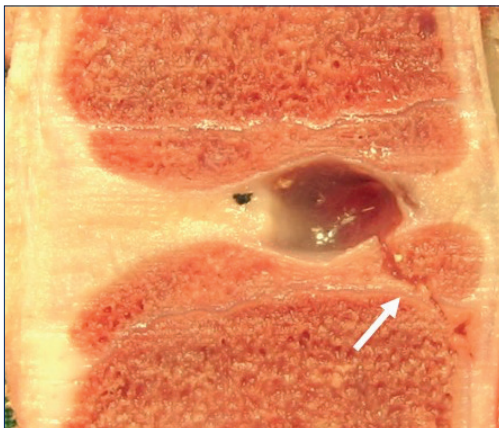


Figure 21. Macroscopic view of FSU number 8.

The failure injury of a fracture through the endplate, growth zone and the dorsal part of the vertebral body.

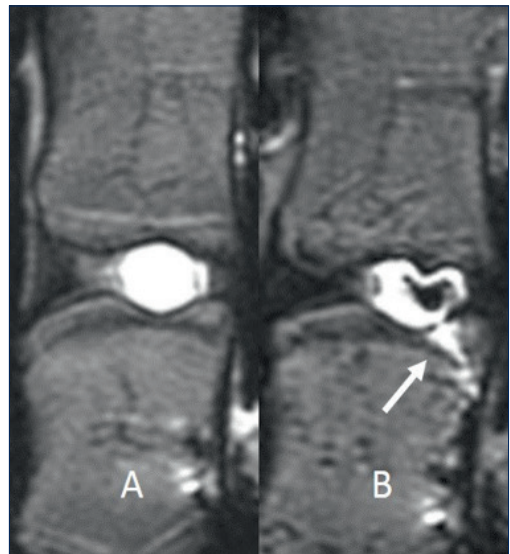


Figure 22. MRI of FSU number 8.

Before loading (A) and after load protocol (B), with arrow highlighting the failure injury of a fracture through the endplate, growth zone and the dorsal part of the vertebral body, with nucleus leakage.

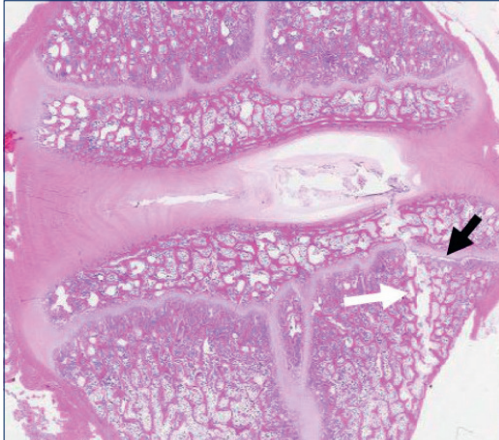


Figure 23. Histological view of FSU number 8.

The failure injury of a fracture (white arrow) through the endplate, growth zone and the dorsal part of the vertebral body. There is also a separation fracture of the endplate from the vertebral body (black arrow).

Study II

The fatigue effect of young porcine lumbar FSUs display both MRI and histological changes in the endplate and the growth zones due to repetitive flexion or extension.

Introduction

The spine in adolescent athletes is often subjected to high repetitive loads in different magnitudes and motions. The potential fatigue effect of such loading is not fully clarified but may correlate to the increased prevalence of spinal abnormalities and low back pain that are common among young athletes. Several studies have examined the biomechanical mechanisms of fatigue and failure of FSUs but mainly through axial loading and with failure strength as main endpoint. The aim of this study was to investigate the fatigue

responses and potential failure injuries of young porcine lumbar FSUs subjected to repetitive flexion and extension loading with MRI and histology.

Methods

Eight young (6 month) porcine lumbar FSUs were subject to repetitive pivot flexion and eight to extension loading by a protocol of 20 000 cycles at 1 Hz with a load of 700 N. All FSUs (N=16) were examined with MRI and histology post loading. Three FSUs were examined with MRI as controls. Three additional FSUs were non-loaded histology controls.

Results

No failure injuries were seen in either the MRI or histology examinations. Fatigue responses were seen as MRI signal differentiation, mainly in the growth zone and in the endplate. Fifteen (94%) of the loaded

FSUs have decreased signal in the growth zone of the superior vertebra and 12 (75%) in the inferior vertebrae. Fourteen (88%) FSUs have increased signal in the superior vertebral body. Fourteen (88%) FSUs have a reduced signal in all or any endplate. Eleven (69%) discs display reduced disc height and three (19%) discs have a reduced disc signal that corresponds to Pfirman grade 2. The histological results displayed reduced content in both intracellular as well as in the extracellular matrix reduction at the cartilage cells in the

endplate and growth zone area in all loaded FSUs. There was no difference between the flexion and extension loaded FSUs.

Conclusion

Repetitive loading of young porcine FSUs in both extension and flexion causes consistent MRI and histological changes in the growth zones and endplates which could be a first sign of fatigue and an explanation for disc, apophyseal and growth zone injuries seen among adolescent athletes.

table 6 Basic Characteristics of the FSUs.

FSU	Load	Angle	Level	Distance from B-line
1	Flexion	10	L4-L5	10
2	Flexion	12	L2-L3	11
3	Flexion	12	L4-L5	12
4	Flexion	10	L2-L3	12
5	Flexion	10	L4-L5	13
6	Flexion	13	L2-L3	12
7	Flexion	15	L4-L5	12
8	Flexion	15	L2-L3	14
9	Extension	9	Th12-L1	10
10	Extension	10	L2-L3	10
11	Extension	10	L4-L5	10
12	Extension	9	Th12-L1	10
13	Extension	9	L2-L3	10
14	Extension	8	Th12-L1	10
15	Extension	9	Th12-L1	10
16	Extension	10	L4-L5	10

Angle in degrees. FSU= Functional spinal unit. Distance in mm. B-line as in figure 2.

table 7 MRI signal of the vertebral body of the loaded FSUs.

FSU	Superior Growth zone, V/D	Superior vertebral body, V/D	Inferior Growth zone, V/D	Inferior vertebral body, V/D
1	-/-	+/0	0/0	0/-
2	-/-	+/0	-/-	-/0
3	-/-	0/0	-/-	0/0
4	-/-	+/+	-/-	+/+
5	-/-	+/+	-/-	0/0
6	-/-	+/+	0/0	0/0
7	-/-	+/-	-/-	0/0
8	-/-	+/+	-/-	+/+
9	-/-	+/+	0/0	0/+
10	-/0	+/+	-/-	+/-
11	-/-	+/0	-/-	+/+
12	0/0	+/+	0/0	+/+
13	-/-	+/+	-/-	+/0
14	-/-	+/+	-/-	+/+
15	-/-	0/0	-/-	0/+
16	-/-	+/+	-/-	-/0

According to superior or inferior vertebra and ventral (V) or dorsal (D) location of the FSUs. Grading as reduced (-), normal (0) or increased (+). All controls displayed 0 in all columns.

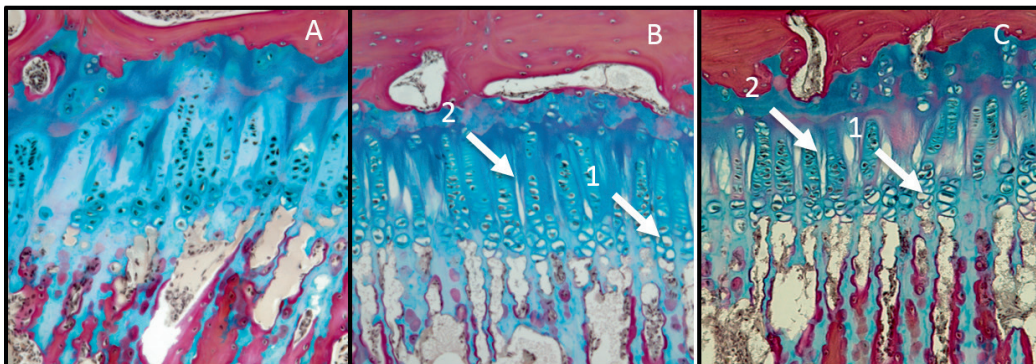


Figure 24. Visualization of the histological results in x10 magnification.

Control (A), flexion (B) and extension (C) FSUs, where the reduction of intracellular content (1) and extracellular matrix (2) are highlighted with white arrows. Slices colored to turn bone red and cartilage blue.



Figure 25. The MRI results of repetitive flexion.

Un-loaded control (A) and FSU after repetitive flexion (B). Decreased signal in both the superior (1) and inferior growth zones (2) and endplates in the flexed FSU.

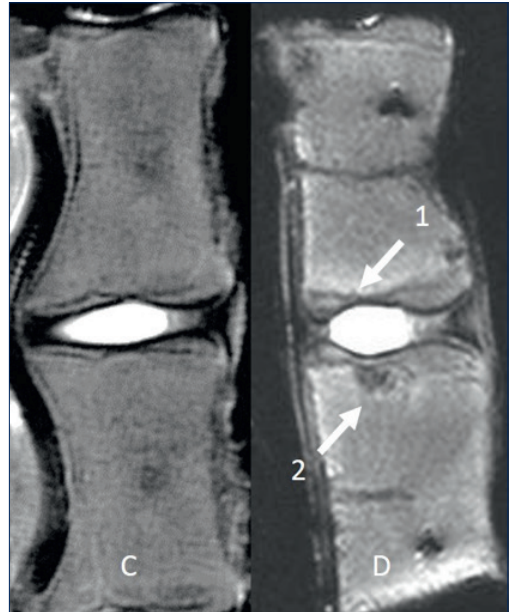


Figure 26. The MRI results of repetitive extension.

Un-loaded control (C) and FSU after repetitive extension (D). Reduced signal in the superior growth zone (1) and in inferior end plate (2) in the extended FSU.

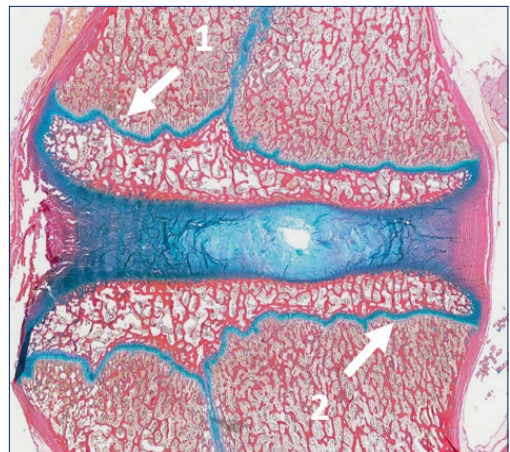


Figure 27. Histological overview of a flexed FSU.

