The loading, shape and motion of the lumbar spine

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Für meine Eltern und Bettina

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Abstract

Low back pain (LBP) is one of the most challenging health-economic problems of modern societies that are subjected to demographic change. Due to its multifactorial causes and a lack of scientific knowledge, currently employed therapy concepts for LBP, for pain in the lumbar spine in particular, are insufficiently successful. However, recent clinical-biomechanical research has emphasized that a deeper understanding of lumbar *spine loading* as well as of lumbar *spine shape* and *motion* are the definitive biomechanical keys for achieving improved prevention, differentiated diagnosis and patient-specific therapy. A detailed understating and consideration of these factors in the evaluation of specific therapeutic approaches, currently does not exist.

The basic objective of this cumulative dissertation is therefore a detailed analysis of lumbar spine *loading*, *shape* and *motion*. In the first part, lumbar spine loading is measured during selected activities that are recognized risk factors for low back pain. The specific focus was to evaluate relevant factors that specifically affect spinal loading. Furthermore, this work aimed to investigate lumbar spine shape and motion during short- and long-term measurements in large asymptomatic cohorts and to investigate age- and gender-related differences, in particular. The findings were subsequently employed in computational modeling studies to evaluate and further develop finite element models of the lumbar spine and to investigate an implant concept regarding spinal loading and motion that is currently very controversially discussed.

The mechanical loading during upper body bending and weight lifting in the sagittal plane was determined and analyzed with an instrumented vertebral body replacement in 265 single measurements and five patients. In particular, the influence of different lifting techniques was thereby investigated. Additionally, a new non-invasive measurement system was further developed, validated and used to determine essential parameters, e.g., lumbar lordosis and range of motion, in standardized, short-term measurements (Standing/Flexion/Extension, number of subjects: n=323) in analogy to the standard procedure employed in a clinical setting. These shape and motion parameters were also determined in long-term measurements (n=208) and compared with values collected using the standard clinical procedure. In the computational section of the dissertation, worldwide currently employed finite element models (FEMs) of the lumbar spine that originated from eight research groups were systematically evaluated. Based on this validation study, the implantation of an artificial disc was investigated in a probabilistic study with several validated FE models in 4000 single simulations to reveal relevant mechanical risk factors.

The spinal loading measurements revealed that a daily upper body inclination of approximately 50° alone can substantially increase the loading of the lumbar spine. Weight lifting resulted in the largest implant loads ever measured (approx. 1600 N) by an instrumented vertebral body replacement. The employed lifting technique did not substantially affect the resultant loading. The analysis of the spinal

shape and motion revealed an enormous variability of these characteristics in the asymptomatic population. A characteristic gender-specific aging process could be demonstrated in standard clinical short-term measurements, which was characterized by a segment-specific reduction of the lumbar lordosis and motion. Furthermore, the specific interplay between the lumbar spine and pelvis during motion also showed age- and gender-specific differences. Using long-term measurements over 24 hours, it was possible to establish for the first time reference values for the daily number of spinal movements in the sagittal plane. The mean values determined for lumbar lordosis and range of motion over 24 hours, as well as the resultant age- and gender-related effects, differed significantly from the results obtained during classical clinical short-term measurements. The results of the computational analyses revealed that the FE models of the lumbar spine currently separately employed worldwide do not individually represent the natural large inter-subject variability of lumbar lordosis and motion shown here. However, a combination of all these models resulted in a valid prediction of loads and motion values measured *in vivo* and *in vitro* and of the inherent inter-subject variability. A computational analysis of an artificial disc identified several mechanical risk factors, e.g., lumbar spine shape and iatrogenic distraction, which can substantially affect spinal loading and motion.

The here presented in vivo values of spinal loading and motion are an essential basis for realistic, preclinical implant testing for developing evidence-based prevention measures and for performing risk assessments for LBP patients. In particular, the presented results of different lifting techniques are in contradiction to current ergonomic guidelines, which can hence be doubted from a biomechanical perspective. Furthermore, the results reveal that a meaningful differential diagnosis and patient-specific therapy must consider the here presented age- and gender-related differences of spinal shape and motion. In particular, age-related reference values appear necessary for the sagittal profile reconstruction. Furthermore, the results obtained from the long-term measurements call into question the entire clinical concept of the standing “sagittal balance,” as actual daily lumbar spine shape and function significantly differ from those of the classical clinical perspective. Considering the here presented large inter-subject variability of lumbar spine loading, shape and motion, the generalizability of single FE models to a patient cohort remains a concern. However, by using several representative models in a probabilistic sensitivity study, mechanical risk factors of a total disc replacement could be validly predicted, clinically verified, and thus directly used for providing improved patient-centered care.

Zusammenfassung

Im demographischen Wandel moderner Gesellschaften stellen Rückenschmerzen eine der größten gesundheitsökonomischen Herausforderung dar. Aufgrund ihrer multifaktoriellen Ursachen und des Fehlens gesicherter wissenschaftlicher Kenntnisse weisen derzeitige Behandlungskonzepte insbesondere im Bereich der Lendenwirbelsäule (LWS) jedoch nur einen unzureichenden Therapieerfolg auf. Klinisch-biomechanische Untersuchungsergebnisse der vergangenen Jahre konnten allerdings zeigen, dass eine tiefergehende Kenntnis der *Belastung* sowie der spezifischen *Form* und *Bewegung* der LWS die entscheidenden biomechanischen Schlüssel für eine verbesserte Prävention, differenzierte Diagnose und patientenspezifische Versorgung sind. Ein detailliertes Verständnis dieser drei Charakteristika und ihre Berücksichtigung bei der Analyse spezifischer Therapiemaßnahmen existiert jedoch bisher nicht.

Das grundlegende Ziel dieser kumulativen Dissertation war daher die detaillierte Analyse der *Belastung, Form* und *Bewegung* der LWS. Im ersten Abschnitt sollte dazu die lumbale *Wirbelsäulenbelastung* bei Aktivitäten, die als Risikofaktoren für Rückenschmerzen gelten, vermessen sowie relevante Lasteinflussfaktoren untersucht werden. Ferner sollte die *Form* und B*ewegung* der LWS in Kurz- und Langzeituntersuchungen anhand großer asymptomatischer Kohorten analysiert werden. Hierbei sollten grundlegende alters- und geschlechtsspezifische Unterschiede herausgearbeitet werden. Das erworbene Wissen wurde anschließend zur Evaluierung und Weiterentwicklung aktueller mechanischer Simulationsmodelle der LWS genutzt und ein klinisch kontrovers diskutiertes Implantat hinsichtlich der auftretenden lumbalen *Belastung* und *Bewegung* in einer probabilistischen Studie untersucht werden.

Die mechanische Belastung bei der Oberkörperneigung und beim Heben von Lasten in der Sagittalebene wurde mit Hilfe eines instrumentierten Wirbelkörperersatzes in 265 Messungen in fünf Patienten bestimmt, analysiert und insbesondere der Einfluss verschiedener Hebetechniken untersucht. Zur Analyse der Form und Bewegung der LWS wurde ein nicht-invasives Messsystem weiterentwickelt, validiert und essentielle Parameter (u.a.: Lendenlordose, Bewegungsausmaß) in standardisierten Kurzzeitmessungen (Stehen/Flexion/Extension; Anzahl Probanden: n=323) analog zum klinischen Standardvorgehen bestimmt. Erstmals wurden Form- und Funktionsparameter auch in Langzeituntersuchungen über 24 Stunden (n=208) vermessen und zum klinischen Standardverfahren in Relation gesetzt. Im numerischen Abschnitt der Dissertation wurden zunächst derzeit weltweit verwendete Finite-Element-Modelle (FEM) der LWS von acht internationalen Forschungsgruppen in einer Vergleichsstudie systematisch evaluiert. Darauf aufbauend, wurde mit Hilfe von mehreren validierten FE-Modellen die Implantation einer künstlichen Bandscheibe in 4000 Einzelsimulationen untersucht und mechanische Risikofaktoren erarbeitet.

Die Belastungsmessungen zeigten, dass bereits eine alltägliche Inklination des Oberkörpers von ca. 50° eine substantielle Steigerung der spinalen Last zur Folge haben kann. Das Heben von Gewichten führte zu den höchsten jemals *in vivo* gemessen Kräften mittels eines instrumentieren Wirbelkörperersatzes. Überraschenderweise hatte die spezifische Hebetechnik keinen Einfluss auf die Belastung. Die Analyse der Form und Bewegung der LWS offenbarte die enorme Vielfalt dieser Charakteristika in der Bevölkerung. In klinisch üblichen Kurzzeitanalysen im Stehen konnte ein charakteristischer, geschlechtsspezifischer Alterungsprozess nachgewiesen werden, welcher eine segmentspezifische Verringerung der Lordose und des Bewegungsausmaßes aufwies. Auch das Bewegungszusammenspiel zwischen LWS und Becken zeigte signifikante alters- und geschlechtsspezifische Unterschiede. Durch die Analyse im 24-h-Alltag konnten erstmals Referenzwerte zur Anzahl der Bewegungen in der Sagittalebene definiert werden. Die mittleren Werte über 24 Stunden zur Lordose und lumbalen Bewegung als auch die ermittelten Einflüsse des Alters und Geschlechts zeigten signifikante Unterschiede im Vergleich zu klassischen Kurzzeitanalysen. Die numerischen Untersuchungen offenbarten, dass weltweit separat eingesetzte FE-Modelle der LWS, die hier aufgezeigte natürliche Variabilität der Form und Bewegung nicht abbilden. Eine Kombination der Modelle führte jedoch zu einer validen Vorhersage von *in vitro* und *in vivo* gemessenen Lasten, Bewegungen und interindividueller Variationen. In der numerischen Analyse einer künstlichen Bandscheibe konnten Risikofaktoren (u.a.: LWS-Form, iatrogene Distraktion) identifiziert werden, welche die spinale Last und Bewegung substantiell beeinflussen.

Die hier aufgezeigten *In-vivo*-Werte zur LWS-Belastung und -Bewegung sind wesentliche Grundlagen für eine realistische präklinische Implantattestung, für die Entwicklung evidenzbasierter Präventionsmaßnahmen sowie zur Risikobewertung von Rückenschmerzpatienten. Insbesondere die Ergebnisse zu unterschiedlichen Hebetechniken stehen in Widerspruch zu gängigen ergonomischen Empfehlungen, welche daher aus biomechanischer Sicht angezweifelt werden können. Die Ergebnisse legen ferner nahe, dass eine aussagekräftige Differentialdiagnose und patientenspezifische Therapie (u.a. Rekonstruktion des sagittalen Profils), die hier aufgezeigten alters- und geschlechtsspezifischen Unterschiede der lumbalen Form und Funktion berücksichtigen sollten. Die erworbenen Langzeitergebnisse stellen jedoch insgesamt das klinische Konzept der stehenden „sagittalen Balance“ in Frage, da sich die alltäglich auftretende Form und Funktion der LWS signifikant von der klassischen, klinischen Perspektive unterscheidet. Unter Beachtung der hier aufgezeigten großen interindividuellen Unterschiede in Last, Form und Bewegung verbleibt die Aussagekraft einzelner FE-Modelle für Patienten*kohorten* fragwürdig. Unter Verwendung repräsentativer Modelle in probabilistischen Sensitivitätsuntersuchungen konnten jedoch Risikofaktoren einer künstlichen Bandscheibe valide vorhergesagt, klinisch verifiziert und so direkt für eine verbesserte Patientenversorgung genutzt werden.

1. Introduction

1.1 General introduction and aims of the dissertation

Low back pain (LBP), particularly chronic LBP, is one of the most serious public health problems worldwide. Numerous epidemiological studies have demonstrated its extraordinarily high levels of lifetime incidence and prevalence [1,2]. In a highly regarded review of different cross-sectional studies, Andersson [1] demonstrated that approximately 70-85% of all people face LBP at some point in their life. Furthermore, Vos et al. [3] highlighted in a systematic comparative analysis that LBP is the leading specific cause of years lived with disability worldwide. This exceptionally high number of affected individuals and serious consequences involved, such as loss of labor productivity or high rates of hospital admission, result in tremendous direct and indirect costs for societies' healthcare systems and economies. In 2008, Wenig and co-workers [4] estimated that the total back pain costs for Germany were €48.96 billion, approximately 2.2% of the German gross domestic product. Due to the demographic changes of an aging society, this socio-economic burden will increase in the future. Consequently, there is a substantial need for a better understanding of the etiology and pathogenesis of LBP, for an improved prevention, for a precise diagnosis that actualizes patient selection for a specific treatment, and for an optimization of currently employed clinical interventions.

Although the causes and treatments of LBP have been within the focus of basic and clinical research during recent decades, the understanding of this disease remains limited, and the rate of its successful treatment is often low. Nevertheless, the rate of lumbar spine surgeries has risen disproportionately compared to other major orthopedic procedures [5,6]. Thus, the evidence-based treatment of these patients has to be doubted. This is an intricate medical treatment situation and there are exceptional clinical difficulties because LBP is a complex multidimensional problem with various interdisciplinary risk factors. In recent years, it has been established that different psycho-social risk factors can cause LBP, e.g., high job demands and low job control [7]. Furthermore, it has also been revealed that a lower socio-economic status (e.g., poverty, low educational level and unemployment [8]) and anthropometric factors (e.g., body mass index [9,10]) are associated with LBP, which must therefore considered in an integral treatment approach.

Aside from these risk factors, recent biomechanical and applied clinical research has emphasized that the loading of the spine as well as the individual spinal shape and its motion are essential individual characteristics, the detailed knowledge and interactions of which are key elements for improving the understanding and treatment of LBP (Fig. 1; e.g., [11–17]). Pioneers in these fields have made crucial contributions to our current scientific knowledge of these characteristics and LBP during the last 60 years. In the early 1960s, Nachemson [18–20] first demonstrated the feasibility of assessing *spinal loading in vivo* and thus paved the way for an understanding of the mechanical risk factors for LBP. In 2005, Roussouly [21] et al. created a fundamental classification system of different *spinal shapes*, which serves today as an essential reference for the preoperative planning of numerous surgical interventions. In the 1980s, Pearcy and co-workers [22–24] radiologically measured *spinal motion* in detail in all anatomical planes during standard, choreographed, standing, upper body motions. These values served for decades as the most basic reference values for biomechanical and clinical research. Based on these measurements and clinical observations, engineers such as Shirazi-Adl et al. [25] and Goel et al. [26] created computational models to non-invasively investigate in detail the specific *loading* of certain spinal structures as well as spinal *motion* to optimize LBP treatment options. However, despite intense research, a complete understanding of spinal *loading*, *shape* and *motion* has yet to be achieved.

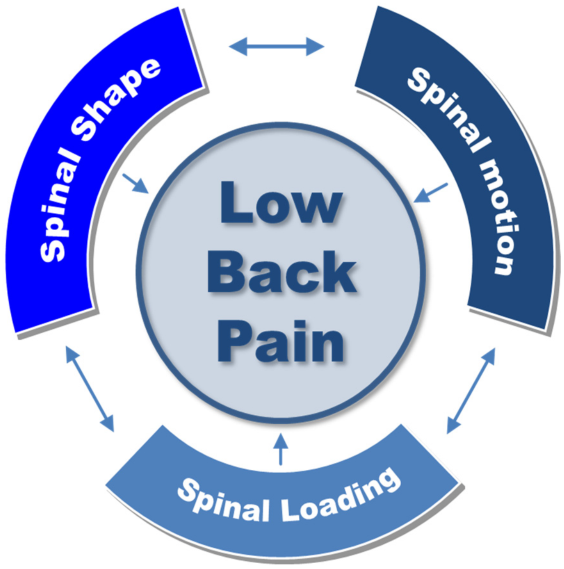

Figure 1: The present dissertation focuses on the investigation of lumbar spine loading, shape and motion, which are essential for improving the understanding, differential diagnosis and treatment of low back pain.

Therefore, the current cumulative dissertation aims to shed light on these characteristics in order to improve the knowledge of mechanical risk factors for LBP, to advance the differential diagnosis of back pain and to improve the currently employed computational research techniques and treatment approaches for LBP. In pursuit of these objectives, the first two studies of this dissertation (paragraphs 2.1 and 2.2) aimed to systematically investigate *in vivo spinal loading* during two essential daily and work-related activities: upper body bending and lifting of heavy weights. Both activities are recognized to be associated with LBP [11,12]. In the second part (paragraphs 2.3-6), lumbar spine *shape* and *motion* and essential influential factors are investigated under standard laboratory conditions, as well as in daily life, over 24 hours. The specific focus was to describe age- and gender-related differences with the aim of achieving a more patient-specific understanding. In the third part, finite element models of the lumbar spine currently employed worldwide, which have become widely used in spinal biomechanics, are thoroughly evaluated with respect to their employed *spinal shapes* and their predicted *loads* and *motion* values; in addition, these models were compared as a validation of a clinically relevant biomechanical analysis (paragraph 2.7). Finally, the knowledge gained overall was employed in a finite element sensitivity study (paragraph 2.8) to investigate in detail the mechanical risk factors for a common clinical treatment option, i.e., total disc replacement, with the aim of directly improving the current clinical care of LBP patients.

1.2 Scientific background and specific objectives

The double-s-shaped human spine is the central load-bearing pillar of the human body. The complex anatomical alignment of the spine is based on the irregular, bony vertebrae, which protect the spinal cord and serve as attachments for the complex muscle and ligament apparatus and for the intervertebral discs, which allow motion in all three main anatomical planes (Fig. 2).

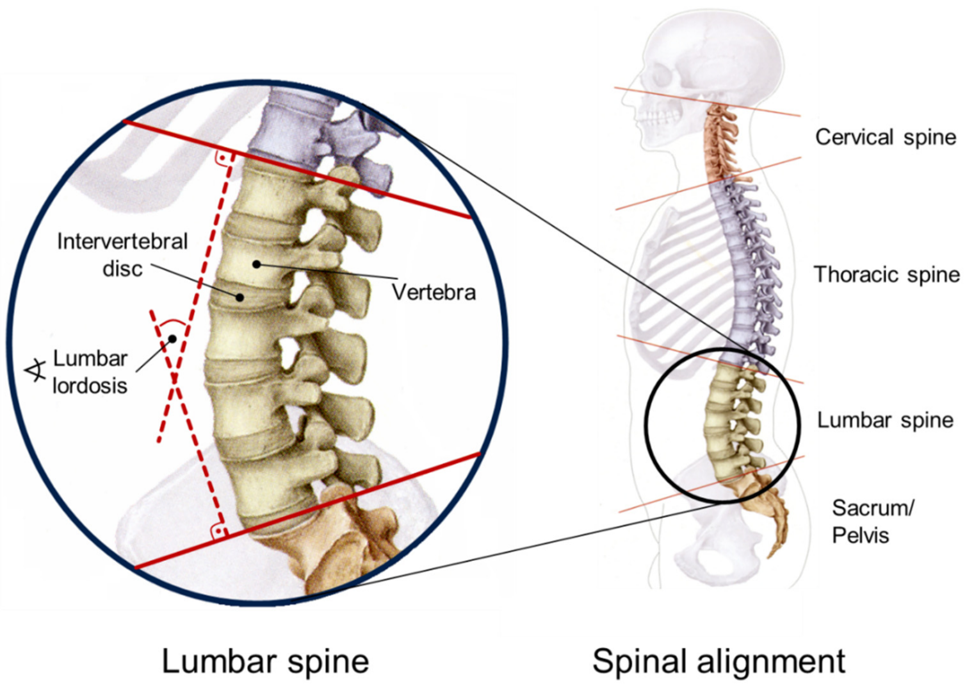

Figure 2: Composition and alignment of the human spine when standing as well as its different specific regions, ranging from the cervical spine to the sacrum. The image on the left demonstrates the lumbar spine in detail and the standard definition for the quantification of lumbar spine curvature (i.e., the lumbar lordosis angle, Cobb et al. [27]). The image is taken and modified from [28].

In a *standing* asymptomatic subject, the alternating composition of the vertebrae and intervertebral discs results in the typical convex forward (cervical and lumbar lordosis) and concave backward curves (thoracic and sacral kyphosis) in the sagittal plane (Fig. 2). Painful degenerative diseases (e.g., degenerative disc diseases or degenerative spondylolisthesis) are frequent in the lumbar spine region, in particular; thus, a major portion of daily clinical problems arise from this region (especially L4-L5, L5-S1) [29,30]. Therefore, the curvature (i.e., lumbar lordosis) and motion of the *lumbar* spine, as well as its loading, are the primary topics of the present dissertation (Fig. 2).

During daily and work-related activities, the spine is highly mechanically loaded and is highly compliant in performing complex motion tasks [23,24,31]. These multifaceted requirements and resultant loads are recognized to play an important role in the etiology of different degenerative pathologies and subsequent LBP. Although it is generally impossible to identify one particular activity as the cause of back pain, several reviews on the epidemiology of LBP have concluded that high spinal loads during frequent upper body bending in the sagittal plane and lifting of heavy weights are considered mechanical risk factors for LBP (e.g., [11,12]) (Fig. 1). However, due to the invasiveness and complexity of direct measurement techniques for determining spinal loading, the loads during these essential activities are still not well understood [32]. The gold standard for assessing spinal loading, i.e., the determination of the intradiscal pressure (IDP) within the nucleus pulposus of an intervertebral disc, was introduced by the work of Nachemson [18,20]. As a basis for these IDP measurements, which were usually performed in the lower lumbar spine (levels: L3-4, L4-5) at small upper body inclinations, it was shown in several *in vitro* investigations that the IDP is linearly related to the acting compression force [33–36]. Since Nachemson's early investigations, essential IDP measurements have been conducted by several researchers, e.g., Andersson et al. [37], Wilke et al. [31,38], Sato et al. [39] and Takahashi et al. [40]. However, during recent decades, only one *in vivo* study conducted by Wilke et al. [31,38], which only included a single volunteer, assessed spinal loading during upper body bending at larger inclinations and even peak flexion, which is assumed to cause high spinal loads. However, a detailed characterization of the typical inclination-load relationship based on the analysis of multiple measurement sessions at larger inclinations was not reported. Furthermore, load variations between different subjects were not assessed. Yet, these issues are required for subject-specific injury prevention, especially in patients after surgery, through the realistic testing of spinal implants and particularly through the validation of biomechanical models [41,42]. Furthermore, understanding this biomechanically complex motion is a prerequisite for the following investigations of the present dissertation, which analyze spinal shape and motion during standing and upper body bending not only under laboratory conditions but also in daily life. It was hypothesized (paragraph 2.1) that upper body bending in a standing position substantially increases spinal loading, even during small inclinations. Furthermore, this work aimed to provide for the first time a detailed description of a typical inclination-load relationship based on an analysis of multiple measurement sessions in several subjects.

Aside from upper body bending, *in vivo* measurements collected by Wilke et al. [38] and Andersson et al. [37] showed that spinal loading is exceptionally high during the lifting of heavy weights. Therefore, different lifting techniques have been very frequently investigated with the aim of reducing spinal loads during the lifting process [43–46]. In particular, the elementary lifting techniques known as “squat” lifting (i.e., leg lifting – knees bent and back straight) and “stoop” lifting (i.e., back lifting – knees straight and back bent) were very controversially discussed during past decades regarding how they affect spinal loading [43,44,47]. The squat technique is frequently assumed to result in lower spinal loads and is thus an elementary component of current ergonomic guidelines and back schools [48,49]. However, an evidence-based and robust recommendation of which of the two techniques results in smaller spinal loads that is based on numerous *in vivo* load measurements in several subjects does not exist. However, a detailed understanding of the high spinal loads occurring during lifting is essential to objectively quantify both work- and recreation-related mechanical risk factors with the overall aim of evaluating work-place safety and introducing effective prevention measures to decrease the rate of LBP. In this study (paragraph 2.2), in agreement with the current scientific consensus, it was hypothesized that the stoop lifting technique results in substantially higher spinal loads than does the squat lifting technique.

In addition to the importance of spinal loading as a mechanical risk factor, the individual shape of the spine and abnormal spinal motion patterns have been shown to play key roles in the development and treatment of painful degenerative pathologies [13,14,16,17,50]. In classic anatomical literature, the alignment of the lumbar spine was considered standardized and uniformly lordotic between the first and fifth lumbar vertebra (Fig. 2) [28]. During this period, differences in the spinal curvature between subjects were usually not in the focus of spinal surgery. However, more recent radiological studies have revolutionized the anatomical and clinical understanding of the lumbar spine and demonstrated that the whole spino-pelvic morphology and orientation can widely vary even among asymptomatic volunteers [51][52].

In 1982, Pierre Stagnara, a pioneer in the field of spinal deformity, emphasized the following:

"The span of possible values of maximum kyphosis and lordosis in subjects with no spinal disease is considerable. ... It is therefore unreasonable to speak of normal kyphotic or lordotic curves." [51].

In addition to the huge amount of variability among subjects, it could be shown that anatomical alignment is a highly individual characteristic. In 1995, the French surgeon G. Duval-Beaupère highlighted that:

"Sagittal spinal morphology varies from one individual to the another and is specific to each person." [53].

Based on these early studies, it could be shown that in a *standing position*, the spatial orientation and morphology of different anatomical entities (e.g., femurs – pelvic bones – sacrum – lumbar spine) are closely related, those of one entity affect those of adjacent entities [52][54]. For instance, it was demonstrated that the individual pelvic incidence is a fundamental morphological parameter [53], which is independent from posture and regulates spinal alignment [52,54] (Fig. 3A). The pelvic incidence is thereby closely correlated to the sacral slope and pelvic tilt (both of which are positional parameters reflecting an individual's posture) and thus with the individual amount of lumbar lordosis. These interrelations resulted in different suggestions for the classification of sagittal alignment, from which Roussouly et al. [21] suggested one of the most influential and widely employed classification systems in 2005 (Fig. 3B). This system is based on four elementary types of sagittal alignment, which differ in aspects such as sacral slope and the resultant segmental and total amount of lordosis.

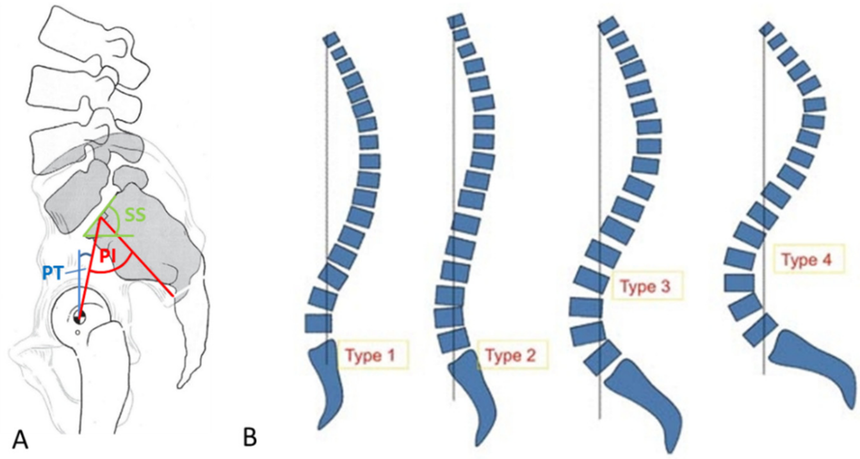

Figure 3: (A) Selection of essential radiological parameters of the spino-pelvic alignment measured in a standing position that characterize the "sagittal balance"; abbreviation: Pelvic Incidence (PI), Sacral Slope (SS), Pelvic Tilt (PT); Picture modified from Tebet [55] (B) The four elementary types of the classification system proposed by Roussouly et al. [21] for the standing sagittal spino-pelvic alignment (Image taken from [56]).

In recent years, it has been shown that these anatomical interrelations and resultant classification systems, which are well known as the so-called "sagittal balance" [57], have major implications for the pathogenesis and treatment of different degenerative pathologies. In a comparative study, Barrey and co-workers [13] for instance demonstrated that specific parameters of sagittal alignment, such as pelvic tilt or sacral slope (Fig. 3A), differ significantly between asymptomatic controls and patients suffering from degenerative disc disease, disc herniation or degenerative spondylolisthesis.

In addition to the analysis of lumbar spine alignment in a standing position and its important implications for LBP, lumbar spine mobility is commonly assessed in a standard procedure during upper body flexion (inclination) *and* extension (reclination) *while standing* for clinical and research purposes. In both positions, i.e., flexion and extension, lordosis is assessed in analogy to the standing position, usually by Cobb's method [27] (Fig. 2). Differences in lordosis between these three positions are calculated to determine the global (whole lumbar spine; Fig. 2) and local (single spinal segment; Fig. 2) range of flexion (RoF = lordosis in standing subtracted from lordosis in flexion), extension (RoE = lordosis in extension subtracted from lordosis in standing) and overall motion in the sagittal plane (sum of RoF and RoE) to characterize the maximal ability of the spine to move. In a radiological study, Pearcy et al. [58] demonstrated that LBP patients show a significantly reduced RoF during these standard measurements in standing compared with asymptomatic controls. Abnormal motion patterns were also measured in patients with disc herniation and nerve root compression in early studies conducted by Stokes and co-workers [16]. Furthermore, several studies have demonstrated that the pre- and postoperative individual spino-pelvic alignment, as well as motion after a surgical intervention, can have major implications for the long-term surgical success [59–61].

Although the findings of previous radiological studies on spinal alignment and motion have been demonstrated to be clinically essential, the current practice for assessing both characteristics, as well as the current state of knowledge of potential influential factors on both parameters, is still very limited. First, it is still a matter of debate how basic factors, such as age and gender, specifically affect local and total lumbar lordosis and mobility [52,54,62–68]. The aforementioned classification system of lumbar lordosis proposed by Roussouly et al. [21] (Fig. 3), which serves as an important clinical reference, is based on young subjects with a mean age of 27 years. However, this is substantially younger than the typical age of patients suffering from painful degenerative spinal diseases. Thus, the detailed effects of aging on total spinal shape and mobility and on certain parts of the lumbar spine, such as the lower, middle or upper lumbar spine, are still controversially discussed and almost unknown. A more patient-specific treatment with respect to disease localization and to a specific patient's age and gender requires a detailed understanding of the influence of these factors. Toward these goals, the present dissertation (paragraph 2.3.) aimed to investigate the gender-specific impact of aging on total and local lumbar spine shape and mobility. The hypothesis that aging significantly reduces total lumbar lordosis and mobility was tested in a cohort of 323 subjects. Furthermore, it was hypothesized that this aging process of lordosis and mobility is gender specific and pronounced differently in different local parts of the lumbar spine (i.e., the upper, middle and lower lumbar spine). In addition, although it can be shown that lumbar lordosis and pelvic orientation are anatomically closely related in a *standing* posture (Fig. 2, 3), their specific interrelation during upper body bending, the so-called "lumbo-pelvic rhythm" (quantified by the lumbar RoF divided by the pelvic RoF in upper body flexion) is still not well understood. Few previous studies have investigated this specific interrelation and demonstrated that during upper body flexion, changes in the lumbar spine dominate in the early part of the flexion motion, whereas changes in pelvic orientation occur mainly during the late flexion phase of the motion [69–71]. However, the impact of age and gender on this interplay has not been investigated at all and is not well understood. However, the understanding of the complex lumbo-pelvic motion is assumed to be essential for a more sophisticated differential diagnosis of LBP that goes beyond the simple determinations of the ranges of motion and that might allow a more targeted subsequent therapy. Moreover, this knowledge is important for obtaining a profound biomechanical understanding of loading during upper body bending and lifting [72–74]. On this basis, in the present dissertation (paragraph 2.4.), the lumbo-pelvic rhythm was investigated in detail, and it was hypothesized that the complex interplay between the pelvis and lumbar spine at different stages of the flexion motion process (i.e., early, middle, late and full flexion) is specifically affected by age and gender.

In addition to these basic research questions, which all have in common that lumbar spine shape and mobility were investigated in standardized *standing, flexion and extension* postures, detailed information of lumbar spine shape and mobility during daily life have not yet been reported. Indeed, all the aforementioned studies and almost all clinical and research practices, including the aforementioned classification system of the spinal alignment by Roussouly et al. [21] and the assessment of spinal mobility by Pearcy et al. [22,23], employ functional radiological measurements in *standing and upper body flexion and extension* as the current “gold standard”. However, it is completely unknown to what extent these assessed values of spinal shape and motion in standing characterize the actual corresponding values that occur during daily life. As life in industrialized countries mainly takes place in sedentary postures [75], differences in lordosis and motion in standing and during daily life seem likely, yet they have remained unstudied and unquantified. This suggests that the standard reference values of spinal mobility assessed in standing would not be representative of those that occur during daily life. Moreover, as standing alignment (in particular, lumbar lordosis) serves as a major reference for almost all instrumented surgical interventions, those differences would also suggest that the pre-operative evaluation for various interventions must be reconsidered and would thus call into question the meaningfulness of classification systems based on a standing position. Furthermore, discrepancies between classical standing and daily life measurements might imply substantially different loading of certain spinal structures and implants during the day than clinically and biomechanically expected. Therefore, in the present dissertation (paragraph 2.5) measurements were conducted during 24-hour periods to offer a new perspective on lumbar lordosis and mobility during daily life. It was hypothesized that lumbar lordosis is highly variable during the 24 hours of the day and significantly differs on average from the clinical reference values assessed during standing. In addition, it was hypothesized that the maximal ranges of motion in the sagittal plane, which are assessed during standard upper body bending in standing, differ significantly from the corresponding actual values. Furthermore, the impact of age and gender on lordosis and lumbar mobility in daily life was investigated, and these effects were compared to those on the standard measurements in standing. In addition to the lordosis and maximal spinal ranges of motion, the presented long-term measurements during daily life can moreover quantify the number of spinal movements in the sagittal plane, which has been unstudied until now. Quantifying the number of lumbar spine movements occurring during the day is important to gain knowledge about "normal" spinal behavior and could thus ideally complement the aforementioned *in vivo* load measurements of standardized activities. As changes in lumbar lordosis are assumed to be accompanied by substantial load changes, their quantification is important for achieving realistic spinal implant testing and for elucidating the etiology of LBP. Therefore, in paragraph 2.6 of this dissertation, the number of lumbar spine movements occurring during daily life was determined as an additional essential parameter. In addition to the quantification of spinal movements, the effects of age and gender were also determined. Despite the aforementioned problems and limitations of the current state-of-the-art methods, there is no doubt that with the current state of knowledge, the individual sagittal alignment still has major implications for the surgical treatment of LBP patients. For instance, Strube et al. [59] showed that individual sagittal alignment can significantly influence clinical outcome of a total disc replacement (TDR). They revealed that sagittal profile types 1 and 4, according to the classification of Roussouly et al. [21], represent a contraindication for TDR in the spinal levels L4-L5 or L5-S1. Besides the static standing alignment, it was shown by Siepe et al. [61] that individual segmental mobility during flexion-extension of the upper body after TDR (quantified by the segmental range of motion) at the index level is an important predictor of postoperative surgical success. They could show that patients who developed painful facet joints within years after having surgery showed a significantly reduced range of motion directly after the intervention. Furthermore, for non-motion-preserving technologies, Pellet et al. [60] could show that an arthrodesis in L5-S1 should be favored in profile types 3 and 4. Although these findings and recommendations are generally helpful for surgical decision-making and rehabilitation, a clear biomechanical explanation of the underlying cause is still missing. A comprehensive mechanical understanding could be very beneficial for attaining more individualized therapies and improved implant designs as well as optimizing surgical procedures. During recent decades, finite element models of the lumbar spine were introduced to analyze these biomechanical risk factors, particularly after the implantation of a spinal implant [76–78]. In cases with a profound and sophisticated validation, these models are employed to predict clinically relevant parameters, such as the loading of facet joints or the segmental range of motion in all main anatomical planes [41,42,79,80]. Furthermore, in comparison to *in vivo* and *in vitro* approaches, these models can offer the advantage of independently assessing the isolated effects of important biomechanical parameters independently, which is very helpful for obtaining a detailed understanding of complex spinal implants and can strongly diminish the need for human or animal specimens in experimental studies. However, to date, the currently employed finite element models are usually based on only one specific or one idealized sagittal alignment [81–87]. Thus, although the aforementioned investigations on the sagittal balance have shown the high clinical importance of individual anatomical alignment for a surgical procedure, this anatomical variability is usually not considered in current finite element model studies. Nevertheless, several specific models that are typically based on only one specific or one idealized sagittal alignment have been developed during recent decades and are referred to as validated, and each has been individually employed in numerous published studies to predict clinical risks (e.g., [84,88,89]). These limitations raise questions on the current comparability of those computational lumbar spine models and their predictive power with respect to an inhomogeneous patient cohort. While a systematic comparison of these models has not been yet performed, it would reveal the range of their results and the comparability with *in vitro* or *in vivo* reference values. Such a comparison is crucial to ensure the quality and validity of future research. Thus, a comparison study (paragraph 2.7) among different research groups around the world was conducted to evaluate for the first time the predictive power, the comparability and the range of results of currently employed finite element models of the lumbar spine.

In light of the current limitations of lumbar finite element models, it appears very promising that a consideration of different sagittal alignments in the finite element analysis of spinal implants might reveal important individual mechanical risk factors and might thus lead to more sophisticated patient-specific treatments. Therefore, in the present dissertation (paragraph 2.8), different spinal geometries were employed in a finite element study to investigate a total disc replacement (TDR) in detail. The TDR was here exemplarily investigated as a major surgical treatment option, which was initially assumed to revolutionize the treatment of LBP patients. As a motion-preserving technology, it was assumed to be clinically superior to a standard spinal fusion procedure, which is assumed to induce adjacent disc disease and subsequent LBP. However, currently, a TDR is one of the most controversially discussed spinal implants, and its success has fallen short of its high initial expectations [90–95]. The current work focuses also on specific surgery-related factors, such as iatrogenic distraction and implant position, which have been discussed to be essential for this surgical intervention. It was hypothesized that the implant location, the individual sagittal alignment and the distraction substantially affect the segmental kinematics at the index level and that the distraction of the segment, in particular, increases the facet joint loads. As these loads have been shown to be highly relevant to postoperative success [96,97], the presented results might directly help to improve the current level of patient care.

2. Publications

2.1 Publication 1: In vivo implant forces acting on a vertebral body replacement during upper body flexion

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Abstract

Knowledge about *in vivo* spinal loads is required for the identification of risk factors for low back pain and for realistic preclinical testing of spinal implants. Therefore, the aim of the present study was to measure the *in vivo* forces on a vertebral body replacement (VBR) during trunk flexion and to analyze in detail the typical relationship between trunk inclination and spinal load.

Telemeterized VBRs were implanted in five patients. *In vivo* loads were measured 135 times during flexion while standing or sitting. The trunk inclination was simultaneously recorded. To reveal elementary differences between flexion while standing and sitting, the force increases at the maximal inclination, as compared to the upright position, were also determined.

Approximately 90% of all standing trials showed a characteristic inclination-load relationship, with an initial increase of the resultant force followed by a plateau or even a decrease of the force at an inclination of approximately 33°. Further flexion to the average maximal inclination angle of 53° only marginally affected the implant loads (~450 N). Maximal forces were measured during the return to the initial standing position (~565 N). Flexion during standing led to a greater force increase (~330 N) than during sitting (~200 N) when compared to the respective upright positions.

The force plateau at greater inclination angles might be explained by abdominal load support, complex stabilization of active and passive spinal structures or intricate load sharing within the implant complex. The data presented here aid in understanding the loads acting on an instrumented lumbar spine.

1. Introduction

Low back pain is one of the most serious public health problems in industrialized countries, affecting approximately 80% of all adults at some point in their lives (Andersson, 1998). In addition to psychosocial factors (Sterud and Tynes, 2013), mechanical loading on the lumbar spine during diurnal activities appears to play a major role in the etiology of low back pain (Hoogendoorn et al., 2000). Furthermore, a comprehensive understanding of activities associated with high spinal loads is a basic requirement for patient risk assessment after surgery and for realistic preclinical testing of spinal implants. Thus, from a mechanical perspective, upper body flexion in the sagittal plane is an essential activity, as it is characterized by the largest range of motion among all the main anatomical planes (Pearcy, 1985), it is frequently performed during daily and work-related activities (Rohlmann et al., 2014), and it is associated with high spinal loads (Nachemson, 1966; Wilke et al., 1999).

Few *in vivo* measurements of spinal loading have been made for upper body flexion during standing, particularly at greater inclination angles. Earlier *in vivo* studies measured the intradiscal pressure (IDP) in single or few subjects and mainly measured in the L4-5 disc at intermediate flexion postures in single measurement sessions (Nachemson (1966); Sato et al. (1999); Takahashi et al. (2006)). Nachemson (1966) demonstrated a substantial load increase of a factor of 1.5 between standing and forward bending at an inclination of 20°. Sato et al. (1999) and Takahashi et al. (2006) confirmed these early measurements but determined an even greater IDP increase, by a factor of between 2.5 and 3.6. More detailed, continuous measurements in a single subject by Wilke et al. (2001) revealed an almost linear pressure increase from approximately 0.5 MPa during standing to 1.08 MPa (a factor of approximately 2.2) at an inclination angle of 36° between the thoracolumbar junction and the sacrum. Using a flexible pressure transducer, Wilke et al. (2001) also measured the IDP for “fingertip to floor” upper body flexion, for which a value of 1.6 MPa was determined (a factor of approximately 3.2). However, only a single pressure value for peak flexion was published, without further information about the continuous motion-loading relationship for higher inclination angles or repetitive measurements. Moreover, only few IDP measurements exist for upper body flexion during sitting, which might be different from standing. Thus, reliable data about spinal loading during upper body flexion in the lumbar spine are rare in the literature.

Apart from direct *in vivo* measurements, several musculoskeletal models have been used to predict and analyze spinal loads and muscle forces during upper body flexion for ergonomic or clinical purposes (Arjmand et al., 2010; de Zee et al., 2007; Han et al., 2012; McGill and Kippers, 1994). Notwithstanding the limitations of computational predictions, validated musculoskeletal models are crucial to the improvement of our understanding of muscle forces and spinal loading *in vivo* in asymptomatic subjects and in patients. However, upper body flexion is characterized by complex interrelations among motion, active and/or passive stabilization (back muscles and ligamentous spine) and the resultant loading. Thus, to increase the confidence level of model predictions, profound and reliable *in vivo* measurements during upper body flexion are an essential prerequisite.

A further possibility to estimate spinal loads is to use instrumented implants, which offer the advantage of multiple repeated measurements. A telemeterized vertebral body replacement (VBR) allows the *in vivo* analysis of implant loads in the anterior spinal column in several individuals over a period of several years (Rohlmann et al., 2013). The aim of this study was thus to determine the relationship in several subjects between upper body trunk inclination and implant loads for trunk flexion in a standing position. Numerous measuring sessions were used to generate a detailed description of a typical inclination-load relationship and to reveal elementary differences in flexion between standing and sitting.

2. Methods

2.1. Telemeterized VBR

The clinically used VBR Synex^{TM} (Synthes, Bettlach, Switzerland) was modified to allow the *in vivo* measurement of three force and three moment components. A hollow cylinder with an original endplate on one side contains strain gauges as load sensors, a telemetry unit, and a coil for the inductive power supply. Screwed-on endplates of different heights allowed the implant height to be intraoperatively adapted to the defect size. The implant has been described in detail elsewhere (Graichen et al., 2007; Rohlmann et al., 2007).

The VBRs were extensively calibrated prior to implantation. Compressive and shear forces were applied onto the implant at 21 different points, causing defined combinations of forces and moments of up to 3,000 N and 20 Nm, respectively. The measurement accuracy was better than 2% for forces and 5% for moments relative to the calibration ranges. The sensitivity of the VBR is less than 1 N for the force components and less than 0.01 Nm for the moment components.

During a measurement, an induction coil was placed around the patient's trunk at the level of the implant for the power supply. The load-dependent signals of the telemetry were received by an antenna on the patient's back and were transmitted to a notebook where the forces and moments were automatically calculated and displayed on a monitor (Graichen et al., 2007). The patients were videotaped during the measurements, and the digital telemetry signals were stored together with the images.

2.2. Ethics Statement

The Ethics Committee of the Charité – Universitätsmedizin Berlin approved the clinical implantation of the telemeterized implant in patients and the study protocol (Registry number 213-01/225-20). All patients gave their written consent to the implantation of the instrumented VBR, the subsequent load measurements and image publication. The subjects' rights were protected throughout the course of the study.

2.3. Patients

Instrumented VBRs were implanted in five patients (WP1-WP5) who had an A3-type compression fracture of a vertebral body (classification after Magerl et al. (1994)). In four patients, the L1 vertebral body was fractured (WP1-WP4), while the L3 vertebral body was fractured in one patient (WP5). Detailed information about the patients is provided in Table 1. In all patients, the vertebral body fracture was first stabilized from the posterior using an internal spinal fixation device. In a second surgery, parts of the fractured vertebral body and the adjacent intervertebral discs were removed, and the VBR was inserted in the corpectomy defect. To enhance the interbody fusion process, autologous bone material was added.

Table 1: Data for patients and surgical procedures

Parameter	Patient				
	WP1	WP2	WP3	WP4	WP5
Sex (Male/Female)	M	M	F	M	M
Age at the time of surgery (years)	62	71	69	63	66
Height (cm)	168	169	168	170	180
Body mass (kg)	66	74	64	60	63
Body mass index (kg/m^2)	23	26	23	21	19
Fractured vertebra	L1	L1	L1	L1	L3
Level of internal fixation device	T12-L2	T12-L2	T11-L3	T11-L3	L2-L4
Implantation date (month/year)	09/2006	11/2006	03/2007	01/2008	07/2008

2.4. Exercises

During each measurement, patients were asked to bend forward while standing. For standardization, trials were only analyzed when the hands were kept close to the legs during the motion. Furthermore, measurements were taken while sitting on a stool (no backrest or armrests). As it has been shown that the position of the arms substantially affects implant loading (Dreischarf et al., 2010), the patients were instructed to let their arms hang laterally for standardization. To avoid any constraints, the patients were generally given no further instructions about how to perform the exercise (with respect to exercise speed, for instance). Load measurements started approximately 2 weeks after surgery and continued as long as 65 months after surgery. In the first few months, patients typically flexed the upper body only slightly and/or with the support of a physiotherapist. Therefore, this study only evaluated exercises performed after 6 months postoperatively. The exercise was usually repeated once or twice during a measuring session. Overall, 135 single measurements (82 standing and 53 sitting), from 37 measuring sessions, in which the patient flexed his or her upper body, were analyzed in the current study.

2.5. Data evaluation

A typical measuring sample is shown in Figure 1 for clarification, where the inclination angle 'α' and the basic loading curves during the motion are indicated. The present study is focused on the resultant force, which is the geometric sum of the three measured force components acting on the implant as the main loading mode (F_x - anterior-posterior shear; F_y - lateral shear; F_z - axial compression). The trunk inclination angle was measured using videotaped images and custom-made software. For this measurement, the angle between a reference vertical line and a straight line fitted to the back of the patient in the region of the lumbar and lower thoracic spine was determined.

In most trials during standing, the load curve for upper body flexion is characterized by the three points marked "A", "B" and "C" (Fig. 1). Therefore, the resultant force and the trunk inclination were evaluated at these three time points.

To reveal elementary differences between flexion while standing and sitting, the maximal inclination angle and the resultant force increase at this time point were additionally determined for all 135 measurements. The resultant force increase is defined as the difference between the force value at the maximal inclination angle and the average force value during upright standing or sitting, as determined on the same day from several trials of an individual patient. This force increase represents the change in force that results from the two different body positions in the absence of dynamic effects, and it is thus appropriate for the validation of computational models.

The average values and ranges of the forces and inclination angles during all measuring sessions were determined. Furthermore, the median values of the resultant forces and trunk inclinations of all patients were evaluated, as were the ranges of individual patient medians.

3. Results

Trunk flexion caused a considerable increase in the resultant force on the VBR with respect to the upright standing position. In approximately 90% of all trials while standing, the resultant force curve initially increased continuously with the inclination. Subsequently, after a certain inclination angle (point A in Fig. 1), the resultant force showed a distinct plateau or a slight decrease. After reaching the maximal inclination angle (point B), the resultant force slightly increased over its plateau value while returning to the initial standing position (point C), resulting in a characteristic relationship between inclination and force, as illustrated in Figure 1.

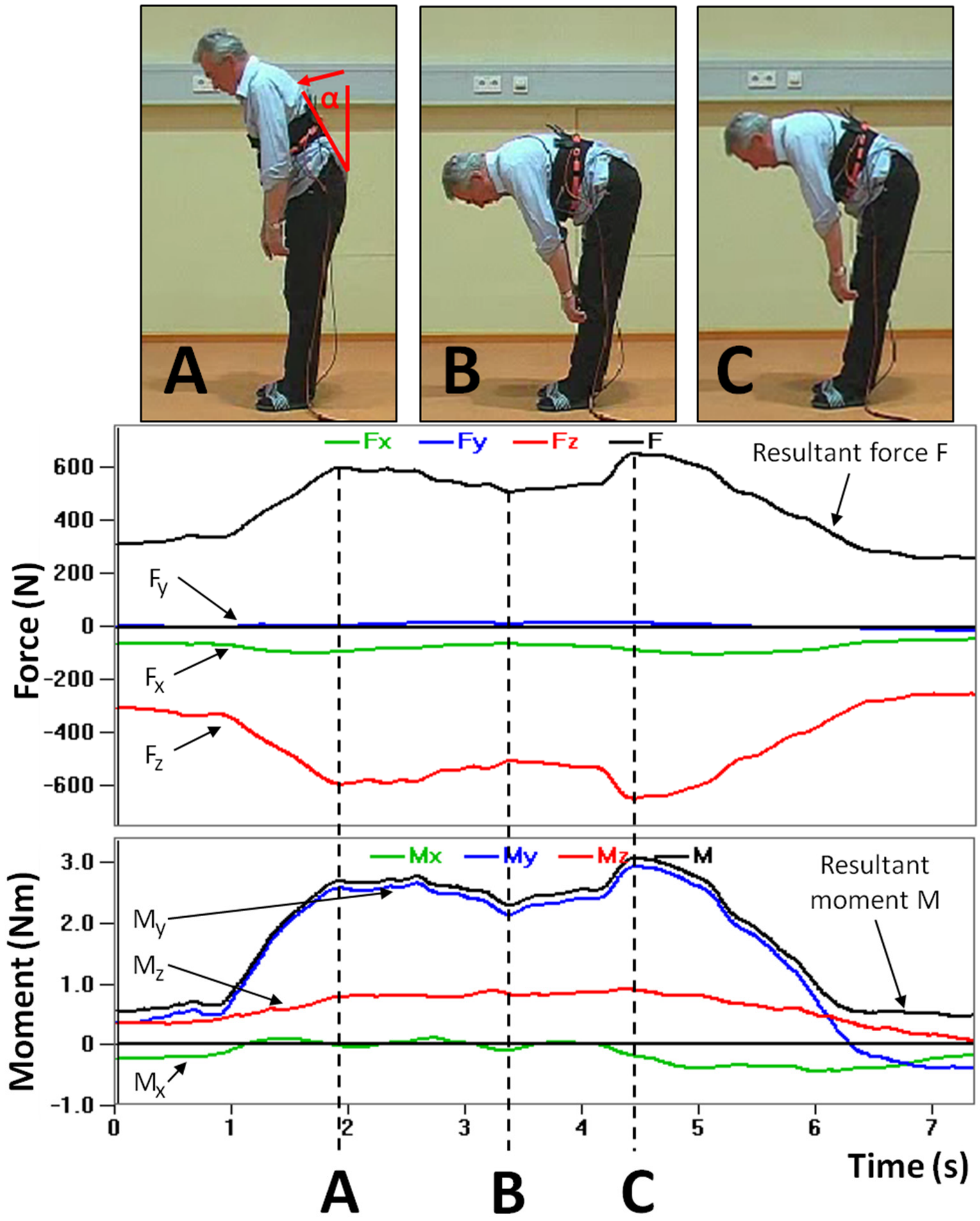
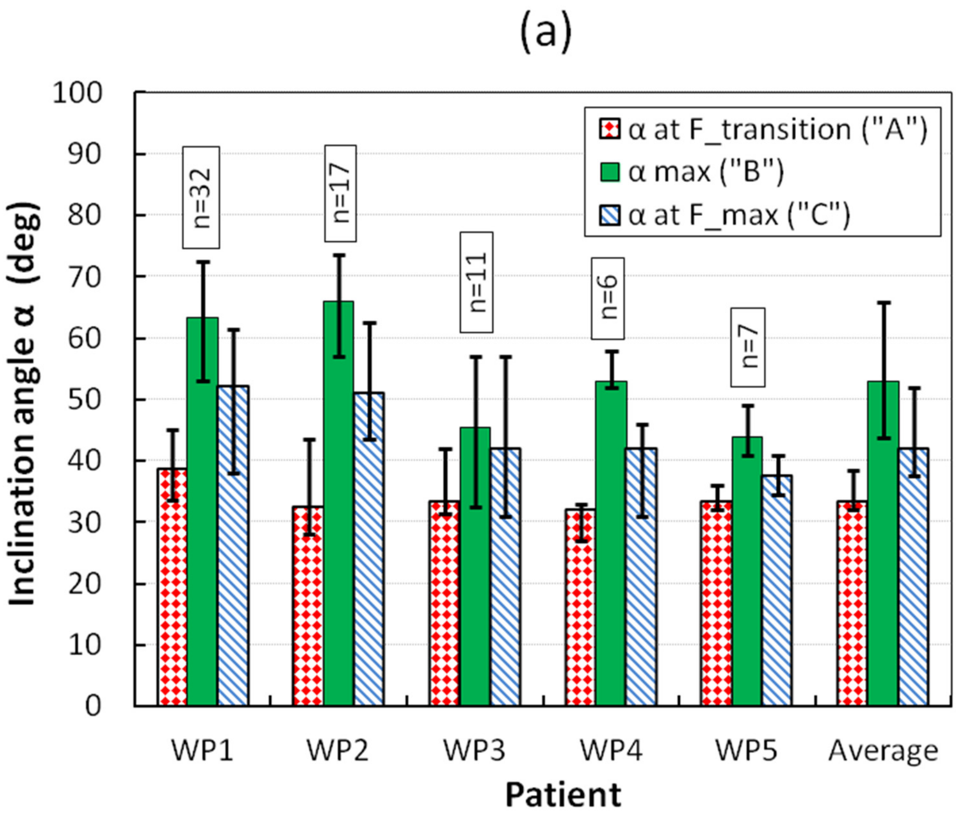


Figure 1: Measured load components (F_x - anterior-posterior shear; F_y - lateral shear; F_z - axial compression; M_x - lateral bending moment; M_y - flexion bending moment; M_z – torsional moment) and the resultant force 'F' and moment 'M' (black lines) for flexion of the upper body. 'α' represents the inclination angle during trunk flexion. At time point "A", the resultant force reached a plateau; at "B", the maximum trunk inclination angle was reached; and at "C", the maximum force occurred when returning to the upright position.

On average, the inclination angle at point A (starting point of the force plateau) was 33°, and the range of median angles for all five patients (Fig. 2a) was rather small (range: 32° to 39°). A further bending of the patients to their maximal inclination angles (point B) of, on average, 53° (range: 44° to 66°), only marginally affected the loading on the VBR (Fig. 2b). In both positions (points A and B), the implant forces were approximately 450 N on average (range: 425 N to 638 N). Maximal implant forces of on average 565 N (range: 450 N to 770 N) were measured during the return to an upright standing position at an average trunk inclination of approximately 42°. However, there was usually a large inter- and intra-individual variation in the resultant force. In the remaining 10% of all trials, no clear plateau and a more irregular pattern with a maximum force was found.



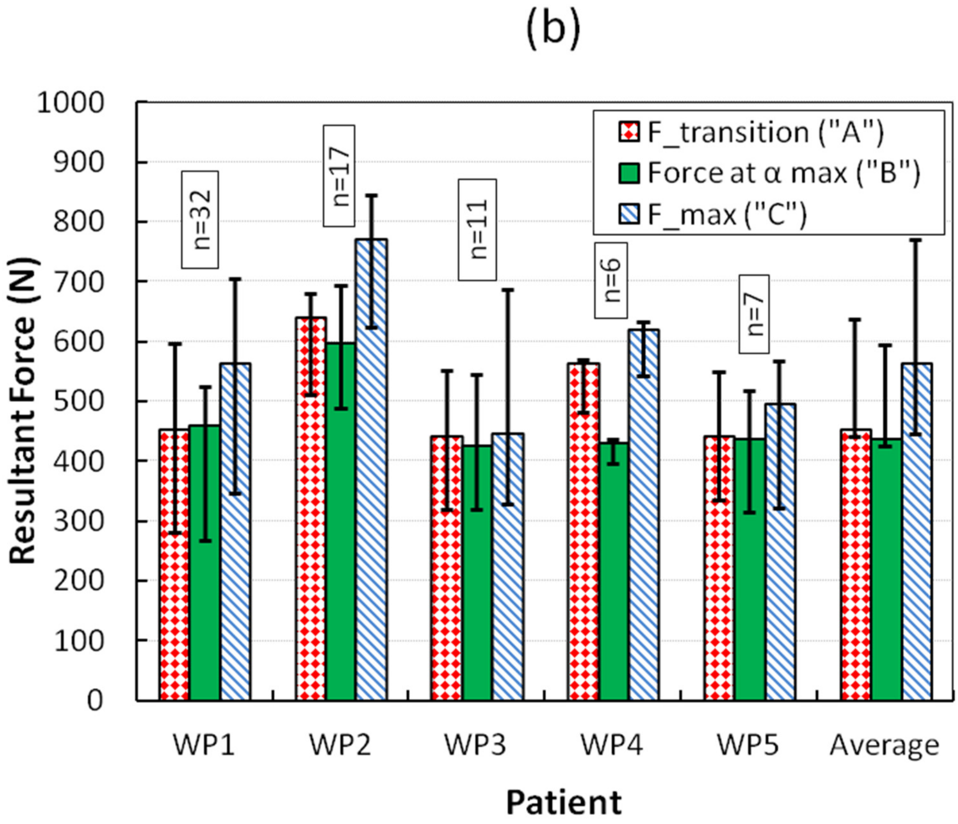


Figure 2: a) Comparison of the inclination angles ('α') at time points "A", "B", and "C" (see Fig. 1) for standing. The median values and ranges are given for each patient (WP1 – WP5). The median value for all patients was also calculated. 'n' represents the number of individual measurements. **b)** Comparison of the resultant implant forces at time points "A", "B", and "C" (see Fig. 1) for standing. The median values and ranges are given for each patient (WP1 – WP5). The median value for all patients was also calculated. 'n' represents the number of individual measurements.

On average, patients reached considerably smaller maximal inclination angles (Fig. 3a) during sitting (30°) than during standing (53°). The force increase at the maximal inclination angle (point B), compared to the corresponding upright position, was smaller in all five patients during sitting (~200 N; Fig. 3b) than during standing (~330 N). For flexion during sitting, the force curve showed a plateau in approximately 75% of all trials. The average trunk inclination angle at point "A" was approximately 21° while sitting and was thus 12° smaller than the corresponding angle in a standing position.

The recorded resultant moments were usually smaller than 4 Nm.

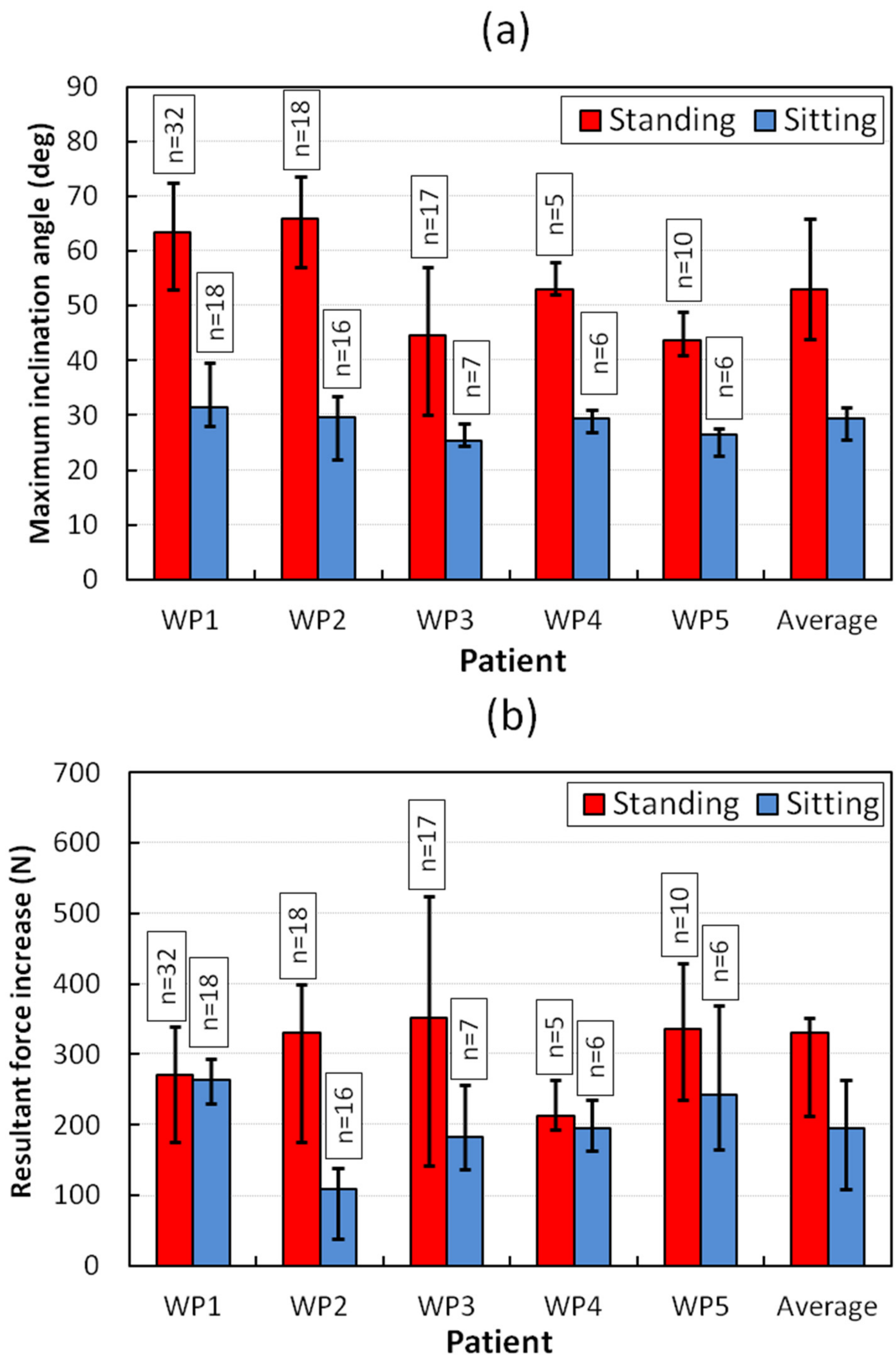


Figure 3:a) Maximum trunk inclination angles and their ranges for flexion while standing and sitting for each patient (WP1 – WP5). The median value for all patients was also calculated. 'n' represents the number of individual measurements. **b)** Force increase of the resultant force at maximal trunk inclination with respect to the upright position. The values are given for flexion while standing and sitting, respectively, for each patient (WP1 – WP5). The median value for all patients was also calculated. 'n' represents the number of individual measurements.

4. Discussion

Forces on a VBR were measured *in vivo* during trunk flexion while standing and sitting in five patients, for a total of 135 single measurements. Simultaneously, the corresponding trunk inclination angles were measured using videotaped images. In general, upper body flexion increased the resultant force on the VBR with respect to the upright position. In most cases, the resultant force curve reached a plateau or even decreased before the maximal inclination angle was reached. After reaching the maximal inclination angles, the resultant force characteristically increased while returning to the upright position. The evaluated force increases and maximal inclination angles were smaller when performing trunk flexion while sitting than while standing.

During trunk flexion, the effective lever arm of the upper body center of mass relative to a certain point in the lumbar spine, and thus the net external moment, is assumed to increase until a trunk inclination of 90° is achieved (Arjmand et al., 2010; Hajihosseinali et al., 2014). After a certain trunk inclination (approximately 30°-45°), the electromyographic (EMG) activity in the global extensor muscles (e.g., the longissimus or iliocostalis) starts to decrease despite the increase in net external moment, an occurrence known as the “flexion-relaxation” phenomenon (Floyd and Silver, 1951; Schultz et al., 1985). During bending, the net external moment is balanced mainly by active spinal components in the initial bending phase. It is then balanced upon further flexion primarily by passive spinal components, including passive muscle forces or ligament forces. These basic mechanical relationships should result in a monotonic increase of the compressive spinal force up to a trunk inclination angle of 90°, when the net external moment reaches its maximum. In accordance with this concept, different sophisticated computational models (Arjmand et al., 2010; Hajihosseinali et al., 2014), simulating an *asymptomatic* subject, indeed predicted a continuous force increase up to a 90° trunk inclination. Typically, the increase initially appears almost linear and subsequently becomes less steep as the maximum inclination is approached. In agreement with these models, *in vivo* intradiscal pressure measurements in one *asymptomatic* individual during flexion showed a nearly linear increase of the IDP for moderate trunk inclinations up to approximately 55°, thus supporting these model predictions for the initial phase of trunk flexion (Wilke et al., 2001). The resultant force on the VBR in *patients* also typically increased continuously with increasing inclination angle, but only in the early phase of trunk flexion (approximately 33°). The resultant implant force did not increase during further inclination.

This finding apparently contradicts the results of the aforementioned computational models of *asymptomatic* individuals.

How is it possible that the implant forces remain constant or even decrease even as the net external moment may increase? One explanation might be that structures other than the extensor muscles (e.g., the thoracolumbar fascia or the supraspinous ligament) support the load during flexion and balance the net external moment more effectively (with larger lever arms), thereby resulting in smaller spinal compressive forces. This idea is supported by the EMG silence at larger inclination angles and by the earlier starting point of the force plateau while sitting. During sitting, the lordosis of the lumbar spine is reduced because of pelvic retroversion, which should increase the passive pretension of the posterior spinal ligaments. Thus, during sitting, these passive structures can support the load earlier and generate an earlier force plateau. However, the force curves did not display a force plateau in all trials for a given patient. If trunk flexion occurs mainly in the hips and if changes in lumbar lordosis are small (different lumbo-pelvic ratios), the passive lumbar structures (e.g., the supraspinous ligament) might be less loaded so that the trunk must be actively balanced by the muscles of the back and lower extremities (Tafazzol et al., 2014). This distinction emphasizes the idea that the way in which an exercise is performed strongly influences the resultant inclination-force curve.

A second explanation for the force plateau might be the intraabdominal pressure and passive support by the abdomen. However, it remains a matter of debate as to what extent intraabdominal pressure actually unloads the spine (Andersson et al., 1977; Cholewicki et al., 1999; Hodges et al., 2001; Marras and Mirka, 1996; McGill and Norman, 1987; Nachemson et al., 1986). During maximal trunk flexion, the abdomen is compressed, especially when sitting with the trunk in contact with the thighs. This compression may partially explain the flattening of the implant loading curve at greater trunk inclinations (Arjmand and Shirazi-Adl, 2006; Calisse et al., 1999). The maximum measured inclination angle and the transition angle (Fig. 1; point A), as well as the force changes, were smaller when flexion was performed while sitting than while standing, corroborating the unloading effect of the abdomen. In addition, the position of the arms may differ between flexion while sitting and standing, with a slightly more ventral arm position while standing than while sitting. This may partly also explain the larger force increase observed during standing than during sitting. In agreement with the present study, Wilke et al. (2001) and Sato et al. (1999) also measured smaller IDP values during trunk flexion while sitting than while standing.

The *in vivo* measurements reported in a single subject by Wilke et al. (2001) show no pressure plateau for intermediate trunk inclinations. However, for inclination values of up to 90°, no complete inclination-force curve was shown. In a further *in vivo* study, Takahashi et al. (2006) measured the IDP during intermediate trunk inclination in three asymptomatic subjects and published individual force curves for all three volunteers. In two of them, a linear increase of the IDP was measured, similar to the measurements of Wilke et al. (2001). However, despite the similar anthropometric characteristics of all three male asymptomatic subjects, the load increase in one volunteer was only about half the total spinal loading and appeared strongly non-linear. The load characteristic of this subject tended to have near-maximal compressive spinal forces at an earlier state of trunk flexion, a result more similar to those presented here. The reasons for the differences among subjects were not discussed by Takahashi et al. (2006). This large overall inter- and intra-individual variability in spinal load measurements severely complicates comparisons of measured results among different studies and hampers an adequate validation of computational models, as most influencing factors are difficult to measure *in vivo* or are unknown.

There are multiple factors that might explain the aforementioned differences between load measurements using a vertebral body replacement in *patients* and IDP measurements in *asymptomatic* subjects and that might also explain the large measurement variation across subjects within these studies. The main advantage of measurements using telemeterized implants over IDP measurements is the possibility of taking multiple repeated measurements in several individuals over several years. This advantage allows the assessment of the large inter- and intra-individual variability, which was also observed in other instrumented joints (such as hip, knee and spine; Damm et al., 2013; Kutzner et al., 2010; Rohlmann et al., 2014). The variability in spinal implant loads arises, for instance, from anatomical variations among subjects (e.g., geometric variability in thoracic kyphosis, lumbar lordosis and pelvic morphology and individual spinal material properties), from differences in performing the movement task (e.g., differences in head position, arm position, knee extension, or back extension, individual lumbo-pelvic ratio or exercise speed), from diurnal variations in spine biomechanics (e.g., water content of the disc and load history of spinal structures), from individual fitness level (e.g., BMI and body constitution and, thus, variability in centers of mass) or from differences because of sex and age.

On the other hand, measurements with an instrumented VBR have several limitations, which make an exact interpretation of the results and a comparison with IDP measurements difficult. In contrast to IDP measurements, which are usually taken in young, *asymptomatic* volunteers with non-degenerated intervertebral discs, the spinal motion and loading in an aged, instrumented spine that has been treated with a VBR are substantially altered (Cripton et al., 2000; Rohlmann et al., 2002). Because of the insertion of the VBR and the internal spinal fixation device, several adjacent segments are fused. Thus, the complete spinal compressive force is not transferred via the vertebral body replacement. In a finite element model study, Zander et al. (2009) estimated that approximately 82% of the total spinal load is transferred via the VBR, 6% via the remaining vertebra and 12% via the internal fixators under pure compression. The overall load sharing between the vertebral body replacement, the internal fixation device, and the remaining bone might moreover be posture-related and dependent on the state of fusion throughout the postoperative time (Rohlmann et al., 2013) and is thus in detail unknown. Because of the rigid implant and posterior fixation device, a moment transmission at the bridged segments is possible, which locally necessitates a smaller moment compensation than in the healthy state and also explains why the measured loads on a VBR are usually smaller than estimates for an *asymptomatic* spine (Dreischarf et al., 2013; Zander et al., 2014 submitted). Furthermore, in contrast to IDP measurements, which are usually taken at the L4-5 disc, load measurements were taken at L1 (WP1-WP4) and L3 (WP5) in the upper and middle lumbar spine. Any of these factors might affect the resultant inclination-force relationship and measured absolute force values.

In addition to the abovementioned limitations, the following points warrant discussion. The advanced telemetry techniques have only been implanted in a small cohort of five patients. Although the methods used are almost unique, no inferential statistical evaluation was possible because of the small cohort. In the present study, the upper body trunk inclination was only estimated from videotapes and not measured with more sophisticated approaches. This approach was taken because our patients were at an older age and declined additional time-consuming measurements. The absolute values of the assessed angles are thus difficult to compare with those measured in other studies on asymptomatic subjects using more sophisticated measurement techniques (e.g.: Tafazzol et al., 2014). Furthermore, because the patients measured in the present study were older, they flexed their upper bodies to only an average of 53°, with maximal values observed in patient “WP2“ of an average of 66°. These values are smaller than the maximal values measured in asymptomatic subjects (Tafazzol et al., 2014). In addition to the maximal trunk inclination angle, the position of the arms during the exercise (close to the legs, hanging down) had a strong effect on the resultant forces. Hence, for the sake of consistency, only those trials where the hands were kept close to the legs were included in this study. Furthermore, the velocity of the movement can influence the resultant absolute force values and the force pattern (Bazrgari et al. 2008). The entire movement usually lasted 5 to 7 seconds in all five patients (Fig. 1) and can thus be characterized as “intermediate” velocity. This characterization is consistent with the study of Bazrgari et al. (2008), who found differences of less than 4% when compared to slow movements. Moreover, multiple differences in the performance of upper body flexion (e.g., exercise speed, position of the head, inclination angle reached) can also affect the resultant inclination-force curve and might explain why, in some trials, the force curve had no distinct plateau and a more irregular increasing trend. For a detailed presentation, the loading curves of various flexion exercises performed by all five patients, with corresponding videos, are available at ‘www.orthoload.com’.

In summary, a VBR experiences high loads during trunk flexion as compared to the upright standing or sitting position. Maximal forces of on average 565 N were measured during the return to the initial standing position after forward bending of the upper body. The force increases on the implant at maximal inclination and the transition inclination angles were lower when trunk flexion was performed while sitting than while standing. The data presented here aid in our understanding of the loads acting on an instrumented lumbar spine during daily and work-related activities and help to validate musculoskeletal models.

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2.2 Publication 2: In Vivo Loads on a Vertebral Body Replacement during Different Lifting Techniques

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Abstract

The repeated lifting of heavy weights has been identified as a risk factor for low back pain (LBP). Whether squat lifting leads to lower spinal loads than stoop lifting and whether lifting a weight laterally results in smaller forces than lifting the same weight in front of the body remain matters of debate.

Instrumented vertebral body replacements (VBRs) were used to measure the *in vivo* load in the lumbar spine in three patients at level L1 and in one patient at level L3. Stoop lifting and squat lifting were compared in 17 measuring sessions, in which both techniques were performed a total of 104 times. The trunk inclination and amount of knee bending were simultaneously estimated from recorded images. Compared with the aforementioned lifting tasks, the patients additionally lifted a weight laterally with one hand 26 times.

Only a small difference (4%) in the measured resultant force was observed between stoop lifting and squat lifting, although the knee-bending angle (stoop 10°, squat 45°) and trunk inclination (stoop 52°, squat 39°) differed considerably at the time points of maximal resultant forces. Lifting a weight laterally caused 14% less implant force on average than lifting the same weight in front of the body.

The current *in vivo* biomechanical study does not provide evidence that spinal loads differ substantially between stoop and squat lifting. The anterior-posterior position of the lifted weight relative to the spine appears to be crucial for spinal loading.

1. Introduction

During daily activities, the human lumbar spine is subjected to high loads while providing a high compliance to perform complex motion tasks. These multifaceted requirements appear to be closely related to the high incidence of low back pain (LBP), which is associated with high rates of disability from work and thus tremendous costs for society (Vos et al., 2012; Wenig et al., 2009). Numerous epidemiological studies on the relationship between physical loads and the occurrence of LBP note lifting, in particular the lifting of heavy weights at higher frequency, as a risk factor for LBP (Frymoyer et al., 1983; Hoogendoorn et al., 2000; Kelsey et al., 1984; Palmer et al., 2003). Therefore, a better biomechanical understanding of the spinal loading of the lumbar spine during different lifting techniques and potential influencing factors is of prime importance.

During the last decades, the spinal loading during stoop lifting (i.e., back lifting – knees straight and back bent) and squat lifting (i.e., leg lifting – knees bent and back straight) have been frequently investigated and controversially discussed (Hsiang et al., 1997; van Dieën et al., 1999). For a detailed biomechanical understanding of these two basic techniques, a reliable, objective and valid measurement of the loading during both approaches is required. However, the complexity and invasiveness of such a measurement have resulted in only a few attempts to directly measure *in vivo* spinal loading, in particular during complex activities such as lifting. By measuring the intradiscal pressure (IDP) in the nucleus pulposus of the L3-L4 disc, Nachemson and Elfström (1970) compared both techniques in six healthy volunteers lifting two 10-kg barbells from a chair. Their results indicated that stoop lifting increased the load by a factor of ~2.3 with respect to upright standing with 10 kg in each hand, substantially more than with the squat technique. Andersson et al. (1976) measured similar but small, non-significant tendencies in four healthy volunteers (L3-L4). In a summary study on several IDP measurements, Nachemson et al. (1981) concluded that both lifting techniques result in load differences of only approximately 10% when lifting a weight of 10 kg. However, more recent measurements in only one healthy volunteer by Wilke et al. (2001) demonstrated an approximately 35% increased pressure in L4-L5 while lifting a crate from the ground with the stoop compared with the squat lifting technique. These IDP measurements during lifting allow a unique understanding of the spinal loading. However, the results of these studies remain limited due to the small number of measured subjects who were typically only measured once during a single measurement session; thus, intra-individual variations were not assessed.

Furthermore, important influencing factors, such as the amount of trunk inclination and knee bending performed, were mostly not evaluated or quantified.

To overcome these drawbacks, alternative non-invasive approaches were developed and employed to estimate spinal loading during lifting in a controlled laboratory environment. Van Dieën et al. (1994) and Rabinowitz et al. (1998) used stadiometry and quantified spinal loading by precisely measuring spinal shrinkage after performing several minutes of repeated lifting. Both groups observed non-significant differences between stoop and squat lifting. In a review study, van Dieën et al. (1999) compared numerous published investigations in which mainly net-moments or model estimations of the spinal compression forces during both techniques were determined. These researchers concluded that the biomechanical literature does not support the utilization of squat or stoop lifting. In contrast, recent combined approaches using a hybrid dynamic kinematics-based finite element model and *in vivo* kinematics measurements by Bazrgari et al. (2007) advocated squat over stoop lifting because of predicted smaller net moments, muscle forces and spinal loads. In addition to these two basic lifting concepts, wherein the weight is placed in front of the body, lifting a weight placed laterally to the body with one hand may be required during daily activities. However, only a few studies (e.g., Davis and Marras, 2005; Faber et al., 2009; Marras and Davis, 1998) investigated the potential differences between these two main weight locations and their influence on spinal loading. Thus, due to these partially conflicting results from past investigations and the lack of literature values, direct approaches that objectively quantify loading during lifting in several individuals and measurement sessions could shed light on the ongoing discussion regarding spinal loading during different lifting techniques.

A telemeterized vertebral body replacement (VBR) enables the *in vivo* measurement of implant forces in the lumbar spine in multiple repeated measurements and can be used to investigate potential influencing factors on spinal loading in several subjects (Rohlmann et al., 2007). In the present study, patients with instrumented VBRs performed numerous lifting exercises to compare squat lifting with stoop lifting and to determine the influence of the initial weight location. We hypothesized that

1. the stoop lifting technique results in a substantially increased load while lifting a weight in front of the body from the ground compared with the squat lifting technique, and
2. lifting a weight laterally with one hand results in smaller implant forces than lifting the same weight in front of the body.

2. Methods

2.1. Telemeterized vertebral body replacement

To measure the *in vivo* loads in the lumbar spine, standard VBRs (Synex^{TM}, Synthes, Bettlach, Switzerland) were modified by inserting strain gauges, a telemetry unit, and a coil for an inductive power supply. These modifications allow measurements of all three force and three moment components acting on the implant. To intraoperatively allow adaptation of the implant to the individual defect size, screwed-on endplates of different heights were employed.

Prior to the implantation, each VBR was extensively calibrated by applying various well-defined combinations of compressive and shear forces onto the implant in a calibration chamber. The loads caused defined combinations of forces and moments, for which the measurement accuracy was better than 2% for forces and 5% for moments relative to the calibration ranges. The sensitivity of the VBR was less than 1 N for the force components and less than 0.01 Nm for the moment components. A detailed description of the implant, its modifications and calibration can be found elsewhere (Rohlmann et al., 2013; 2007).

The power for the implant was supplied by an inductive coil, which was placed around the patient's trunk during the measurement. Furthermore, an antenna was attached to the patient's back, which received the load-dependent signals of the telemetry. These signals were transmitted to a computer, where the forces and moments were calculated and displayed on a monitor. During all measurement sessions, the patients were videotaped, and the digital telemetry signals and the video data were synchronously stored together.

2.2. Ethics statement

All the patients signed a written informed consent form, in which they agreed to the implantation of the instrumented VBR, implant load measurements and the publication of their images. The subjects' rights were protected throughout the course of the study. The Ethics Committee of the Charité – Universitätsmedizin Berlin approved the implantation of the implant in patients and the study protocol (Registry number: 213-01/225-20).