Highlighted are the cranial-anterior growth zone (1), caudal-posterior growth zone (2).

Study III

Assessment of long distance running according to fatigue and failure injuries in spine the spine and the prevalence of low back pain, a cross sectional study.

Introduction

Studies have shown that athletes have a higher prevalence of back pain and a greater number of spinal abnormalities on MRI, such as disc degeneration, compared to non-athletes. Athletes are subjected to a wide range of motions that can cause both fatigue and failure injuries in the spine. The development of different injuries appears to primarily relate to cumulative load and the implied motions. The associations between running and both fatigue and failure injuries such as spinal MRI abnormalities and have not been clarified and neither has the potential correlation to LBP. The objective was to investigate the amount of MRI abnormalities in the thoraco-lumbar spine and the prevalence of back pain in male elite long distance runners compared to a control group of non-athletes in the corresponding age.

Methods

Study participants were 22 male elite long distance runners (runner group) and 25 male

non-athletes (control group) of 18-28 years of age. Elite long distance running was defined as running five times a week for at least the last five years and not participating in any other sport. Back pain was assessed by a three part self-reported questionnaire. Sagittal T1 and T2 weighted MRI examinations from Th5 to sacrum was conducted to evaluate MRI abnormalities according to study protocol.

Results

The mean age of the runner group was 23 years (range 18-28 years) and for the control group was 23 years (range 21-25). The runners reported a significant higher lifetime prevalence of back pain (45%), compared to the control group (12%) ($P=0.011$). No statistical significant difference was found in the amount of MRI verified spinal abnormalities ($P=0.614$) or type of abnormalities between the groups. No statistically significant correlation between back pain and MRI abnormalities was established.

Conclusion

Elite level male long distance runners have a significant higher prevalence of back pain but demonstrate no significant difference in the amount or type of spinal abnormalities compared to non-athletes. Further prospective studies are needed to validate the results.

table 8 Number of current training hours per week stratified by controls and runners. Number and (%).

Number of weekly exercise hours (h)	Controls, n=25	Runners, n=22
>11 h	0	14 (63%)
9-11 h	0	6 (27%)
6-8 h	0	2 (9%)
3-5 h	6 (24%)	0 (0.0)
0-2 h	16 (64%)	0 (0.0)
0 h	3 (12%)	0 (0.0)

table 9 Prevalence of back pain stratified by controls and runners. Chi-square test, $p = 0.011$. Number and (%).

Back pain.	Controls, n=25	Runners, n=22
No back pain	22 (88%)	12 (55%)
Back pain	3 (12%)	10 (45%)

table 10 Presented below is every unique individual with one or more abnormality for each pathology and (%).

MRI abnormality	Controls, n=25	Runners, n=21	P-value
Disk-signal	16 (64%)	11 (52%)	> 0.05
Disk-bulging	11 (44%)	8 (38%)	> 0.05
Disk-height	18 (72%)	14 (67%)	> 0.05
Apophyseal injury	0	0	> 0.05
Shape vertebrae	4 (16%)	6 (29%)	> 0.05
Schmorl's nodes	17 (68%)	8 (38%)	> 0.05
Disk hernia	2 (8%)	0	> 0.05
Spondylolisthesis	0	0	> 0.05
Retrolisthesis	2 (8%)	2 (10%)	> 0.05
Scoliosis	7 (28%)	4 (19%)	> 0.05
HIZ	4 (16%)	0	> 0.05



Figure 28. MRI comparison, runner vs. control.

A) MRI of a 20 years old runner's spine showing disc degeneration on L5-S1 level.
 B) MRI of the spine of a 22 years old control male with disc degeneration on L4-L5 and L5-S1 levels.

Study IV

The correlation of the repetitive complex spinal loads that mogul skiers are subjected to both spinal abnormalities and LBP. Investigated by MRI and questionnaires in a cross-sectional study.

Introduction

The high amount of traumatic and repetitive spinal loads that athletes are subjected to, are thought to cause both fatigue and failure injuries as seen as spinal abnormalities. Mogul skiers are subjected to many different and complex loads with different motion settings and of different magnitudes on the heavily moguled slope, including two jumps, which they ski on. The aim of this study was to investigate the amount of MRI abnormalities in the thoraco-lumbar spine and the lifetime prevalence of low back pain (LBP) in young elite Mogul skiers compared to a control group of non-athletes in the corresponding age.

Methods

Study participants were 16 elite Mogul skiers and 28 non-athletes of both genders and of 15-20 years of age. Elite mogul skiers were defined as those who were enrolled at Åre/Järpen Alpine Ski High School. LBP was assessed by a three-part questionnaire. Sagittal T1 and T2 weighted MRI examinations from Th5 to sacrum was conducted and evaluated in a blinded manner by a specialized radiologist regarding spinal abnormalities.

Results

The groups differed in gender where the mogul group consisted of 14 male (87%) participants while the control group had

9 male (32%) participants. The mogul skiers exercised significantly more hours per week in mean than the control group. The mogul skiers had significantly more spinal abnormalities in mean (7.25 vs 3.78, $p < 0.023$) compared to the controls. No significant difference was seen regarding the lifetime LBP prevalence between the groups (50 % vs 42 %, $p = 0.555$).

Conclusion

Young elite Mogul skiers, compared to an age matched control group of non-athletes, have an increased risk of developing spinal pathologies potentially due to the different high loads of both traumatic and overuse origin that they are subjected to in their sport. There were no statistical difference regarding lifetime or point prevalence of back pain between both groups and no correlation could neither be found between disc degeneration and back pain in the present study. Future relationship between the MRI abnormalities and LBP cannot be verified by this study design.

table 11 Baseline characteristics, stratified by group.

Baseline characteristics	Controls (n=28)	Mogul Skiers (n=16)
Age, years	16.4 (0.57)	17.6 (1.02)
Male sex, n (%)	9 (32%)	14 (87%)
Female sex, n (%)	19 (68%)	2 (13%)
Height, cm	172 (8.56)	177 (6.90)
Weight, kg	67 (17.91)	70.8 (10.62)
Body mass index, kg/m ²	22.8 (5.15)	22.5 (2.73)

Values are mean and (standard deviation) unless specified otherwise.

table 12 Total amount of abnormalities stratified by groups.

Group (n)	Total	Mean	Standard deviation
Mogul Skiers (n=16)	116	7.25	4.28
Controls (n=28)	111	3.78	4.90

T-test for equality between groups, $p < 0.023$.

table 13 Every unique individual with one or more abnormality for each pathology and (%).

MRI abnormality	Controls (n=28)	Mogul Skiers (n=16)	P-value
Disc-signal	12 (43%)	11 (69%)	0.098
Disc-bulging	13 (46%)	13 (81%)	0.024
Disc-height	0	8 (50%)	<0.001
Apophyseal injury	0	1 (6%)	Na
Shape vertebrae	1 (4%)	1 (6%)	Na
Schmorls nodes	6 (21%)	9 (56%)	0.019
Disc hernia	0	0	Na
Spondylolisthesis	1 (4%)	0	Na
Retrolisthesis	0	0	Na
Scoliosis	8 (29%)	2 (13%)	0.283
HIZ	0	1 (6%)	Na

P-value by Chi-Square Test. Na = not analyzed due to no or few events. Bold style indicating statistical significance.

table 14 Lifetime prevalence of back pain stratified by gender and group, number and (%).

Gender	LBP lifetime	Controls	Moguls	Total
Female	Yes	7 (37%)	0 (0%)	7 (33%)
	No	12 (63%)	2 (100%)	14 (67%)
	Total	19	2	21
Male	Yes	5 (56%)	8 (57%)	13 (57%)
	No	4 (44%)	6 (43%)	10 (43%)
	Total	9	14	23
Total	Yes	12 (43%)	8 (50%)	20 (45%)
	No	16 (57%)	8 (50%)	24 (55%)
	Total	28	16	44

Chi-Square Test, $p = 0.555$ (total lifetime LBP prevalence).