2.3. Patients

Four male patients with telemeterized VBRs participated in the present study (WP1, WP2, WP4 and WP5). All of the patients had an A3-type compression fracture of a lumbar vertebral body (classified according to Magerl et al. (1994)). A detailed description of these patients is provided in Table 1. Three of the patients received a VBR in the first lumbar vertebra "L1"

(WP1, WP2 and WP4), whereas patient WP5 received a VBR in the third lumbar vertebra “L3”. Prior to the VBR implantation, the unstable burst fracture was stabilized posteriorly using an internal spinal fixation device. In a second surgery, parts of the fractured vertebral body and the adjacent intervertebral discs were removed, and the VBR was implanted into the corpectomy defect. Autologous bone material was employed to enhance the interbody fusion process.

Table 1: Data for patients, surgical procedures and investigated lifting tasks.

	Patient			
	WP1	WP2	WP4	WP5
Sex (Male/Female)	M	M	M	M
Age at the time of surgery (years)	62	71	63	66
Height (cm)	168	169	170	180
Body mass (kg)	66	74	60	63
Body mass index (kg/m²)	23	26	21	19
Fractured vertebra	L1	L1	L1	L3
Levels of internal fixation device	T12-L2	T12-L2	T11-L3	L2-L4
Implantation date (month/year)	09/2006	11/2006	01/2008	07/2008
Stoop lifting				
Measurement sessions	5	5	4	3
Number of lifting tasks	18	12	11	8
Squat lifting				
Measurement sessions	5	5	4	3
Number of lifting tasks	20	13	13	9
Lifted weights	2×10.8 kg; 1×10 kg; 1×7 kg; 1×4.3 kg	4×10.8 kg; 1×7 kg	2×10 kg; 1×7 kg; 1×4.3 kg	1×10 kg; 1×4.3 kg; 1×4 kg
Lifting laterally vs. in front of the body				
Measurement sessions	3	3	2	1
Number of lifting tasks frontally	19	15	13	5
Number of lifting tasks laterally	7	7	7	5
Lifted weights	2×10.8 kg; 1×10 kg	3×10.8 kg	2×10 kg	1×10 kg

2.4. Exercises

During several measurement sessions at different postoperative time points, the patients were asked to lift a bottle crate in front of their body from the ground. Prior to the lifting tasks, the patients were introduced to the two basic concepts: stoop lifting and squat lifting. For squat lifting, the patients were taught to keep their backs as straight as possible and to bend their knees to lift the crate. In contrast, for stoop lifting, the patients were taught to keep their knees straight and to lift the crate by bending the upper body. Without further instructions, the patients subsequently lifted the crate 2 to 4 times using both techniques in the same session (Fig. 1). Overall, stoop and squat lifting were compared in four patients in 17 measuring sessions, in which both techniques were performed a total of 104 times (Table 1).

To evaluate the influence of the initial location of the weight on the implant loading, patients lifted an identical crate laterally with one hand in addition to the aforementioned lifting tasks with the weight in front of the body. For this assessment, the crate was located laterally to the feet, and patients were asked to lift the weight with one hand (Fig. 3). No further instructions concerning the individual lifting performance were provided. Both crate locations were compared in a total of 9 measurement sessions, in which lifting a weight laterally was performed 26 times in total.

In general, when the two lifting techniques were compared during a session, the weight of the crate was identical. For clarity, Table 1 displays how often each patient completed each of the aforementioned tasks.

2.5. Data evaluation

This study focused on the resultant force (F_{res}) as the main loading mode acting on the VBR during all the investigated lifting tasks (Fig. 1). The F_{res} is the geometric sum of the three measured force components: anterior-posterior shear (F_x), lateral shear (F_y) and axial compression (F_z).

During all lifting tasks, the maximal resultant force throughout the complete lifting process was determined. The median of all the maximal forces was separately calculated for stoop and squat lifting of several repetitions both individually for each patient and for each measurement session. Only median values from the same session were directly compared with each other to evaluate potential load differences between both lifting techniques (load ratio: F_{res} for squat lifting/F_{res} for stoop lifting). Furthermore, to evaluate differences in trunk inclination and knee-bending angle during stoop lifting and squat lifting, the videotaped images of all measurements were analyzed. For this assessment, a custom-made program was employed to determine the trunk inclination (α), which is the angle between a reference vertical line and a straight line fitted to the back of the patient in the region of the lumbar and lower thoracic spine (Fig. 1). Furthermore, the knee-bending angle (β) was determined, which estimates the amount of knee bending during the lifting tasks. Both angles were compared between stoop and squat lifting for characteristic time points. For both techniques, α and β were determined for the time point at maximal resultant force. In addition, the maximal trunk inclination (α_{max}) for stoop lifting and the maximal knee-bending angle (β_{max}) for squat lifting during the lifting task were estimated. Finally, the median values of the trunk inclinations, knee-bending angles, maximal implant forces and resultant load ratios as well as their ranges were determined individually for each patient and among all the patients.

Stoop-lifting and squat-lifting tasks were typically performed with a similar number of repetitions during a measurement session. For both techniques, the median value of all the maximal resultant forces was determined in a measurement session to determine the average peak force for lifting a weight in front of the body. Subsequently, to evaluate elementary differences between both crate locations, the results were compared with the median of the resultant maximal forces for lifting the same weight laterally during the same session (Table 1).

3. Results

3.1 Stoop lifting vs. squat lifting

Depending on the lifted weight, the implant forces reached absolute maxima from all sessions of ~1090 N for WP1, ~1420 N for WP2, ~1635 N for WP4, and ~1400 N for WP5 (Fig. 1).

The evaluation of the trunk inclination and knee bending during the lifting tasks confirmed that the patients followed the given instructions and performed each lifting technique differently (Fig. 2). At the time point with maximal resultant forces, patients exhibited substantially more knee bending during squat lifting (median: $\beta_{Fres\text{-}max}$=45°, range: 38-54°) compared with stoop lifting (median: $\beta_{Fres\text{-}max}$=10°, range: 5-12°). Furthermore, patients bent their upper body more during stoop lifting (median: $\alpha_{Fres\text{-}max}$=52°, range: 48-67°) than during squat lifting (median: $\alpha_{Fres\text{-}max}$=39°, range: 29-40°). However, maximal resultant forces were not observed at maximal inclination during stoop lifting. Maximal forces were typically observed shortly after the crate lift-off, when the upper body was slightly more straightened

(Fig. 1). Therefore, maximal values for the trunk inclination were observed prior to the time point with maximal forces and reached an average of α_{max}=63° (range: 59-70°). For squat lifting, maximal forces were also measured slightly after crate lift-off with less knee bending compared with the maximal angle of knee-bending reached during the time point of the crate lift-off. In this case, maximal knee bending values of β_{max}=56° (range: 52-66°) were measured.

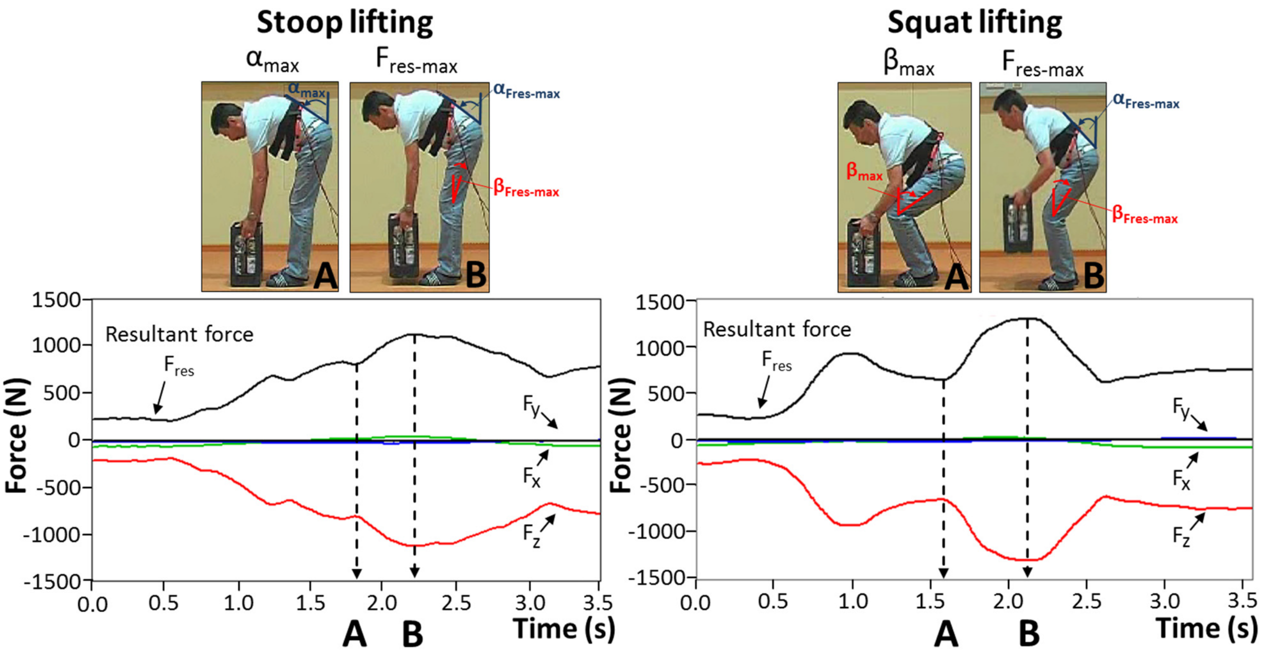

Figure 1: Force curves for lifting a weight using stoop and squat lifting. The time point "A" corresponds to the maximum trunk inclination (α_{max}) and maximum knee-bending angle (β_{max}), whereas time point "B" corresponds to the maximum resultant force ($F_{res\text{-}max}$).

Although both lifting techniques were performed differently, they caused almost similar maximal implant forces with 4% higher resultant forces on average in squat than in stoop lifting. In two patients, the resultant forces during squat lifting were slightly smaller on average. The median “squat/stoop” load ratios were 98% for WP1 (range from all measuring sessions: 93-108%) and 90% for WP5 (85-104%). In the other two patients, the ratios were slightly increased, i.e., 109% for WP2 (100-117%) and 118% (113-120%) for WP4.

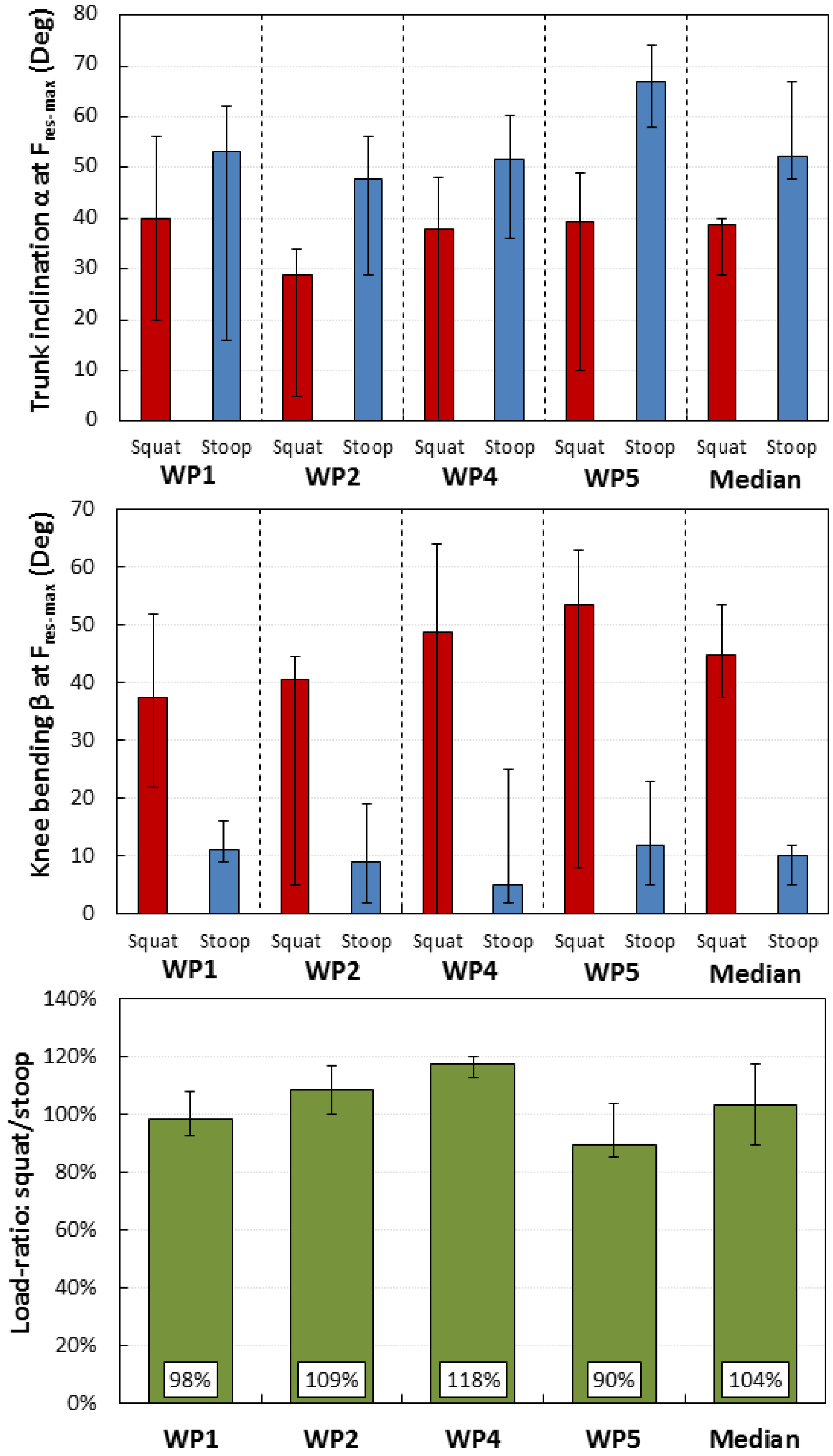

Figure 2: Trunk inclination (α, top) and knee-bending angle (β, middle) at maximum resultant force ($F_{res-max}$) for stoop and squat lifting. Individual medians and ranges for all four patients are presented. The median value for all patients was also calculated. The diagram at the bottom presents the medians and ranges of the load ratio "squat/stoop" for these patients.

3.2 Comparison of lifting a weight laterally and in front of the body

In 8 of 9 measurement sessions, the resultant force in all four patients was slightly increased when lifting the weight in front of the body compared with laterally (Fig. 3). On average, the difference between both lifting techniques was 14% (range: -1-25%). In only one session, the maximal forces were nearly similar between both techniques with differences of 1%.

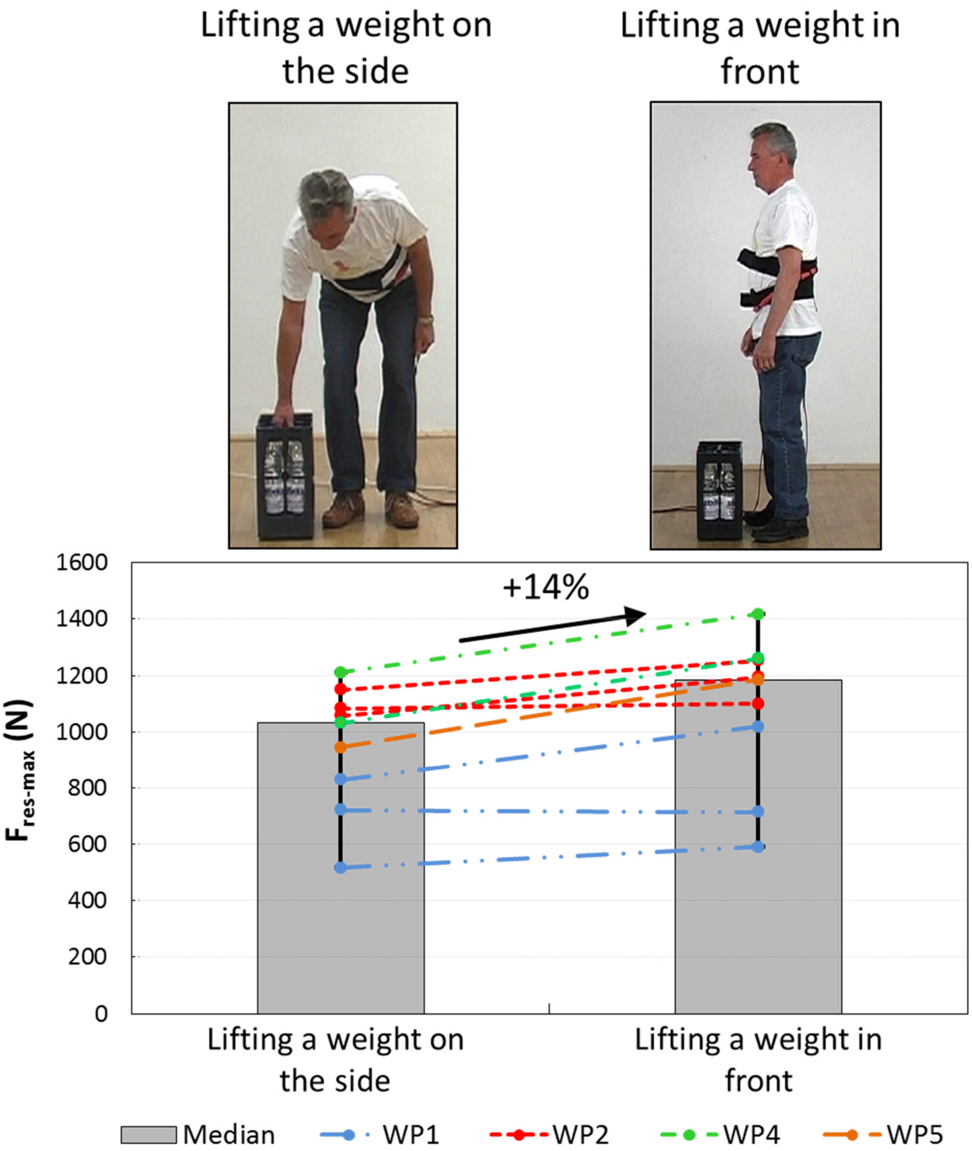

Figure 3: Lifting a weight on the side and lifting a weight in front of the body - comparison of the median maximum resultant force ($F_{res-max}$). In 8 of 9 measuring sessions, the maximal resultant force was increased for lifting a weight in front of the body compared with lateral lifting.

4. Discussion

The effects on spinal loading of different lifting techniques, in particular stoop lifting and squat lifting, as well as the initial location of the weight (frontal vs. lateral) are controversially discussed. In the present study, both techniques and locations were directly compared *in vivo* by measuring the implant forces acting on a VBR in four patients during numerous measurement sessions. Stoop lifting and squat lifting resulted in similar maximal implant forces with an average difference of 4% when the same weight was lifted in front of the body. Lifting an identical weight laterally with only one hand resulted in slightly reduced maximal forces compared with lifting the weight in front of the body with two hands.

Lifting a weight from the ground is a biomechanically complex task. When the weight acts in front of the body, the gravitational force of the weight creates a high forward bending moment, which must be counteracted during lifting. Depending on the thorax, lumbar and pelvis rotations, mainly active but also passive spinal components (passive muscle forces, ligament forces) contribute to the lifting process (Bazrgari et al., 2007). Previous direct *in vivo* measurements emphasized considerable spinal loading during lifting that may approach the failure load of the lumbar vertebrae (Brinckmann et al., 1988, 1987). Rohlmann et al. (2014) confirmed this exceptionally high loading during lifting by investigating approximately 1,000 different activities, among which lifting weights resulted in the highest loads measured among all the activities. In agreement, Wilke et al. (2001) measured the IDP and investigated various daily activities. Again, the highest loads occurred during lifting a weight from the ground. Thus, due to this high loading, numerous studies have investigated potential influencing factors (e.g., lifting technique, weight of the lifting object, gender, lifting speed, size of the weight, load-splitting, weight location, spinal posture, mental processing (Bush-Joseph et al., 1988; Davis et al., 2002; Faber et al., 2009; Kingma et al., 2010; Marras and Davis, 1998; Marras et al., 2003; van Dieën et al., 1999)), and in particular differences, between stoop and squat lifting to biomechanically better understand the spinal loading during lifting. In a previous review of 27 different biomechanical studies, van Dieën et al. (1999) demonstrated that both techniques resulted in non-significant load differences and equal or slightly increased net moments or compression forces for the squat technique. Consistent with this conclusion but in contrast to our first hypothesis, the present investigation confirms that both techniques result in similar spinal loads. However, inter-individual differences between subjects occurred with a maximal difference in load ratios of 28% between patient WP4 (squat/stoop: 118%)

and WP5 (90%). Thus, although all the patients were similarly introduced to both techniques, the resultant execution of the lifting task can differ depending on the individual subject's fitness, flexibility and coordination skills. This results in differences in the achieved median trunk inclinations and knee-bending angles not only among but also within patients, which can partly explain the inter-individual as well as the intra-individual load variations. In addition, differences in neuromuscular patterns between patients were not controlled/measured in this study, although these differences could influence the individual spinal loading. Furthermore, in the present study, the velocity during lifting was not controlled and thus could differ between investigated techniques and patients (Buseck et al., 1988; Bush-Joseph et al., 1988). Moreover, the initial position of the crate was not precisely defined, and the complex motion path of the crate during the lifting process can differ. In general, the crate was positioned slightly in front of or in line with the toe tips, and the patients lifted the weight at their own preferred speed for safety and convenience. In agreement with the argumentation of van Dieën et al. (1999), those variations in lifting speed, crate position or the general individual lifting execution could influence the specific loading of a selected measurement. However, these factors must be considered as integral components of the lifting technique during daily life, in which the lifting of weights is usually accomplished in an unstandardized manner. Therefore, in the present study, only a few instructions were given to the patients to measure realistic values of daily life. From a biomechanical perspective, a certain lifting technique that is assumed to result in smaller spinal loads must be robust against those uncertainties. Furthermore, it should be noted in general that in the present study only the spinal loading was directly measured and not the overall occupational safety. The occupational safety must however be considered for an evidence-based recommendation of a certain lifting technique.

Early studies by Andersson at al. (1976) previously demonstrated that the distance between the body and the weight is of greater importance than the lifting technique. In the present study, the crate was typically slightly in front of or approximately in line with the toe tips for both stoop and squat lifting and thus clearly generally in front of the body. Only a few measurements in one of our subjects confirmed that, when the size of the weight allows lifting the crate between the feet and thus substantially closer to the body with a lower trunk inclination and a smaller forward bending moment, a load reduction can be achieved. This observation may explain the larger IDP differences of ~35% between squat lifting (performed in between the feet) and stoop lifting measured by Wilke et al. (2001). This observation further confirms the conclusion of van Dieën et al. (1999) that squat lifting resulted in lower net moments compared with stoop lifting when the weight was lifted from a position between the feet. Following the same principle, lifting a weight laterally resulted in smaller implant forces than lifting in front of the body given the smaller anterior-posterior distance of the weight, which requires lower muscle forces to counteract the external load. In addition, the degree of inclination of the trunk might differ between different weight locations, with less trunk inclination during lifting laterally compared with lifting frontally, which, however, could not be verified in the present study. Furthermore, when lifting a weight in front of the body, the weight of both arms acts in front of the body and thus will induce larger bending moments compared with lifting a weight laterally, where both arms are usually closer to the body. Thus, the second hypothesis that lifting a weight laterally results in smaller implant forces than lifting the same weight placed in front of the body was confirmed.

Telemeterized VBRs allow the direct *in vivo* assessment of lumbar loads within multiple repeated measurements. In contrast to IDP measurements, usually taken in the L3-4 or the L4-5 disc, loads were determined at the spinal level of “L1” (WP1, WP2, WP4) or “L3” (WP5). However, the load differences between stoop lifting and squat lifting may be level-dependent and different in the lower and upper lumbar spine. Bazrgari et al. (2007) investigated both techniques in a computational model and observed only small differences of approximately 4% at level T12-L1. However, at level L5-S1, larger differences of up to ~17% for both techniques during lifting a weight of 180 N were predicted. Therefore, it must be noted that the present results are only valid for the investigated spinal levels in the upper (L1) and middle (L3) lumbar spine. Furthermore, it should be emphasized that the spinal loading is not completely transferred by the VBR but is also partly transferred by the remaining vertebra and internal fixators. Therefore, the measured absolute forces are difficult to interpret and thus were directly compared between the lifting techniques within the same measurement session by determining the “load ratio”. Furthermore, the load sharing might be slightly dependent on the lifting technique. Moreover, the participating patients were of an older age, and additional time-consuming measurements to precisely determine the upper-body inclination or knee bending using a more sophisticated approach were not possible. Thus, both angles (α, β) were estimated exclusively from the video recordings. In addition, the position of the weight relative to the instrumented level plays an important role for the resultant loads acting on the VBR.

However, a precise measurement of this distance was not possible in the present study. Furthermore, smaller loads were lifted in various measurement sessions (e.g., 4 kg) to not overstress patients shortly after the surgery. For detailed presentations, the load-time patterns and patient videos from various lifting exercises of all the patients are available at www.OrthoLoad.com.

In conclusion, large forces act on a VBR during lifting *in vivo*. On average, only small differences were measured when using the stoop or squat technique to lift a weight from the ground in front of the body. Based on our data and from a biomechanical perspective, neither of the two lifting techniques ensures smaller spinal loads. Lifting the same weight laterally with one hand resulted in slightly reduced maximal forces. The distance of the weight in the anterior-posterior direction appears to be crucial and should be minimized during lifting to reduce the resultant spinal loading.

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2.3 Publication 3: Age-related loss of lumbar spinal lordosis and mobility - a study of 323 asymptomatic volunteers.

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Abstract

Background: The understanding of the individual shape and mobility of the lumbar spine are key factors for the prevention and treatment of low back pain. The influence of age and sex on the total lumbar lordosis and the range of motion as well as on different lumbar sub-regions (lower, middle and upper lordosis) in asymptomatic subjects still merits discussion, since it is essential for patient-specific treatment and evidence-based distinction between painful degenerative pathologies and asymptomatic aging.

Methods and Findings: A novel non-invasive measuring system was used to assess the total and local lumbar shape and its mobility of 323 asymptomatic volunteers (age: 20-75 yrs; BMI < 26.0 kg/m²; males/females: 139/184). The lumbar lordosis for standing and the range of motion for maximal upper body flexion (RoF) and extension (RoE) were determined.

The total lordosis was significantly reduced by approximately 20%, the RoF by 12% and the RoE by 31% in the oldest (>50 yrs) compared to the youngest age cohort (20-29 yrs). Locally, these decreases mostly occurred in the middle part of the lordosis and less towards the lumbo-sacral and thoraco-lumbar transitions. The sex only affected the RoE.

Conclusions: During aging, the lower lumbar spine retains its lordosis and mobility, whereas the middle part flattens and becomes less mobile. These findings lay the ground for a better understanding of the incidence of level- and age-dependent spinal disorders, and may have important implications for the clinical long-term success of different surgical interventions.

Introduction

The individual shape of the lumbar spine is an essential predictor for different lumbar degenerative pathologies and for the success of various surgical interventions [1–5]. Moreover, the mobility of the lumbar spine is discussed as an indicator for abnormal spinal mechanics [6,7]. The influence of the factors age and sex on the total lumbar lordosis and the range of motion (RoM) still merits discussion, because it is essential for a patient-specific treatment, for example, with regard to patient age and disease localisation, and evidence-based distinction between painful degenerative pathologies and asymptomatic aging. Despite their influence, the impact of these factors on certain regions of the lumbar spine and its mobility, including upper, middle and lower lumbar spine, remains unknown.

Most studies on the effect of age showed that lumbar lordosis decreases or remains constant during the lifetime [8–21]. Only a few studies demonstrated an increase in lumbar lordosis with aging [22,23]. Studies investigating sex-related differences in lordosis showed either a slightly greater lordosis in females or no significant dependency on sex [24–27]. However, several of these studies investigating age and sex were limited in their sample sizes, did not differentiate between males and females and subjects with or without low back pain. Moreover, in almost all of these studies the whole lumbar lordosis was usually described by a single angle (e.g. Cobb's method), which strongly simplifies the complex lumbar curvature [28–30]. A more detailed analysis, including of different lumbar sub-regions, may reveal that the upper, middle or lower lumbar lordosis are affected specifically, for example, by aging.

In addition to the individual shape of the lumbar lordosis, it is generally accepted that the total RoM in flexion-extension is reduced with increasing age [6,31–39]. However, similar to lumbar lordosis, it remains unknown, which lumbar sub-region is affected dominantly by aging in males and females. Knowledge about local changes in spinal function with aging may therefore help to optimise and adapt the treatment to the diseased spinal level.

Because detailed segmental diagnostic X-ray examinations are ethically questionable in healthy individuals and very laborious in large cohorts, a new technological approach was first identified and further developed by our group [40], which would allow analysis of the total and local lordosis as well as the spinal function (e.g. by means of RoM). Using this sophisticated, strain-gauge based tool that had been validated previously, the present study investigated the effect of age and sex on the lordosis and on the RoM for the whole lordosis as well as for the different lumbar sub-regions in asymptomatic volunteers across the adult lifespan. It was hypothesised that:

(1) aging reduces the total lumbar lordosis and the total range of motion in flexion (RoF) and extension (RoE) of the lumbar spine,
(2) locally, the change in lordosis and mobility with aging varies between different lumbar sub-regions,
(3) the total lumbar lordosis is larger in females than in males.

Materials and Methods

Measuring system

The lumbar and thoraco-lumbar shape and the mobility of the spine in the sagittal plane were dynamically determined with the Epionics SPINE system (Epionics Medical GmbH, Potsdam, Germany). The system has the advantage over X-ray techniques that the volunteers are not exposed to radiation and thus several repeated measurements are possible. Furthermore, different sub-regions of the lumbar lordosis, including the lower, middle and upper lordosis, can be analysed. The high accuracy and reliability of the system was reported previously [40,41].

The system consists of two flexible sensor strips, which are placed in hollow plasters onto the volunteers' back (Fig. 1). Each of the strips are positioned paravertebrally approximately 7.5 cm from the mid-sagittal plane while the lowest part of the strips is positioned at the level of the posterior superior iliac spine (approximately first sacral vertebra). Each sensor strip consists of twelve 25-mm-long single sensor units (Epionics segments: S1-S12) containing strain-gauge technology. Each sensor unit detects the local back curvature as illustrated in Fig. 1. The data from all 12 sensors is collected at 50 Hz and saved locally on a small storage unit (12.5 cm x 5.5 cm; mass: 120 g) carried on a belt, allowing free unhampered movements of the volunteer. An accelerometer is located at the lower end of each sensor strip to assess the orientation of the sensors in relation to earth's gravitational field. A detailed description of the system has been published elsewhere [40,41].

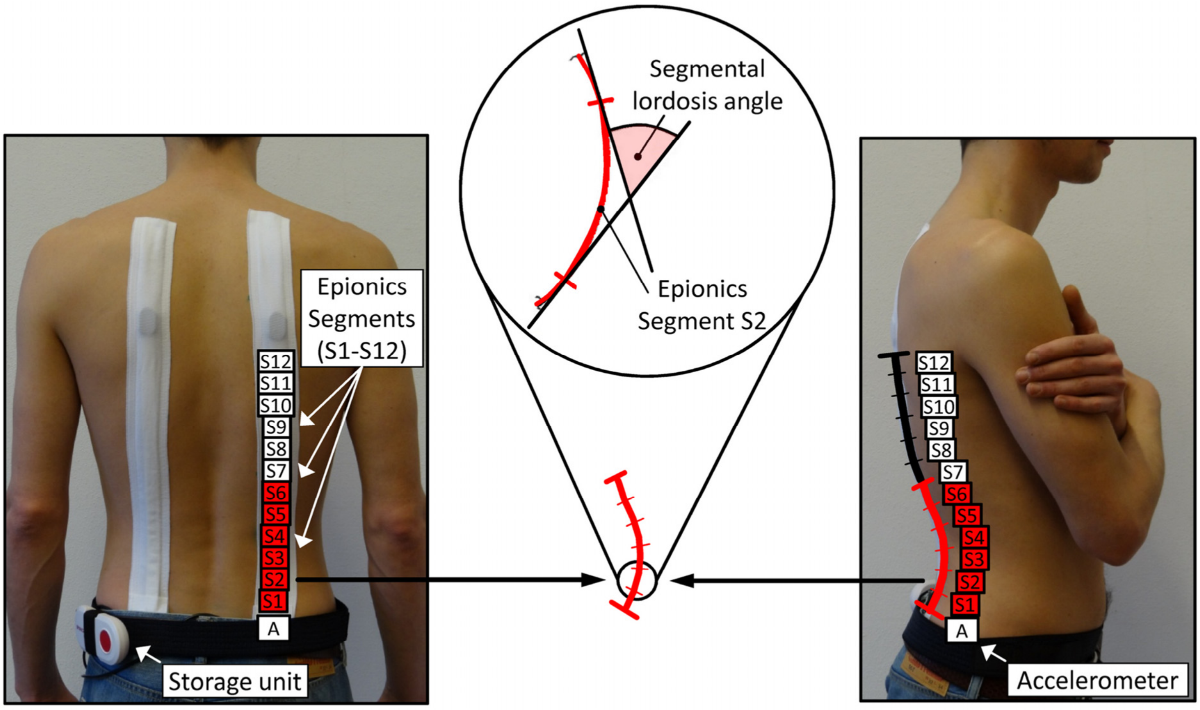

Figure 1: Epionics SPINE system with the positions of the Epionics segments S1-S12. On average, the lumbar lordosis is covered by the first six segments (shown in red). Middle: Schematic sketch of the definition of the determined segmental angle is shown for a single exemplary sensor unit S2.

Volunteers

Measurements were performed on 429 asymptomatic volunteers (198 males, 231 females). Subjects were free from acute low back pain and had no low back pain within the previous 6 months. Furthermore, volunteers had no previous spinal surgery.

Own validation and previously published studies showed that there is a significant correlation (Spearman's correlation: 0.86, $p < 0.01$ [42]) between the total lumbar lordosis measured on the back and the radiologically determined lordosis in subjects with a BMI < 26.0 kg/m². Moreover, this value of 26.0 kg/m² is considered as the normal-weight limit for subjects with an age similar to the mean age of the here investigated cohort (National Research Council, [43]) and was set to the BMI-limit in the present study.

The volunteers were classified for sex and assigned to four age groups: 20-29 years, 30-39 yrs, 40-49 yrs and >50 yrs, as was done in previous studies (e.g.: [15,44]).

Table 1: Number of volunteers and mean values (standard deviation) for age, body height, body weight and body mass index

		All	20-29yrs	30-39yrs	40-49yrs	>50yrs
Volunteers	**entire cohort**	323	115	70	71	67
	female	184	66	40	41	37
	male	139	49	30	30	30
Age (in years)	**entire cohort**	38.6 (14.0)	25.1 (2.7)	34.0 (3.3)	44.5 (3.2)	60.3 (7.9)
	female	38.4 (14.1)	24.8 (2.7)	34.0 (3.3)	44.2 (3.3)	60.8 (8.0)
	male	38.9 (13.7)	25.6 (2.8)	34.0 (3.3)	44.9 (3.1)	59.6 (7.8)
Body height (in cm)	**entire cohort**	173.0 (9.5)	173.8 (9.3)	173.2 (9.3)	172.9 (9.2)	171.5 (10.2)
	female	167.6 (6.9)	168.3 (7.0)	167.7 (6.4)	168.0 (7.2)	165.8 (7.0)
	male	180.1 (7.4)	181.2 (6.5)	180.6 (7.1)	179.6 (7.2)	178.4 (9.2)
Body weight (in kg)	**entire cohort**	67.6 (10.1)	66.9 (10.0)	66.7 (10.2)	68.6 (10.0)	68.6 (10.4)
	female	61.7 (7.5)	60.7 (6.8)	61.0 (8.2)	62.8 (7.6)	62.8 (7.7)
	male	75.4 (7.5)	75.1 (7.2)	74.3 (7.2)	76.6 (6.7)	75.8 (8.8)
BMI (in kg/m^2)	**entire cohort**	22.5 (2.0)	22.0 (1.9)	22.2 (2.2)	22.9 (2.0)	23.2 (1.8)
	female	21.9 (2.1)	21.4 (1.9)	21.7 (2.3)	22.2 (2.1)	22.8 (1.9)
	male	23.2 (1.7)	22.9 (1.7)	22.8 (1.9)	23.7 (1.4)	23.7 (1.4)

Measurement protocol

The volunteers performed standardised motion choreographies in the sagittal plane. For guidance and standardisation, the volunteers watched a video prior to the exercise, which explained and demonstrated the exercise. Starting from a relaxed standing position, the volunteers were asked to perform a maximal upper body flexion and extension with extended knees up to six times. Before each exercise, the subjects were measured in a relaxed standing position. Each volunteer performed the movements at his or her own preferred speed.

Data analysis

All Epionics sensor segments (S1-S12, Fig. 1) and the total lumbar lordosis were evaluated for the three investigated body positions: standing, maximal flexion and maximal extension of the upper body. The results of the left and right sensor strips were averaged. The total lumbar lordosis in standing of each volunteer was determined individually as the sum of all lordotically curved segments. The total angles for flexion and extension were calculated individually as the sum of the segments, which were identified as being lordotic during upright standing. The total RoF and RoE in the lumbar spine for each subject were calculated as the maximal or minimal angle difference with respect to standing.

Statistical Analysis

Descriptive statistics (mean, standard error, standard deviation) were analysed using SPSS 21.0 (SPSS Inc., Chicago IL, USA). The Kolmogorov-Smirnov test was performed to evaluate the normal distribution for each investigated group. In addition, the Levene's test was performed to test equality of variance. A two-way analysis of variance (ANOVA) with the factors age and sex was performed to evaluate the effects on the total lumbar lordosis, total RoF and total RoE. Subsequently, the mean values of the lordosis, RoF and RoE of the Epionics segments of different age groups were compared sex-specifically using a one-way ANOVA followed by post-hoc analysis using Scheffé's test. A p-value < 0.01 was considered as statistically significant.

Ethics Statement

This study was approved by the Ethics Committee of the Charité – Universitätsmedizin Berlin (registry number EA4/011/10). The procedure of this study was explained to each volunteer in detail and they signed a written informed consent, which allows spinal shape determinations with the Epionics SPINE device.

Results

Volunteers

Due to the defined BMI-threshold of 26.0 kg/m², 106 volunteers were excluded from the initial sample of 429, which resulted in a final number of 323 subjects (males: 139, females: 184). The mean values for body height, body weight and BMI for all the age cohorts are given in Table 1.

Total and local lumbar lordosis during standing

The Kolmogorov-Smirnov test showed that the lumbar lordosis followed a normal distribution for both sexes. Two-way ANOVA demonstrated that the total lumbar lordosis was only significantly associated with age, but not with sex (Table 2).

Table 2: Results of two-way analysis of variance (ANOVA) for age and sex for each of the three dependent variables: lumbar lordosis, range of flexion and range of extension.

	p-value	*Partial Eta-squared*
Total lumbar lordosis		
Age	**<0.001***	0.123
Sex	0.017	0.018
Age x Sex	0.287	0.012
Total range of flexion		
Age	**<0.001***	0.080
Sex	0.134	0.007
Age x Sex	0.212	0.014
Total range of extension		
Age	**<0.001***	0.132
Sex	**<0.001***	0.088
Age x Sex	0.188	0.015

*Statistically significant (p<0.01)

For the whole sample, this reduction of the total lordosis with age occurred with each consecutive age group (Fig. 2 top; Table 3). There was a significant reduction of approximately 7.4° (≈20%) between the youngest and the oldest cohort. This decrease was more evident in females, who showed a significant reduction of 7.9°, than in males with 6.7°, which was only close to significant (*p=0.034*). For both sexes, there was only a small lordosis reduction between 20-29yrs and 30-39yrs. In the following aging process, females showed a continuous decrease, while the reduction in males mostly occurred between the ages 30-39yrs and 40-49yrs. The smallest total lordosis in males was measured within the 40-49yrs group. Post-hoc comparison demonstrated no statistical differences between the 40-49yrs and >50yrs age groups (*p=0.977*) in males, whereas there was a significant reduction of the lordosis between the 20-29yrs and the 40-49yrs age groups (*p=0.009*).

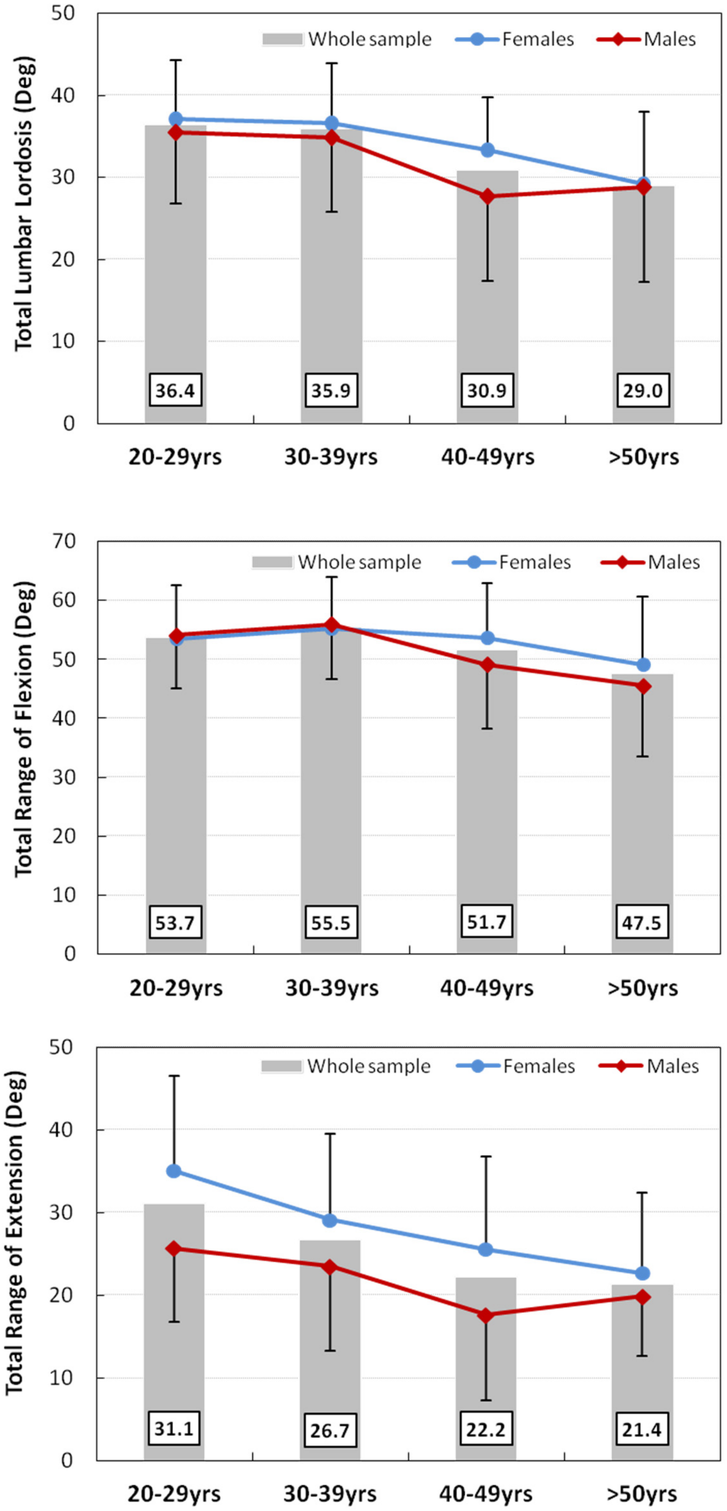

Figure 2: Mean values of the total lumbar lordosis (top), total range of flexion (middle) and total range of extension (bottom) in all four investigated age groups for the whole cohort (grey columns). The red lines represent males and the blue lines females. Error bars represent the standard deviation.

On average, the first six Epionics segments (S1-S6) were lordotic in the present cohort (Figs. 1, 3 A) and are therefore presented here. Epionics segments above those were part of the thoraco-lumbar transition and lower thoracic kyphosis. Locally for both sexes, the greatest loss of lordosis occurred in the middle part of the lordosis with a tendency towards the upper part. Generally, less reduction was observed towards the thoraco-lumbar and lumbo-sacral transitions (Fig. 3B; Table 3). The largest absolute loss of lordosis between the youngest and oldest cohorts occurred in the Epionics segment S4 with values of 2-3°. The lower segments S1 and S2 and the upper segment S6 showed no significant differences for the whole sample, nor for males and females separately. For the relative change, the lordosis of the youngest cohort was set to 100% in Fig. 3 C. In males, the largest relative reduction of the lordosis occured in S6 (to 54% of the reference) with continuously less reduction towards the most caudal segment S1 (to 101%). In females, the largest relative reduction occurred in S5 (to 69%), with continuously less reduction to the most caudal segment S1 (to 80%) and furthermore less in S6 (to 81%).

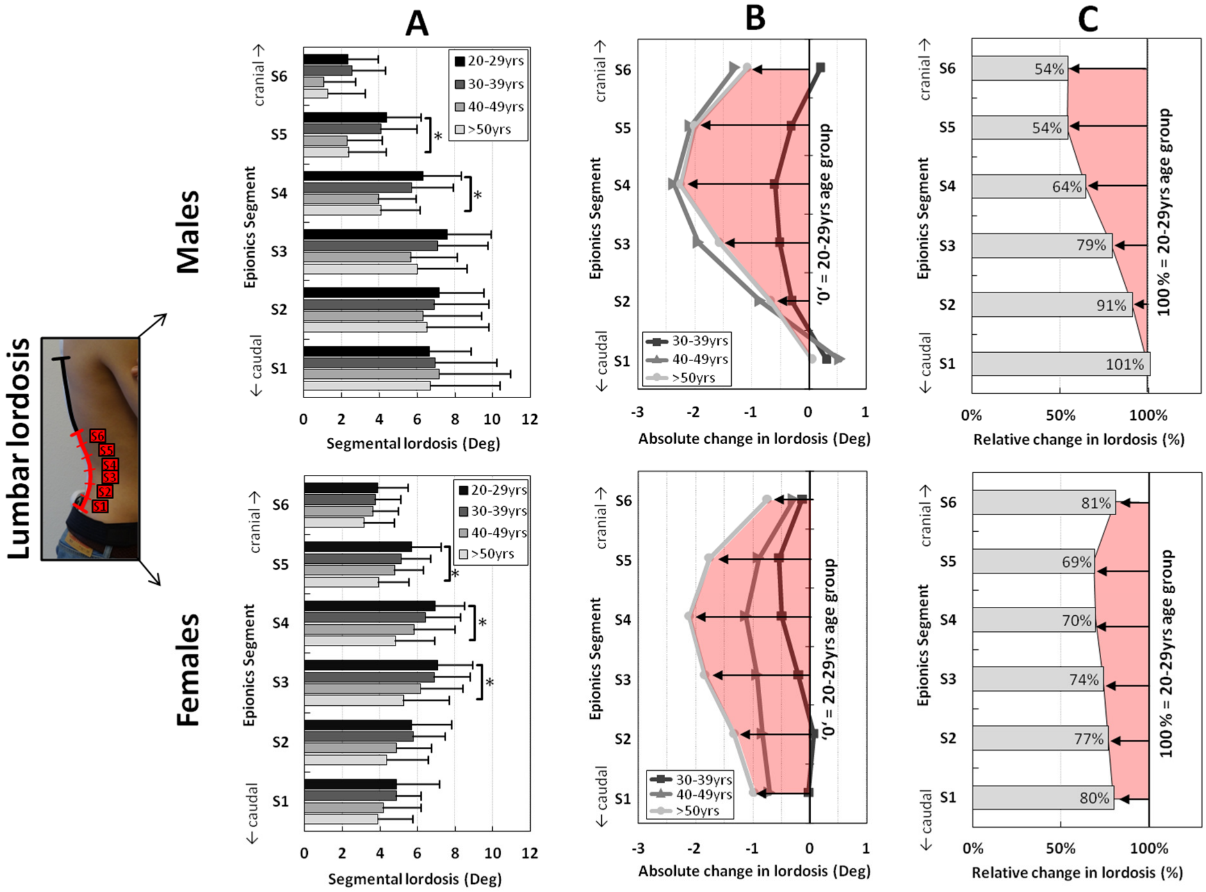

Figure 3: Mean values of the segmental lordosis for the Epionics segments S1 to S6 in all investigated age groups **(A)**. Males (above) and females (below) are shown separately. Error bars represent the standard deviation. **(B):** Absolute change in segmental lordosis for the Epionics segments S1 to S6 in all investigated age groups in relation to the youngest cohort (20-29yrs) for males (above) and females (below) separately. The youngest cohort is normalised to 'zero' as a reference. The red area highlights the pattern of the absolute change between the oldest and youngest cohorts. **(C):** Relative change in segmental lordosis for the Epionics segments S1 to S6 between the oldest and youngest age groups for males (above) and females (below) separately. The youngest cohort is normalised to 100% as a reference. Values indicate the percentage of lordosis that the oldest cohort possesses in relation to the youngest cohort. The red area highlights the pattern of the relative changes between the oldest and youngest cohorts

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Table 3: Mean total lumbar lordosis (standard error; standard deviation) for investigated age groups. All measurements are in degrees.

	Parameter	20-29yrs	30-39yrs	40-49yrs	>50yrs	*ANOVA* *p*-value*	*Post-hoc: 20-29yrs vs. >50yrs***
Entire cohort (n=323)	**Total Lumbar Lordosis**	36.4 (0.7; 7.9)	35.9 (1.0; 8.1)	30.9 (1.0; 8.7)	29.0 (1.2; 10.0)	**<0.001**	**<0.001**
	S1 Lordosis	5.6 (0.2; 2.4)	5.8 (0.3; 2.6)	5.4 (0.4; 3.2)	5.2 (0.4; 3.1)	0.599	0.752
	S2 Lordosis	6.3 (0.2; 2.3)	6.3 (0.3; 2.3)	5.5 (0.3; 2.5)	5.4 (0.4; 2.9)	0.020	0.085
	S3 Lordosis	7.3 (0.2; 2.1)	7.0 (0.3; 2.3)	6.0 (0.3; 2.3)	5.6 (0.3; 2.5)	**<0.001**	**<0.001**
	S4 Lordosis	6.7 (0.2; 1.8)	6.1 (0.2; 2.0)	5.0 (0.3; 2.3)	4.5 (0.3; 2.1)	**<0.001**	**<0.001**
	S5 Lordosis	5.1 (0.2; 1.8)	4.7 (0.2; 1.8)	3.7 (0.2; 2.1)	3.2 (0.2; 1.9)	**<0.001**	**<0.001**
	S6 Lordosis	3.2 (0.2; 1.8)	3.2 (0.2; 1.6)	2.5 (0.2; 2.0)	2.3 (0.2; 2.0)	**0.001**	0.015
Males (n=139)	**Total Lumbar Lordosis**	35.5 (1.2; 8.7)	34.9 (1.7; 9.1)	27.6 (1.9; 10.2)	28.8 (2.1; 11.6)	**0.001**	0.034
	S1 Lordosis	6.6 (0.3; 2.2)	7.0 (0.6; 3.3)	7.2 (0.7; 3.8)	6.7 (0.7; 3.7)	0.881	0.999
	S2 Lordosis	7.2 (0.3; 2.3)	6.9 (0.5; 2.9)	6.3 (0.6; 3.1)	6.5 (0.6; 3.3)	0.576	0.801
	S3 Lordosis	7.6 (0.3; 2.3)	7.1 (0.5; 2.7)	5.7 (0.4; 2.5)	6.0 (0.5; 2.6)	**0.003**	0.065
	S4 Lordosis	6.3 (0.3; 2.0)	5.7 (0.4; 2.2)	4.0 (0.4; 2.0)	4.1 (0.4; 2.1)	**<0.001**	**<0.001**
	S5 Lordosis	4.4 (0.3; 1.8)	4.1 (0.3; 1.9)	2.3 (0.3; 1.8)	2.4 (0.4; 2.0)	**<0.001**	**<0.001**
	S6 Lordosis	2.4 (0.2; 1.6)	2.6 (0.3; 1.8)	1.1 (0.3; 1.7)	1.3 (0.4; 2.0)	**0.001**	0.075
Females (n=184)	**Total Lumbar Lordosis**	37.1 (0.9; 7.2)	36.6 (1.2; 7.3)	33.3 (1.0; 6.4)	29.2 (1.4; 8.8)	**<0.001**	**<0.001**
	S1 Lordosis	4.9 (0.3; 2.3)	4.9 (0.2; 1.3)	4.2 (0.3; 2.0)	3.9 (0.3; 1.9)	0.041	0.119
	S2 Lordosis	5.7 (0.3; 2.1)	5.8 (0.3; 1.7)	4.9 (0.3; 1.8)	4.4 (0.4; 2.2)	**0.003**	0.016
	S3 Lordosis	7.1 (0.2; 1.9)	6.9 (0.3; 1.9)	6.2 (0.3; 2.2)	5.2 (0.4; 2.4)	**<0.001**	**0.001**
	S4 Lordosis	6.9 (0.2; 1.6)	6.4 (0.3; 1.9)	5.8 (0.3; 2.2)	4.8 (0.3; 2.1)	**<0.001**	**<0.001**
	S5 Lordosis	5.7 (0.2; 1.6)	5.1 (0.2; 1.5)	4.8 (0.2; 1.5)	3.9 (0.3; 1.6)	**<0.001**	**<0.001**
	S6 Lordosis	3.9 (0.2; 1.6)	3.8 (0.2; 1.3)	3.6 (0.2; 1.4)	3.1 (0.3; 1.6)	0.118	0.133

Bold values indicate statistical significance (p<0.01).
*p-values base on one-way ANOVA. **Post-hoc comparison using Scheffé's test.

These local changes in males and females led to a characteristic change between the 'young' and the 'old' lordosis as illustrated in Fig. 4.

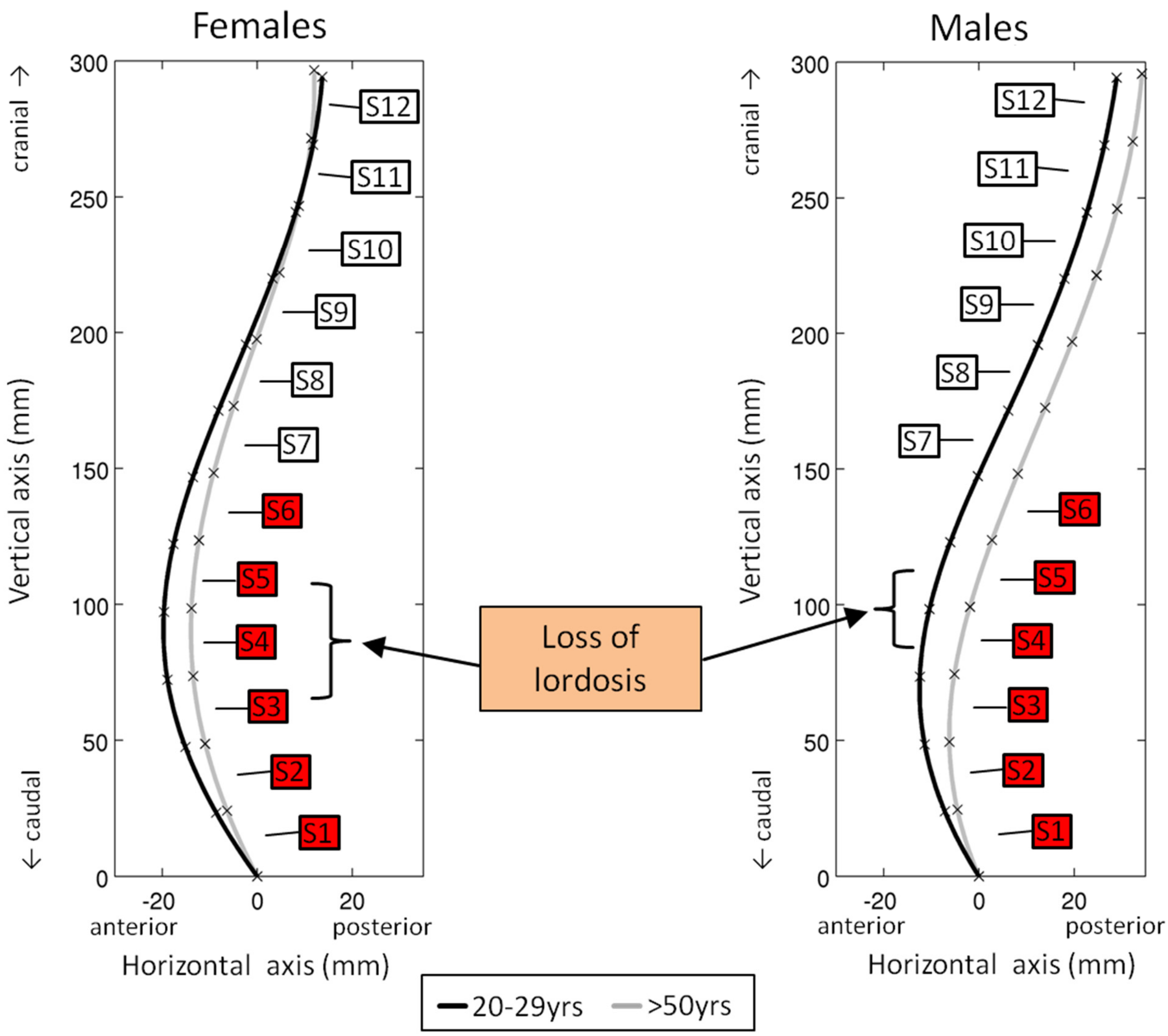

Figure 4: Age-related postural adaptations of the 12 Epionics segments between the oldest and youngest age cohorts for females (left) and males (right).

Total and local range of flexion and extension during standing

The Kolmogorov-Smirnov test showed that the RoF and RoE were normally distributed in male and female cohorts. The total RoF and RoE were significantly associated with age (Table 2). Moreover, the total RoE, but not the total RoF, was significantly associated with sex.

For the whole sample as well as for males and females separately, the total RoF showed no significant difference between the 20-29yrs and 30-39yrs age cohorts, but a consecutive decrease for the subsequent age groups (Fig. 2 middle; Table 4). Although significant, the total RoF was reduced by only approximately 12% (6.2°) when comparing the youngest and oldest cohorts of the whole sample. This decrease was only significant for males, with a loss of 8.6°. In females, the reduction was only 4.2°.

Males and females showed similar local patterns for the reduction of the RoF with increasing age. This local reduction was most dominantly in the middle part (S3, S4) of the lumbar region (Fig. 5 A,B; Table 4). In general, the Epionics segments close to the thoraco-lumbar and lumbo-sacral transition (S1, S6) showed non-significant absolute changes with increasing age. Males tended to display a slightly greater reduction relative to the youngest cohort than females, with the greatest loss in segment S5 (to 73% of the reference; Fig. 5 C). In females, the largest relative reduction occurred in S4 (to 80%).

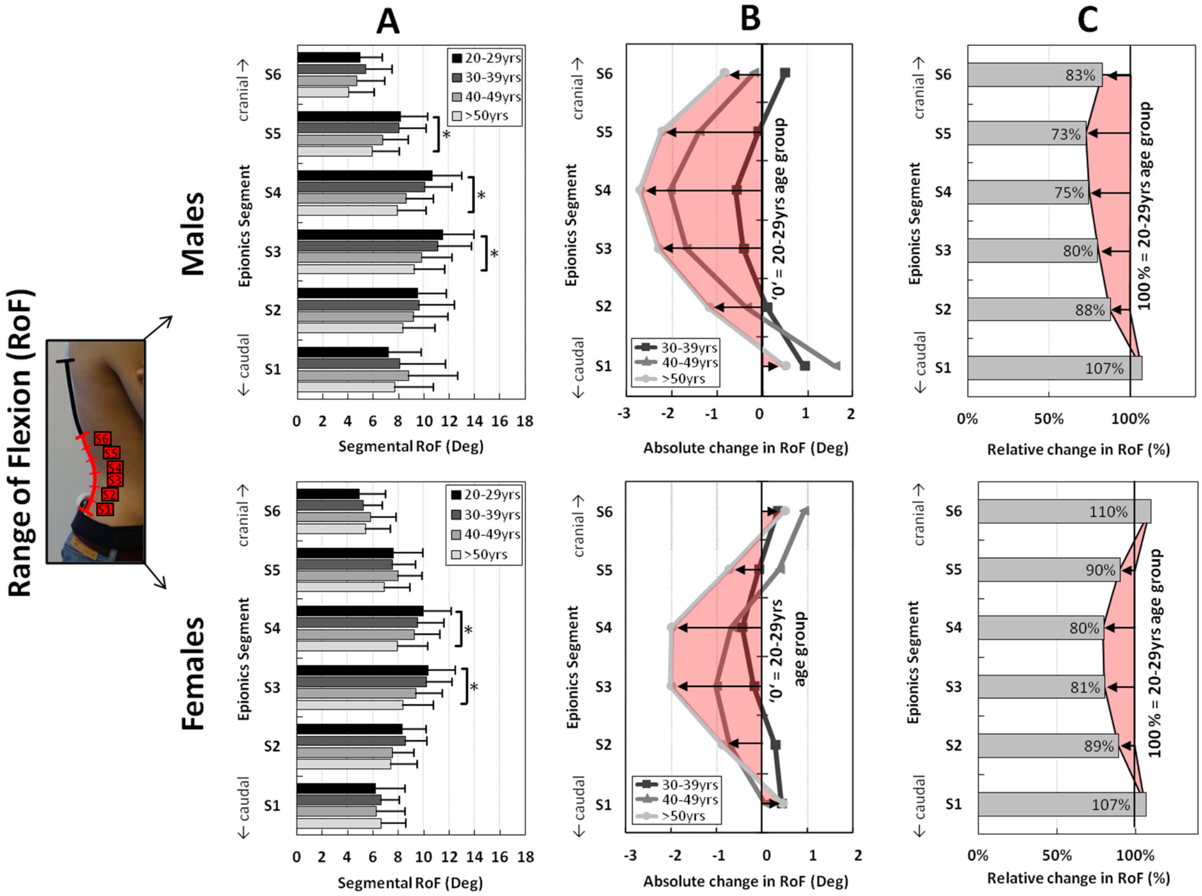

Figure 5: Mean values of the segmental range of flexion (RoF) for the Epionics segments S1 to S6 in all investigated age groups **(A)**. Males (above) and females (below) are shown separately. Error bars represent the standard deviation. **(B):** Absolute change in the segmental RoF for the Epionics segments S1 to S6 in all investigated age groups in relation to the youngest cohort (20-29yrs) for males (above) and females (below) separately. The youngest cohort is normalised to a value of 'zero' as a reference. The red area highlights the pattern of the absolute change between the oldest and youngest cohort. **(C):** Relative change in the segmental RoF for the Epionics segments S1 to S6 between oldest and youngest age groups for males (above) and females (below) separately. The youngest cohort is normalised to 100% as a reference. Values indicate the percentage of the RoF the oldest cohort possesses in relation to the youngest cohort. The red area highlights the pattern of the relative changes between the oldest and youngest cohorts.

The total RoE of the whole sample was reduced for each consecutive age cohort and was significantly decreased by approximately 31% when comparing the youngest and oldest cohort (Fig. 2 bottom; Table 4). The loss of the RoE was more pronounced and only significant in females (12.4°). Males showed a smaller reduction of only 5.8°. Independent of age, males had a smaller total RoE than females.

For the local RoE, males and females both showed the largest absolute reduction in the middle part of the lordosis (S3; Fig. 6 A,B) and, similar to the local RoF, less reduction towards the transition zones. However, in females, the absolute and relative reductions were more pronounced in the middle and lower Epionics segments (Fig. 6 C). Males showed no significant and only small relative changes in the Epionics segment S1. In both sexes only small non-significant changes in the RoE occurred in segments close to the thoraco-lumbar transition (S5, S6).

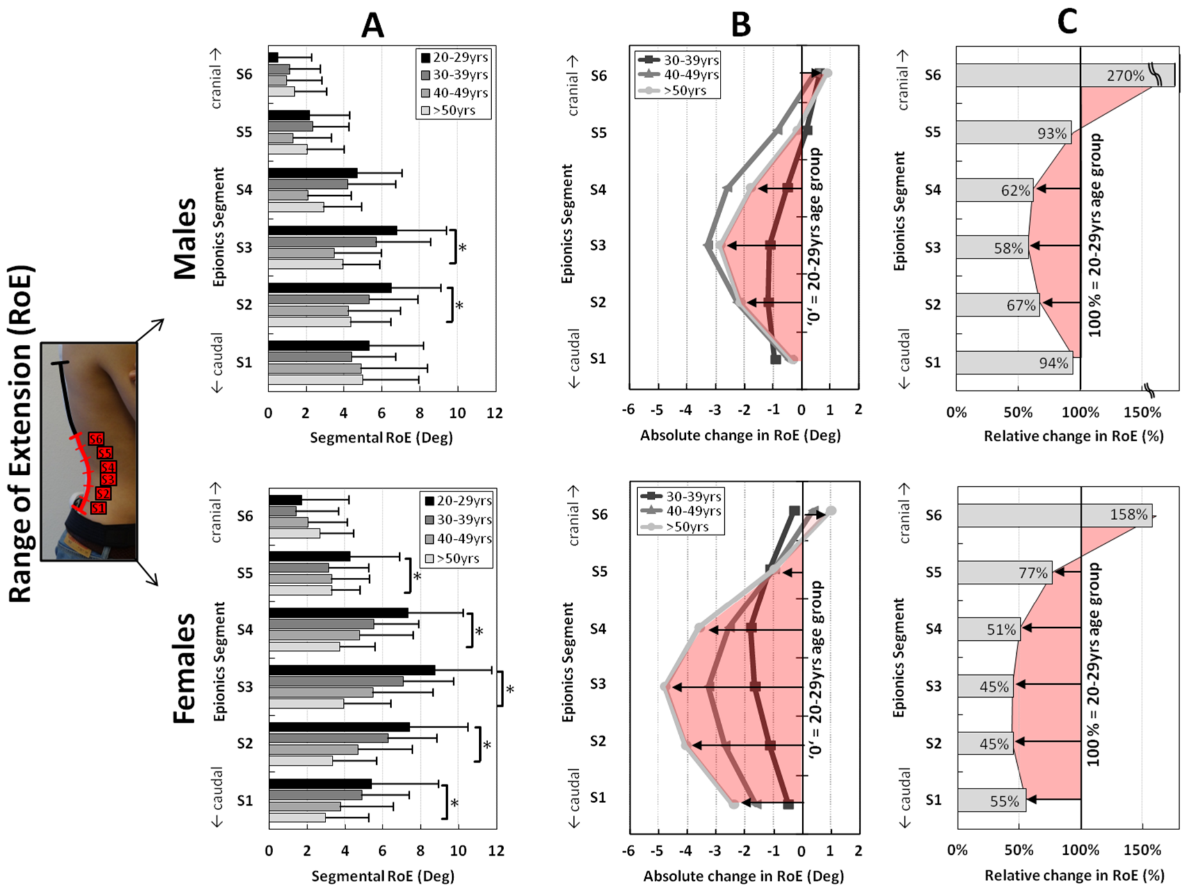

Figure 6: Mean values of the segmental range of extension (RoE) for the Epionics segments S1 to S6 in all investigated age groups **(A)**. Males (above) and females (below) are shown separately. Error bars represent the standard deviation. **(B):** Absolute change in the segmental RoE for the Epionics segments S1 to S6 in all investigated age groups in relation to the youngest cohort (20-29yrs) for males (above) and females (below) separately. The youngest cohort is normalised to 'zero' as a reference. The red area highlights the pattern of the absolute change between the oldest and youngest cohort. **(C):** Relative change in the segmental RoE for the Epionics segments S1 to S6 between the oldest and youngest age groups for males (above) and females (below) separately. The youngest cohort is normalised to 100% as a reference. Values indicate the percentage of the RoE the oldest cohort possesses in relation to the youngest cohort. The red area highlights the pattern of the relative changes between oldest and youngest cohorts.

Table 4: Mean range of flexion (RoF) and range of extension (RoE) (standard error; standard deviation) for investigated age groups. All measurements are in degrees.

	Parameter	20-29yrs	30-39yrs	40-49yrs	>50yrs	*ANOVA p*-value*	*Post-hoc: 20-29yrs vs. >50yrs***
Entire cohort (n=323)	**Total range of flexion**	53.7 (0.8; 9.0)	55.5 (1.1; 8.8)	51.7 (1.2; 10.2)	47.5 (1.4; 11.8)	**<0.001***	**0.001***
	RoF S1	6.6 (0.2; 2.5)	7.3 (0.3; 2.7)	7.3 (0.4; 3.3)	7.1 (0.3; 2.5)	0.270	0.720
	RoF S2	8.8 (0.2; 2.2)	9.0 (0.3; 2.3)	8.2 (0.3; 2.3)	7.8 (0.3; 2.3)	**0.006***	0.046
	RoF S3	10.9 (0.2; 2.3)	10.6 (0.3; 2.4)	9.6 (0.3; 2.2)	8.7 (0.3; 2.4)	**<0.001***	**<0.001***
	RoF S4	10.2 (0.2; 2.3)	9.7 (0.3; 2.1)	9.0 (0.2; 2.1)	7.9 (0.3; 2.3)	**<0.001***	**<0.001***
	RoF S5	7.8 (0.2; 2.2)	7.7 (0.2; 1.9)	7.5 (0.2; 2.0)	6.4 (0.3; 2.1)	**<0.001***	**<0.001***
	RoF S6	4.9 (0.2; 1.9)	5.3 (0.2; 1.7)	5.4 (0.3; 2.1)	4.8 (0.3; 2.1)	0.211	0.986
	Total range of extension	31.1 (1.1; 11.3)	26.7 (1.3; 10.6)	22.2 (1.4; 11.5)	21.4 (1.1; 8.8)	**<0.001***	**<0.001***
	RoE S1	5.4 (0.3; 3.3)	4.7 (0.3; 2.4)	4.2 (0.4; 3.1)	3.9 (0.3; 2.8)	**0.007***	0.017
	RoE S2	7.0 (0.3; 2.9)	5.9 (0.3; 2.6)	4.5 (0.3; 2.8)	3.8 (0.3; 2.3)	**<0.001***	**<0.001***
	RoE S3	7.9 (0.3; 3.0)	6.5 (0.3; 2.8)	4.6 (0.4; 3.1)	3.9 (0.3; 2.2)	**<0.001***	**<0.001***
	RoE S4	6.2 (0.3; 3.0)	5.0 (0.3; 2.5)	3.6 (0.3; 2.9)	3.4 (0.2; 2.0)	**<0.001***	**<0.001***
	RoE S5	3.4 (0.2; 2.6)	2.8 (0.2; 2.0)	2.5 (0.3; 2.2)	2.7 (0.2; 1.8)	0.038	0.311
	RoE S6	1.2 (0.2; 2.3)	1.3 (0.2; 2.0)	1.6 (0.2; 2.0)	2.1 (0.2; 1.8)	0.032	0.048

	Parameter	20-29yrs	30-39yrs	40-49yrs	>50yrs	*ANOVA* *p*-value*	*Post-hoc: 20-29yrs vs. >50yrs***
Males (n=139)	**Total range of flexion**	54.1 (1.3; 9.0)	55.9 (1.7; 9.2)	49.1 (2.0; 10.9)	45.5 (2.2; 12.0)	**<0.001***	**0.005**
	RoF S1	7.2 (0.4; 2.6)	8.1 (0.7; 3.6)	8.8 (0.7; 3.9)	7.7 (0.6; 3.1)	0.191	0.931
	RoF S2	9.5 (0.3; 2.3)	9.6 (0.5; 2.8)	9.2 (0.5; 2.8)	8.3 (0.5; 2.5)	0.182	0.274
	RoF S3	11.5 (0.3; 2.4)	11.1 (0.5; 2.6)	9.8 (0.4; 2.4)	9.2 (0.4; 2.4)	**<0.001***	**0.002**
	RoF S4	10.6 (0.3; 2.3)	10.1 (0.4; 2.2)	8.6 (0.4; 2.2)	7.9 (0.4; 2.3)	**<0.001***	**<0.001***
	RoF S5	8.2 (0.3; 2.1)	8.1 (0.4; 2.1)	6.8 (0.4; 2.0)	5.9 (0.4; 2.1)	**<0.001***	**<0.001***
	RoF S6	4.9 (0.3; 1.8)	5.4 (0.4; 2.0)	4.7 (0.4; 2.2)	4.0 (0.4; 2.0)	0.072	0.334
	Total range of extension	25.7 (1.3; 8.8)	23.5 (1.9; 10.2)	17.6 (1.9; 10.3)	19.9 (1.3; 7.2)	**0.001***	0.061
	RoE S1	5.3 (0.4; 2.9)	4.4 (0.4; 2.3)	4.9 (0.6; 3.5)	5.0 (0.5; 2.9)	0.601	0.973
	RoE S2	6.5 (0.4; 2.6)	5.3 (0.5; 2.6)	4.2 (0.5; 2.7)	4.3 (0.4; 2.1)	**<0.001***	**0.005**
	RoE S3	6.8 (0.4; 2.6)	5.7 (0.5; 2.9)	3.5 (0.5; 2.5)	3.9 (0.4; 2.0)	**<0.001***	**<0.001***
	RoE S4	4.7 (0.3; 2.4)	4.2 (0.5; 2.5)	2.1 (0.4; 2.3)	2.9 (0.4; 2.0)	**<0.001***	0.013
	RoE S5	2.2 (0.3; 2.1)	2.4 (0.3; 1.9)	1.3 (0.4; 2.0)	2.0 (0.4; 1.9)	0.184	0.990
	RoE S6	0.5 (0.3; 1.8)	1.1 (0.3; 1.6)	1.0 (0.3; 1.9)	1.4 (0.3; 1.7)	0.160	0.204
Females (n=184)	**Total range of flexion**	53.4 (1.1; 9.1)	55.2 (1.4; 8.6)	53.6 (1.5; 9.3)	49.2 (1.9; 11.5)	0.041	0.199
	RoF S1	6.2 (0.3; 2.3)	6.6 (0.2; 1.5)	6.3 (0.3; 2.2)	6.6 (0.3; 1.9)	0.633	0.788
	RoF S2	8.3 (0.2; 1.9)	8.5 (0.3; 1.7)	7.5 (0.3; 1.7)	7.4 (0.3; 2.1)	0.012	0.151
	RoF S3	10.4 (0.3; 2.1)	10.2 (0.3; 2.1)	9.4 (0.3; 2.1)	8.4 (0.4; 2.4)	**<0.001***	**<0.001***
	RoF S4	9.9 (0.3; 2.2)	9.5 (0.3; 2.2)	9.3 (0.3; 2.0)	7.9 (0.4; 2.4)	**<0.001***	**<0.001***
	RoF S5	7.6 (0.3; 2.3)	7.5 (0.3; 1.8)	8.0 (0.3; 1.9)	6.9 (0.3; 2.0)	0.126	0.392
	RoF S6	4.9 (0.3; 2.0)	5.2 (0.2; 1.5)	5.8 (0.3; 2.0)	5.4 (0.3; 2.0)	0.121	0.677
	Total range of extension	35.1 (1.4; 11.4)	29.1 (1.6; 10.4)	25.6 (1.8; 11.2)	22.7 (1.6; 9.7)	**<0.001***	**<0.001***
	RoE S1	5.3 (0.4; 3.6)	4.9 (0.4; 2.5)	3.8 (0.4; 2.8)	3.0 (0.4; 2.3)	**<0.001***	**0.002**
	RoE S2	7.4 (0.4; 3.1)	6.3 (0.4; 2.6)	4.7 (0.4; 2.8)	3.4 (0.4; 2.3)	**<0.001***	**<0.001***
	RoE S3	8.7 (0.4; 3.0)	7.1 (0.4; 2.7)	5.5 (0.5; 3.2)	4.0 (0.4; 2.5)	**<0.001***	**<0.001***
	RoE S4	7.3 (0.4; 2.9)	5.5 (0.4; 2.4)	4.8 (0.4; 2.8)	3.7 (0.3; 1.9)	**<0.001***	**<0.001***
	RoE S5	4.3 (0.3; 2.6)	3.2 (0.3; 2.1)	3.3 (0.3; 2.0)	3.3 (0.2; 1.5)	0.026	0.192
	RoE S6	1.7 (0.3; 2.5)	1.4 (0.4; 2.2)	2.1 (0.3; 2.1)	2.7 (0.3; 1.8)	0.067	0.205

Bold values indicate statistical significance (p<0.01).
*p-values base on one-way ANOVA. **Post-hoc comparison using Scheffé's test.

Discussion

This study investigated the effect of age and sex on the lordosis and the RoM of the whole lumbar spine as well as for different lumbar sub-regions in asymptomatic volunteers across the adult lifespan. The results of the present study emphasise the importance of the factor age on the lumbar lordosis and the RoM. We demonstrated that the age-related changes in the lordosis and the RoM differ between men and women and are strongly level dependent. The lordosis and RoM in the middle part of the lumbar spine are dominantly reduced with aging, with less reduction towards the lumbo-sacral and thoraco-lumbar transitions. The sex affects only the RoE.

The loss of total lordosis with aging as demonstrated in this study (Fig. 4) is in agreement with measurements in the literature [9,11,17] and corroborates our first hypothesis. This study provides evidence that this aging process is not uniform throughout lifespan and differs between males and females. In both sexes, the decrease of lordosis appears only marginal between 20-29yrs and 30-39yrs. While in females the process of aging is subsequently more continuous, the loss of lordosis in males mostly occurs between the 30-39yrs and 40-49yrs age groups. This discontinuous loss of lordosis explains why in some studies, in which only cohorts older than 40 years with no young control group were investigated, no significant loss of lordosis was found [14,20]. In the present study, a high inter-subject variability was found, which necessitates a sufficient cohort size with a homogeneous composition to detect these age effects. Furthermore, in the present study, asymptomatic subjects were investigated, whereas in other studies subjects with acute or chronic low back pain participated. However, the change in lordosis during aging differs between asymptomatic and symptomatic subjects, because the latter may already have, for example, a flat sagittal alignment or spinal diseases that affected the spinal curvature during an earlier stage of life [1–3]. Similar to the lordosis in standing, aging is also the crucial factor for a reduction in total RoM, especially in extension, where it is reduced by 31% between the oldest and youngest cohorts. This is consistent with previous studies [38,39,45].

In opposite to our third hypothesis, the lumbar lordosis was not significantly different between both sexes, which is in agreement with several studies [9,14,24,26], however in opposite to other investigations [12,46]. The present study suggests that the difference in lordosis between men and women is small and varies between age groups. This might partly explain why studies with varying cohort sizes and different mean ages show contradictory results.

Furthermore, in this sample, only subjects with a BMI < 26.0 kg/m² participated, which resulted in a mean BMI of 22.5 kg/m². Therefore, the impact of being overweight or obese was not investigated.

Currently, a detailed investigation of the age effect on certain regions of the lordosis and its motion is lacking in the literature. In accordance with our second hypothesis, the lower Epionics segments were less affected by aging than the middle segments, which characteristically changes the total lordosis and 'concentrates' the lordotic shape of the lumbar spine to the lower segments. Only one radiological study on a small cohort supports our findings of a significant correlation between age and lordosis loss restricted to the middle lordosis (L3-4) [9]. Only a trend was observed in the adjacent segments L2-3 and L4-5, and no significant influence was found in L5-S1. Previous studies reported a close relationship between the morphology of the pelvis, as, for example, characterised by the pelvic incidence [47], and the degree of total lumbar lordosis [25,26,48,49]. The level specific changes in lumbar lordosis during aging suggest that different parts of the lumbar spine may substantially change their relationship to the individual pelvic incidence.

In analogy to the aging process of the lordosis, the RoM characteristically changes with age. The RoM in the middle lumbar lordosis also decreases, whereas the RoM next to the thoracic and sacral transitions only shows a small change. Therefore, not only the lower lumbar lordosis but also its mobility is preserved during aging. These facts may have important implications for the spinal loading and the prevalent degeneration process in the lower lumbar spine during life, and could help to understand the mechanical challenges the lower lumbar spine has to withstand. However, these results also have consequences for the treatment of degenerative spinal diseases. Because the shape and motion differently change for certain regions of the lumbar spine, an age- and lumbar level-specific treatment may be important for long-term patient satisfaction.

This study emphasises that a reduction of the lordosis in symptomatic subjects with a severe, painful degenerated lumbar spine partly consists of a natural adaptive process during aging, which also occurs in asymptomatic subjects. Knowledge of this physiological loss of lordosis in asymptomatic individuals may, however, be essential for surgical reconstruction concepts of the sagittal alignment of the spine. In these concepts, the degree of lordosis is estimated mostly with the help of the individual pelvic incidence of the patient, which is assumed to be independent of posture and age (e.g.: lumbar lordosis = pelvic incidence ± 9°; [50]). Because of the physiological loss of lordosis with aging, the relationship between the lumbar lordosis and pelvic incidence appears to also be dependent on age. Therefore, an optimal patient-specific reconstruction may require an age dependent estimation of the lordosis.