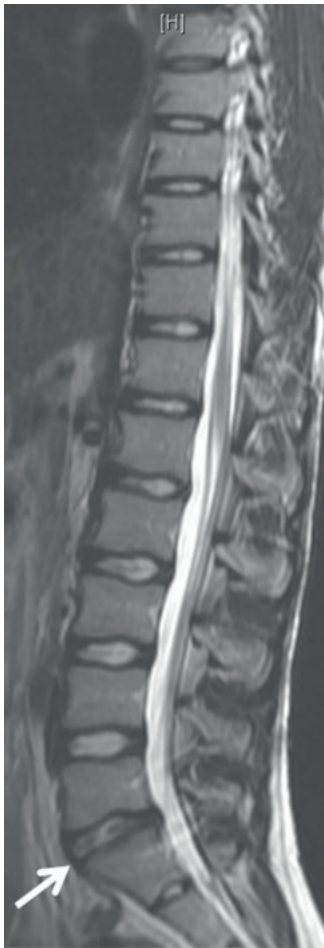
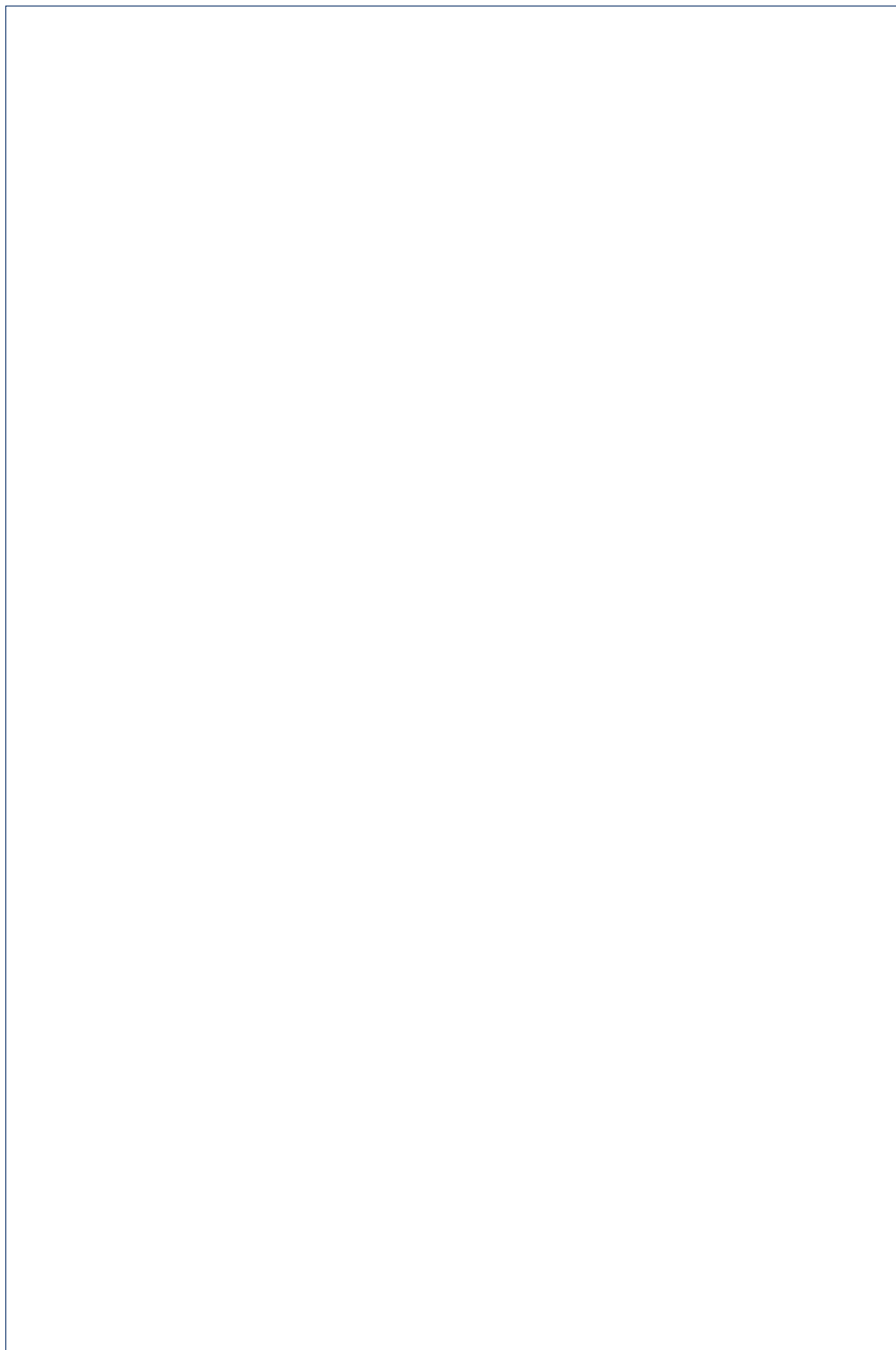


Figure 29. Disc degeneration.

Sixteen year old Mogul skier with disc degeneration at the L5-S1 level.



discussion

Experimental studies

The results from the experimental studies were that the vibrated FSUs in study I were not any more sensitive to axial compression than earlier non cyclic loaded FSUs from young porcine. The endplate and the growth zone were the weakest parts in young porcine vibrated FSUs. In study II a majority of all cyclic loaded FSUs in flexion and extension displayed signal changes in both the vertebral bodies and the disc. The growth zones and endplates were affected in particular potentially highlighting the areas of developing fatigue. There were no displayed differences between the results in the extended and flexed FSUs.

Materials, Porcine FSUs

Experimental studies of the spine are mainly done with either cadaveric or porcine FSUs. Most cadaveric studies are done with spines of high or adult age and are therefore not suitable to investigate the developing or young spine due to the major biomechanical, activity conditions and pathological differences due to ageing alone but also to age correlated injuries [35, 38-41]. In the experimental studies a well-used and established porcine model was used and the protocols were based on earlier studies in the same settings [40, 61, 69, 104]. Young thoracic and lumbar porcine spinal models are considered a suitable anatomical animal model for experimental studies [72] even if the porcine spine display some anatomical differences [73] like different vertebral body size

[64] and reduced range of motion [64, 65] that needs to be considered when assessing the results from porcine studies. The young porcine FSU and the human FSU have many similar cellular [71, 76-78] and biomechanical properties [66-7]. These similarities seem to be adequate since the human and young porcine FSUs display similar responses to fatigue and failure loading [71, 74, 76, 77] making the young porcine spine a good experimental model to the investigation of fatigue and failure responses in spinal FSUs.

The chosen pigs for the two experimental studies were domestic Swedish male porcine of an age around 6 months and a weight around 75 kg and the examinations displayed that the growth zones were not closed. BMC was not measured for any of the specimens considering that they were all healthy young male pigs, but internal conditions like BMC and EP size are vital in loading biomechanics. During the tests the FSUs were covered with saline-soaked gauze to prevent dehydration but since the majority of all adjacent soft tissue was taken away from the spine the environment was very different in this in-vitro experimental model rather than an in-vivo situation. High water content structures such as the intervertebral disc did lack several important factors for maintaining integrity like the absence of adjacent tissue pressure that to some extent counter balance applied load on the disc and affecting the viscoelastic behavior of the disc. This is however a general problem in all experi-

mental tests of FSUs in the literature and is one of many factors that needs to be considered when addressing the clinical relevance of experimental findings.

In study I eight FSUs were used and as control group regarding ultimate load, the results from an earlier study was used [104]. The control study had the same study settings (experimental lab, pre loading preparations and test environment) and equipment and FSUs from porcine of the same breed, gender and age but with the exception that the control FSUs were compressed to failure without prior fatigue loading. No power calculation was done due to no good pilot studies in the same settings regarding ultimate load and due to the objective endpoints of the study. This renders the study result an unknown possibility to display a statistical type 2 error.

In study II, sixteen FSUs were separated in two groups. No power calculation was done ahead of the study due to the experimental objective study design.

Study protocol

The study protocols in both studies were chosen to resemble normal every day behavior in load magnitude, frequency and duration. The motions chosen were to investigate the fatigue effect in axial compression and in flexion correlating to different motion settings clinically.

Motion

Two different motion settings were used in the biomechanical studies. In study I, an axial low magnitude repetitive load-

ing was followed by a strong axial load to failure in the neutral position. This was a biomechanical experimental set-up model that could presumably correlate to a clinical situation of a long distance running followed by gym exercise or a heavy lift. The repetitive flexion/extension motion in study II were more complex load motions that were a set-up that could resemble the spinal flexion-extension motion that occurs during alpine skiing. Even if the mogul skiing motion is more complex, including both lateral bending and rotation in different settings, the mechanical procedure in the present model was simplified to repetitive flexion or extension loading. The flexion test had a mean angle of 12° while the extended test had a mean angle of 9° which were chosen due to have comparable method to an earlier study by Baranto et al. [61] and to correlate it to the maximum flexion of the human lumbar back [105].

In experimental models, the applied loads and motions to the FSUs are in general static or cycled while a typical clinical movement is a very complex movement constituting of several movement vectors that are difficult to exam in an experimental model. The transfer to a specific clinical situation of results from experimental studies may be difficult since human daily activity, especially in sports, includes a complex pattern of motions and a long-term cumulative load exposure. The result of simplified test protocols might underestimate the risk of reaching the fatigue limits in real life activity and, as a consequence, underestimate the risk for injury to the spine. The motion itself is also very

important load properties and can have several differences, considering a flexion motion is a moment (Nm) rather than a load and constitutes of different properties, meanwhile compression in a static flexed position is instead a load and not a moment. Earlier research have displayed different fatigue and failure responses due to different applied motions especially among adult specimens [35, 51] meanwhile EP, apophyseal and growth zone injuries are common in the adolescent spine independent on motion type [40, 61].

Preload

Preload is used in many studies to resemble the normal non-external load that is applied to the spine and is in many studies around 300-500 N for a set time period [46, 50]. In the present studies no specific preload was used due to the designs viscoelastic differences existing and thereby are the conditions not clinically equal. The experimental studies were at low load magnitude thereby correlating the first period of cycles of load to normal non-injurious loading which, could be considered the studies preload.

Load magnitude

Load magnitudes in experimental models are usually derived from the in-vivo pressure measurements from human intervertebral discs [79, 80, 82]. The erect position is in many experimental studies correlated to an externally applied load of 500 N that is derived from an assumed area of the EP of 1000 mm² since the normal upright position correlates to a disc pressure of around 500kPa. The normal adult human lumbar EP is around 1500 mm²

[31] and the porcine EP is generally smaller, dependent on breed, making it important to consider the external load in correlation to the applied area. Different studies have displayed a wide range of results regarding the ultimate strength of both cadaveric and porcine FSUs dependent on both internal and external properties and is somewhere between 2-14 kN, displaying the maximum load magnitude / failure load of a FSU [45-53]. When discussing the results of different studies it is always important to consider if the results are described as force/load (N) or in stress (N/m²) and thereby taking the EP area in consideration or not.

In study I the chosen repetitive sinusoidal load magnitude was 1000 N correlating to the load that is derived during a run or a jog [81]. In study II the sinusoidal load was set to 700 N which was chosen due to be a third of the maximum loading capacity in flexion and extension loading before injury develops according to results of earlier studies [61, 362].

Load duration and number of cycles

The load duration is very important due to the effect on the spine depends on the cumulative load that it has been subjected to. Earlier studies support that the load magnitude is inversely correlated to the load duration in relation to the development of fatigue and failure injuries but is affected by motion type [35, 58].

Both study I and study II were loaded with a total of 20,000 cycles correlating roughly to the distances covered in sports like Australian football [89], soccer [90] or a 10 km walk with a stride length of 0.5 m.

Load frequency

The chosen frequency of study protocols are important when considering what clinical situation that they meant to resemble. The frequency in study I was set to 3 Hz due to be faster than a walk [83] but slower than a mechanical induced frequency as a cab and car driver is subjected to [86]. The FSUs in study II were loaded at a frequency of 1 Hz which was chosen to its correlation to the stride frequency during a normal distance run [84].

Load rate

Two different set-ups to control the load rate where load control is the set load that the FSU will be put under [54, 127] meanwhile strain control is the amount of displacement the FSU is subdued to and usually measured by mm/s [125, 128]. The load rate was controlled by load control during the fatigue procedure in both study I and study II. In the compression to failure section in study I the load rate was set to 1 mm/s and thereby strain controlled.