Although the results presented here are consistent with radiological measurements, it should be noted that the Epionics SPINE system determines the curvature of the back and not directly the shape of the spine. Multiple studies previously demonstrated that the curvature and motion measured on the back and the spine significantly correlate with each other [42,51,52]. In our own preliminary validation studies, we could additionally show that the correlation between the back and spinal shape is poor in overweight and obese persons, which limits this study to normal-weight subjects (BMI < 26.0 kg/m^2). However, this study investigated the spinal shape and motion of a large asymptomatic cohort for which a radiological study design is ethically not supportable. Furthermore, this study is limited by investigating the motion only in the sagittal plane, although the motion of the lumbar spine in other anatomical planes such as during axial rotation and lateral bending might be affected by aging as well.

In conclusion, this study characterises the adaptive response of the lumbar spinal shape and its mobility as a function of age in asymptomatic males and females. While the lower part of the lumbar spine retains its lordosis and mobility, the middle part flattens and becomes less mobile. This may have important implications for the clinical long-term success of different surgical interventions, for instance for the surgical reconstruction of the sagittal alignment. Furthermore, the results can help to better understand the incidence of level- and age-dependent spinal disorders, and are essential for patient specific treatments and an evidence-based distinction between painful degenerative pathologies and asymptomatic aging.

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2.4 Publication 4: The effects of age and gender on the lumbopelvic rhythm in the sagittal plane in 309 subjects

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Abstract

Frequent upper body bending is associated with low back pain (LBP). The complex flexion movement, combining lumbar and pelvic motion, is known as "lumbopelvic rhythm" and can be quantified by dividing the change in the lumbar spine curvature by the change in pelvic orientation during flexion movement (L/P ratio). This parameter is clinically essential for LBP prevention, for diagnostic procedures and therapy; however, the effects of age and gender, in detail, are unknown.

The Epionics SPINE system, utilizing strain-gauge technology and acceleration sensors, was used to assess lumbar lordosis and sacrum orientation during standing and lumbar angle and sacrum orientation during maximal upper body flexion in 309 asymptomatic subjects (age: 20-75 yrs;♂: 134; ♀: 175). The effects of age and gender on these characteristics as well as on the resultant range of flexion (RoF) and lumbopelvic rhythm were investigated.

Aging significantly reduced lumbar lordosis by 8.2° and sacrum orientation by 6.6° during standing in all subjects. With aging, the lumbar RoF decreased by 7.7°, whereas the pelvic RoF compensated for this effect and increased by 7.0°. The L/P ratio decreased from 0.80 to 0.65 with age; however, this decrease was only significant in men. Gender affected sacrum orientation in standing and in flexion as well as the L/P ratio.

This study demonstrated the effects of age and gender on lordosis, sacrum orientation and lumbopelvic rhythm. These findings are of importance for the individual prevention of LBP, and provide a baseline for differentiating symptomatic from asymptomatic age- and gender-matched subjects.

1. Introduction

Frequent upper body bending is a risk factor for the development of low back pain (LBP) (Damkot et al., 1984; Hoogendoorn et al., 2000; Punnett et al., 1991). Therefore, physicians and physiotherapists have focused on understanding the complex pattern of this movement, which combines lumbar spine motion and pelvic rotation at the same time. During upper body bending, the lumbar spine and pelvis contribute differently to the total amount of motion in different phases of flexion movement, which is known as the "lumbopelvic rhythm". This rhythm can be quantified by dividing the change in the curvature of the lumbar spine by the change in pelvic orientation during flexion movement (the lumbopelvic (L/P) ratio). It has been shown that in young asymptomatic volunteers, the lumbar spine dominates in the early phase of flexion, whereas in the late flexion phase, the motion mainly arises from the pelvis (Dolan and Adams, 1993; Esola et al., 1996; Granata and Sanford, 2000; Kim et al., 2013; McClure et al., 1997a; Porter and Wilkinson, 1997; Tafazzol et al., 2014). Detailed knowledge about lumbopelvic motion is clinically essential for LBP prevention and diagnostic procedures and therapy (Laird et al., 2014; 2012) as well as for sophisticated biomechanical analyses of upper body motion in computational models that aim to predict lumbar spine loading (Tafazzol et al., 2014). To establish an improved individualized and patient-specific approach, the effects of age and gender on the lumbopelvic rhythm must be understood. However, these effects remain elusive.

For a sophisticated understanding of the lumbopelvic rhythm, the analysis of the lumbar spine and pelvis during standing and in full flexion is a prerequisite. Although there is a strong anatomical correlation between lumbar lordosis and pelvic morphology (Barrey et al., 2007; Vaz et al., 2002), several studies have investigated the effects of age and gender on lumbar lordosis and the pelvis separately. The majority of studies found either no differences (Jackson and McManus, 1994; Vialle et al., 2005) or a decrease in lordosis during aging (Gelb et al., 1995; Korovessis et al., 1998). Studies that have examined gender-related differences have reported either slightly greater lordosis in females (Schroder et al., 2014) or no significant differences at all (Gelb et al., 1995; Korovessis et al., 1998; Vaz et al., 2002). Studies on the effects of gender and age on pelvic morphology have not identified any gender-related differences in parameters such as pelvic incidence and pelvic tilt (Vaz et al., 2002) and have reported only weak correlations between age and pelvic tilt (Korovessis et al., 1998; Mac-Thiong et al., 2011). Investigations on upper body flexion have focused mainly on the spine, demonstrating a reduction in the spinal range of motion with increasing age (Dvorak et al., 1995; Intolo et al., 2009; Troke et al., 2005). The effect of gender on lumbar motion is still controversially discussed, with partly more or less motion in males than in females (McGregor et al., 1995; Russell et al., 1993; Troke et al., 2001; Van Herp et al., 2000). However, only a few studies have investigated age- and gender-specific differences in lumbopelvic rhythm to elucidate potential deviations in the interaction between the lumbar spine and the pelvis during flexion movement. Only Dolan and Adams (1993) examined the effect of aging, however in sitting and found no effect of age on lumbopelvic rhythm. Gender-related effects were only investigated by Esola et al. (1996), who did not find any significant differences between males and females. Due to these findings, most subsequent studies neglected the impact of age and gender or included sample sizes that were too small to explore these fundamental effects (Table 1).

Therefore, this study aimed to investigate, in a large asymptomatic cohort, the effects of age and gender initially on lumbar angle and sacrum orientation during standing and in upper body flexion as well as in particular on the resultant lumbopelvic rhythm by employing a novel motion capture device.

It was hypothesized that

1) Age and gender significantly affect lumbar angle and sacrum orientation in standing and during flexion.

2) As a consequence, age and gender specifically affect the resultant L/P ratio for full flexion and for single phases of the flexion process.

Table 1: Literature values for asymptomatic subjects (f=females; m=males) from previously published studies and data regarding their lumbar and pelvic ranges of flexion (RoF) and lumbopelvic ratios (L/P ratios). L/P ratios for full flexion are calculated by dividing the maximum lumbar RoF by the maximum pelvic RoF. The results of the current study are shown for comparison.

Author	Mean Age (yrs)	Age Range (yrs)	Measurement Technique	Subjects	Gender	Lumbar RoF (°)	Pelvic RoF (°)	L/P Ratio
Mayer et al. (1984)	31.0	19-51	Inclinometer + X-ray	13	6f/7m	55.0	66.0	0.83
Esola et al. (1996)	27.5	-	3D optoelectric motion analysis	21	8f/13m	43.0	70.0	0.61
Porter et al. (1997)	26.0	18-36	3D motion analysis	17	17m	68.6	58.3	1.18
Kim et al. (2013)	23.8	-	3D motion capture system	16	-	48.5	56.6	0.86
Tafazzol et al. (2014)	25.3	-	Inertial tracking device	8	8m	60.2	53.0	1.14
Range						**43.0-68.6**	**53.0-70.0**	**0.61-1.18**
Current Study	38.4	20-75	Epionics SPINE system	309	175f/134m	52.1	72.1	0.72

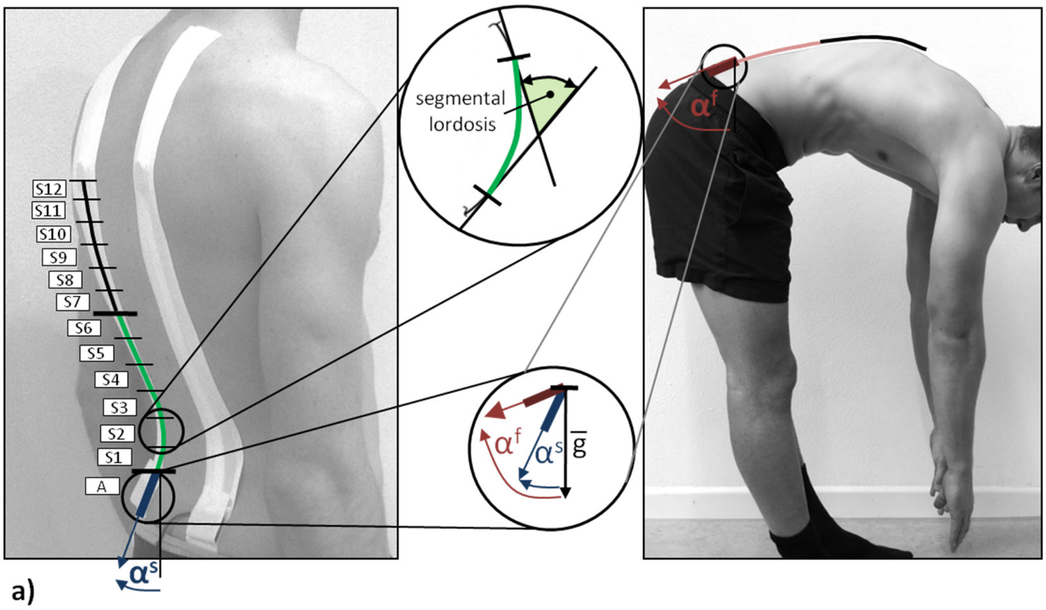
2. Material and Methods

2.1. Measurement system

The Epionics SPINE system (Epionics Medical GmbH, Potsdam, Germany) was used to measure lumbar spinal shape and motion as well as sacrum orientation (as a representation of pelvic orientation) and rotation in the sagittal plane (Fig. 1a). The system consisted of two flexible sensor strips that utilize strain gauge sensors located alongside flexible circuit board strips. These provided a sensitive measure of electrical resistance, and thus the aperture angles (Figure 1a middle), in accordance with the curvature in each of the twelve 2.5-cm-long segments (Epionics segments: S1-S12). During a measurement, the sensor strips were inserted into two hollow plasters attached to the back paravertebrally, 7.5 cm away from the spinal column on each side. The Epionics segments detected the local back curvature by means of lumbar lordosis (similar to the X-ray assessment of lordosis introduced by Cobb (Cobb, 1948)), as illustrated in Figure 1a (middle). The resultant segmental angles were derived from the measured segmental radius as follows:

$$\text{angle in degrees} = (\text{arc length x } 360)/(2\pi \text{ x radius }).$$

The lower end of each strip was aligned with the posterior superior iliac spine, which was approximately in line with the first sacral vertebra. A tri-axial accelerometer was located at this end, allowing the system to determine the sacrum orientation as depicted in Figure 1a. This acceleration sensor determined the spatial orientation of the sensor relative to the vertical direction of the earth's gravitational field. The sensor strips were connected to a storage unit (size: 12.5 cm x 5.5 cm; mass: 80 g) that collected data with a frequency of 50 Hz. The system's sensor strips exhibit high accuracy and repeatability (ICC>0.98) with test-retest reliability ICC values of >0.98. Previous studies confirmed the suitability of the system for assessing lumbar and pelvic motion (Consmuller et al., 2012a, b; Pries et al., 2015).



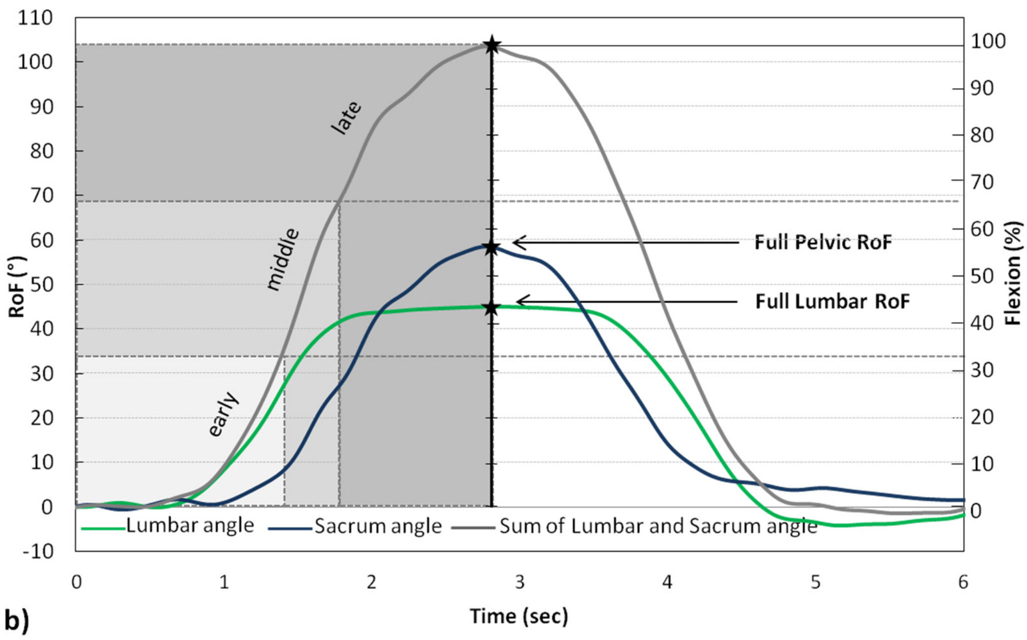


Figure 1a) The Epionics SPINE system affixed to a volunteer's back in standing (left) and in flexion (right). Lumbar lordosis is the sum of all of the Epionics segments lordotically curved in standing; on average, the lordosis was between S1 and S6 (highlighted in green during standing and in light red for flexion). The orientation of the sacrum was assessed via the accelerometers (blue in standing and dark red in flexion) in terms of the angle "α^s" for standing and "α^f" for flexion with respect to the earth's gravitational field ("$\bar{g}$").

Figure 1b) Example of a flexion curve (grey) decomposed into lumbar flexion (green) and pelvic rotation (blue). In maximal upper body flexion, the sum of the change in lumbar angle and sacrum orientation was at its maximum. For the incremental analysis of flexion, the values of each lumbar angle and sacrum angle corresponding to 0, 33, 66 and 100% of total flexion were obtained, and the differences between 33 and 0% (early), 66 and 33% (middle), and 100 and 66% (late) were determined.

2.2. Ethics

The Ethics Committee of the Charité – Universitätsmedizin Berlin approved this study (registry number EA4/011/10). All of the volunteers were informed of the study's procedure, and they signed a written consent granting their permission to conduct the measurements.

2.3. Subjects

This study examined data obtained from 429 subjects from a previously published cohort on the measurement of lumbar spinal posture and motion (Consmuller et al., 2012a). These subjects had no pain in the lower back or in the pelvis in the six months prior to the measurements and no history of spinal or pelvic surgery. Recent studies, such as those by Adams et al. (1986), Guermazi et al. (2006), and Stokes et al. (1987) as well as our own validation studies, have found a significant correlation between lumbar lordosis assessed via the back shape and radiologically determined lordosis only for subjects with a body mass index (BMI) <26.0 kg/m². Therefore, to ensure valid results with a strong correlation between back shape and underlying spinal structures, 106 volunteers with a BMI higher than 26.0 kg/m² were excluded from the study. Moreover, 14 subjects were excluded due to missing sacrum orientation values caused by a malfunction in the acceleration sensors, resulting in 309 evaluated subjects (175 females; 134 males) with a mean age of 38.4 ± 14.0 yrs (38.2 yrs for females, 38.5 yrs for males). The mean height was 173.0 ± 9.5 cm (167.4 cm for females, 180.3 cm for males), the mean weight was 67.5 ± 10.1 kg (61.4 kg, 75.5 kg) and the mean BMI was 22.5 ± 2.0 kg/m² (21.9 kg/m², 23.2 kg/m²). The volunteers were classified by gender and assigned to three age groups: 20-35 yrs (n=155), 35-50 yrs (n=100) and >50 yrs (n=54).

2.4. Measurement protocol

All of the volunteers were measured five times during relaxed upright standing after being equipped with the Epionics SPINE system. From this upright reference position, maximum upper body flexion was performed five times at the volunteers' preferred velocity while keeping the knees extended (Fig. 1a).

2.5. Data analysis

The lumbar angle (lordosis when negative; kyphosis when positive) was at first individually calculated by summing all of the Epionics segments that were lordotically curved in the individual volunteer shown by the transition from lordosis to kyphosis while standing (Fig. 1a, average lordosis range of all subjects highlighted in green (S1-S6)) accounting for differences in the volunteers' anthropometrics. The corresponding data from the left and right sensors were averaged. These lordotic Epionics segments served as individual reference for determining the lumbar angle during flexion (Fig. 1a). The sacrum orientation was determined based on the orientation of the accelerometer, as denoted by the angles "α^s" for standing and "α^f" for flexion in Fig. 1a.

In maximal upper body flexion, the sum of the change in the lumbar angle and sacrum orientation was at its maximum (Fig. 1b). At this point, the corresponding lumbar and sacrum angles were determined ("Lumbar angle in full flexion"; "Sacrum orientation in full flexion") and utilized to calculate the full lumbar and pelvic range of flexion (RoF; Fig. 1b). These values were calculated by subtracting the lumbar angle and sacrum orientation in standing from the corresponding values in full flexion. From these ranges, the L/P ratios for full flexion were calculated by dividing the lumbar RoF by the pelvic RoF. Moreover, the process of full flexion was divided into three distinct phases: 0-33% (early), 33-66% (middle) and 66-100% (late flexion) (Fig. 1b). The incremental changes in both parameters for these three phases were calculated and divided by each other. The resultant L/P ratios can be interpreted as the corresponding average slope of the curve segments for early, middle and late flexion, as depicted in Figure 2a and b. This procedure was similar to that reported for instance by Esola et al. (1996), and it aimed to characterize the lumbar-pelvic interrelation at selected stages of the flexion process.

All data were processed using in-house developed MATLAB routines (MATLAB R2009b, MathWorks, Inc., Natick, MA, US.).

2.6. Statistics

Descriptive statistics were analyzed using SPSS 21.0 (SPSS Inc., Chicago IL, USA). The Kolmogorov-Smirnov test was used to evaluate the normal distribution for each investigated age or gender group. Levene's test was used to test for variance homogeneity. For normally distributed data and variance homogeneity, the effects of age and gender were investigated using a two-way analysis of variance (ANOVA). For gender-specific analyses, the entire cohort was subsequently separated by gender and the effect of age was analyzed using one-way ANOVA. All of the analyses were followed by post hoc Scheffé's test.

In cases in which data were not normally distributed, the non-parametric Kruskal-Wallis test was used to analyze the effect of age, followed by the post hoc Mann-Whitney U test with

Bonferroni correction. The effect of gender was evaluated using the two-tailed Mann-Whitney U test. *P-values* less than 0.01 were considered statistically significant.

3. Results

3.1. Standing, full *flexion and range of flexion*

According to the Kolmogorov-Smirnov test, lumbar angle and sacrum orientation in standing and in full flexion as well as lumbar and pelvic RoF were normally distributed in all of the investigated groups.

For the entire cohort, the mean lumbar lordosis during standing was -33.8° (Fig. 2a), with no significant differences between genders (males, -32.4°; females, -34.9°; Fig. 3a, Table 3). The mean sacrum orientation during standing was 19.5° (Fig. 2a) and was significantly different between males (17.4°) and females (21.1°; Fig. 3a). During aging, lordosis in standing significantly decreased by 7.3° in males (Fig. 4a, Table 2) and by 8.9° in females (Fig. 4c), in comparing the youngest to the oldest cohort. The decrease in lordosis during aging was accompanied by a significant reduction in sacrum orientation from 20.4° to 14.2° in males (Fig. 4a, Table 2) and from 23.0° to 16.2° in females (Fig. 4c).

In full flexion, no significant differences in lumbar angle or sacrum orientation could be detected between the youngest and oldest cohort (Table 2). The sacrum orientation in full flexion significantly differed between males (81.5°) and females (99.4°; Table 3).

The lumbar RoF significantly decreased with aging in males (reduction of 9.1°) and in females (6.5°; Table 2). In contrast, the pelvic RoF increased with aging and appeared to compensate for the reduction in the lumbar RoF. However, only in males did the values for pelvic RoF show a significant increase by 12.8° during aging. The increase in females was 3.0°, which was not significant (Table 2). It should be noted that the aforementioned significant changes in the lumbar and pelvic RoF with aging were caused only by the change in lumbar angle and sacrum orientation in the starting upright standing position, not by the value reached in full flexion.

Table 2: Effects of aging on all of the investigated parameters. For normally distributed data, the mean and standard deviation are presented. The p-values are based on one- and two-way ANOVAs and post hoc comparisons using Scheffé's test. For non-normally distributed data, median and ranges are provided. The p-values are based on the Kruskal-Wallis test and post hoc comparison using Mann-Whitney U with Bonferroni correction. Bold values indicate statistical significance ($p<0.01$).

Parameter	Subjects	20-35 yrs Mean (SD)	36-50 yrs Mean (SD)	>50 yrs Mean (SD)	ANOVA p-values	Post hoc analysis 20-35 yrs. vs >50 yrs
Lumbar lordosis in standing (°)	**Entire cohort**	-36.8 (7.8)	-32.0 (8.7)	-28.6 (10.2)	**<0.001***	**<0.001***
	Males	-36.1 (8.7)	-28.7 (9.9)	-28.8 (12.0)	**<0.001***	**0.007***
	Females	-37.4 (7.1)	-34.3 (6.8)	-28.5 (8.7)	**<0.001***	**<0.001***
Sacrum orientation in standing (°)	**Entire cohort**	21.9 (6.3)	18.2 (7.7)	15.3 (8.1)	**<0.001***	**<0.001***
	Males	20.4 (6.9)	14.6 (7.7)	14.2 (9.8)	**<0.001***	**0.004***
	Females	23.0 (5.6)	20.8 (6.6)	16.2 (6.2)	**<0.001***	**<0.001***
Lumbar angle in full flexion (°)	**Entire cohort**	17.3 (6.7)	20.0 (8.6)	17.8 (8.6)	0.017	0.913
	Males	18.5 (5.7)	21.4 (7.7)	16.8 (8.1)	0.020	0.536
	Females	16.3 (7.3)	19.1 (9.1)	18.7 (9.1)	0.113	0.403
Sacrum orientation in full flexion (°)	**Entire cohort**	91.9 (16.5)	90.8 (15.3)	92.4 (14.5)	0.503	0.979
	Males	80.2 (13.0)	80.4 (11.7)	86.8 (12.7)	0.070	0.087
	Females	100.9 (12.9)	98.4 (13.1)	97.2 (14.5)	0.325	0.426
Lumbar RoF (°)	**Entire cohort**	54.1 (9.0)	52.0 (10.4)	46.4 (11.0)	**<0.001***	**<0.001***
	Males	54.6 (8.7)	50.0 (11.4)	45.5 (12.0)	**0.001***	**0.001***
	Females	53.7 (9.2)	53.4 (9.5)	47.2 (10.3)	**0.005***	**0.007***
Pelvic RoF (°)	**Entire cohort**	70.1 (17.2)	72.7 (14.3)	77.1 (16.7)	**0.003***	**0.010***
	Males	59.8 (14.8)	65.8 (13.1)	72.6 (16.4)	**0.001***	**0.001***
	Females	77.9 (14.7)	77.6 (13.2)	80.9 (16.3)	0.557	0.618

L/P Ratio		20-35 yrs Median (Range)	36-50 yrs Median (Range)	>50 yrs Median (Range)	Kruskal-Wallis-Test p-values	Post hoc analysis 20-35 yrs. vs >50 yrs
Full flexion	**Males**	0.91 (0.21-2.57)	0.77 (0.26-1.50)	0.65 (0.27-1.57)	**<0.001***	**<0.001***
	Females	0.69 (0.29-1.48)	0.70 (0.26-1.20)	0.65 (0.17-1.24)	0.062	0.093
Early flexion	**Males**	3.44 (-68.27-22.05)	1.73 (0.47-6.02)	1.33 (0.46-6.37)	**<0.001***	**<0.001***
	Females	2.54 (-12.86-24.18)	2.10 (0.71-35.28)	1.73 (0.64-4.16)	**0.002***	**0.001***
Middle flexion	**Males**	0.93 (0.16-2.69)	0.80 (0.07-2.07)	0.66 (0.26-1.62)	0.081	0.090
	Females	0.61 (0.22-1.59)	0.70 (0.25-1.32)	0.63 (0.09-1.26)	0.361	0.999
Late flexion	**Males**	0.22 (-0.04-0.91)	0.22 (-0.02-0.77)	0.21 (0.03-0.54)	0.541	0.999
	Females	0.11 (-0.06-0.72)	0.16 (-0.05-0.45)	0.15 (-0.06-0.57)	0.271	0.636

Table 3: Effects of gender on all of the investigated parameters. For normally distributed data, the mean and standard deviation are presented. The p-values are based on two-way ANOVA. For non-normally distributed data, the median and range are provided. The p-values are based on the two-tailed Mann-Whitney U test. Bold values indicate statistical significance (p<0.01).

Parameter	**Males Mean (SD)**	**Females Mean (SD)**	**ANOVA p-values**
Lumbar lordosis in standing (°)	-32.4 (10.3)	-34.9 (7.9)	0.036
Sacrum orientation in standing (°)	17.4 (8.3)	21.1 (6.5)	**<0.001***
Lumbar angle in full flexion (°)	19.1 (7.0)	17.6 (8.3)	0.373
Sacrum orientation in full flexion (°)	81.5 (12.7)	99.4 (13.2)	**<0.001***
Lumbar RoF (°)	51.5 (10.8)	52.5 (9.7)	0.267
Pelvic RoF (°)	64.1 (15.3)	78.3 (14.5)	**<0.001***
L/P Ratio	**Males Median (Range)**	**Females Median (Range)**	**Mann-Whitney U Test p-values**
Full flexion	0.81 (0.21-2.57)	0.68 (0.17-1.48)	**<0.001***
Early flexion	2.33 (-68.27-22.05)	2.16 (-12.86-35.28)	0.652
Middle flexion	0.84 (0.07-2.69)	0.64 (0.09-1.59)	**<0.001***
Late flexion	0.22 (-0.04-0.91)	0.14 (-0.06-0.72)	**<0.001***

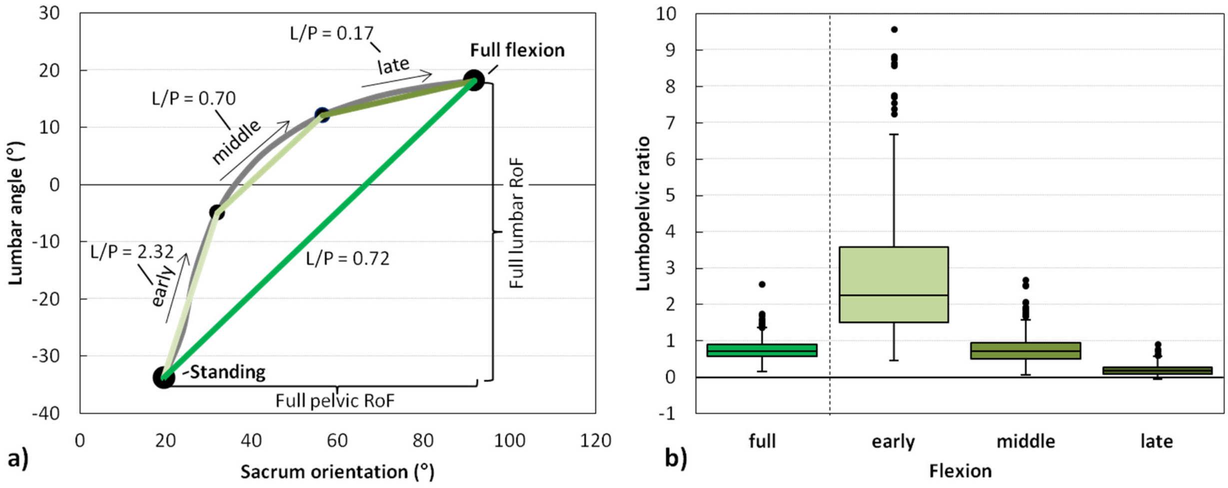


Figure 2a) Plot of mean lumbar angle (y-axis) versus sacrum orientation (x-axis) showing the L/P rhythm for the entire cohort during flexion. The black dots, indicating 0, 33, 66 and 100% of full flexion, divide the curve into segments that depict the early, middle and late stages of flexion. The average slope of each single segment can be interpreted as the corresponding L/P ratio.

2b) L/P ratios for full flexion and for incremental early, middle and late flexion in the entire cohort. Black dots represent outliers greater than 1.5 times the interquartile range.

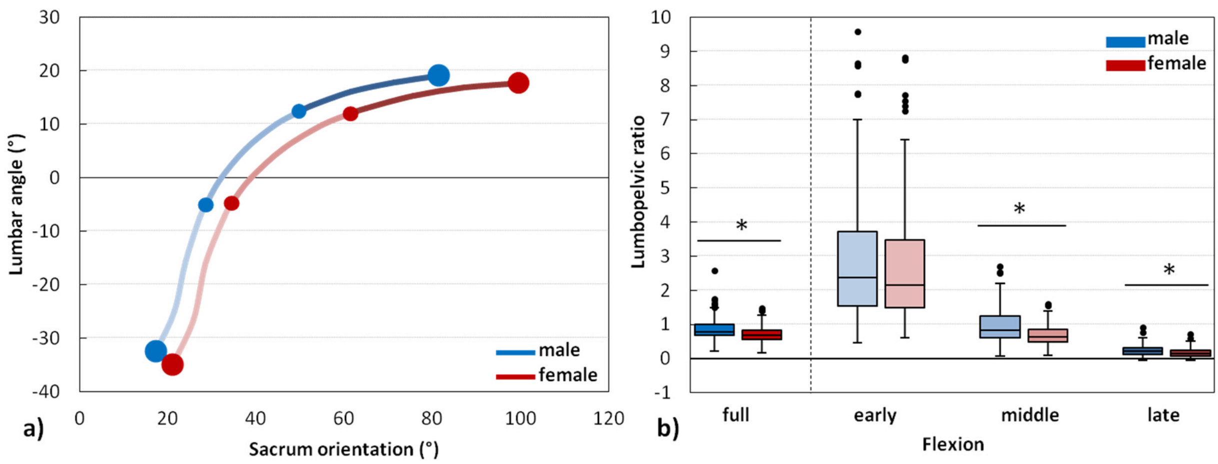


Figure 3a) L/P rhythm for males and females separately. The red and blue dots divide the curve into segments that depict the early, middle and late stages of flexion. The average slope of each single segment can be interpreted as the corresponding L/P ratio.

b) L/P ratios for full flexion and for incremental early, middle and late flexion for males (blue) and females (red) separately. Black dots represent outliers greater than 1.5 times the interquartile range. Asterisks indicate statistical significance ($p < 0.01$).

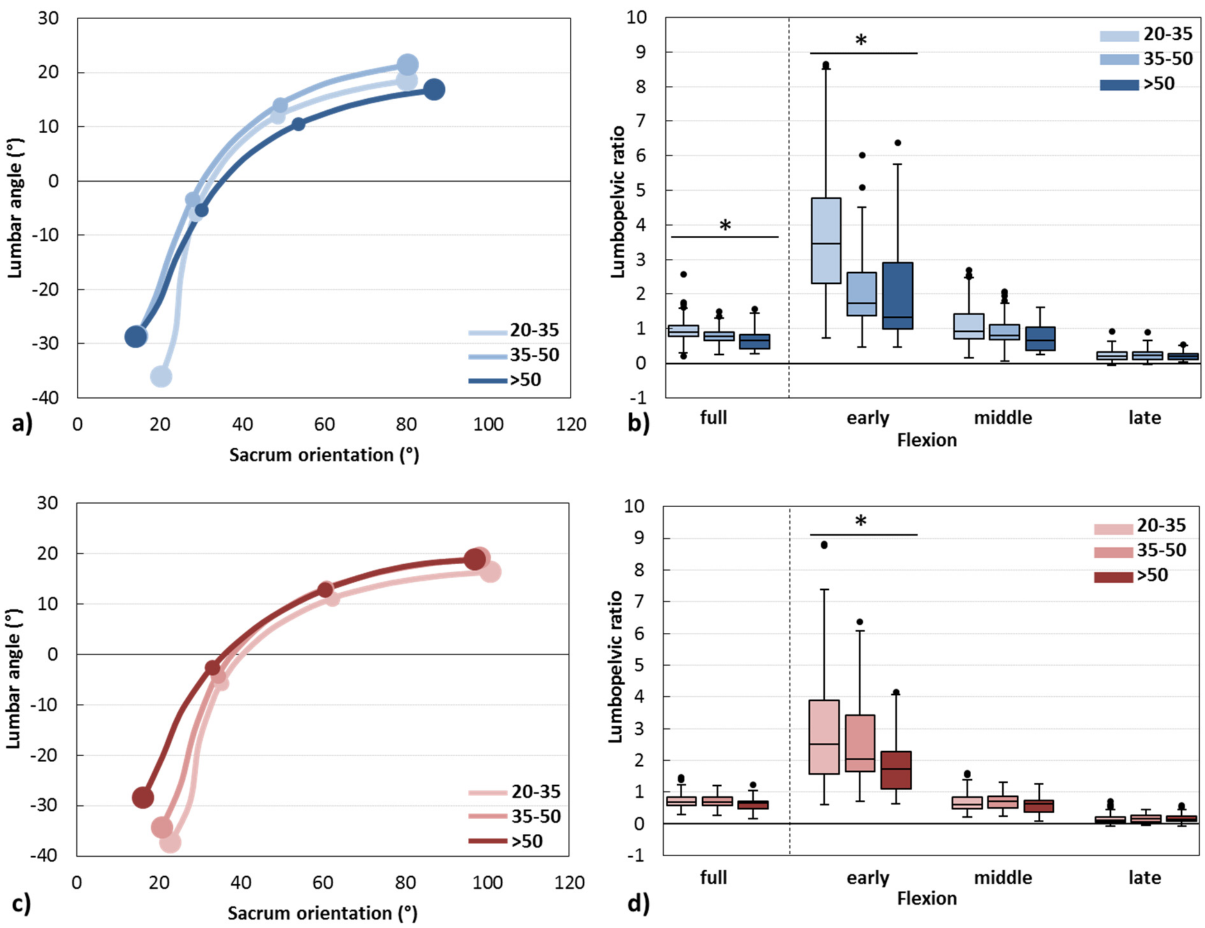


Figure 4a and c) L/P ratios for different age groups (in years) divided by gender. The red and blue dots divide the curve into segments that depict the early, middle and late stages of flexion for a) males and c) females. The average slope of each single segment can be interpreted as the corresponding L/P ratio in Figure 4b and d.

Figure 4b and d) L/P ratios for full flexion and for incremental early, middle and late flexion presented for b) males and d) females. Black dots represent outliers greater than 1.5 times the interquartile range. Asterisks indicate statistical significance ($p < 0.01$).

3.2. L/P ratios for full, early, middle and late flexion

According to the Kolmogorov-Smirnov test, the L/P ratios for full, early, middle and late flexion were not normally distributed, and they showed large inter-subject variability. Fourteen extreme outliers for the L/P ratio in early flexion (values more than three interquartile ranges below the first quartile or above the third quartile) among the 309 values were excluded only from the boxplots to provide a better graphical depiction, but not from the inferential statistical evaluations.

The L/P ratios for full flexion significantly differed between females (0.68) and males (0.81) (Fig. 3b, Table 3), indicating an overall larger contribution of the pelvis in females compared with males. With aging, the L/P ratio for full flexion significantly decreased in males from 0.91 to 0.65 (youngest cohort compared with the oldest cohort; Fig. 4b, Table 2), whereas in females, the changes were small and not significant (Fig. 4d). This result indicates a smaller contribution of the lumbar spine and a greater contribution of the pelvis to flexion motion with increasing age.

Overall, the specific L/P ratio characteristically changed during the course of flexion motion. The early part of flexion was primarily accomplished by the lumbar spine, whereas the motion occurred mainly in the pelvis during the late phase of flexion (Fig. 2). Therefore, the incremental L/P ratio decreased from 2.32 during early flexion to 0.70 during middle flexion and to 0.17 during late flexion for the entire cohort (Fig. 2b). Significant differences between males and females were only observed during middle and late flexion (Fig. 3b), with significantly larger L/P ratios observed in males. Age affected the L/P ratio only in early flexion, with significantly larger values observed in the youngest cohorts of males and females compared with those in the corresponding oldest cohorts (Fig. 4b, d).

4. Discussion

Upper body flexion in the sagittal plane is an essential daily activity and is frequently performed during work-related activities (Freitag et al., 2012; Jansen et al., 2001). This movement is associated with high spinal loads (Takahashi et al., 2006; Wilke et al., 1999) and is considered a risk factor for the development of LBP (Damkot et al., 1984; Hoogendoorn et al., 2000; Punnett et al., 1991). The complex pattern of this movement, which combines spinal and pelvic motion, has, in principle, been demonstrated by few studies (Table 1). However, gender and age factors have been neglected, or no effects have been found. The present study demonstrated the essential effects of age and gender in a large asymptomatic cohort, initially on lumbar angle and sacrum orientation in standing and flexion and in particular on the resultant L/P ratios. In agreement with our first hypothesis, aging significantly reduced lumbar lordosis as well as sacrum orientation during standing. With increasing age, the lumbar RoF decreased, whereas the pelvic RoF compensated for this effect and increased. This phenomenon resulted in an altered L/P ratio for full flexion, which significantly decreased with aging, corroborating the second hypothesis. Moreover, males showed a more vertically oriented sacrum in standing, a significantly smaller angle of sacrum orientation in full flexion

and a smaller pelvic RoF compared with females, indicating different L/P ratios between genders, especially during middle and late flexion, which is in agreement with the second hypothesis.
The mean values of the lumbar and pelvic RoF as well as the resultant L/P ratios for the entire cohort obtained in the present study are consistent with previously reported values (Table 1), which were measured by several different methods (Dolan and Adams, 1993; Esola et al., 1996; Mayer et al., 1984; McClure et al., 1997b; Porter and Wilkinson, 1997; Tafazzol et al., 2014). No L/P ratios of studies that included lifting tasks, such as those of Granata and Sanford (2000) or Maduri et al. (2008), were included in the comparison, as these data show discrepancies with the results presented in Table 1, which may be related to the influence of the weight and the lifting task itself (different coordination of the lumbar spine and pelvis). The loss of lordosis in standing and the loss of RoF with aging are similar to those reported in previous studies that investigated the effects of age and gender on lumbar lordosis or the pelvis separately (Dvorak et al., 1995; Gelb et al., 1995; Intolo et al., 2009; Korovessis et al., 1998; Milne and Lauder, 1974; Troke et al., 2005). Moreover, in agreement with the literature and clinical observations, aging affected sacrum orientation (Gelb et al., 1995; Mac-Thiong et al., 2011), resulting in a more vertically oriented sacrum with increasing age. Higher L/P ratios were reported in previous studies that included only males (Table 1; e.g., Porter and Wilkinson (1997): 17 males, L/P ratio of 1.18) than in studies involving both genders (e.g., Esola et al. (1996): 8 females and 13 males, L/P ratio of 0.61), which indirectly supports the results of the present study, in which females exhibited smaller L/P ratios for full flexion compared with those obtained for males. In agreement with this finding, the present study is the first to clearly demonstrate that age and gender substantially affect the combination of lumbar and pelvic motion.
With increasing age, the entire flexion movement pattern changes in a gender-specific manner. The shift from less lumbar to more pelvic motion during aging is essential for diagnostic procedures, therapy planning and monitoring in clinical examinations or in physiotherapy. This finding emphasizes that a sophisticated evaluation of a patient’s ability to move requires a more detailed assessment of and differentiation between spinal and pelvic motion as well as a determination of the relationship dictating this motion. Commonly used functional assessments, such as the fingertip-to-floor distance, have been utilized to describe a patient’s mobility and to document functional changes before and after therapy (Ekedahl et

al., 2012; Moll and Wright, 1971). However, those tests are unable to differentiate between spinal and pelvic components and therefore cannot discriminate whether, for example, a loss in mobility with aging is caused by a loss of spinal or pelvic motion. Moreover, in this study, the changes in the RoF during aging were caused by a change in the standing starting position, not by the maximum value reached in flexion. This result demonstrates that the sole assessment of lumbar and pelvic ranges of flexion has important limitations because it does not consider the starting and ending positions of the flexion movement but only the range between the two.

Several *in vivo* studies measuring the intradiscal pressure (Takahashi et al., 2006; Wilke et al., 1999) or the loads on a telemeterized vertebral body replacement (Dreischarf et al., 2015) as well as computational predictions (Bazrgari et al., 2008) have demonstrated that the lumbar spine is highly loaded during upper body flexion. Using a kinematics-driven musculoskeletal finite element model of the spine, Tafazzol et al. (2014) further demonstrated that the overall compression and shear loading for a given trunk flexion was substantially affected by the individual L/P ratio. The authors' computational predictions suggested a load decrease at spinal level L5-S1 for larger L/P values, particularly at small to moderate trunk flexion angles. As such, the quantification of age- and gender-related changes in the L/P ratio may indirectly highlight changes in lower back loading. The present study demonstrates that aging significantly reduces the L/P ratio, especially in the early flexion phase, which implies a higher loading of lumbar spinal structures in an older cohort relative to a young cohort during the same trunk flexion angle. Therefore, this altered movement pattern in the elderly might be an important reason for the higher risk for LBP at an older age, especially because many daily routine tasks, such as vacuuming or washing the dishes, are performed in a bent position similar to early flexion.

This study focused mainly on the motion of the lumbar spine and pelvis and neglected thoracic kyphosis and thoracic mobility. Although it is generally accepted that only little motion occurs in the thoracic region (Mannion et al., 2004; Steinbeis, 1999), this component should be considered in future studies analyzing upper body bending. Although the current study's results agree with those reported in the literature (also obtained using non-invasive measurement methods; Table 1), it should be noted that all of the employed tools, including the Epionics SPINE system, measure back and not directly the spine curvature. To ensure valid results with a strong correlation between back shape and underlying spinal structures, subjects with a BMI higher than 26.0 kg/m² were excluded, thus limiting the results of this study to a normal-weight population. The acceleration sensors estimate the sacrum orientation as a representation of the overall pelvic orientation. In standard anatomical literature (Moore, 1992), the sacrum is described as part of the pelvic girdle, whose orientation was estimated herein from the posterior. This procedure is in accordance with other non-invasive measurement approaches (Granata and Sanford, 2000; Maduri et al., 2008; Tafazzol et al., 2014) but does not directly reflect pelvic parameters such as pelvic tilt, which can be obtained only from radiographs. As an amphiarthrosis, the iliosacral joint has almost no flexibility in particular at advanced age, which has been confirmed for instance by in vivo measurements by Wilke et al. (1997). Therefore, the sacral and pelvic ranges of motion are assumed to be equal. Taking the mean pelvic RoF of the present study of ~72° and a rotation of 1.6° in the iliosacral joint (Wilke et al., 1997) as a worst case, there would be a difference of ~2% between sacrum and pelvic rotation. Therefore, potential differences between pelvic and sacrum ranges of motion in the present study are very small.

This study highlights the effects of age and gender on the complex interrelation between the lumbar spine and sacrum orientation in standing and during flexion. The presented results emphasize that for an individualized functional analysis, it is essential to consider age- and gender-specific changes in the lumbar spine, sacrum orientation and their relationship during flexion motion (lumbopelvic rhythm) as these characteristics have major implications regarding spinal loads and the development of LBP.

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2.5 Publication 5: Differences between clinical "snap-shot" and "real-life" assessments of lumbar spine alignment and motion - What is the "real" lumbar lordosis of a human being?

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Abstract

The individual lumbar lordosis and lumbar motion have been identified to play an important role in pathogenesis of low back pain and are essential references for preoperative planning and postoperative evaluation. The clinical "gold-standard" for measuring lumbar lordosis and its motion are radiological "snap-shots" taken while standing and during upper-body flexion and extension. The extent to which these clinically assessed values characterise lumbar alignment and its motion in daily life merits discussion.

A non-invasive measurement-system was employed to measure lumbar lordosis and lumbar motion in 208 volunteers (age: 20-74yrs; ♀/♂: 115/93). For an initial short-term measurement, comparable with the clinical "snap-shot", lumbar lordosis and its motion were assessed while standing and during flexion and extension. Subsequently, volunteers were released to their daily lives while wearing the device, and measurements were performed during the following 24h.

The average lumbar lordosis during 24h (8.0°) differed significantly from the standardised measurement while standing (33.3°). Ranges of motion were significantly different throughout the day compared to standing measurements. The influence of the factors age and gender on lordosis and its motion resulted in conflicting results between long- and short-term-measurements.

In conclusion, results of short-term examinations differ considerably from the average values during real-life. These findings might be important for surgical planning and increase the awareness of the biomechanical challenges that spinal structures and implants face in real-life. Furthermore, long-term assessments of spinal alignment and motion during daily life can provide valid data on spinal function and can reveal the importance of influential factors.

Keywords: lumbar lordosis; range of motion; aging; gender; sagittal alignment

1. Introduction

Low back pain (LBP) is the leading cause of disability worldwide, resulting in tremendous direct and indirect costs (Connelly et al., 2006; Vos et al., 2012). Although the reasons for LBP are multidimensional, the individual sagittal alignment and motion of the lumbar spine have been identified as elementary characteristics that play an important role in the pathogenesis and treatment of LBP (Chaléat-Valayer et al., 2011; J.-C. Le Huec et al., 2014). A valid, objective and reliable measurement of lumbar spine curvature and its motion is essential, as it serves as an important reference for the planning of various surgical interventions and the evaluation of patients' spinal function (Mehta et al., 2015). Currently, the "gold-standard" for assessing lumbar lordosis and its motion in clinical short-term examinations is to obtain functional radiological measurements in the standing position and during upper body flexion and extension (e.g., using Cobb's method; (Cobb, 1948)). However, the extent to which these clinically assessed values characterise the "real" lumbar alignment and motion during daily life merits discussion.

In the field of spinal musculoskeletal diseases, long-term measurements of the lumbar spine that determine lumbar lordosis and its motions in everyday life have not been reported. However, especially in the analysis of dynamic postural changes, the oversimplification of complex and diverse daily spinal alignment and motion to single static measurements in the standing position (upright, flexed, extended) seems obvious yet remains unstudied. Measurements in a standing position seem even more questionable, as life in industrialised countries takes place predominantly in sedentary postures (Matthews et al., 2008). The actual average sagittal alignment and motion of the lordosis during 24 hours might therefore be substantially different from the clinically assessed standing reference. This discrepancy would imply a different loading of certain spinal structures and implants during the day (Wilke et al., 1999), and may therefore require a reconsideration of pre-operative evaluation for different surgical interventions. Knowledge of the alignment and motion of the lumbar spine in daily life is therefore vital for improving the understanding of the aetiology of different degenerative spinal disorders, revealing the true impact of essential factors such as age and gender, optimising the planning of surgical interventions, and designing implants that are adapted to patients' individual conditions in daily life.

Therefore, in this study the alignment and motion of the lumbar lordosis was measured with the help of a non-invasive measurement tool in 208 asymptomatic volunteers over a period of

24 hours and using a standardised measurement procedure during standing, which is similar to a clinical assessment. The current investigation aims to quantify the extent of differences in lumbar lordosis and its motion between daily life and standard standing measurements. Furthermore, the influence of age and gender on lordosis and its motion were investigated and compared between daily life measurements and standard standing measurements.

2. Materials and Methods

2.1. Study participants

All the participating volunteers were free of acute LBP, and none had experienced LBP within six months prior to the measurement and had previous spinal surgery.

Initially, 297 volunteers completed short-term measurements (STMs) and long-term measurement (LTMs) with the Epionics SPINE system (Epionics Medical GmbH, Potsdam, Germany) that assesses spinal shape via back shape measurements. Several studies have demonstrated that the shape and motion measured on the back and the spine significantly correlate with each other (Adams et al., 1986; Guermazi et al., 2006; Stokes et al., 1987). However, our own preliminary validation studies found that this correlation is poor in overweight and obese persons. Therefore, for the present study, 89 volunteers with a body mass index (BMI) higher than 26 kg/m^2 were excluded from the initial cohort to ensure a high correlation between the shape of the back and that of the spine.

The volunteers were classified by gender and assigned to three age groups as in previous studies (e.g., (Consmüller et al., 2012; Nourbakhsh et al., 2001)): 20-35 yrs, 35-50 yrs, and >50 yrs. The mean values for age, body height, body weight and BMI are provided in Table 1.

Table 1: Number of volunteers and the mean (± standard deviation) of age, height, weight and body mass index (BMI) for the investigated age groups and for males and females separately.

	All	20-35 yrs	35-50 yrs	>50 yrs
Volunteers (female/male)	208 (115/93)	88 (44/44)	72 (45/27)	48 (26/22)
Age (years; female/male)	40.3 (40.9/39.5)	27.4 (27.0/27.8)	42.3 (42.4/42.1)	60.9 (61.9/59.8)
Body height (cm; female/male)	173.0 ± 9.6 (167.4/179.9)	174.8 ± 9.6 (168.2/181.4)	171.7 ± 9.5 (167.6/178.6)	171.5 ± 9.5 (165.7/178.4)
Weight (kg; female/male)	68.0 ± 9.9 (62.1/75.4)	68.5 ± 10.0 (61.4/75.7)	67.2 ± 9.6 (62.9/74.3)	68.3 ± 10.2 (61.8/76.0)
BMI (kg/m²; female/male)	22.7 ± 2.0 (22.1/23.3)	22.3 ± 1.9 (21.7/23.0)	22.7 ± 2.1 (22.4/23.3)	23.1 ± 1.9 (22.5/23.9)

2.2. Ethics statement

The Ethics Committee of the Charité – Universitätsmedizin Berlin (registry number EA4/011/10) approved this study. The procedure was explained to all the volunteers in detail, and the participants provided written informed consent permitting the spinal shape determinations in the present study.

2.3. Measurement system

In the present study, participants were measured with the Epionics SPINE system (Fig. 1), which allows for the dynamic assessment of lumbar and thoraco-lumbar spinal alignment and motion in the sagittal plane. The system enables short-term measurements considering a standard choreography, including flexion and extension, similar to clinical functional X-ray evaluations as well as long-term measurements incorporating measurements up to 24 hours without restrictions for the subject.

The Epionics SPINE system consists of two flexible sensor strips that each consist of twelve 25-mm long sensor units (Epionics segments: S1-S12) that utilise strain gauge technology. The sensor strips are inserted into two hollow plasters, which are attached to the back paravertebrally at a distance of ~7.5 cm from the mid-sagittal plane. Each sensor unit detects the local curvature, as illustrated in Fig. 1A. The lowest part of the strips is positioned relative to the posterior superior iliac spine, which is approximately in line with the first sacral vertebra. A tri-axial accelerometer is located at the lower end of each sensor strip to determine the orientation of the sensor segments relative to the earth's gravitational field. The sensor strips are connected to a portable storage unit (size: 12.5 cm x 5.5 cm; mass: 80 g) that records the data at 50 Hz. The system has a high accuracy and reliability and is described in greater detail elsewhere (Consmüller et al., 2012; Taylor et al., 2010).

2.4. Measurement protocol

The measurements in this study consisted of two parts: a preceding standardised short-term measurement in the standing position (comparable to the clinical "snap-shot"; duration: approximately 15 minutes) and a functional long-term measurement during daily life over a period of 24 hours.

Prior to the measurements, volunteers were equipped with the Epionics SPINE system and were at first asked to perform a standardised short-term motion choreography in the sagittal plane. The choreography started with relaxed standing, from which volunteers performed maximal upper body flexion and extension, both with extended knees (Fig. 1B). This procedure was performed at the volunteers' preferred speed and was repeated five times. For guidance, the volunteers watched a video prior to the choreography that demonstrated and explained the exercises. After the STMs, the volunteers were released to their daily lives while wearing the system and were asked to return after 24 hours (described as LTM; Fig. 1C).

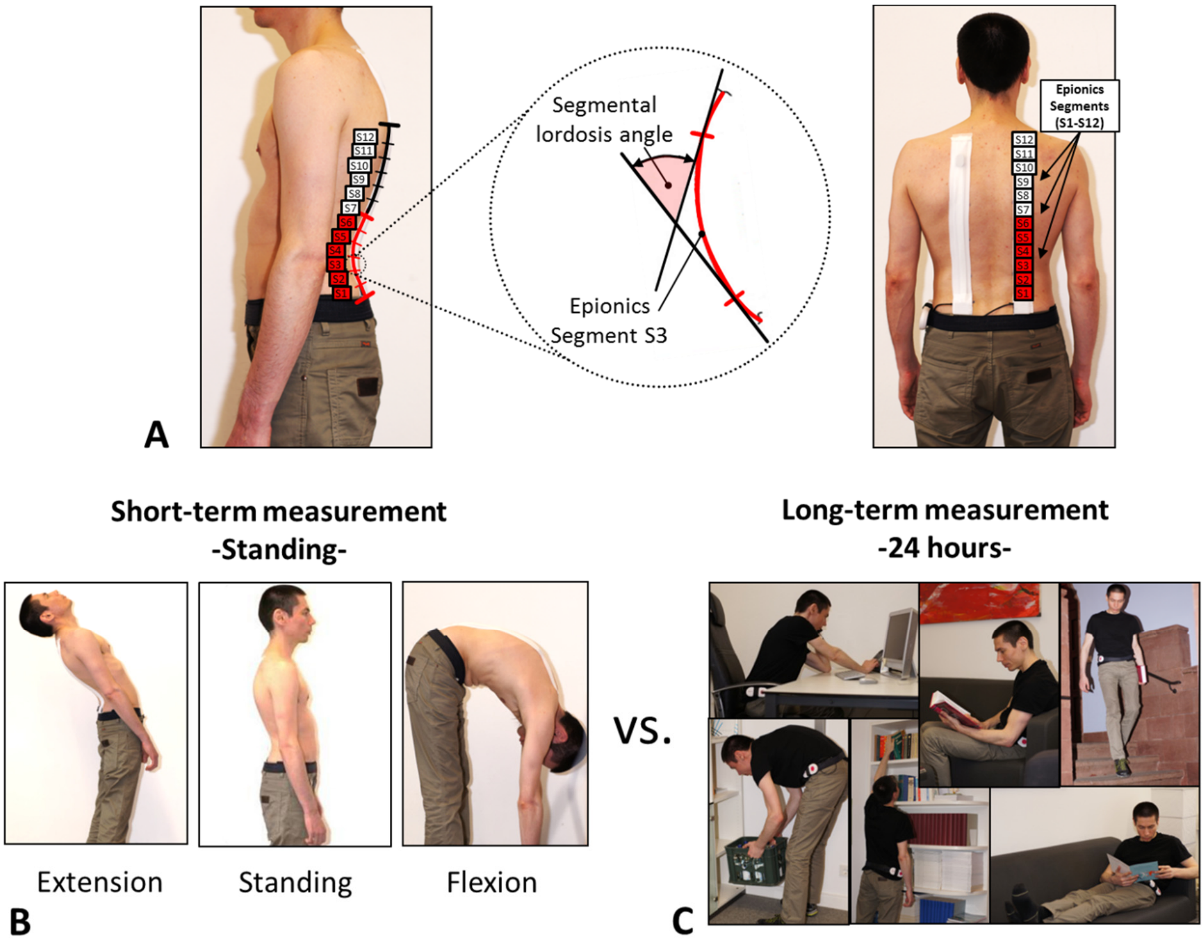

Figure 1: (A) Epionics SPINE system and the positions of the Epionics segments (S1-S12). On average, the first six Epionics segments covered the lumbar lordosis (shown in red) in the entire cohort. The definition of the determined segmental angle is shown for a single exemplary sensor unit (S3) in a schematic. **(B)** Measurements were conducted standardized in standing and in maximal upper body flexion and extension. **(C)** Subsequently, volunteers wore the device for 24 hours while attending to their daily lives.

2.5. Data collection

2.5.1. Standardised short-term measurement

All twelve Epionics segments were evaluated for upright standing and for upper body flexion and extension. During standing, the lordotic segments, which correspond to the lumbar spine region, were individually determined for each subject, and these segments served as the reference segments for further evaluations (Fig. 1A). All local angles of the reference segments were individually summed in the standing, maximal flexion and extension positions to determine the lumbar lordosis while standing as well as the lumbar curvature during maximal flexion and extension. The resultant range of flexion (RoF) and range of extension (RoE) were subsequently calculated as the angle differences from the standing reference. The values of the left and right sensor strip were averaged, and finally, the mean of the five repetitions was determined.

2.5.2. 24 hour long-term measurement

The data from each participant were collected over 24 hours from the Epionics segments, and the instantaneous lumbar lordosis was individually calculated for each time point (summing the local angles of the reference segments). Subsequently, the average lumbar lordosis during the day as well as the amount of time spent within a certain lordotic posture were calculated. In addition to the lordosis, the lumbar RoF and RoE during the day were calculated by subtracting the standing reference from the maximal and minimal angles, respectively, occurring during 24 hours.

All data were processed using in-house-developed MATLAB routines (MATLAB R2009b, MathWorks, Inc., Natick, MA, US.).

2.6. Statistical analysis

Descriptive statistics (mean and standard deviation) were analysed, and normal distribution was tested for each investigated age and gender group by using the Kolmogorov-Smirnov test. Furthermore, Levene’s test was used to test the equality of variances. The average lumbar lordosis and the RoF and RoE from short-term measurements were specifically compared to the corresponding values from the long-term measurements using paired t-tests. Additionally, a two-way analysis of variance (ANOVA) with the factors of age and gender and a post hoc analysis (Scheffé’s test) were performed separately for the STMs and LTMs to evaluate their effects on the lordosis, RoF and RoE. A *p-value* <0.01 was considered statistically significant. Data were analysed using SPSS 21.0 (SPSS Inc., Chicago IL, USA).

3. Results

3.1. Differences between short-term and long-term measurements for all participants

The lumbar lordosis in standing during STMs was on average 33.3° and differed significantly ($p<0.001$) from the average lordosis during 24 hours (8.0°) by approximately 25° (Fig. 2A) across the entire cohort. This difference between STMs and LTMs was significant in men and women (Fig. 3A) as well as in all the investigated age groups (Fig. 4A). During the day, the volunteers adopted various different lordotic postures (Fig. 1C, 2B) and spent only approximately 9% of the day in postures with a lumbar lordosis, which was within the range of 5° larger and 5° smaller than the lordosis determined in the standing short-term reference

(Fig. 2B; violet diagonal-striped area). Only approximately 1% of the day was spent in a lordosis more than 5° larger than during standing (Fig. 2B; horizontally striped area), and approximately 90% of the day was spent in a lordosis that was more than 5° smaller than the standing lordosis (Fig. 2B; vertically striped area).

The average RoF measured during 24 hours was significantly larger (~13%; *p<0.001*; Fig. 2C) than that during the standardised standing measurement, whereas the RoE was significantly smaller (~20%; *p<0.001*). These effects were also significant in men and women separately as well as in all the investigated age groups (Figs. 3C; 4C).

3.2. Effects of gender

In the STMs, men (32.5°) and women (33.8°) showed no significant differences in lordosis (*p=0.195*); however, women (9.3°) exhibited a slightly, but significantly, larger lordosis during long-term measurements than men (6.4°) (*p=0.002;* Fig. 3A). In both gender groups, the lordosis during the 24-hour period was highly variable (Fig. 3B), with similar average deviations between the STMs and LTMs in both genders (men: 26.1°; women: 24.5°).

The RoF was not affected by gender in either the STMs (*p=0.335*) or the LTMs (*p=0.107*). However, for both the STMs and LTMs, the RoE was significantly smaller in men than in women (STM: *p=0.001*; LTM: *p=0.009;* Fig. 3C).

3.3. Effects of aging

Whereas age significantly influenced the lordosis in the standing position (with 8.4° less lordosis in the oldest compared to the youngest age cohort; *p<0.001;* Fig. 4A), the loss of lordosis with aging based on the 24-hour measurement was small (3.0°) and not significant. In all the age groups, the lumbar alignment was highly variable during the day (Fig. 4B), with a tendency toward less variability with increasing age. This effect was also reflected by a smaller deviation between the average daily lordosis and the standing reference with increasing age (20-35 yrs: 27.7°; 35-50 yrs: 24.3°; >50 yrs: 22.3°; Fig. 3B).

In both the STMs and LTMs, the RoF and RoE were significantly reduced with aging (all *p*-values *≤0.001*; Fig. 4C). This reduction was more pronounced for the RoE and more evident in the LTMs.

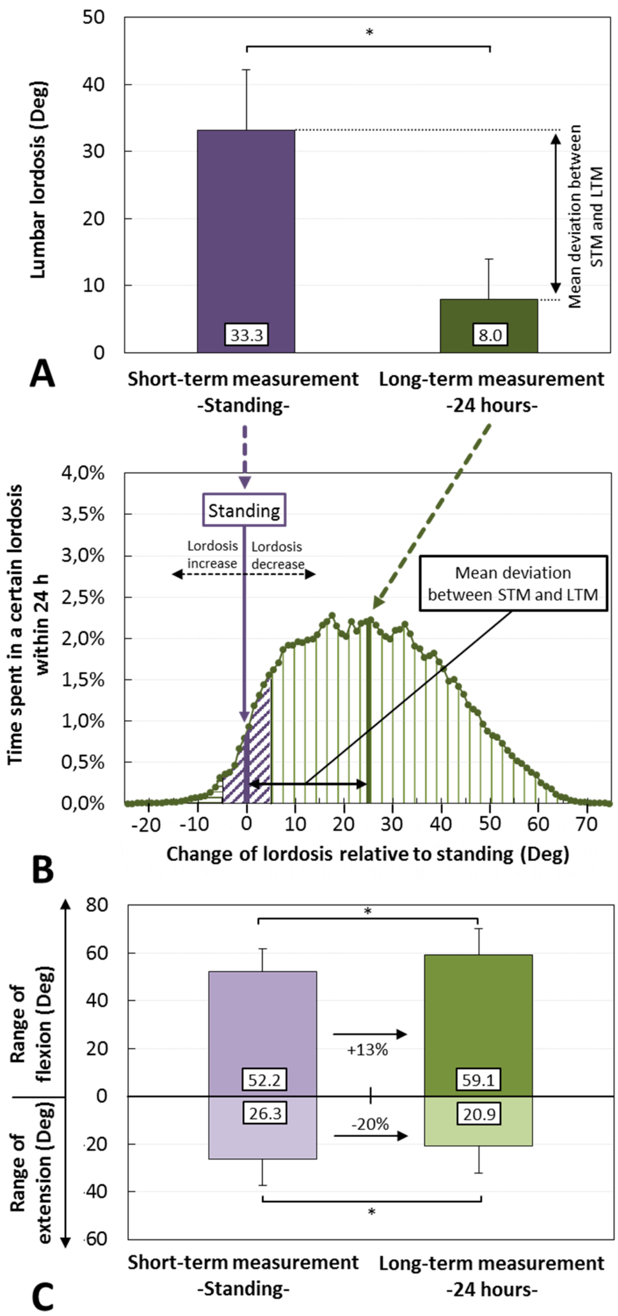

Figure 2: (A) Difference in average lumbar lordosis measured during the standardised short-term measurements (STMs) while standing and during the 24-hour long-term measurements (LTMs) for the whole cohort. **(B)** Time spent in a certain lordotic posture within 24 hours (average for all 208 volunteers). "0°" corresponds to the lumbar lordosis measured in standing. Values >0° indicate a reduced lordosis, and values <0° indicate an increased lordosis compared to standing. Approximately 9% of the daytime was spent in a lordosis range of ±5° compared to the lordosis measured while standing (violet diagonal-striped area). Approximately 1% of the day was spent in a lordosis more than 5° larger than that during standing (horizontally striped area), and 90% of the day was spent in a lordosis that was more than 5° smaller than the standing lordosis (vertically striped area). **(C)** Differences in the RoF and RoE between the short-term assessment (standardised flexion-extension choreography while standing) and the long-term assessment (24 hours).

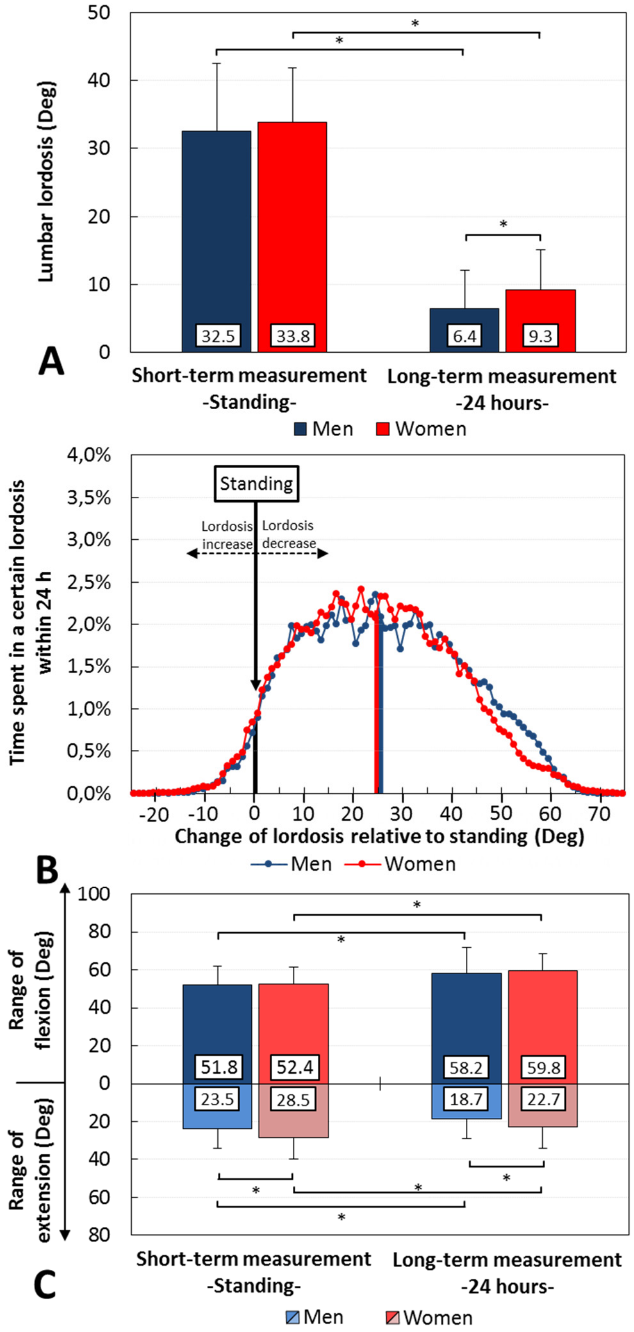

Figure 3: (A) Difference in average lumbar lordosis measured during 24 hours and during the standardised short-term measurements (STMs) while standing for males and females separately. **(B)** Time spent in a certain lordotic posture over 24 hours (average for males and females separately). "0°" corresponds to the lumbar lordosis measured in standing. Values >0° indicate a reduced lordosis, and values <0° indicate an increased lordosis compared to standing. **(C)** Differences in the RoF and RoE between the short-term assessment (standardised flexion-extension choreography while standing) and the long-term assessment (24-hour measurement) for males and females separately.

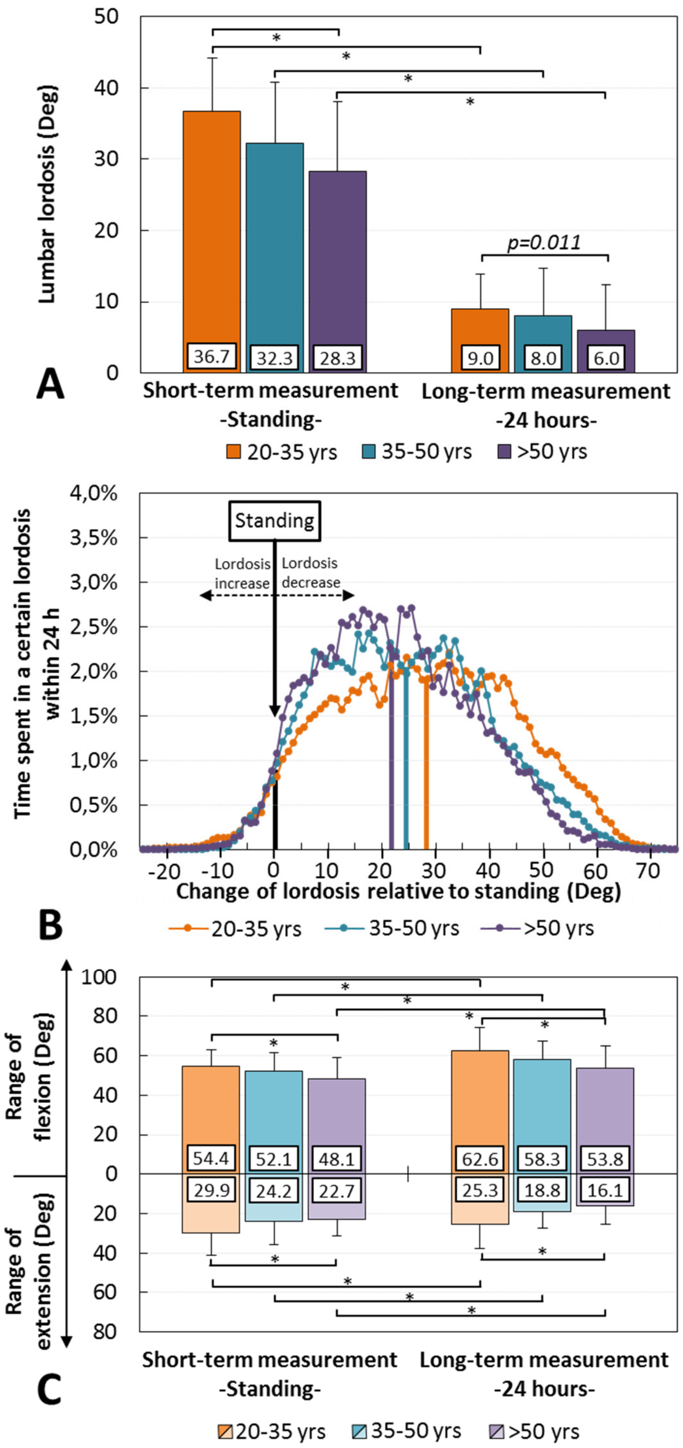

Figure 4: (A) Influence of age on the average lumbar lordosis measured during 24 hours and during the standardised short-term measurement (STM) while standing for all three investigated age groups. **(B)** Influence of age on the time spent in a certain lordotic posture within 24 hours (average for all three investigated age groups). “0°” corresponds to the lumbar lordosis measured while standing. Values >0° indicate a reduced lordosis, and values <0° indicate an increased lordosis compared to standing. **(C)** Influence of age on the RoF and RoE measured in the short-term measurements (standardised flexion-extension choreography while standing) and in the long-term measurements (24-hour measurement) for all the investigated age groups.

4. Discussion

The individual sagittal alignment and motion of the lumbar spine are elementary characteristics for the pathogenesis and treatment of LBP. However, the valid assessment of these parameters is limited to radiological short-term examinations, which offer only a "snap-shot" of the actual performance in "real-life". Until today, results of functional long-term measurements during daily life have not been reported. The present study reveals the actual sagittal alignment and motion of the lumbar spine throughout the entire day and shows that both parameters differed significantly from their corresponding values in short-term assessment. In particular, the average lumbar lordosis during the day is significantly smaller than that during the short-term measurements. Moreover, age and gender influence the lordosis and motion in the short-term measurement differently than they do during long-term measurement.

The radiologically assessed lumbar spinal alignment is "state-of-the-art" and plays an important role in the surgical planning of almost all instrumented spinal surgeries. To overcome the inherently large anatomical variability, recent studies have classified different anatomical parameters (e.g., pelvic incidence (Legaye et al., 1998) or sacral slope in Roussouly's classification (Roussouly et al., 2005)) to define a "well-balanced" radiologic sagittal alignment (Mac-Thiong et al., 2010; Vialle et al., 2005) with the aim of objectifying patient selection for a specific treatment as well optimising the surgical intervention (Pellet et al., 2011; Strube et al., 2013). All of these concepts employ radiographs of patients in a standing position and determine the lumbar lordosis as a single scalar value. However, the present study revealed that the lumbar lordosis is not a constant single value but rather is highly variable and on average significantly smaller during the day than what is observed in the standing "snap-shot". The current clinical aim of achieving a "balanced standing profile" might be reconsidered, as this profile only represents a minor fraction of the daily sagittal alignment in our sedentary society. The dominance of sitting postures during the day (Matthews et al., 2008), in particular in patients and the elderly, leads to a reduction in the lumbar lordosis over a wide range of time (Vaughn and Schwend, 2014). The resultant discrepancy after surgical treatment between the iatrogenically corrected spinal alignment, which is based on a radiographic "snap-shot" of an upright standing person, and the individual spino-pelvic complex in a prevailing sedentary posture may therefore induce additional mechanical stresses, in particular at the transition between treated and untreated segments (especially after multilevel deformity correction). This paradoxical situation might be a crucial contributor to long-term clinical failure. These results also question the meaningfulness of a classification of the sagittal alignment in a standing position. As a consequence, the present study supports the idea that a radiological evaluation in a sitting posture may be more appropriate for analysing sagittal alignment, as it is more comparable to the average daily posture.

As a basic requirement for the specific individualised evaluation and treatment of patients, the effects of age and gender on lumbar alignment and range of motion (RoM) have been investigated in numerous studies. In agreement with the majority of the literature (Boulay et al., 2006; Dreischarf et al., 2014; Dvorák et al., 1995; Gelb et al., 1995; Milne and Lauder, 1974), the lumbar lordosis while standing showed non-significant gender differences, but both lumbar lordosis and RoM were significantly reduced with increasing age. However, the results of the present study question the validity of the extrapolation of these findings to daily life, as these effects can substantially differ from corresponding effects obtained in long-term measurements. For instance, women showed a slightly but significantly larger lordosis than men did in the LTMs, which is in contrast to the results of the STMs. Furthermore, the influence of age on lumbar lordosis while standing diminished during the LTMs. In addition to age and gender effects, the results emphasise that the RoM differs significantly between LTMs and STMs. Therefore, a valid and meaningful evaluation of specific influential factors as well as of the individual patient's spinal function requires a long-term analysis of the patient's daily life.

The presented results have major implications for evaluating and developing an *in vivo* biomechanical understanding of spinal implants and adjacent native tissues after implantation as well as for performing in vitro or in silico investigations. Important radiological short-term measurements, such as those by Pearcy et al. (1984) or Dvorak et al. (1991), have provided insights into spinal motion during upper body bending while standing as well as essential reference values for various research fields. However, the present results reveal that during daily life, the RoF is approximately 13% larger than that during standard upper body flexion measurements. During flexion, this difference in RoF implies an overall more demanding loading scenario in vivo during the day than is usually assumed. Furthermore, the present results demonstrate that the lumbar spine is in a much more flexed position on average during daily life. However, this result indicates a substantially different "working point" during the day, a potentially different load direction and a different average loading (load sharing) of implants and adjacent spinal structures than are usually assumed. These essential details are not currently considered in computational model studies or *in vitro* tests of the lumbar spine. A functional X-ray analysis of patients in standing, flexion and extension is essential for the clinical examination and evaluation of the spinal curvature in the sagittal and coronal plane (e.g., for deformity surgery). The results presented herein offer a real-life perspective of lumbar lordosis and its motion only in the sagittal plane during various daily activities, and these results may help to better evaluate X-rays in comparison to daily life. However, in the present study, spinal shape was assessed via non-invasive measurements of back shape. These indirect measurements can thus not replace X-ray measurements in a clinical setting. Several studies have demonstrated a significant and strong correlation between back and spinal shape (Adams et al., 1986; Guermazi et al., 2006; Stokes et al., 1987); however, our own validation studies revealed a high correlation only in subjects with a BMI <26, which limits the investigation to normal-weight volunteers. The present study focused on asymptomatic subjects, although previous studies have emphasised specific differences in alignment and motion between patients with LBP and asymptomatic volunteers (Chaléat-Valayer et al., 2011). The current study can be regarded as a basis for a sophisticated analysis of patients with chronic LBP in future studies. Furthermore, in this study, motion was investigated in the sagittal plane only, although the motion of the lumbar spine in other main anatomical planes, such as during axial rotation and lateral bending, might also differ between LTMs and STMs. Precise segmental measurements of lumbar motion in other anatomical planes are currently not possible with the employed system. Furthermore, the current study focuses on the lumbar spine. During motion in the sagittal plane, the pelvis and thoracic spine also contribute to the overall motion; however, such parameters were not assessed in the current study. In general, it must be noted that short-term and long-term analyses each have important advantages and disadvantages. Short-term analyses under laboratory conditions are important because they provide controlled and standardized biomechanical analyses of a subject's activity as well as clearly interpretable data. In contrast, the long-term analyses of daily life cannot be interpreted as exactly because activity is not controlled and daily life is characterized by a variety of unstandardized activities. However, long-term measurements characterise the "real" behaviour of subjects and thus provide a 24-hour perspective on lordosis and spinal motion. Therefore, both approaches were performed in this study, and the results were compared. The investigated age and gender groups of the presented long-term analysis may differ with regards to occupational status and leisure activities. Therefore, based on a sample of 208 subjects, the measured values characterise only the average work and lifestyle aspects of these groups. Further differentiation with respect to the type of occupation or different parts of the day was not possible in this study.

In conclusion, currently utilised short-term radiological examinations ("snap-shots") differ from average "real-life" evaluations of lumbar alignment and motion during the day. Lumbar lordosis is not constant but rather is highly variable during the day, and on average, it is considerably smaller during the day than in the standing position. This basic knowledge might be important for surgical planning and potentially improve the understanding of the outcome of different interventions and of postoperative problems. Moreover, these results will increase the knowledge regarding the biomechanical challenges faced by spinal structures and implants in daily life. Furthermore, long-term assessments of spinal alignment and motion during daily life can provide valid results of spinal function and can reveal the importance of influential factors, such as the impact of aging and gender.

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2.6 Publication 6: Measurement of the number of lumbar spinal movements in the sagittal plane in a 24-hour period

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Abstract

Purpose: Little is known about the number of spinal movements in the sagittal plane in daily life, mainly due to the lack of adequate techniques to assess these movements. Our aim was to measure these movements in asymptomatic volunteers.

Methods: Two sensor strips based on strain gauge technology (Epionics SPINE system) were fixed on the skin surface of the back parallel to the spine on a total of 208 volunteers without back pain. First, the lordosis angle was determined during relaxed standing. The volunteers were then released to daily life. The increases and decreases in the back lumbar lordosis angle over a period of 24 hours were determined and classified into 5° increments. Changes in the lordosis angle greater than 5° were considered.

Results: The median number of spinal movements performed within 24 hours was approximately 4400. Of these movements, 66% were between 5° and 10°. The proportions of higher-magnitude lordosis angle changes were much lower (e.g., 3% for the 20-25° movement bin). Surprisingly, the median total number of movements was significantly higher (29%) in women than in men. Large inter-individual differences were observed in the number of movements performed. The volunteers spent a median of 4.9 hours with the lumbar spine flexed between 20° and 30° and only 24 minutes with the spine extended relative to the reference standing position. A median of 50 full-flexion movements and zero full-extension movements were recorded.

Conclusions: These data illustrate the predominantly small range of movement of the spine during daily activities and the small amount of time spent in extension. These unique data strongly contribute to the understanding of patients' everyday behavior, which might affect the development and testing of spinal implants and the evaluation of surgical and nonsurgical treatments.

Introduction

The lumbar spine tolerates a large range of motion (RoM) in the sagittal plane [1, 2]. The RoM of the lumbar segment may be of clinical utility for distinguishing healthy subjects from those with spinal disorders. Therefore, the measurement of mobility in clinical practice is of great importance to the functional assessment of patients with back pain and the evaluation of rehabilitation efficiency [3].