Radiologic examinations

In study I the FSUs were examined with plain radiography, CT and MRI before and after experimental loading making the investigations paired. In study II the FSUs were radiologically examined with MRI after the experimental loading and compared to unloaded controls making them subject to un-paired controls. Of these study regimes the first with paired controls is the better where it reduces the possibility of confounding findings that are not derived from the mechanical tests.

The radiographs were assessed in a test re-test manner in both study I and II but no ICC, inter or intra rater reliability tests were done in either study and thereby not validating the assessment. The study protocols were based on the same injury definition protocol but varied regarding that study I did emphasize failure injury location and type whereas study II assessed potential fatigue response in the vertebra and also included disc degeneration determination according to Pfirman et al. [257].

There are several radiologic exams available to assess the spine clinically but MRI is generally considered as the Gold standard in relation to different spinal abnormalities. There is still reliability and validity issues predominantly with different MRI assessment classifications and high inter- and intra-rater agreement variability regarding different abnormalities and especially when severity level is determined [283]. Disc degeneration alone has several different classifications [256-258, 291-293] systems where all have pro and cons considering the still unclear and difficult condition that they are meant to assess. The Pfirman grading [257] is a step-by-step assessment and is weighted where some disc changes are needed to have occurred before further degeneration classification can happen. Since the degenerative process is not clarified this could be debated and probably would a classification that included all parts of the disc be a better and more representative classification system.

Histology and macroscopic examinations

The preparation of the histology sections included segmentation of the FSUs with a bench saw, which has previously been shown to cause very little structural changes to the slices [40, 61]. The slices were examined macroscopically and in study I digital photographs were taken and further assessed. To reduce the risk of potential damage from the slice preparation the histology slices were taken from the middle of the sawn slices in both study I and study II. The same experienced histology specialist conducted the histology examinations in both studies in a blinded manner but no reliability test was performed. In study II the histology assessment was done with a protocol that correlated to the MRI protocol and thereby increased the comparison between the two examinations.

Biomechanical properties

The median compression load at failure in study I was 8.35 kN (range 5.6-8.7 kN). The median deformation for all cases was 2.24 mm (range 2.3-2.7 mm) and stiffness was 3.45 kN/mm (range 3.5-4.5 kN/mm). No biomechanical properties were investigated in study II.

The compression load at failure in study I did not display any significant difference towards the control study [104] inclining that the attributed repetitive axial loading did not affect the ultimate strength of the FSUs. The results are though affected by the lack of power and possible confounders such as individual factors as BMC and the specimens were not matched with

disc, EP and vertebral size that all could affect the results even if the macro anatomy of the pigs and the test conditions were similar. The results are also in the reported level of the ultimate strength of both porcine and human FSUs in the literature [45-53] even if the results are greatly affected by the different internal and external properties of each experiment making relation between different experiments sometimes difficult. When comparing the results to a study with degenerated FSUs from young porcine [40] in the same study settings, a distinct difference can be noted where the degenerated FSUs had greater value of higher ultimate strength compared to the FSUs in study I. This could be correlated to the increased stiffness that degenerated discs develop and result from the load is transferred in different ways in degenerated FSUs with a higher axial load bearing in the dorsal bony segments and in the AF and thereby potentially not affecting the weak spots in the EP and growth zones that are affected by normal discs. Degenerated discs in young vertebrae are therefore potentially more resistant to a higher load magnitude but have less fatigue resistance.

Radiological results

The radiological examinations in study I displayed that failure was seen as endplate fracture in all cases in both the MRI, macroscopic and histological examinations whereas CT detected seven fractures and plain radiography could detect only one fracture of all the FSUs. The MRI evaluations were thereby equal to the Gold standard of histology in localizing failure injuries. The MRI examinations were better

than CT and plain radiology in localizing the FSU injuries but no reliability test was performed to validate the results, however, since the FSUs were examined pre and post-loading the actual findings were derived from the mechanical tests. The correlation of any radiological finding and clinical problem is still not available thereby affecting the risk of reporting non-clinically important findings and thereby over diagnosing.

In study II, the MRI examinations displayed signal differentiation in the same location as the histological results. The consistent results are of clinical importance since the MRI examinations also are possible in-vivo, in contrast to the histology examinations.

Histology results

In study I, the MRI and histological exams displayed the same results regarding failure location and injury type. In study II did the MRI and histological exams correlate and display the same location for signal reduction and reduction of both intracellular and extracellular content and no failure injuries were visible in neither examination. This implies that the results could be due to the potential reduction of polysaccharides and hyaluronic acids inside the cell and in the matrix due to mechanical vibration. These are key players in maintaining the cellular and matrix fluid levels and if these are damaged and reduced the fluid levels decrease in the affected tissues.

The results suggest that the histology is still the Gold standard of structural injury detection but cannot assess early fatigue

responses that do not cause fatigue injuries but rather affect flow and viscoelastic properties.

Fatigue and failure results

In study I the failure location was seen in all cases as dorsal EP fractures that corresponded through the epiphyseal plate to the growth zone and thereafter to and out of the dorsal corner of the vertebral body.

Study II displayed MRI signal changes in the growth zones, EP and in the vertebral bodies in a majority of the FSUs, while the histological results displayed changes in the cartilage cells and extracellular content in the endplate and growth zones. The lack of injuries as fatigue response was due to either too few repetitions or too low load magnitude.

The signal reduction in the EP and in the growth zones in study II correlate to the failure location in study I and could correspond to the first step of fatigue and failure in the FSU. The failure location in study I has the same configuration as in the control study [104] and also as studies in the same experimental setting with either axially loaded degenerated porcine FSUs [40] and in young porcine FSUs loaded in flexion or extension to failure [61]. The fatigue response in study II were the FSUs were subjected to repetitive flexion and extension is located in the same areas but did not manifest any injuries and therefore, the fatigue effect hard to judge. The axial repetitive fatigue loading that was performed in study I did not affect the ultimate strength and did not change the failure location implying that neither the load motion nor disc condition have a primary

impact of failure location in young porcine FSUs. The results also concurred with the general opinion that compressive loading has a typical failure injury in the EP area of the adult FSUs [104, 140, 363, 364] even if the failure type may differ with less vertebral fractures to more injuries in the EP-AF junction area. The effect of repetitive loading has previously been shown to display an increased weakening between the AF and the vertebra and thereby increasing the risk of DH as failure injury [19]. The risk is even higher if the attributed motion load is of flexion design, but this could not be seen in neither study I or study II potentially due to both mechanical and age related differences to adult FSUs.

The fatigue response in study I was only measured with ultimate strength, but in study II the fatigue response was the main endpoint. The applied load magnitude and duration were in both studies too low to inflict any permanent fatigue injuries. The fatigue effect in study II included signal intensity changes but also changes to the disc morphology. A majority of the FSUs displayed disc height reduction, relocation of the NP in relation to applied motion load and less distinct NP boundaries compared to controls. Disc height reduction is an elastic fatigue response and correlates to the discs viscoelastic properties but still concurs with earlier findings of disc height reduction due to repetitive loading in both experimental and clinical studies [186, 365-367]. In the flexed FSUs the NP was moved dorsally and among the extended the NP relocated anteriorly. This is in accordance to earlier findings that display the NP as a semi enforced structure

and not only gelatinous [21, 26, 27] and can thereby relocate and halt in the new location, which has also been seen clinically and experimentally [96, 97].

The majority of the fractures in study I were located in the inferior vertebra which does not correlate to the adult failure response where the superior vertebra is at greater risk due to less bone structure compared to the inferior vertebra. This difference could be due to the fact that the used FSUs were of young age and thereby not yet clinically affected by BMC and bone density issues meanwhile the growth zones are still open and clinically the weak spot for the failure response.

The results from study I and study II support the theory that the MRI signal differentiation are consistent to histological changes and can be seen as a first step towards the failure that injuries may occur in the growth zone and in the endplates in young porcine FSUs. Early fatigue changes as disc signal reduction can be seen clinically on MRI after a normal 1 hour run [186], which potentially correlate with the experimental results to normal clinical exposure. Injuries in the growth zone and EP are often seen among adolescent athletes and this could be due to the athletes having increased exposure to both peak, and repetitive loads compared to non-athletes, causing both traumatic and overuse injuries. The increased cumulative amount of spinal load due to increased exercise duration and frequency that many athletes are exposed to could reduce the time for recovery and biomechanical hysteresis and thereby increasing the risk of injury development.

Clinical studies

The results from study III displayed that the included runners had a significantly higher lifetime prevalence of LBP compared to the gender matched control group of a similar age. There was no significant difference regarding the amount of spinal abnormalities. Study IV is the first study concerning spinal abnormalities and LBP among mogul skiers in the literature and displayed that the mogul skier group had significantly more spinal abnormalities compared to the age matched control group. There was no significant difference regarding lifetime prevalence of LBP.

Sample size

In study III the participants consisted of twenty-two elite male long distance runners and a control group of 25 non-athletic subjects. Study IV consisted of 16 mogul skiers and a control group of 28 non-athletes. The low sample size in both studies are due to many reasons, where the total number of ideal participants are very few due to that Sweden is a small country with few inhabitants making the total number of specialized young athletes very few in each sport. Young athletes in Sweden are often active in several sports at the same time or have very diverse exercise regimes that make the imposed load very varied in magnitude, motion and duration and thereby very hard to correlate clinically. Young persons that do not exercise are also very hard to find without addressing specific subgroups, which then do not reflect the general population.

No good power analysis was performed for either study since no similar or pilot study was available.

A power analysis was done for the runners by calculating the results from an earlier study [159] using similar PROM and MRI protocols for the orienteers. and gave an expected sample size for back pain of 23 and sample size for MRI abnormalities was 9 by using power 0.8. However, this was not used as a vital part of the study plan was due to the facts that the study was low in sample size and orienteers and runners do not have equal loading mechanisms. The lack of an adequate power analysis increases the risk of making the results subject to potential type 2 statistical errors.

Recruitment and drop out

The recruitment of participants in study III was done through contact with the coach of the Swedish National team and coaches of long distance Clubs. The control group was recruited through flyers at the Gothenburg University and the controls were also offered 2 cinema tickets as compensation.

In study IV all 16 mogul skiers who were students at Åre Ski Academy, Järpen, Sweden, agreed to participate and formed the mogul group. Thirty age-matched students at the Östersund and Åre/Järpen High Schools were invited to participate in the control and twenty-eight of the students accepted.

Drop out was no problem in neither study due to the cross sectional design but especially study III had potential selection and

recruitment bias. The unknown number of subjects who refrained to participate in the runner group could potentially have been assessed since the recruitment was done with direct contact. Recruitment of the control group in study III, was done with flyers, and is therefore potentially a very biased group due to selection bias and not a reflection of the general population, which must be considered when discussing the results regarding the external clinical implication. In study IV 94% of the persons who were offered participation in the control group accepted and 100% in the study group.

Confounders and risk factors

The groups were in both studies limited by inclusion and exclusion criteria to decrease the confounders and increase the comparability between the groups. Other techniques to increase the comparability between groups in objective studies are to match the subjects between the control and study groups according to specified determinants such as age, gender, weight etc.

The risk factors for LBP and thereby potential confounders in study III and IV, are not different between studies. Gender is probably the most important among adolescents but increased growth, smoking, high levels of physical activity and competitive sports, psychological factors and poor leg flexibility have been discussed [309, 345]. The potential risk factors for adults are very similar but with the addition of heredity, leg asymmetry, early onset of LBP and age [282, 320, 321, 334]. Different outcomes and risk factors have been pub-

lished in systematic and general reviews [282, 314, 320-325] making risk factors not fully clarified and probably due to many different subgroups that are included in LBP.

Risk factors for spinal injuries and MRI abnormalities are generally not well known except for the general increase due to age and especially during and after the growth spurt, which indicates that the spine is extra vulnerable during that particular time [164, 172-175]. Different studies correlate high physical exercise to early development of many spinal injuries [159, 160, 162, 167-171, 209, 210, 240, 247, 248] and the different load attributes of different sports seem to correlate to different injuries [167, 168].

In study III the groups were only matched in gender and to a major part in age but the runner group had a wider age span due to difficulties to include runners to the study. The definition of an elite level long distance runner was defined as to practice more than 5 times a week for at least the last 5 years; and not to be active in any other sports. Inclusion criteria for the control group were male gender, maximum 2 exercises/week and 20-25 years of age.

The skiers were between 15-20 years of age. Exclusion criteria were previous surgery in the thoraco-lumbar spine, hip, pelvis, and present activity in other sports or active pregnancy. No skiers were excluded due to the inclusion or exclusion criteria. Inclusion criteria for the control group were to be a first year High School student and no previous or present participation in

any organized sport or training more than 2 hours/week. Exclusion criteria were surgery to the thoraco-lumbar spine, hip or pelvis, obesity or active pregnancy.

The basic characteristics of both groups could have been detailed further. In study III groups were gender matched which is probably the most important regarding the result but is then instead only correlating to half the population but were not completely age matched. In study IV the participants were age matched but gender were not equally distributed where the control group consisted of a minority of males (9/28) while the skiers had a majority of males (14/16). The potential effect of the gender mismatch could be that gender may have limited the results through a potential increase of LBP prevalence in the control group. Gender sub-group analysis was very limited due to the small sample size. In study II the weight was not measured but instead asked in the recruitment process meanwhile in study IV it was assessed in the study method.

Cumulative exposure to external loads

Future studies should be gender and age matched and basic parameters such as smoking, cumulative physical exercise, heredity and other factors correlating to the potential risk factors be measured and presented in the basic characteristics to better correlate the result to the general population and address the potential confounders in a good way. The control group in future studies should also be described in the best way possible since it could be affected by different subgroups and thereby not reflecting the general population.

Cumulative exposure to external loads

An important potential risk factor for both LBP and spinal abnormalities is the cumulative exposure to external loads such as physical exercise both in the short and long term. This was addressed in both study III and IV by the inclusion and exclusion criteria and also assessed by a self-answered questionnaire that only addressed the present exercise and not past, and also in the first part of the Swärd and Baranto back pain questionnaire that assesses the number of exercised hours per week.

The cumulative exposure is clinically very hard to determine when normal activities such as spare time activities, school athletics and walking can be done in many ways and in different intensities thereby correlating to different load exposures. This could potentially be reduced in importance with increased sample size but should otherwise be specified at its best to achieve the best characteristics of the study population. There are several different questionnaires regarding the physical exposure in both exercise and daily life [355, 356].

Method

The method in both studies was done with PROM questionnaires and MRI investigations.

PROMs / questionnaires

The questionnaires used in both studies have been used earlier by the study group [159, 160, 162, 169] and consist of the Swärd and Baranto back pain questionnaire, the ODI and the EQ-5D. There are many PROMs evaluating LBP but no Gold

standard, and no validated version regarding LBP among adolescent athletes.

The ODI and EQ-5D (which are created for more adult and aged populations) scoring evaluation were in both studies limited since all participants displayed good health and no disability. Young active persons that are attending High school are in general unlikely to score any disability, and the absence of play that active healthy but injured athletes can have is not assessed in neither of these scores. Therefore both scores have sensitivity and specificity limitation with floor-ceiling effect.

The Swärd and Baranto back pain questionnaire has not been validated by the Cosmin standards [358]. The questionnaire includes two questions regarding the prevalence of back pain and is related to present or earlier back pain and thereby investigating the point prevalence and lifetime prevalence. The total duration of back pain is also assessed, and the numbers of occurrences per year is estimated. The questionnaire also evaluates the severity and impact of LBP with questions regarding both physical exercise changes as in absence of play and normal work and home-related activities.

Point prevalence can be problematic to assess due to it being less common than longer periods of LBP and thereby needs a greater sample size to be able to display both clinically and significant differences between groups. LBP is a very diverse symptom that can last from a couple hours to many years but are still considered as equal in lifetime LBP prevalence evalu-

ations where the number of occasions of LBP is not reflected in lifetime prevalence investigations. The lack of explanations to define the severity of LBP makes bed-disabling LBP equal to minor ache in the lumbar area, which is considered very different in importance in normal clinic. Pain is a very subjective feeling and can be very different between different individuals making it difficult to compare. Since the minimum severity level is not defined this is up to each person to decide what is LBP for them. Athletes could have a higher tolerance for pain due to their potential high risk of injuries and could thereby be accustomed to pain compared to non-athletes. Subjective differences are also more likely to affect the results when sample size is low if a polarized subgroup affects the group results. Definition problems like these make all LBP prevalence evaluations hard to relate and compare clinically

Re-call bias increases with the investigated duration, thereby affecting all lifetime prevalence investigations. Suggestions have been made to investigate LBP and ALBP in duration levels where a one year duration should be used to decrease recall bias [342] which could be suitable to include in future prevalence evaluations.

MRI

The radiologic investigations were done with MRI examinations. MRI is generally considered the Gold standard of examination of all spinal abnormalities.

The MRI protocol of these studies has been used in earlier studies with the study group [159, 160, 162, 169]. The study pro-

tocol consisted of a four level severity assessment of different spinal abnormalities and also dichotomous assessment of absent or existing fracture or spondylo-
listhesis. Disc degeneration was in study III classified according to Pfirrmann et al. (2001) [257] and in study IV according to DeCandido et al. [256].

The assessment of almost all spinal and MRI abnormalities are lacking an established Gold standard. The present study protocol assessed also the severity of many of the spinal abnormalities even if the severity is clearly correlated to neither symptom existence nor symptom level. The assessment is in the result displayed in a dichotomous manner (existing or not) and perhaps future study protocols could benefit from this manner already from the assessment analyze. Future considerations should also emphasis on a consensus how to exam and measure different spinal abnormalities. There are too many assessments and measurements in the literature and a consensus that could be used in future studies would increase the possibility to compare the results between studies.

Degenerative Disc Disease examination

DDD is a difficult condition where the correlation of DD to symptoms has still not been fully clarified. The DDD diagnose is dependent on both disc degeneration and pain whereas disc degeneration is difficult to exam and assess with sufficient sensitivity and specificity due to the high prevalence of normal but aged discs that have the same radiologic attributes on MRI exams.

The examination of disc degeneration is done with several radiologic techniques but is mainly done through MRI. The interpreter often clinically does the assessment of the radiologic findings subjectively but many suggested more or less validated scales and classifications are available [243, 256-258, 286, 291]. Examples of these have been presented in an earlier chapter in this thesis and all have both advantages and disadvantages. The classifications assess the morphological severity of disc degeneration but are seldom validated or correlated to clinical symptoms. Before a well validated and symptom correlated classification has been presented a combination of several classifications should be presented in every disc degeneration study to increase the possibility to compare the results. An ideal assessment should preferably be graded in few steps, potentially dichotomous, for each part of the disc, EP, AF and NP. To decrease the problem with ageing disc a potential step would be to rephrase both ageing disc and degenerated discs to "worn" disc or similar, like it has been done with arthrosis affected joints that suffer from similar definition problems.

The Thompson scale is the assessment of the macroscopic mid-sagittal section of the disc [291], thereby dependent that the slices are perfect examples of the whole disc in one and can only be used in experimental models. The Pfirrmann scale starts with a normal disc that is graded as disc degeneration I even if it is a normal disc. The assessment follows a step-by-step assessment of the disc signal and does not considering other factors such as disc

height, shape and endplate condition [257] but is generally common clinically and has displayed high reliability [286]. The Modic grading is only concerned by the potential change or decrease of endplate signal. Thereby not considering the annulus and the nucleus potential changes or normalization [243]. The Dallas classification is a limited assessment since it is done after discography and is only considering the potential nucleus penetration through the

annulus, thereby not considering endplate conditions [258]. The Decandido classification is a very subjective 4 step assessment of the grey-scale levels of the T2 disc signal [256]. Not considering factors such as potential changes of disc height nor degeneration in the AP or in the EP.

Results

The main findings from study III and study IV are presented in table 15.

table 15 Compilation of results from study III and IV.

Group (study)	Number (m/f)	Age, median (range)	exercise h/ week, median	LBP, lifetime	MRI mean (SD)	MRI median (range)	DD in %
Runners (III)	22 (22/0)	23 (18-28)	>11	45%	5.6 (5)	4 (0-17)	71%
Controls (III)	25 (25/0)	23 (21-25)	0-2	12%	9.2 (7.5)	7 (0-22)	76%
Moguls (IV)	16 (14/2)	17 (15-20)	>11	50%	7.2 (4.3)	6 (3-18)	88%
Controls (IV)	28 (19/9)	16 (16-17)	3-5	42%	3.8 (4.9)	1.5 (0-15)	57%

Low Back Pain

In study III the runners reported a statistical significant higher lifetime prevalence of back pain (45%), compared to the control group (12%) (p=0.011).