In addition to the RoM, the frequency of specific movement patterns during daily activities is of great importance for characterizing the level of activity of patients or the status of a disease such as back pain. Surprisingly, no normative data on the number of certain flexion and extension movements of the lumbar spine are available for asymptomatic, healthy populations. Such data could serve as a benchmark level of activity for comparison with patients suffering from spinal pathologies or as a means of comparing activity levels prior to and after back pain therapies. In addition, this knowledge is of paramount importance for the development of novel therapies for patients suffering from spinal pathologies, such as implants, for which realistic movement data are lacking, and for tissue regeneration studies after back pain therapy (simulation of tissue remodeling or nutrient processes that require a physical stimulus). Knowledge about the number of large movements is also needed for the development and testing of spinal implants. Furthermore, the number of movements might play a significant role in fatigue failure in the aging and degeneration processes of spinal structures and, consequently, the risk of developing low back pain. However, the number and range of lumbar spinal movements performed in daily life are unknown.

Several treatment strategies are utilized in clinical and physiotherapeutic practice to treat patients with low back pain, with varying degrees of effectiveness. Most studies have concluded that active exercises are a valuable therapeutic approach in managing low back pain, despite a lack of consensus on optimal exercise techniques and intensity [4]. However, the amount of physical activity engaged in by healthy individuals remains unknown. How much motion does the lumbar spine undergo in everyday life? “Long-term” motion data, (i.e., the number and extent of lordosis-angle changes in an asymptomatic, healthy population) could be used to improve existing therapies or to develop novel strategies to better treat individuals with back pain caused by a lack of physical activity.

Several devices (e.g., pedometers, actibelts) enable the determination of the frequency of some activities, such as walking and stair climbing, over several hours, without significant restrictions for the subject [5-7]. The number of spinal movements in the back has been measured under laboratory conditions with stationary subjects [8] or at worksites using portable sensors such as 3D-SpineMoveGuard [9-11]. However, no data exist regarding the number of spinal movements during daily activities measured over a period of 24 hours. A device that allows measurements over a longer period is required to establish a database of data on movements and their frequencies and would allow population-based studies of spinal kinematics in healthy subjects.

Therefore, the present study aimed to measure people's spine movements in typical day-to-day life. The device used in this study was based on advanced strain-gauge technology (Epionics SPINE, Epionics Medical GmbH, Potsdam, Germany) and allowed the long-term measurement of back shape in the thoracolumbar spine region. The activities of the subjects were nearly unrestricted by the system. The number of different magnitudes of lordosis angle changes was measured in asymptomatic volunteers over a period of 24 hours. The effects of sex, age, and body mass index (BMI), as well as the time the volunteers spent in certain positions, were determined.

Material and Methods

Measurement system

The measurement system Epionics SPINE consists of two flexible sensor strips, two tri-axial accelerometers, and a small storage box (Fig. 1). The storage box has a total weight of 120 g. Each sensor strip has 12 predetermined 25-mm-long segments, which measure the segment angles at a frequency of 50 Hz using strain-gauge technology. The accelerometers are located at the lower end of the sensor strips and measure the sensor's orientation in relation to the earth's gravitational field. The sensors are connected to the storage and power unit. Under laboratory conditions, the measurement accuracy is approximately 0.5° for the complete system (unpublished data from the manufacturer). The sensor strip exhibits a high repeatability (ICC>0.98), with test-retest reliability ICCs of >0.98 [12].

The sensor strips were inserted in special hollow plasters glued to the volunteers' backs to the right and left of the spine at a mid-line-distance of 15 cm. The most caudal sensor was placed at a standard location at the level of the posterior superior iliac spine.

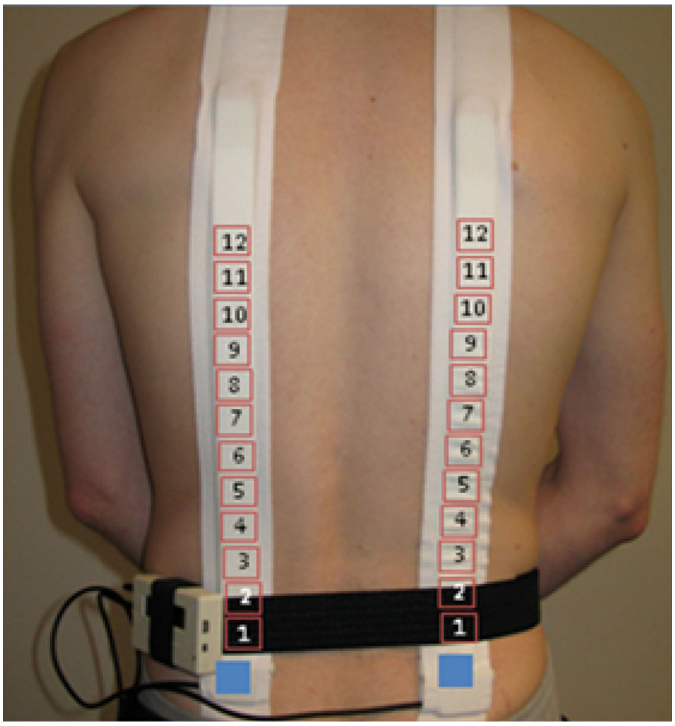

Figure 1: *Epionics SPINE system with numbered sensor segments (red squares) and acceleration sensors (blue). (from Consmüller et al. [13])*

Subjects

This study is related to a previously published study on the measurement of lumbar spine posture and range of motion [13] that included 429 volunteers. These volunteers did not suffer from back pain in the previous 6 months and had never undergone spine surgery [13, 14]. In a subgroup of 208 volunteers with a BMI up to and including 26 kg/m², back shape was also successfully measured over a period of slightly longer than 24 hours. The median age of that group was 39.0 years (range 20 to 74 years).

Ethics statement

The study was approved by the local Ethics Committee (registry number EA4/011/10). All subjects were informed about the details of the procedure and the scientific research purpose of the measurements. Subjects provided written informed consent to participate.

Measurement protocol

The volunteers were equipped with Epionics SPINE and then asked to perform a short sequence of choreographed exercises such as maximum upper body flexion and extension while standing with extended knees, left and right lateral bending, and left and right axial rotation. Each exercise was performed five times, with upright standing as a reference position. Prior to the exercises, each volunteer was shown a video clip of a person performing the exercises to standardize the respective movements. After this choreographed sequence, the volunteers were released to their daily life; the only restriction was not to bathe or shower. After slightly more than 24 hours, the volunteers returned, the device was removed, and the measured data were stored on a PC. The starting time for the measurements varied between 8:00 am and 5:00 pm.

Data analysis

First, the thoracolumbar lordosis angle (LA) of the back was determined for a standing posture. During the short choreographed sequence, the relaxed standing position was adopted up to 6 times, and the median LA for this posture was chosen as a reference value. The entire LA was calculated as the sum of the segment angles starting from the most caudal sensor strip segment to the first segment with a different sign (transition from lordosis to kyphosis). Thus, the system includes all individual lumbar spinal levels, which can be different from volunteer to volunteer because the amount of lumbar lordosis as well as the inflection point from lordosis to kyphosis can differ in asymptomatic subjects [15]. The approximate spinal levels included in the lumbar lordosis angle were usually T12 to S1. The data from the corresponding left and right sensor segments were averaged because they should deliver similar results due to symmetry [13]. The LA was calculated from these data for each volunteer, and this position was defined as the reference position. The measured segments that define the LA during standing were also used for calculating the LA changes during the long-term measurements.

For each volunteer, exactly 24 hours of data (4.32 million frames) were evaluated to determine the number of movements. The recorded row data from the sensor strips were filtered using an eighth-order low-pass Butterworth filter with a cut-off frequency of 5 Hz to eliminate noise. During daily activity, many different movements in the sagittal plane are possible, but not all movements started from the reference position. Flexion of the lumbar spine is characterized by a decrease in the LA relative to the reference position, and extension is characterized by an increase [16]. However, the LA may change in either direction when the spine is already flexed or extended. A LA vs. time (24 hours) curve was created, and all local maxima and minima were determined. Then, internally developed MATLAB routines were used to determine the positive or negative changes in the LA at each time point. Only movements greater than 5° were counted, and only the maximum value for a movement after moving in the opposite direction by at least 5° was counted. Increment ranges of LA with an interval of 5° were defined, and the measured changes in the LA were assigned to the corresponding bins. Thus, two histograms were created representing increases and decreases in the LA. By selecting and comparing the corresponding subgroups, the effects of sex, age, and BMI on the number of movements were determined. Of the 208 volunteers (115 female, 93 male), 92 subjects were 20 to 35 years old, 74 subjects were 36 to 50 years old, and 42 subjects were 51 to 75 years old. The median BMI of the subjects was 22.6 kg/m² (range 17 to 26 kg/m²).

The number of movements within the flexion region of the lumbar spine and the number of movements within the extension region over 24 hours were also determined. The flexion region of the lumbar spine was defined as the region in which the lumbar spine flattened relative to the reference position or even became kyphotic. The complimentary region in which the magnitude of the LA increased relative to the LA for the reference standing position was defined as the extension region. Furthermore, the number of movements starting from and returning to the reference LA (±5°) was determined for bin sizes of 10°. The amount of time the volunteers spent within a certain range of the LA with respect to the reference position was also calculated.

Most of the measured data were not normally distributed, and the studied subgroups were of unequal size. Therefore, the Mann-Whitney U test (for gender) and the Kruskal-Wallis non-parametric one-way analysis of variance method (for age) were applied to determine if the subgroups originated from the same distribution. A Bonferroni post-hoc test was applied to identify age subgroups that differed significantly. A significance level of 0.01 was employed for all tests.

Lower angular limit of movement measurement

To estimate the lower angular limit of movement measurements in volunteers, the number of movements in the lumbar spine with increasing or decreasing LA within 24 hours was counted from 1° to 15°, with a bin sizes of 1°.

Results

None of the volunteers exhibited signs of an allergic reaction to the plasters.

24-hour movement profiles

Figure 2 depicts the deviation from the reference LA measured over a period of 24 hours for 5 subjects. The resting periods are clearly recognizable by the reduced number of changes in the LA. Please note the differences in activity levels and motion ranges within and between subjects.

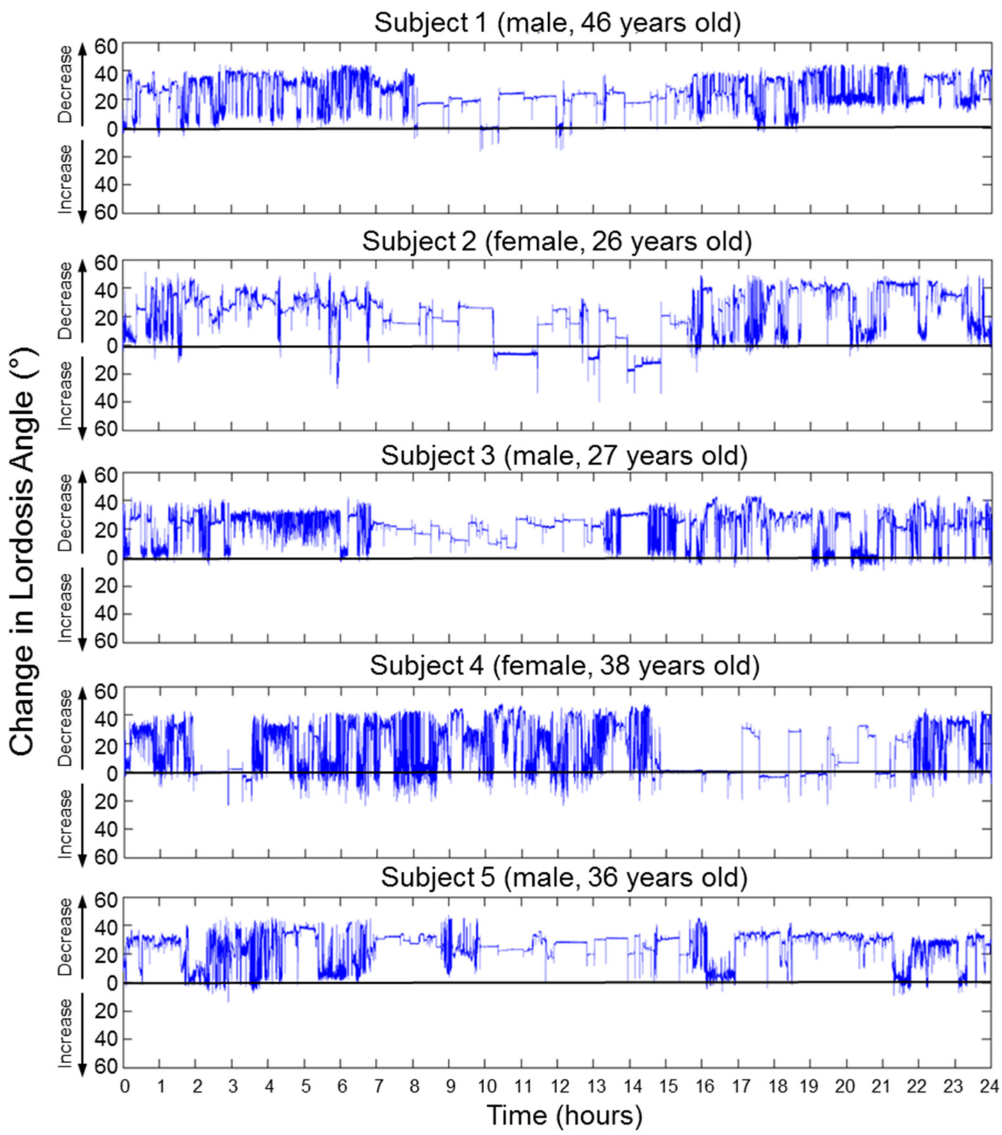

Figure 2: Five examples of the change in the magnitude of lordosis angle (LA) over 24 hours. The difference between the measured LA and the reference LA for a relaxed standing position is shown. The 'zero hour' could range between 8 am and 5 pm. Zero degrees refers to a relaxed standing position.

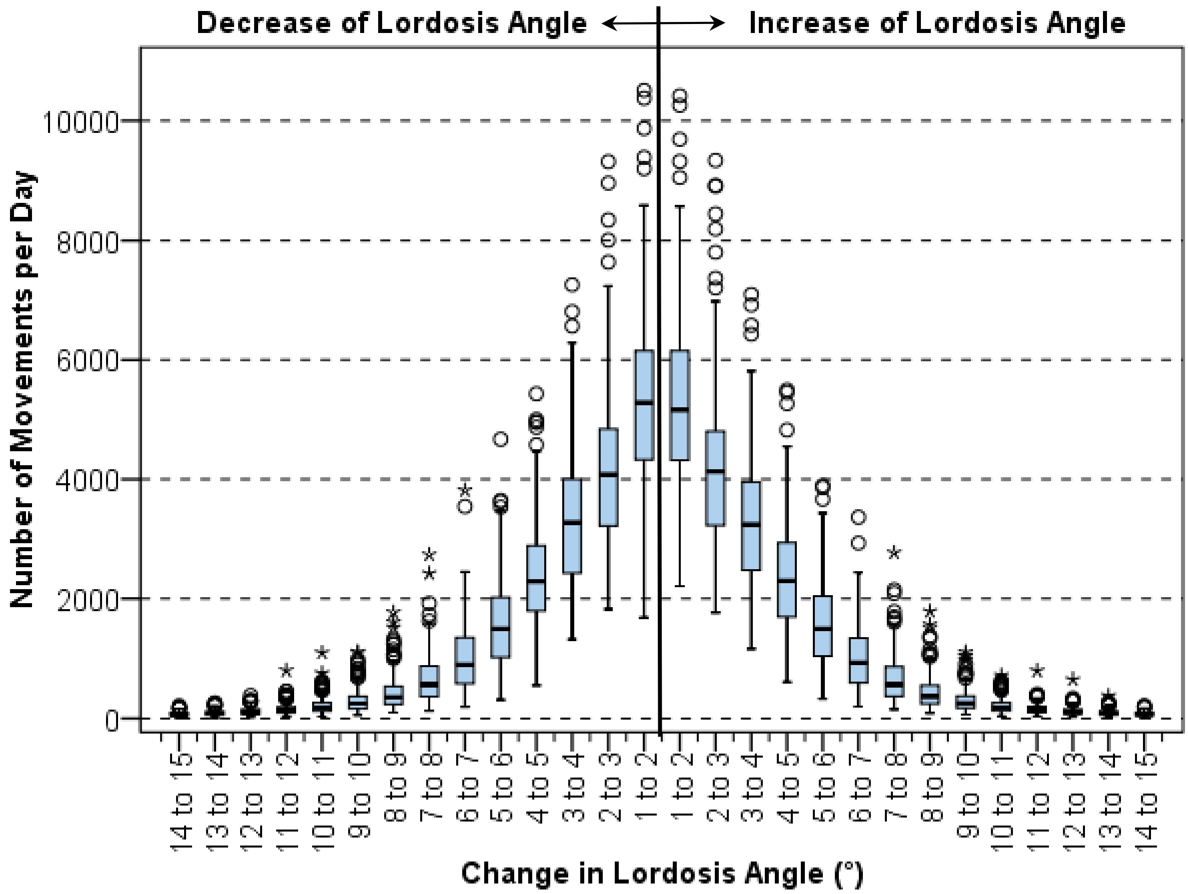

Figure 3: Number of movements with changes in the lordosis angle up to 15° and a bin size of 1° over a period of 24 hours. Please note that the changes in lordosis angle are all relative to the previous position or posture and are not relative to erect standing. The whiskers of the box-plots represent the extreme values or the 1.5 interquartile ranges. Outliers are shown as circles (up to 3 times the interquartile range) or stars (greater than 3 times the interquartile range)

Lower limit of movement measurement

Over 24 hours, the participants performed, on average, nearly identical numbers of movements in the different motion ranges for increases and decreases in the LA (Fig. 3). Therefore, for the sake of simplicity, only the values representing an LA increase are presented. Although the data for the motion ranges of 1° to 5° appeared very reasonable, we considered the detection of movements of less than 5° by the measuring system to be unreliable for a long-term study.

Number of movements associated with a change in LA

The median total number of movements with an LA change greater than 5° was approximately 4400 (range 1248 to 13029) within 24 hours. Most of these movements (66%) were very small, with LA changes of 5° to 10°, and the median number of these movements was approximately 2915 (range 741 to 9897) (Fig. 4). Larger changes in the LA occurred less often. The median number of LA changes between 10° and 15° was 17% of the total number of movements, and the median number of LA changes between 15° and 20° was 6%. The median number of LA changes of greater than 45° was 21 for a period of 24 hours. For the various movement bins, the data for the changes in the LA were not normally distributed. Median values of LA changes were 51.9° (19° to 74°) for full flexion and 25.1° (3° to 62°) for full extension. The median value of LA during standing was 33.8° (4° to 57°). On average, full flexion was reached or exceeded 50 times (0 to 805). The value for full extension was 0 times (0 to 84).

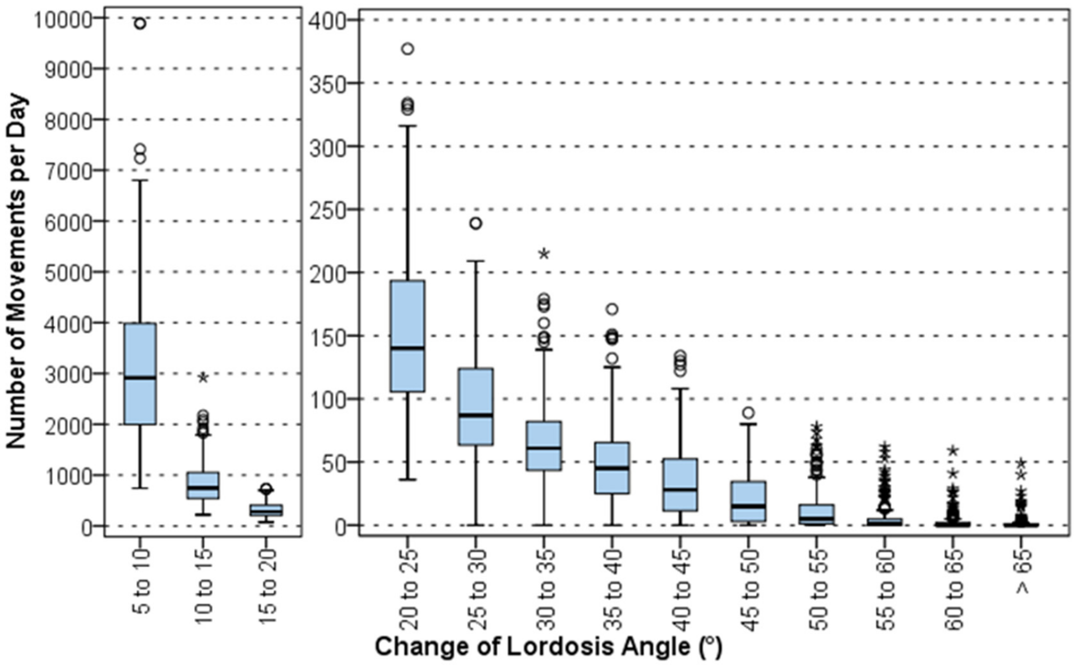

Figure 4: Number of movements with an increase in the lordosis angle measured over 24 hours in 208 volunteers. Please note that the changes in lordosis angle are all relative to the previous position or posture and are not relative to erect standing. An approximately equal number of additional movements were made in which the angle was decreasing. Note the different scales for the number of movements. The whiskers of the box-plots represent the extreme values or the 1.5 interquartile ranges. Outliers are shown as circles (up to 3 times the interquartile range) or stars (greater than 3 times the interquartile range)

The median number (num) of movements in a 5° bin can be estimated by using the following exponential equation:

$$num = a \cdot e^{b \cdot LA} + c \cdot e^{d \cdot LA} \quad (1)$$

where a=31,200, b=-0.3376, c=798.3, d=-0.08104; and R^2=0.9999. LA represents the mean value for the lordosis angle range in degree units, with an interval of 5°.

Effect of BMI

The BMI, which ranged from 17 to 26 kg/m², did not have a significant effect on the number of LA changes in either men or women.

Effect of sex

Generally, women performed significantly more movements than men (Table 1, Fig. 5). Overall, the median number of movements was 4978 for women and 3846 for men, representing a 29% greater number of movements by women. The influence of sex on the number of movements was significant for LA changes between 10° and 40° and for the total number of movements. The median number of movements for the various movement bins with more than 10 movements was, on average, 41% higher for women than for men (Table 1).

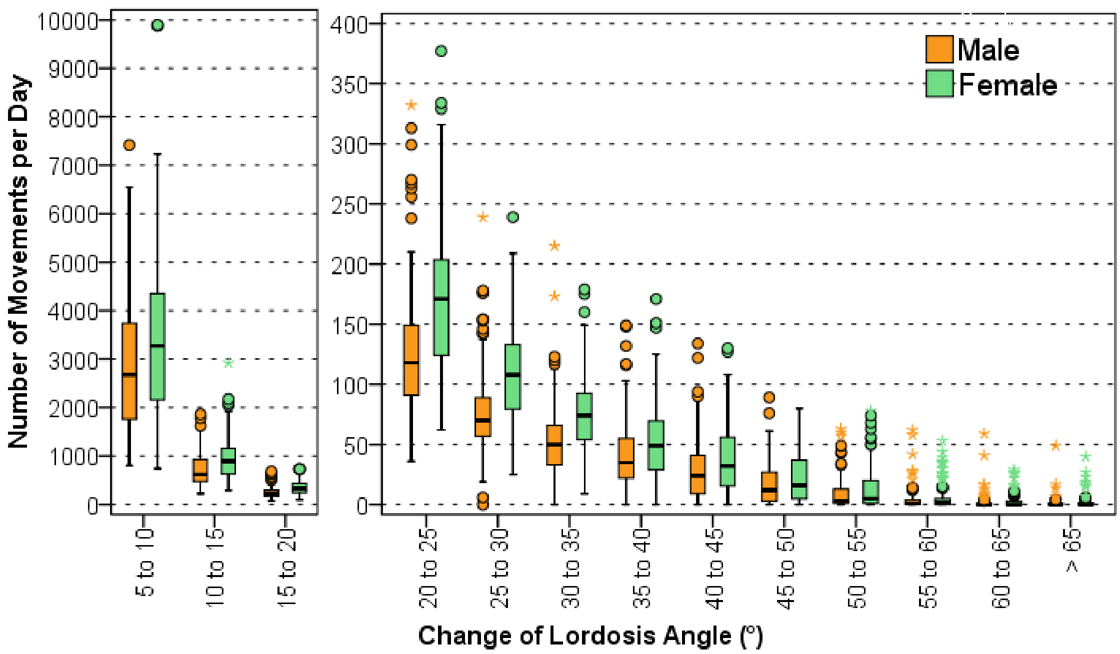

Figure 5: Effect of gender on the number of movements with an increase in the lordosis angle. An approximately equal number of additional movements were made in which the angle was decreasing

Table 1 Median number of movements for various movement bins depending on gender and calculated *p*-value

Change in LA	Gender		%-difference	*p*-value (Mann-Whitney U-Test)
	Male	Female		
5° to 10°	2677	3273	22.3	0.011
10° to 15°	615	891	44.9	**<0.001**
15° to 20°	226	335	48.2	**<0.001**
20° to 25°	118	171	44.9	**<0.001**
25° to 30°	70	108	54.3	**<0.001**
30° to 35°	50	74	48.0	**<0.001**
35° to 40°	35	49	40.0	**0.002**
40° to 45°	24	32	33.3	0.028
45° to 50°	12	16	33.3	0.102
50° to 55°	3	5	66.7	0.306
5° to 65°	3846	4978	29.4	**<0.001**

LA = lordosis angle; **bold:** *p*-value < 0.01

Effect of age

Age had only a minor effect on the number of movements, although the median value was mostly lower for the oldest age group than for the youngest one (Fig. 6). The Bonferroni post-hoc test indicated that age had a significant influence on the number of movements in men only for LA movement bins of 10° to 15°, 15° to 20° and 45° to 50° (Table 2). For women, the effect of age was not significant.

Table 2 Median number of movements for various movement bins classified by gender and age and with calculated *p*-values.

Male				
	Age (years)			
Change in LA	20 to 35	36 to 50	51 to 74	*p*-value (Kruskal-Wallis Test)
5° to 10°	3030	2244	1759	**0.009**
10° to 15°	716	544	472	**<0.001**
15° to 20°	258	214	169	**0.005**
20° to 25°	122	106	115	0.273
25° to 30°	72	71	68	0.392
30° to 35°	52	54	32	0.036
35° to 40°	45	36	18	**0.008**
40° to 45°	28	23	6	**0.005**
45° to 50°	22	11	2	**<0.001**
50° to 55°	9	3	0	**0.001**

Female				
	Age (years)			
Change in LA	20 to 35	36 to 50	51 to 74	*p*-value (Kruskal-Wallis Test)
5° to 10°	3623	3212	2308	0.013
10° to 15°	965	872	685	**0.007**
15° to 20°	365	330	300	0.462
20° to 25°	171	172	171	0.918
25° to 30°	99	114	112	0.391
30° to 35°	68	77	71	0.113
35° to 40°	49	59	42	0.115
40° to 45°	36	40	16	0.023
45° to 50°	25	16	8	**0.008**
50° to 55°	10	5	1	**0.009**

LA = lordosis angle; **bold**: *p*-value < 0.01

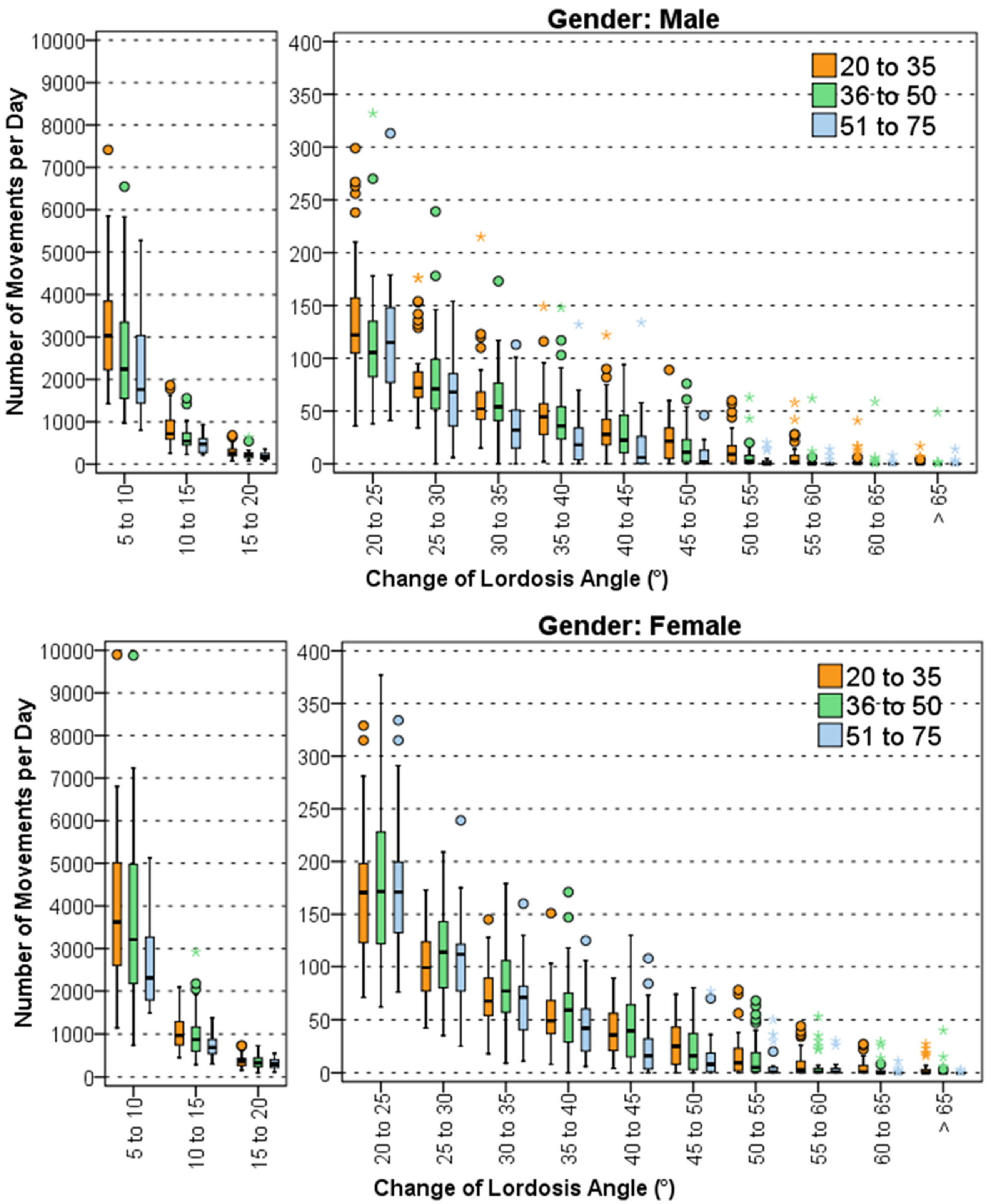

Figure 6: Effect of age on the number of movements with an increase in the lordosis angle. An approximately equal number of additional movements were made in which the angle was decreasing. The data for men and women are shown in the upper and lower halves, respectively. The *p*-values are based on a Bonferroni post-hoc test.

Time spent within different LA ranges

Figure 7 shows the time spent within various ranges of LA changes. On average, less than 2% (24 minutes) of the 24 hours was spent with the lumbar spine extended relative to the reference LA. Most of the time (20.3% or 4.9 hours of the day) was spent in the flexion region, with an LA change of 20° to 30° relative to the reference LA. A total of 63% of the day (15.1 hours) was spent in the lumbar flexion region with an LA change of 10° to 40°, and 94% of the day (22.6 hours) was spent between 0° and 50°.

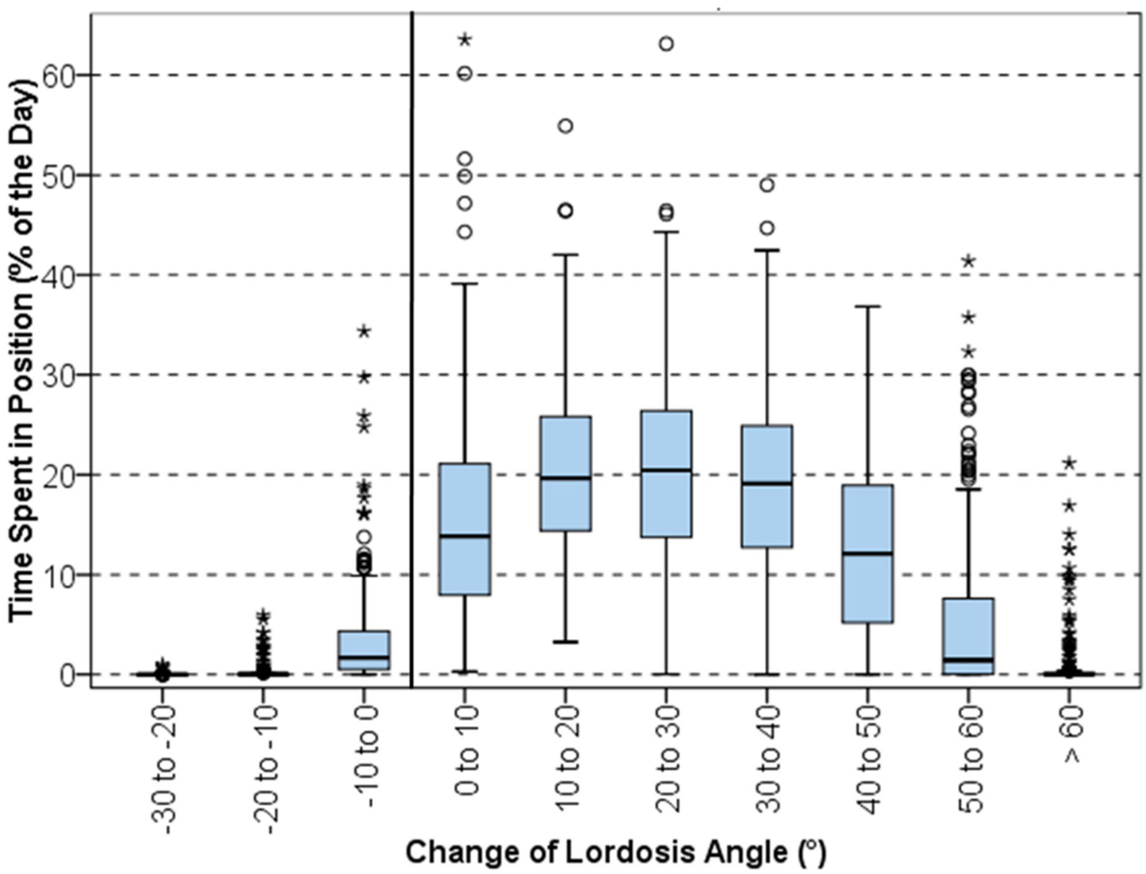

Figure 7: Time spent in various bins of changes in the lordosis angle within 24 hours. The changes from the reference position (vertical line) are given for 208 volunteers.

Number of movements starting from the reference LA

Compared to the total number of movements, few movements started from and returned to the reference LA ± 5° (Fig. 8). A median of 580 movements were in the range between 5° and 15° flexion. The second highest median value was only 77 movements for the 15° to 25° movement bin. Flexion movements from the erect standing position were much more frequent than extension movements for all groups of subjects.

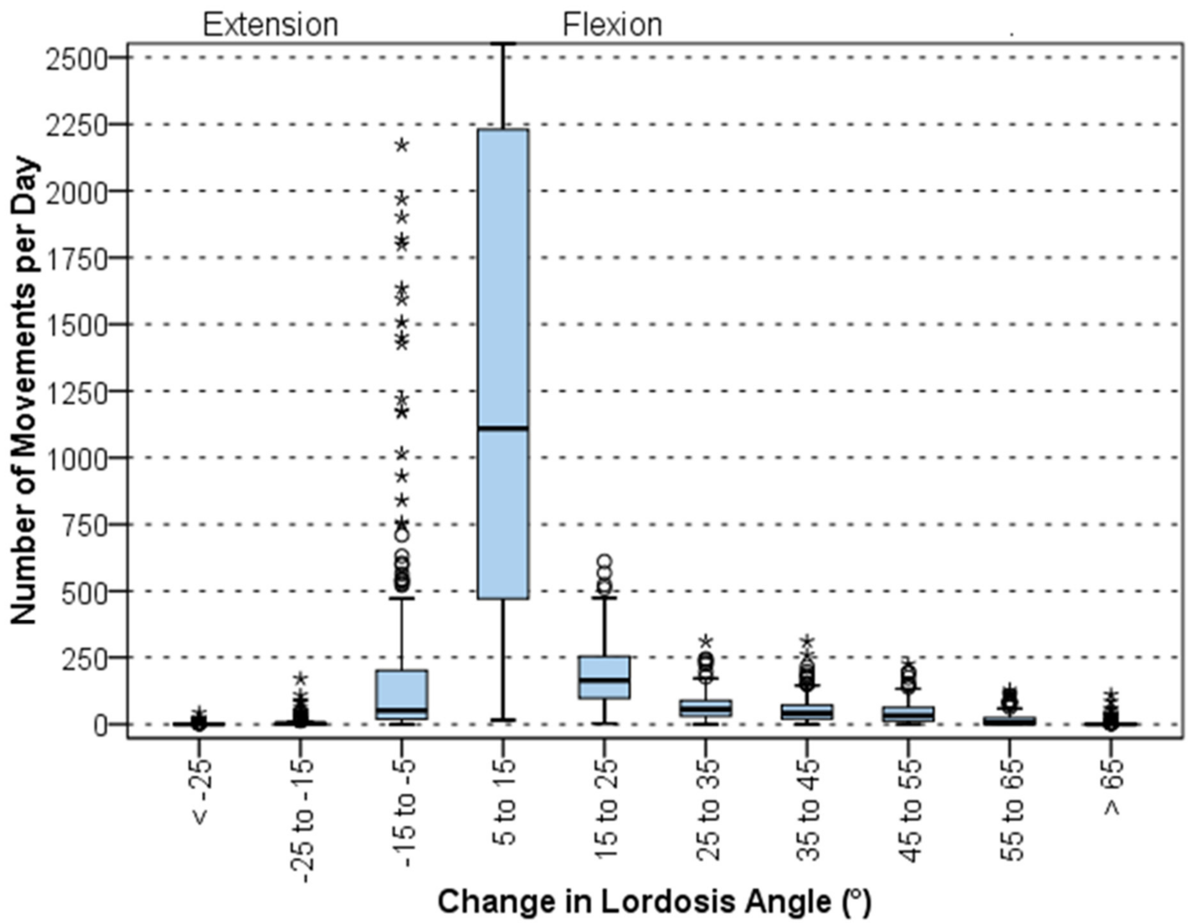

Figure 8: Number of movements starting from and returning to the reference lordosis angle (±5°) measured over 24 hours in 208 volunteers. For the movement bin 5° to 15°, the upper range value was 4850 movements, and the maximum outlier in this bin was 9069 movements.

Discussion

Low back pain and its prevention are highly relevant clinical concerns in aging societies in industrialized countries. Movement and activity are essential to maintain function and structure and to avoid low back pain. However, little is known about the normal activities in asymptomatic individuals and in subjects suffering from back pain. The objective of the present study was to investigate the number and extent of lumbar LA changes in asymptomatic healthy volunteers over a period of 24 hours. Our long-term aim is to establish a database of spinal activity patterns to enable the differentiation of subjects with and without motion pathologies to improve the efficiency of rehabilitation programs.

To be conservative, we established a threshold value of 5° for the entire lumbar spine when counting movements, although the data for the 1° to 5° range also appeared reliable. In some individuals, breathing while lying in a prone position generated a change in LA of approximately 4°. During walking, the change in the LA was usually less than 5°.

The number of different LA changes was measured over 24 hours in 208 asymptomatic volunteers. The numbers of movements leading to an increase in the LA were nearly equal to those leading to a decrease in the LA. This result implies that, on average, the magnitude of forward bending movements was the same as that of backward bending movements. However, the number of movements in the flexion region (LA smaller than the LA for the reference standing position) was much higher than that in the extension region. Furthermore, much more time was spent with the lumbar spine flexed relative to the reference standing position than extended. The average overall time during which the lumbar spine was extended was only 24 minutes. High facet-joint compressive forces in the lumbar region are frequent during extension [17-20]. However, the accumulated duration of high facet-joint forces was minor. The numbers of movements, the various starting points of these movements, and the time spent in the various positions must be considered, particularly when studying the behavior of a spinal implant.