No statistical significant difference was seen in study IV regarding the lifetime LBP prevalence between the mogul and control group (50 % vs 42 %, p=0.555).

Confounders that also impact the clinical significance of the results affected both studies. In study III, age was not matched in the groups and the control group displayed a very low LBP lifetime prevalence,

which could be due to potential selection bias and thereby not reflecting the general population but rather an unknown specific sub group with reduced prevalence of LBP. As discussed earlier, all results regarding lifetime prevalence are also subjected to limitations due to potential definition problems as well as re-call bias. The groups also differed widely in amount of exercise hours, which could also affect the results. Studies have displayed that active participation in sports can be both beneficial [339] and a risk towards LBP and is probably dependent on the demands of the sport [168]

In study IV gender was not matched and could thereby affect the results. However did female gender not display higher lifetime prevalence of LBP when the results were analyzed in subgroups. That female gender is a risk factor for LBP is however not certain since gender is not presented as a risk factor in all systematic reviews regarding LBP even if many studies display a correlation [282, 314, 320-325]. There was no difference in weight between the two groups in study IV.

The presented prevalence of LBP in study III and IV are in accordance to the lifetime prevalence presented in a meta-analysis that ranged between 34-46% among children and adolescents [343]. This also supports the notion that the control group in study III could potentially be biased due to its very low lifetime prevalence when considering that the adult age range is higher. In both studies the amount of exercise hours differed greatly between the controls and the athletes. The effect is hard to judge since both too much and too little physical exercise has been discussed as potential risk factors for LBP. The low lifetime prevalence in the control group of study III suggests that absence of exercise correlates to LBP reduction when considering that the runner group probably has a more age-matched life time prevalence of low back pain and the two groups in study IV both display prevalence in accordance to the runner group even though they have lower age. Studies have displayed that active participation in sports can be both beneficial [339] and a risk towards LBP and is dependent on the demands of the sport [168]. No major difference is

seen when comparing the runners with the skiers regarding lifetime LBP prevalence. The sports and applied spinal loads are very different where the mogul skiers are subjected to much higher impact and repetitive loads compared to the runners but any effect on LBP prevalence is not evident in the results. This implies that the groups have different LBP etiologies where the runners potentially are suffering from muscular generated LBP meanwhile the skiers could have LBP due to spinal injuries to a higher degree.

Spinal abnormalities

The results from study III could not display a statistical significant difference between the groups in total amount of abnormalities in mean (6.6 vs 9.2, $p>0.05$) nor in independent spinal abnormalities on MRI.

The mogul skiers had statistical significantly more spinal abnormalities in mean (7.25 vs 3.78, $p<0.023$) compared to the controls, and the amount of disc bulging, disc height, and Schmorls node was statistical significant compared to the expected difference between the groups.

The study protocols differed in assessment of DD but were otherwise similar in both studies. The main endpoints in both studies were total amount of spinal abnormalities since not a clear correlation was shown between present or future symptoms and different spinal abnormalities, therefore, this is hard to determine what spinal abnormalities are of clinical importance. The assessment of spinal abnormalities does not consider causation, severity or clinical importance of the specific spi-

nal abnormalities and includes highly discussed abnormalities such as disc bulging that affect the clinical significance of the endpoint.

In study III were the spinal abnormalities distributed in a wide range in both groups where both groups had participants that had no spinal abnormalities. The runner group did have fewer abnormalities, which implies that they had only some runners with many abnormalities but the majority quite few meanwhile the abnormalities were more evenly distributed in the control group.

In study IV there is a distinct difference between the skiers and the controls that could be due to the mogul skiing exposure, since this is the main known difference between the groups regarding risk factors for spinal abnormalities. The control group displays a low mean and median but with a high range implying that some subjects have many spinal abnormalities meanwhile the majority have very few. The differences between the groups are also displayed in the amount of DD that is statistically significantly higher in the mogul group.

table 16 Number of unique individuals with one or more abnormality for each pathology and (%), stratified by group and study.

MRI abnormality	Runners III (n=21)	Controls III (n=25)	Skiers IV (n=16)	Controls IV (n=28)
Disc signal	11 (52%)	16 (64%)	11 (69%)	12 (43%)
Disc bulging	8 (38%)	11 (44%)	13 (81%)	13 (46%)
Disc height	14 (67%)	18 (72%)	8 (50%)	0
Apophyseal inj.	0	0	1 (6%)	0
Shape vertebrae	6 (29%)	4 (16%)	1 (6%)	1 (4%)
Schmorls nodes	8 (38%)	17 (68%)	9 (56%)	6 (21%)
Disk hernia	0	2 (8%)	0	0
Spondylolisthesis	0	0	0	1 (4%)
Retrolisthesis	2 (10%)	2 (8%)	0	0
Scoliosis	4 (19%)	7 (28%)	2 (13%)	8 (29%)
HIZ	0	4 (16%)	1 (6%)	0

Studying the results in detail display that many of the MRI abnormalities are changes in disc signal, disc bulging, disc height and Schmorls nodes while more structural injuries such as disc herniation, spondylolisthesis and apophyseal injuries were very few. When comparing the runners and the mogul skiers regarding spinal abnormalities the mogul skiers have more in both mean and median with a more tight range even if they are younger and less exposed

to spinal abnormalities due to age. The main differences seen are increased disc bulging and Schmorls nodes in the skier group that both could be correlated to external compression loads. This implies that the repetitive and sudden spinal loads of high magnitude that the mogul skiers are subjected to are correlated to increased risk of developing spinal abnormalities compared to the repetitive loading of low magnitude that the runners are exposed to.

Correlating LBP to spinal abnormalities

Neither study could display an existing correlation between LBP and any spinal abnormalities or DD. A very interesting finding of these studies is the reverse findings for a high amount of spinal abnormalities and very low LBP lifetime prevalence in the control group of study III. The clinical importance of different spinal abnormalities is hard to evaluate due to the poor

evidence and correlation between spinal abnormalities and LBP. The design of the studies cannot determine any future correlation of any of the spinal abnormalities or DD to LBP. DD is a condition that is without remodelling and cure and it is highly plausible that early DD will eventually evolve to symptomatic DDD, which has been seen in earlier studies [159].

General discussion

All studies included in this thesis are either experimental or of cross sectional design with low sample size. Moreover, they are not able to give any clear scientific answers for the general population but are instead able to raise new questions and hypotheses.

Fatigue and repetitive loading

The fatigue is dependent on duration, frequency, angle and load. The human spine seem very resistant against low fatigue loading meanwhile high load amplitude correlate to fatigue and failure responses where the motion and the morphologic age of the specimen determine injury type. The fatigue seems to be first of elastic deformation where the disc and vertebrae can withstand the load and remodel itself towards future demands. The more advance stages of fatigue include plastic deformation where minor injuries and changes occur in particular in the end plate and in the growth zone that are also the location for failure injuries among young porcine FSUs.

This is supported by the included studies where low load fatigue demonstrated in clinical study III whilst experimental study I and II did not display increased levels of failure. The ultimate load is not changed due to repetitive axial compression among porcine FSU which is supported by the fact that the elite runners in study III did not display a significant higher mean amount of radiologic abnormalities compared to age matched controls. The fatigue created by repetitive flexion and extension in experimental study II did not display any injuries or end point failure but affected instead several factors concerning the fluid levels and the viscoelastic flow. These changes were situated in the endplates and the growth zones in particular highlighting this to be a sensitive area of fatigue and the same location for failure in the ultimate strength tests in experimental study I. In the clinical study IV the mogul skiers have more spinal abnormalities than the controls, which could be derived of the repetitive and high load amplitudes they are subjected to during their skiing. Thereby affected by both potential fatigue that together with the potential increased amount of sudden high ultimate loads (im-

pact) in more complex movement angles and direction creating more complex loading patterns and failure mechanisms.

Failure mechanism in relation to age

Failure of the disc is dependent on several factors of both internal and external origin. Among young individuals, the potential fatigue load and the failure load combine to two distinct kinds of endpoint, apophyseal injuries and endplate injuries whereas traumatic disc hernias are less common. The apophyseal and endplate injuries seem to develop due to avulsion or fracture in the growth zone, which is the weakest part of the FSU. The annulus with its complex fibre structure is more resistant to the load.

When the spine matures, the endplates calcify and strengthen and initial disc degeneration may have been sustained. These changes alter the biomechanical properties and DH is the most probable endpoint when subjected to adequate loads. The NP appears not to push through the AF but rather orient its way through the adjacent bundles to form clefts in the lamellae guided by the load axis. The main load to cause

DH seem to be flexion in combination with compression. Rotation and extension have secondary impact but increases the risk of disc injuries. Repetitive loading is dependent on the magnitude more than duration and frequency to have an impact on both fatigue and failure outcome.

Due to age and daily activities wear and tear increases disc ageing and degeneration therefore making the disc shrink and fragile. This causes increased loading on accessory tissues such as the facet joints making them subject to increased amounts of load and the increased risk of arthritis.

During the later stage of life with even more disc stiffness and disc degeneration, the spine failure endpoint becomes a vertebral fracture due to changed biomechanical properties in both the disc and in the vertebrae. Disc degeneration and disc height reduction shift the load from the nucleus to the annulus and the posterior bony segments [133], where the reduction can generate increased bone loss due to Wolff's law, and thereby an even greater risk of vertebral fracture.

Limitations

General limitations

The included studies were of experimental and cross sectional design of low sample size and thereby not able to give any clear answers for the general population.

Experimental studies

There are several important limitations in the design of the experimental studies. No power analyse was done in either study to calculate the risk of a statistical type 2 error. The control group in study I was derived from an earlier study and thereby being object to several potential biases. The controls in study II were different FSUs regarding the histology and MRI examinations consisted of only three specimens for each examination.

The experimental studies were performed with dead porcine spines that are not fully equal the human spine in neither anatomy nor biomechanical properties. An in-vitro experimental model inherently lack of several important factors for maintaining integrity in a high water content structure such as the intervertebral disc. Most notably is the absence of tissue pressure that to some extent counter balance load on the disc.

In study I the MRI examinations of the study and the control groups were performed with different MRI machines that could limit the assessments. Different examiners performed the MRI assessments in the studies and in neither study were any validity or reliability tests conducted. The sectioning process prior to the histo-

logical preparation was done in a frozen state with a bench saw with a risk of causing traumatic injuries in the FSUs. An experienced histology specialist evaluated the histology examination but no reliability test was conducted in either study, and in study II were no statistical analyses possible due to the absence of morphometric assessment.

Clinical studies

There are several important limitations in the clinical studies that affect both the validity and the external significance.

No power analyse was performed in either study. There are several potential confounders in the study groups. The selection process in study III was potentially affected by selection bias. The study groups were not fully matched according to age and gender. Several potential risk factors for LBP and spinal abnormalities were not assessed in either study. The cumulative physical activity is very hard to exam and assess appropriately.

The PROMs in the studies were not validated, and potentially affected by re-call bias. LBP was not clearly defined and thereby making it subjective. The MRI protocol was not validated and no reliability test was performed regarding the MRI assessment. The spinal abnormalities are not related to clinical significance making them subject to increased risk of false positive assessment.

Strengths

General

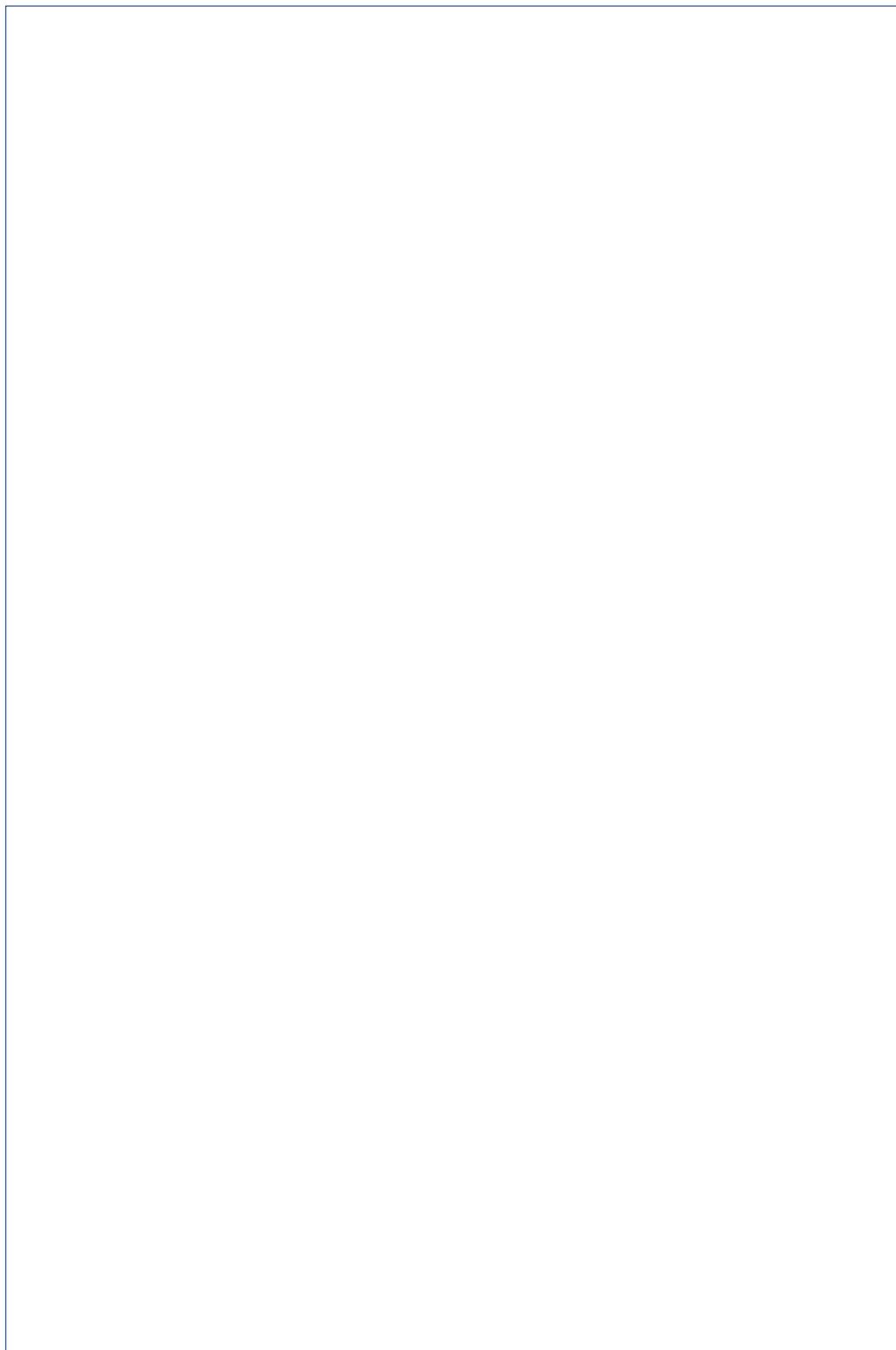
This thesis combine experimental and clinical studies.

Experimental studies

The experimental studies have clinically related load protocols.. The studies were performed with young porcine lumbar spines that is one of the best experimental materials for experimental tests regarding young and adolescent human spinal pathologies. The method included both histological and MRI analyses that both are the Gold standard for examining several spinal pathologies. The results from the MRI and histological examinations were consistent in both studies, which increase the external reliability.

Clinical studies

Study IV is the first clinical study that evaluates spinal abnormalities and LBP among young mogul skiers. The athlete participants in both studies are of Swedish elite level. The study method is well established, and include previously used MRI protocol and PROMs. The Swård-Baranto questionnaire assess many important factors regarding LBP such as the cumulative physical activity, the severity and the occurrence. The statistical assessments of radiological findings do not address assessed but not validated severity and are dichotomous in both studies. Statistical significant differences are detected in both clinical studies.



conclusion

Fatigue and failure responses in the spine are dependent on several factors and are mainly localized to the endplate and growth zone in the young spine according to experimental tests.

Repetitively axially loaded young porcine lumbar FSUs did not display any statically significant different behavior to axial compression to failure than non-vibrated FSUs. The endplate and the growth zone were the weakest parts in the axially repetitively loaded FSUs.

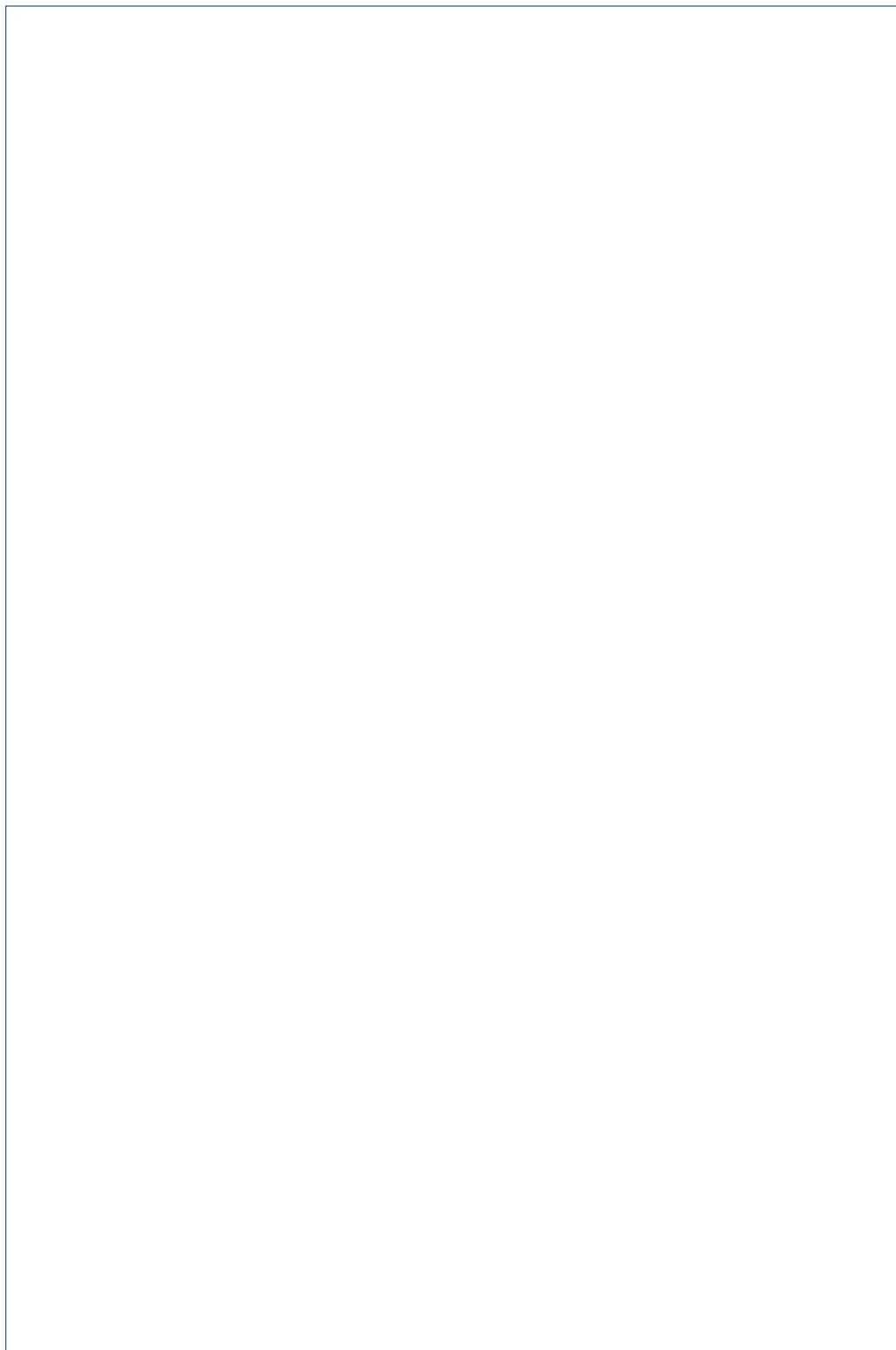
Low magnitude repetitive loading in both extension and flexion causes consistent histological changes and MRI signal changes in both the disc and vertebral bodies with a focus in the growth zones and endplates of young lumbar porcine FSUs.

A group of elite level male long distance runners had statistically significant higher

lifetime prevalence of LBP, but no significant difference in the amount or type of spinal abnormalities on MRI compared to a gender matched group of non-athletes.

Young elite mogul skiers had statistically significant higher frequency of MRI abnormalities in the thoraco-lumbar spine but no significant difference regarding the lifetime prevalence of LBP compared to an age matched control group of non-athletes.

When comparing mogul skiers and long distance runners the mogul skiers appear to have more spinal abnormalities in mean and a higher lifetime prevalence of LBP.



future perspective

General

To increase the knowledge about spinal injuries and LBP among the population as a whole and especially among risk groups such as young athletes appears to be very essential. To thereby implement preventive measures to reduce the prevalence and the impact of the spinal injuries and symptoms.

Experimental studies

To develop study protocols that involve complex set-ups to resemble daily activities in both motion and load.

To address load properties in stress rather than load to increase external comparison between studies.

To analyze the existing experimental studies in a systematic review.

To further investigate the human spine and to determine the aetiology of different fatigue and failure injuries.

Clinical studies

Future considerations should emphasize on a consensus how to examine and assess different spinal abnormalities. There are too many assessments and measurements in the literature and a validated consensus that could be used in future studies would increase the possibility to compare the results and make them more reliable.

To investigate the aetiology and pathogenesis of many of the spinal abnormalities

to increase the clinical significance and the correlation to both present and future symptoms.

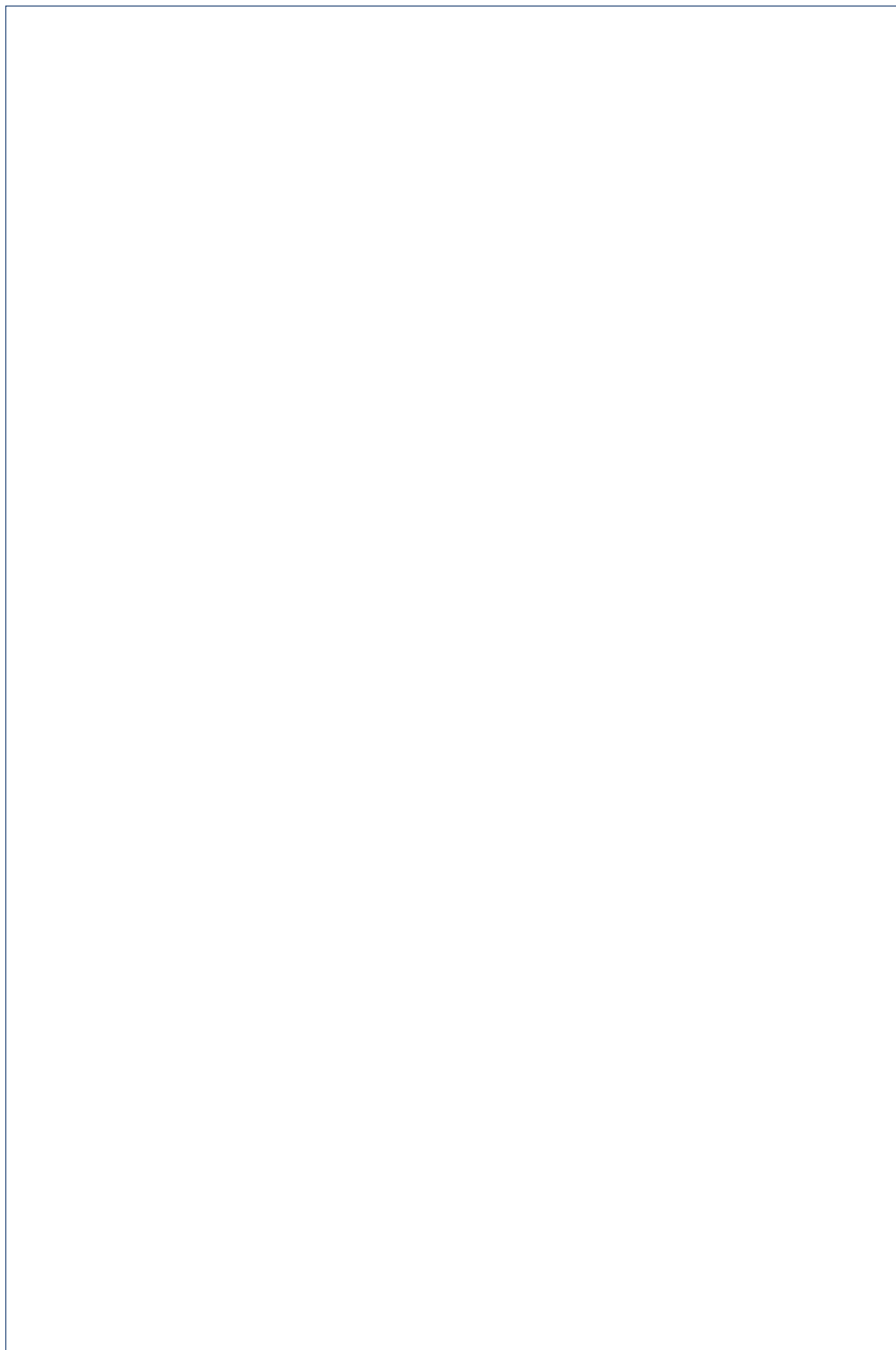
To establish a clear and generally accepted definition of LBP that considers severity, duration, occurrence and location. Severity could potentially be measured in absence of planned activities and work meanwhile the lowest pain level is harder to distinguish. Duration should address the minimum time for a LBP episode where a one week episode would be adequate. Occurrence is important when considering that some exposure could cause several occurrences per year and thereby gives high clinical importance that is not seen in the present LBP prevalence measurements. Location is defined in the literature as is pain localized under the costal margin and above the gluteal folds with or without leg pain, and should be used more generally while many studies still use different definitions.

To establish a validated questionnaire suited for young athletes. The Swärd-Baranto questionnaire is a well-used questionnaire but is not validated. The questionnaire addresses several important factors as low back pain severity, occurrence, and clinical impact and is a good base for further validation.

To further analyse the LBP risk factors and divide it into more accurate subgroups to achieve greater clinical significance.

To increase the knowledge among the profession but also among the trainers, parents and athletes on how to avoid early spinal injuries and to increase the salutogenic factors regarding LBP among young athletes and in the general population.

To establish new ways of assessing spinal loads during activities potentially through motion analyse and simulated computerized programs.



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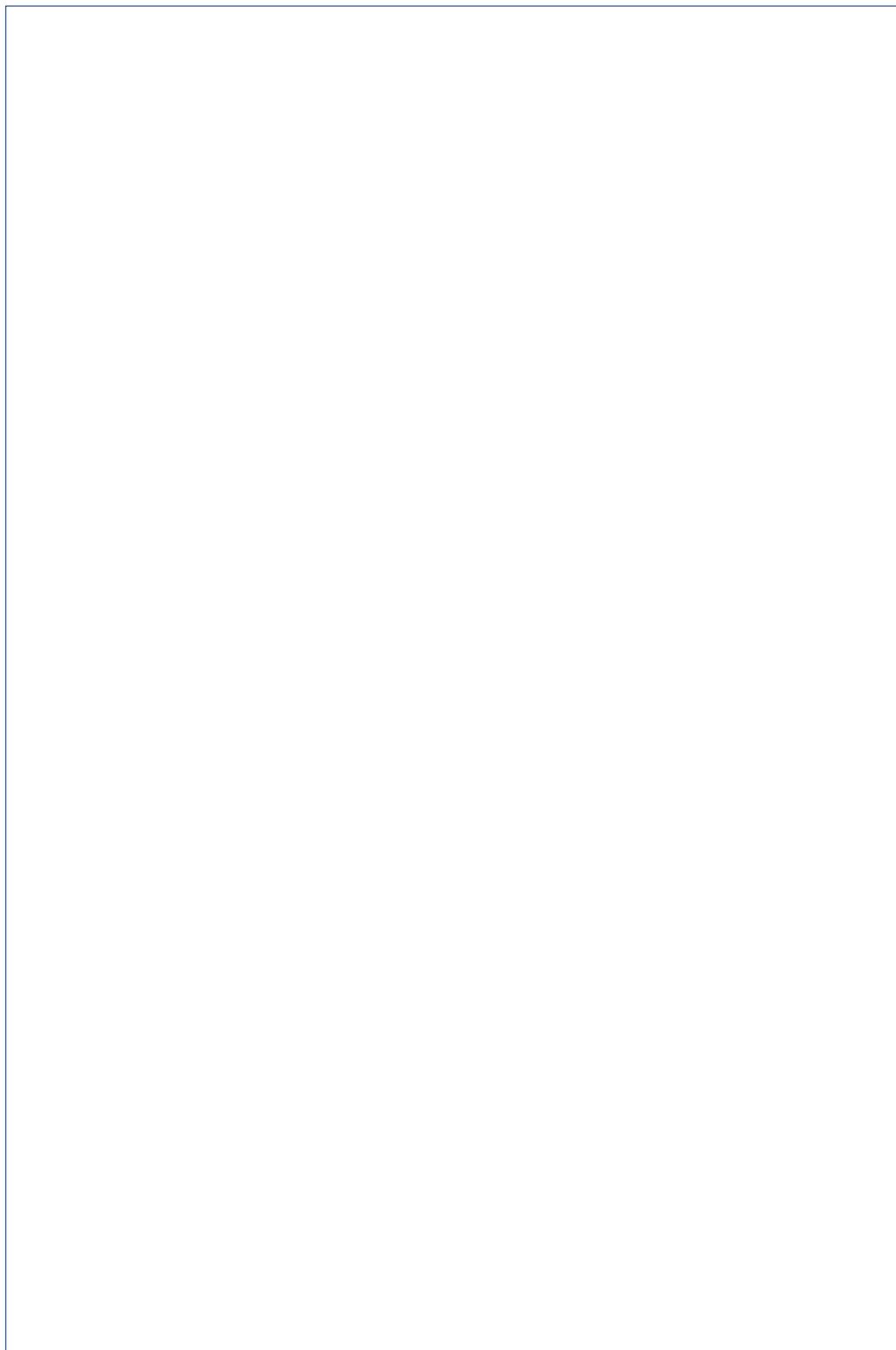
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