On average, women performed significantly more spinal movements than men did. This finding is in contrast to the number of steps taken per day. Bassett et al. [5] measured physical activity in U.S. adults using a pedometer and observed greater numbers of steps for males than for females (5340 vs. 4912 steps per day), with the exception of the age group 60+ years. The mean number of steps per day in that study was 5117, which is much higher than the number of movements in the spine (4400 per day) counted in the present study. Similar results for the number of steps per day were obtained for a Japanese population, although the activity level of the Japanese population was higher [21]. In that study, men took, on average, 7321 steps per day, compared to 6267 steps per day by women. Generally, the steps per day were lower in the older age groups, while the 40- to 49-year-old age group took a similar number of steps per day, or even more steps per day, compared to the youngest (18 to 29 years old) age group.

The number of movements was relatively high (approximately 2915) for small LA changes but much lower for larger LA changes. The number of movements starting from the reference LA was much lower than the number starting from other positions. The outliers in Fig. 8 for small-flexion movements were most likely caused by volunteers who were jogging on that day. During sitting and lying, the LA usually differs from the reference LA for relaxed standing, but during standing, many movements also start from a position other than the reference LA position. This pattern should also be considered when spinal implants are preclinically tested. Because most of the time the lumbar spine is flexed, starting the testing from a flexed position should be considered. The magnitude of deformation could also vary. Extrapolating our data to 1 year, we identified an average of more than 1,000,000 movements between 5° and 10° but fewer than 8,000 movements greater than 45°.

Subjects with a BMI higher than 26 kg/m² were not included in the present study because the effect of bias by thick soft tissue at the level of the lumbar spine could not be excluded. This factor was of particular concern in the case of women with a BMI higher than 30 kg/m², in whom the back shape differs from the spinal shape. Surprisingly, when we included subjects with a BMI higher than 26 kg/m², we did not observe a significant influence of the BMI on the number of movements; however, further studies are needed to evaluate the exact BMI values for which the system delivers reliable results.

The changes in the LA were measured in the thoracolumbar region on the back and not directly in the spine. A direct measurement of the number of spinal movements during a day is not yet possible. However, the number of back-shape changes can be measured. Spinal-shape changes almost always result in changes to the back shape. Stokes et al. [22] compared surface and radiographic lumbar spinal motion measurements and found a correlation coefficient of 0.58. Using an electronic inclinometer for measuring lumbar curvature, Adams et al. [23] found a correlation coefficient of 0.91 between inclinometer recordings and flexion angles measured from x-rays. Due to the soft tissue between the spine and skin, the magnitude of spine and back motions may differ even from subject to subject. However, the first results of an ongoing study indicate that there is a good correlation between the LA measured with the Epionics SPINE system and the radiologically determined Cobb angle.

Only the changes in the lumbar LA were evaluated in the present study because in the sagittal plane, the angular deformations of the thoracic spine are small compared with those of the lumbar spine [13]. In addition to pure movements in the sagittal plane, movements with superimposed lateral bending or axial rotation were also counted.

The starting time of the measurements varied between 8 am and 5 pm. Thus, diurnal variations in the spinal shape during standing and in the ranges of flexion and extension may have had a small effect on the numbers of movements that started from and returned to the relaxed standing position (Fig. 8).

In conclusion, for the first time, the number of different changes in the LA has been measured in a large cohort over a period of 24 hours without motion restrictions of the subjects. A comparison of these data with those for patients suffering from back pain may provide deeper insights into patient pathology. These data will also be very important for designing and testing spinal implants, evaluating various surgical procedures, and simulating tissue remodeling and nutrient processes that require a physical stimulus.

The foundation for a database of spinal kinematics has now been established. Future studies should investigate population-based differences, changes in subjects with specific back pain or spinal disorders, and the effects of therapies. This information would further enhance our ability to diagnose spinal pathologies and disorders and to improve prevention and rehabilitation interventions.

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2.7 Publication 7: Comparison of Eight Published Static Finite Element Models of the Intact Lumbar Spine: Predictive Power of Models Improves When Combined Together

Dreischarf M, Zander T, Shirazi-Adl A, Puttlitz CM, Adam CJ, Chen CS, Goel VK, Kiapour A, Kim YH, Labus KM, Little JP, Park WM, Wang YH, Wilke HJ, Rohlmann A, Schmidt H

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This publication is only a supplementary study to this thesis and not part of the evaluation.

Abstract

Finite element (FE) model studies have made important contributions to our understanding of functional biomechanics of the lumbar spine. However, if a model is used to answer clinical and biomechanical questions over a certain population, their inherently large inter-subject variability has to be considered. Current FE model studies, however, generally account only for a single distinct spinal geometry with one set of material properties. This raises questions concerning their predictive power, their range of results and on their agreement with *in vitro* and *in vivo* values.

Eight well-established FE models of the lumbar spine (L1-5) of different research centers around the globe were subjected to pure and combined loading modes and compared to *in vitro* and *in vivo* measurements for intervertebral rotations, disc pressures and facet joint forces.

Under pure moment loading, the predicted L1-5 rotations of almost all models fell within the reported *in vitro* ranges, and their median values differed on average by only 2° for flexion-extension, 1° for lateral bending and 5° for axial rotation. Predicted median facet joint forces and disc pressures were also in good agreement with published median *in vitro* values. However, the ranges of predictions were larger and exceeded those reported *in vitro*, especially for the facet joint forces. For all combined loading modes, except for flexion, predicted median segmental intervertebral rotations and disc pressures were in good agreement with measured *in vivo* values.

In light of high inter-subject variability, the generalization of results of a single model to a population remains a concern. This study demonstrated that the pooled median of individual model results, similar to a probabilistic approach, can be used as an improved predictive tool in order to estimate the response of the lumbar spine.

1. Introduction

Accurate and clinically relevant modeling of complex biological systems such as the human lumbar spine remains challenging, yet promising, with the potential to substantially enhance the quality of patient care. Due to its ability to represent intricate systems with material nonlinearities, irregular loading, and geometrical and material domains, the finite element (FE) method has been recognized as an important computational tool in various biomedical fields (Zhang and Teo, 2008) and has been widely adopted for describing spinal biomechanics (Schmidt et al., 2013). In comparison to in vitro or in vivo approaches, computational methods are advantageous in offering cost efficient and powerful response solutions while at the same time effectively dealing with the ethical concerns related to the use of live animals in experiments. Moreover, use of computational models may greatly diminish the need for experimental investigations that utilize post mortem human and animal specimens. For example, finite element models provide improved insight into the functional mechanisms of the spine by assessing the isolated effect of various parameters independently - a feature that has been invaluable with respect to the design/optimization of spinal implants (Fagan et al., 2002a; Schmidt et al., 2013; Zhang and Teo, 2008).

Despite the proven success of computational studies in other disciplines, the FE method's role in clinical spine research has sometimes been questioned (Viceconti et al., 2005). The uncertainty and high variability of tissue material properties, the anatomical complexity of spinal structures (Panjabi et al., 1992; 1993), and the unknown loading (Rohlmann et al., 2009; Wilke et al., 1998) and boundary conditions, particularly in vivo, has cast doubt on the accuracy and reliability of FE model predictions. The inherent geometric and material property differences among individuals and alterations in these parameters due to age, sex and degeneration may limit the widespread applicability of the reported results. To gain confidence in and to enhance the predictive quality of FE models, recommendations have been made on how to develop suitable models in order to address research questions within an adequate degree of predictive accuracy (Anderson et al., 2007; Jones and Wilcox, 2008; Oreskes et al., 1994; Roache, 1998; Viceconti, 2011; Viceconti et al., 2005). These standards comprise three main steps: code verification, sensitivity analyses of uncertain model input parameters, and task-specific validations of the model.

The verification of the code poses the least concern as the vast majority of computational studies nowadays employ extensively verified, commercially available FE software. The analysis of the sensitivity to alterations in geometrical (Dupont et al., 2002; Meijer et al., 2011; Natarajan and Andersson, 1999; Niemeyer et al., 2012; Noailly et al., 2007; Robin et al., 1994), material (Fagan et al., 2002b; Lee and Teo, 2005; Rao and Dumas, 1991; Shirazi-Adl, 1994a; Zander et al., 2004) or loading parameters (Dreischarf et al., 2011; 2012; Rohlmann et al., 2009), however, demands more time and effort and has hence only occasionally been carried out. It has been shown that the range of motion (RoM) of a lumbar motion segment is strongly affected by the disc height (Meijer et al., 2011; Natarajan and Andersson, 1999; Niemeyer et al., 2012; Robin et al., 1994) and material properties (e.g. ligament properties (Zander et al., 2004)). Furthermore, appropriate loading conditions (Dreischarf et al., 2011; 2012) are necessary to realistically simulate relevant tasks under maximal voluntary motion measured in vivo (Pearcy, 1985; Pearcy et al., 1984; Pearcy and Tibrewal, 1984; Wilke et al., 2001).

The term 'validation' merits attention as it remains controversial. Validation is commonly used to indicate that model predictions are consistent with observations. However, it is intractable to completely validate numerical models because it is not possible to account for the multiplicity of their inherent degrees of freedom in an experiment (Oreskes et al., 1994). It is, however, generally accepted that greater number and diversity of corroborating observations between a model and experimental data increases the probability that the model predictions are not flawed (Oreskes et al., 1994; Viceconti et al., 2005). To increase the confidence in a model, the number of free independent parameters employed to construct the model should remain low to decrease the risk of non-uniqueness. Detailed experimental data on the lumbar spine that would allow for a thorough validation of model predictions remain, however, limited. For example, measurements are often only performed at a single level. Model validation is therefore often performed by comparing the calculated results with the limited data that is available from in vitro studies (Moramarco et al., 2010; Zander et al., 2009). However, experimental setups, specimens, loading and boundary conditions substantially differ among various studies (Brinckmann and Grootenboer, 1991; Kettler et al., 2011; Rohlmann et al., 2001b; Wilke et al., 1994), and these differences are often neglected with regard to the resulting data. Furthermore, the validation of numerical models should preferably include as many relevant outputs as possible (Woldtvedt et al., 2011), as some may be more sensitive to model assumptions than others under specific loading conditions. Moreover, for clinically relevant parameters such as the facet joint forces (FJF), which have considerable dependence on loading and geometry, almost no in vivo data exist (Wilson et al., 2006).

Well-established FE models should incorporate the aforementioned three steps to meet the conditions for a meaningful numerical study. Despite these requirements, most FE studies account for only one spinal geometry with one set of material properties and are validated with very few available experimental data. This raises questions with regard to the reliability/comparability of their predictions under various conditions, on the range of results of these numerical predictions, and on their agreement with in vitro values. Concerns also exist when attempting to validate predictions with in vivo data under complex combined loading modes (e.g. compression and bending). To address these issues, one may compare the salient predictions of peer-reviewed models obtained under nearly identical loading and boundary conditions. For this purpose and due to the importance and complexity of the lumbar spine, this novel multicenter study was undertaken to compare the results of eight well-established FE models of the lumbar spine that have been developed, validated and applied for many years in different research centers around the globe. Tasks simulated consist of pure and combined bending, torsion and compression loads in order to better compare model predictions with each other and with the published in vitro and in vivo data. The objective is to evaluate the predictive power of individual estimations versus the median of all estimations. It is hypothesized that the median predictions of FE models when combined could more closely approximate the experimental data than the predictions of individual models.

2. Materials and Methods

2.1. Inclusion criteria

Ten different research groups, working in the field of spinal FE modeling were invited to participate in the present study. Only validated models of the lumbar spine (L1-5) that were previously published in peer reviewed journals were considered. A model was considered to be validated when its predictions compared favorably with available measurements under simple loading conditions. From ten groups, eight agreed to participate, one declined due to lack of resources and one did not respond to the invitation. In the current study, complex combined loading modes were employed, for which not all models were validated previously. Thus, all results of the present study were anonymized to increase the number of participating groups. Only the first author (M.D.) had access to the non-anonymized data, and all research groups agreed to the current publication. The models were arbitrarily numbered from 1 to 8.

2.2. Study design

The first part of this study served as an in vitro validation attempt. Here, FE models were subjected to pure moments and pure compression under standardized loads recommended in experimental studies (Wilke et al., 1998). Results were compared with previously published in vitro values (Brinckmann and Grootenboer, 1991; Rohlmann et al., 2001b; Wilson et al., 2006). The second part served as a validation for the simulation of physiological movements of maximal voluntary motions in different planes. Therefore, previously published loading recommendations were employed, and the results were compared with available in vivo data (Pearcy, 1985; Pearcy et al., 1984; Pearcy and Tibrewal, 1984; Wilke et al., 2001) in which subjects were requested to perform maximal motions.

2.3. Finite element models of the intact lumbar spine

All osseoligamentous FE models employed in this study included at least five lumbar vertebrae and four intervertebral discs (L1-5, Fig. 1). FE models simulated the intact lumbar spine under static loading conditions. Detailed information about the geometry, material properties and validation of each model are described elsewhere (Ayturk and Puttlitz, 2011; Kiapour et al., 2012a; Little et al., 2008; Liu et al., 2011; Park et al., 2013; Schmidt et al., 2012; Shirazi-Adl, 1994b; Zander et al., 2009). For a better evaluation of all models, Tables 1 and 2 list the global mechanical and geometrical properties of the employed FE models.

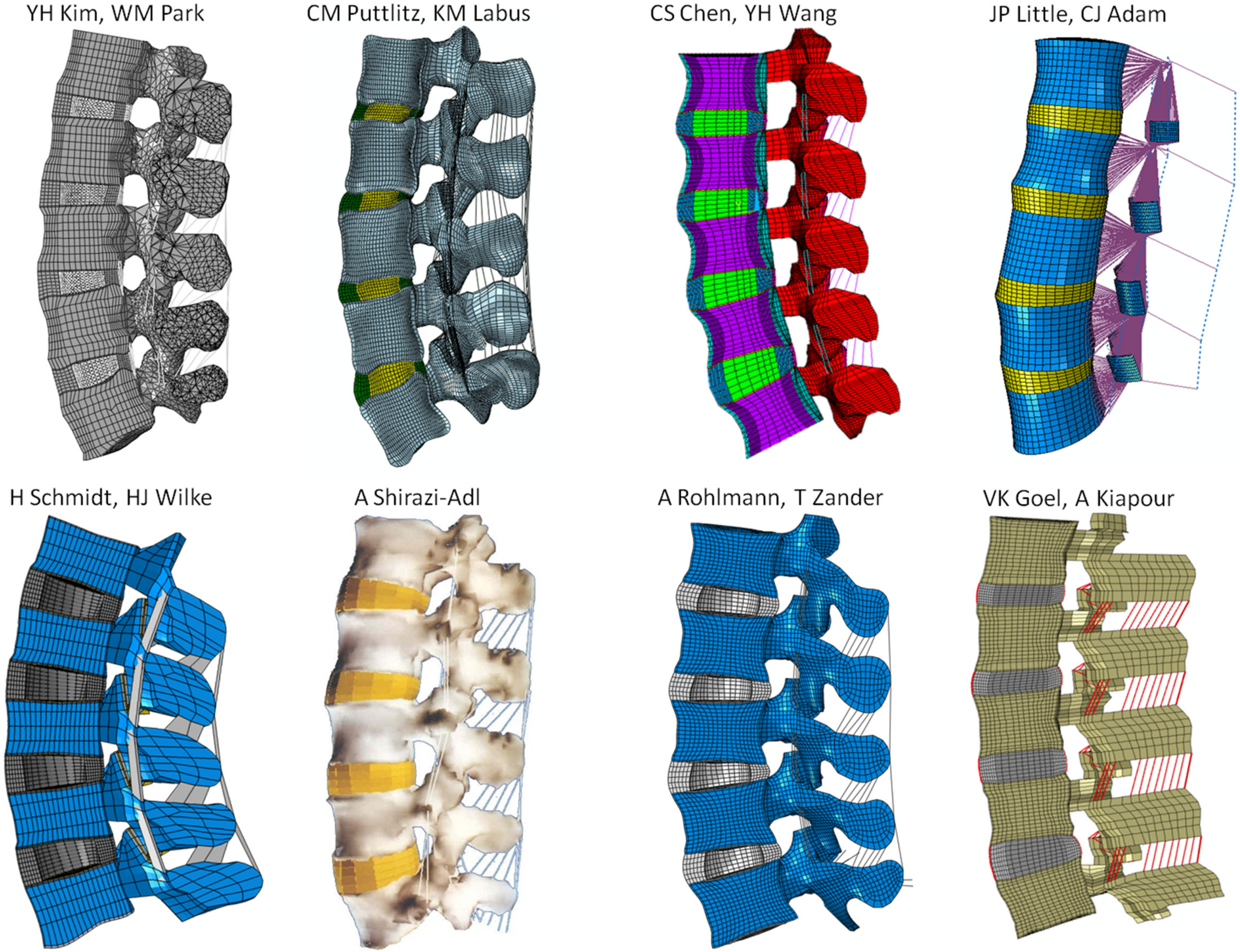

Figure 1: Finite element models of the L1-5 lumbar spine of all eight participating groups.

Table 1: Mechanical properties of different finite element models

Component	YH Kim WM Park	CM Puttlitz KM Labus	CS Chen YH Wang	JP Little CJ Adam	H Schmidt HJ Wilke	A Shirazi-Adl	A Rohlmann T Zander	VK Goel A Kiapour
Cortical bone	E = 12,000 MPa ν = 0.3	E_{11} = 8,000 MPa E_{22} = 8,000 MPa E_{33} = 12,000 MPa ν_1 = 0.4 ν_2 = 0.35 ν_3 = 0.3	E_1= 22,000 MPa E_2= 11,300 MPa ν_1 = 0.484 ν_2= 0.203	E=11,300 MPa ν =0.2	E_1 = 22,000 MPa E_2 = 11,300 MPa ν_1 = 0.484 ν_2 = 0.203	Rigid	E = 10,000 MPa ν = 0.3	E = 12,000 MPa ν = 0.3
Cancellous bone	E = 100 MPa ν = 0.2	Based on CT images	E_1= 200 MPa E_2= 140 MPa ν_1= 0.45 ν_2= 0.315	E=140 MPa ν =0.2	E_1 = 200 MPa E_2 = 140 MPa ν_1 = 0.45 ν_2 = 0.315	Rigid	E_1 = 200 MPa E_2 = 140 MPa ν_1 = 0.45 ν_2 = 0.315	E = 100 MPa ν = 0.2
Posterior bony elements	E = 3,500 MPa ν = 0.25	E = 3,500 MPa ν = 0.3	E = 3,500 MPa ν = 0.25	Quasi-rigid	E = 3,500 MPa ν = 0.25	Rigid, attached to vertebral body by two deformable beams	E = 3,500 MPa ν = 0.25	E = 3,500 MPa ν = 0.25
Ground substance of annulus bulk	Hyperelastic – Mooney-Rivlin c_1 = 0.18 c_2 = 0.045	Hyperelastic – Yeoh c_{10} = 0.0146 c_{20} = -0.0189 c_{30} = 0.041	Hyperelastic – Mooney-Rivlin c_1 = 0.42 c_2 = 0.105	Hyperelastic – Mooney-Rivlin c_1 = 0.7 c_2 = 0.2	Hyperelastic – Mooney-Rivlin c_1 = 0.56 c_2 = 0.14	Linear hypoelastic E = 4.2 MPa ν = 0.45	Hyperelastic – neo-Hookean c_1 = 0.3448 c_2 = 0.3	Hyperelastic – neo-Hookean c_1 = 0.3448 c_2 = 0.3
Nucleus pulposus	Incompressible fluid-filled cavity	E = 1.0 MPa ν = 0.49	Incompressible fluid	Incompressible fluid	Incompressible fluid-filled cavity	Incompressible fluid	Incompressible fluid-filled cavity	Incompressible fluid
Fibres of annulus	Non-linear, dependant on distance from disc centre, 6 layers - criss-cross pattern,	Non-linear, two families of fibers A_3 = 0.03 (MPa) b_3 = 120.0 (unitless)	Non-linear, 12 layers -criss-cross pattern,	Tension-only, embedded inear elastic elements, 8 layers with alternating orientation	Non-linear stress-strain curve , 16 layers - criss-cross pattern	8 layers of fiber-reinforced membranes with through annulus depth-dependent thickness and nonlinear properties	Non-linear, dependant on distance from disc centre, 14 layers - criss-cross pattern	8 layers of fiber-reinforced continuum elements with criss-cross pattern
Ligaments	Non-linear stress-strain curve	Exponential force-displacement curves	Linear stress-strain curve	Piecewise nonlinear elastic with individual ligament lengths at each spinal level	Non-linear stress-strain curve	Collection of uniaxial elements with nonlinear properties	Non-linear stress-strain curve	Uniaxial 2D elements with theoretically defined cross-sectional area with nonlinear hypoelastic properties
Cartilage of facet joints	Hard frictionless contact, Young's Modulus: 11 MPa, Poisson's ratio: 0.4, Initial gap: 0.5 mm	neo-Hookean, c_{10} = 2	Soft contact, Friction coef: 0.1, Initial gap: 0.5 mm	Finite-sliding, frictionless tangential contact with 'softened', exponential normal contact, Initial gap: 0.8 mm	Hard frictionless contact, Young's Modulus: 35 MPa, Poisson's ratio: 0.4, Initial gap: 0.4 mm	Soft frictionless contact with variable gap distances and a gap limit for contact initiation of 1.25 mm	Soft frictionless contact, Initial gap: 0.5 mm	Soft frictionless contact using gap elements with initial clearance of 0.5 mm
Employed data for validation	Panjabi et al. (1994) Guan et al. (2007)	Panjabi et al. (1994) Niosi et al. (2008) Sawa and Crawford (2008) Ayturk (2007)	Atlas and Deyo (2001) Lin et al. (2013) McMillan et al. (1996) Yamamoto et al. (1989) Shirazi-Adl (1994c) Chen et al. (2001)	Pearcy (1985) Nachemson (1960)	Heuer et al. (2007b) Heuer et al. (2007a) Rohlmann et al. (2001b) Heuer et al. (2008)	Shirazi-Adl (1994b) Shirazi-Adl (1994c)	Heuer et al. (2007b) Brinckmann and Grootenboer (1991) Rohlmann et al. (2001b) Wilson et al. (2006) Rohlmann et al. (2001a) Wilke et al. (2003)	Kiapour and Goel (2009) Goel et al. (2005) Goel et al. (2007) Kiapour et al. (2012b)
Solver	Abaqus 6.10*	Abaqus 6.11*	ANSYS 11.0**	Abaqus 6.9.1*	Abaqus 6.10*	In-house FE solver	Abaqus 6.10*	Abaqus 6.10*

* SIMULIA Inc. Providence, Rhode Island, USA **Swanson Analysis Systems, Inc, Houston, PA, USA

Table 2: Geometrical properties of different finite element models

Component	Kim Park	Putlitz Labus	Chen Wang	Little Adam	Schmidt Wilke	Shirazi-Adl	Rohlmann Zander	Goel Kiapour	**Median (range)**
Origin of the model	CT-scan of living subject (lying), male, age: 26 years	CT-scan, cadaver specimen, female, age: 49 years	CT-scan of living subject (lying), male, age: 19 years	CT-scans, cadaver specimen, female, age: 59 years	CT -scan, cadaver specimen, male, age: 46 years	CT-scans, cadaver specimen, male, age: 65 years	CT -scan, average values were taken from literature	CT-scan, cadaver specimen, male	
Lumbar lordosis – L1-L5 cobb angel (deg)	37	35	27	26.1	44	32.7	28	19.1	30.4 (19.1-44.0)
Disc diameter L4-5 (mm)									
- lateral	50.8	49	58	39	49	50.3	50	49.8	49.9 (39.0-58.0)
- sagittal	33.4	32	43.1	28	35	34.4	37	35.2	34.7 (28.0-43.1)
Disc thickness L4-5 (mm)									
- anterior	11.4	16.0	19.4	14	15	15.8	11.5	13.7	14.5 (11.4-19.4)
- lateral	7.9	11.1	13.7	9.8	13.5	13.4	9.0	13.2	12.2 (7.9-13.7)
- posterior	7.8	7.1	11.2	8.5	12	11.2	6.0	9.2	8.9 (6.0-12.0)
Cross-sectional area L4-5 (mm^2)									
- disc	1460	1332	2075.5	N/A	1380	1455	1480	1210	1455 (1210-2076)
- nucleus	560	478	894.6		552	653	624	563	563 (478-895)

2.4. Loads and boundary conditions

In 6 of 8 simulations, Dirichlet boundary conditions were applied at the most caudal lumbar vertebra L5 to fix all displacement degrees of freedom. Model 3 and 4 however also included the L5-S1 level and were constrained at the S1 level.

For the first part of this study, pure bending moments of 7.5 Nm were applied in all three anatomical planes (Wilke et al., 1998). For model comparison, the entire L1-5 range of motion (RoM) and the facet joint forces (FJF) at all segments were compared. Subsequently, the FE models were loaded under compression (up to 1000 N) and the L4-5 intradiscal pressure (IDP) predictions were compared. Since the osseoligamentous lumbar spine is inherently unstable (Crisco et al., 1992), the follower load technique was employed (Dreischarf et al., 2010; Patwardhan et al., 1999; Shirazi-Adl and Parnianpour, 2000) to apply the compression. This technique minimizes artifact bending moments expected in compression loading (Cripton et al., 2000).

For the second part, all models were subjected to compression in combination with bending and torsion as shown in Table 3. These loads were taken from FE model studies that simulated most realistically maximal voluntary motions as measured in vivo (Pearcy, 1985; Pearcy et al., 1984; Pearcy and Tibrewal, 1984; Wilke et al., 2001). The intervertebral rotations (IVR), IDP values, and FJF were analyzed for each model at all segments. In each model, left and right FJF at all levels were averaged for both sides during extension. In torsion and lateral bending, the sides under higher load were chosen for the sake of comparison.

For both parts, the median and ranges of all FE model predictions were calculated for each loading case in order to compare the FE predictions with the reported in vitro and in vivo results.

Table 3: Loading modes for the simulation of different body positions

Body position	Compressive force (N)	Moment (Nm)	References
Flexion	1175	7.5	Rohlmann et al. (2009)
Extension	500	7.5	Rohlmann et al. (2009)
Lateral bending	700	7.8	Dreischarf et al. (2012)
Axial rotation	720	5.5	Dreischarf et al. (2011)

3. Results

3.1. Participating groups

Seven of eight groups completed all calculations for the first part of this study. Due to resource limitations, one group only presented results under pure moments and not pure compression. Six of the eight groups participated in the second part as two groups did not participate due to resource limitations. One of the six participating groups was not able to deliver results for the load case upper body flexion, due to convergence problems.

3.2. Part 1 – Pure moments and pure compression

Under pure moments, the median total L1-5 rotation of all FE models (Fig. 2a, each 2nd column) differ by only approximately 2° in flexion-extension (FE median: 34°, FE range: 24°-41°), 1° in left-right lateral bending (35°, 25°-41°), and 5° in left-right axial rotation (17°, 11°-22°) from in vitro median values (Fig. 2a, red columns). All three FE median values are within the in vitro range. Two of eight FE models predict rotations slightly outside the in vitro range in flexion-extension and in axial rotation. In lateral bending, all eight models are within the measured range. All FE models demonstrate, albeit to different degrees, a stiffening effect with increasing load resulting in non-linear moment-rotation curves (Fig. 2b).

Median FJF of all levels differ considerably between the models in all moment loading cases (Fig. 2c). Furthermore, the forces between the levels considerably vary within the models. In extension and axial rotation, two of seven models predict FJF well outside of the in vitro range. The segmental FJF of all models are on average 0 N in flexion, 32 N in extension, 12 N in lateral bending and 87 N in axial rotation (Fig. 2c). The medians of the predicted FJF are very close to the centre of the experimentally measured ranges (Fig. 2c, shown in red error bars) for extension (in vitro: 30 N, FE median: 32 N) and axial rotation (in vitro: 83 N, FE median: 87 N). However, the FJF ranges predicted by all models exceed the in vitro data range.

Results of all models indicate that under axial compressive loading, the IDP increases almost linearly with the applied load (Fig. 2d). Six of seven models predict L4-5 IDP within the in vitro range under 1000 N compression. Only one model considers an initial IDP offset at 0 N (model 5: 0.13 MPa), which leads to IDP values slightly out of range at compression of 300 N. One model predicts IDP values smaller than experimental measured values.

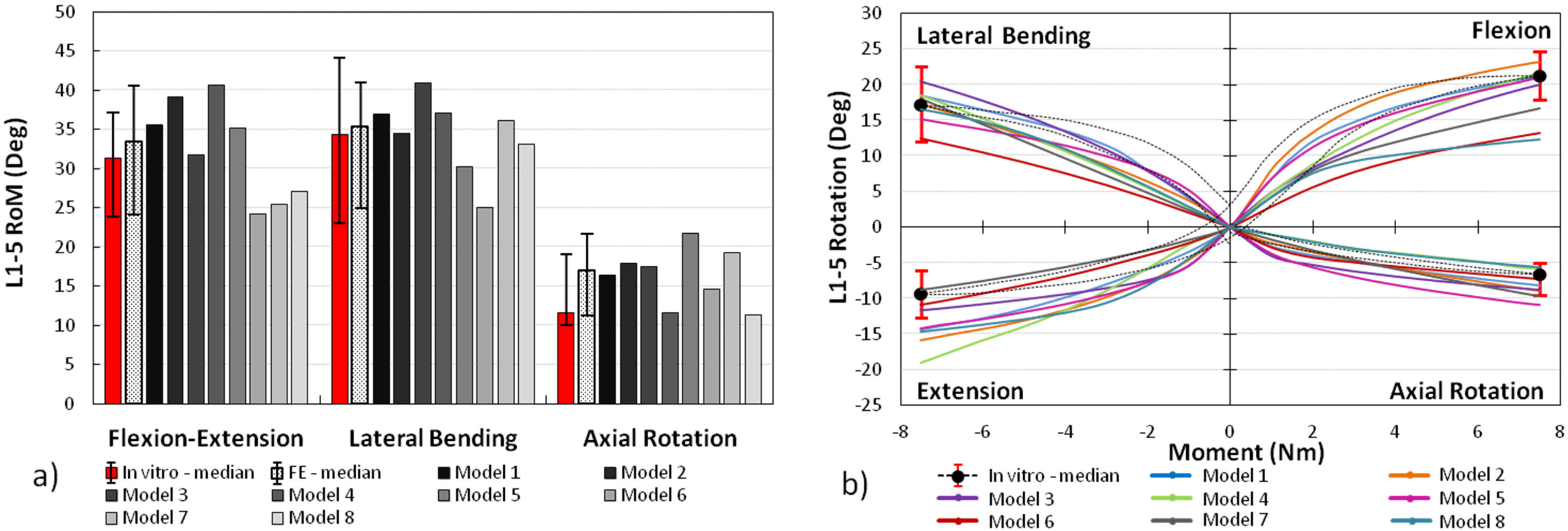

Figure 2: a) Predicted L1-5 range of motion (RoM) under pure moments (3rd to 10th bar). The second dotted bar represents the median value of all eight models and its range represents the range of results of all models. The red bars show the *in vitro* median value and the range of results of ten L1-5 specimens (Rohlmann et al., 2001b). b) Non-linear load-deflection curves (L1-5) of all eight models under pure moments. Black dotted lines represent the median curves of ten L1-5 specimens(Rohlmann et al., 2001b). The red ranges represent their range of results for a moment of 7.5 Nm.

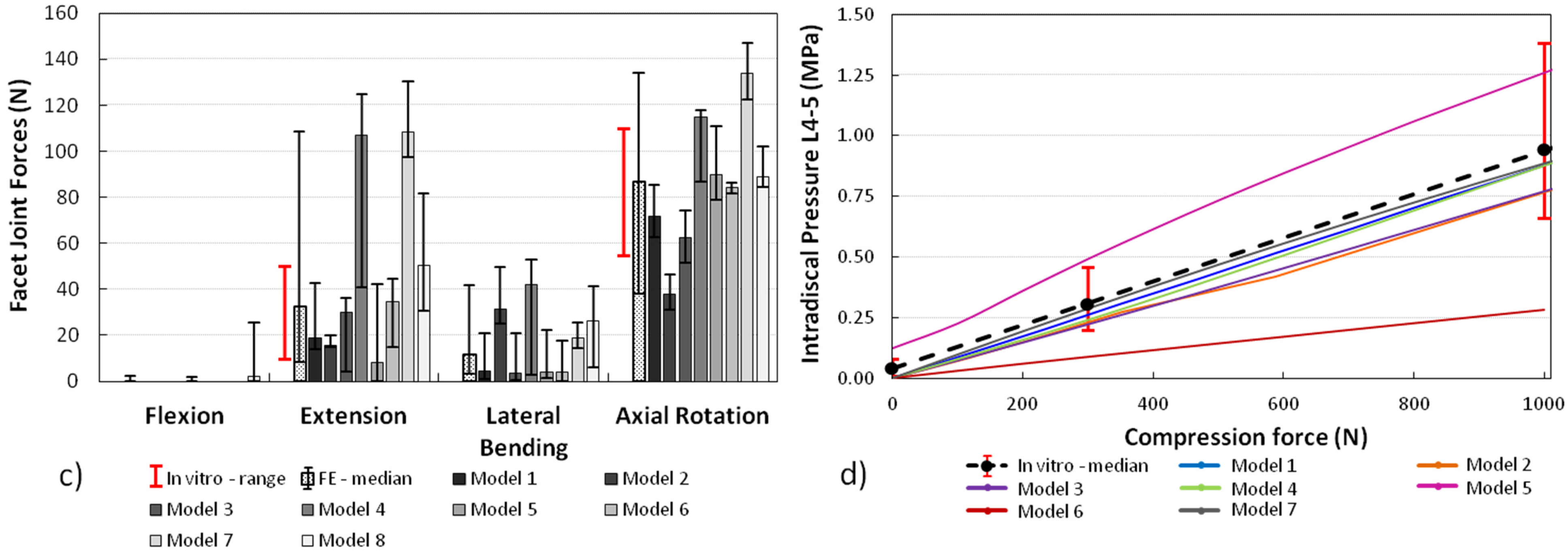

Figure 2: c) Median facet joint forces of all spinal levels (L1-5) for each finite element model (2^{nd} to 8^{th} bar), whereas the ranges represent minimal and maximal forces predicted in each model. The dotted bars demonstrate the median facet joint forces of all eight finite element models and their ranges. The red ranges represent the range of facet joint force measured *in vitro* in L1-5 specimens (Wilson et al., 2006). d) Predicted intradiscal pressure in L4-5 nucleus vs. applied compression force. Red black dotted line and red ranges represent the median relationship for fife L4-5 segments and its range of results for 0 N, 300 N and 1000 N, respectively (Brinckmann and Grootenboer, 1991).

3.3. Part 2 – Combined compression-bending and compression-torsion

Except for flexion, all predicted segmental median IVRs are within the in vivo measured range (Fig. 3 a-d; each red and dotted bar). In flexion, under 7.5 Nm moment and 1175 N compression, all FE models predict smaller IVR than seen in vivo under maximal voluntary bending with maximal deviations of approximately 9°. Only for the segment L1-2 are the predictions within the in vivo range. The predictions of all FE studies are, however, very similar. For lateral bending and axial rotation, all segmental IVRs of all FE models are within the in vivo range and close to the in vivo median values. For extension, almost all predicted IVR are within the in vivo ranges, except for one case at L1-2 and one at L4-5.

Median FE values of IDP predicted at L4-5 disc are close to the corresponding in vivo values for lateral bending, extension and axial rotation (Fig 4, each red and dotted bar). The predicted median IDP for flexion is slightly smaller than what has been measured in vivo. There are large variations in the predicted IDP values between all models, especially in extension. It has to be noted that the in vivo pressure data were measured in one single subject (Wilke et al., 2001) under maximal voluntary motion.

Predicted total FJF of all FE models are, on average, approximately 38 N in extension, 14 N in lateral bending and 60 N in axial rotation (Fig 5). In flexion, the facet joints remain unloaded. Computed FJF considerably differ between FE models, especially in lateral bending. Under these combined loading conditions, no measured FJF has been reported, making comparison of these predictions intractable.

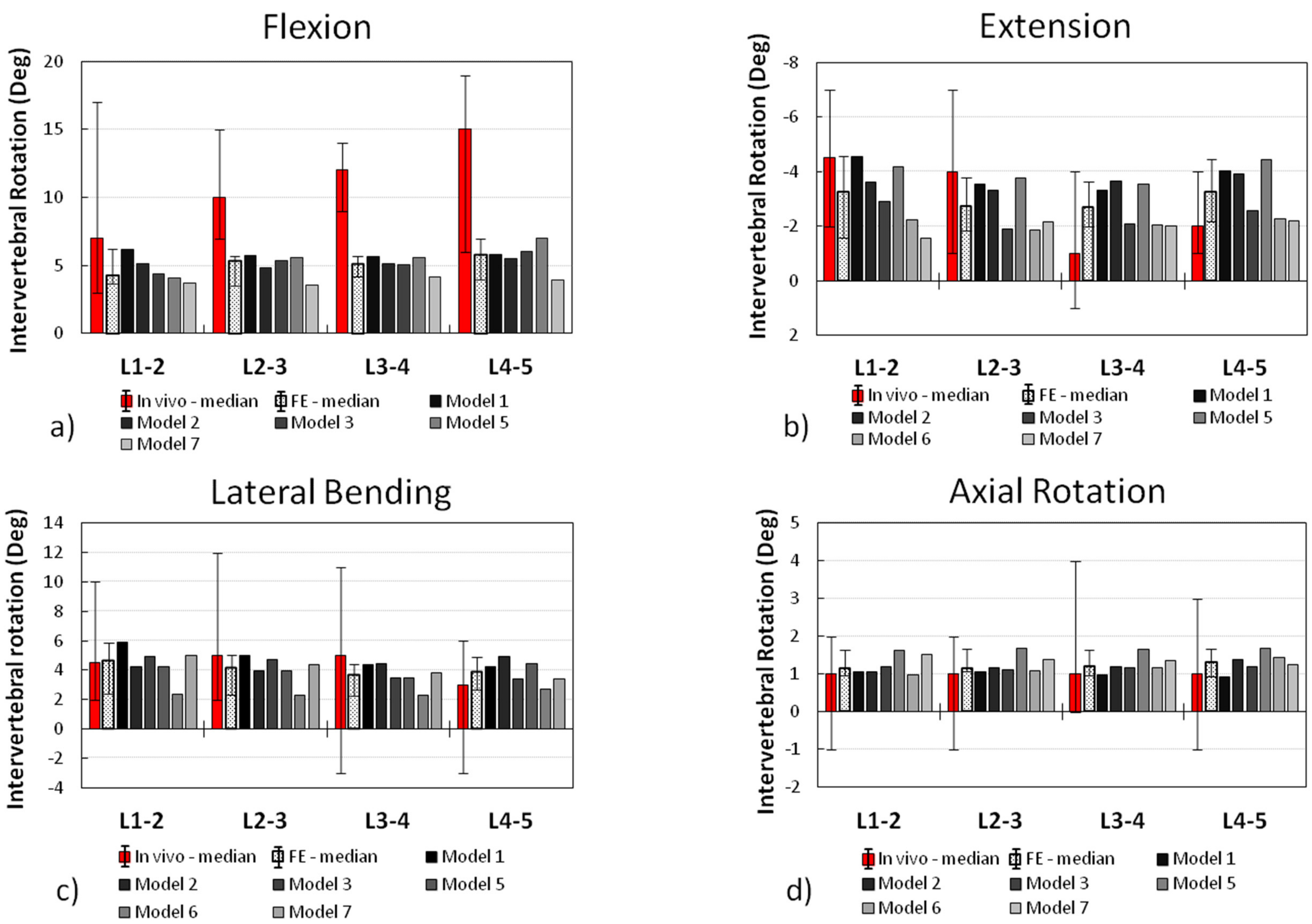

Figure 3): Comparison between predicted intervertebral rotations in different spinal levels of up to six finite element models and median *in vivo* values (Pearcy and Tibrewal, 1984; Pearcy et al., 1984; Pearcy, 1985) (red bars) for the loading cases flexion (a), extension (b), lateral bending (c) and axial rotation (d). The dotted bars represent the segmental median values of all models and their range of results.

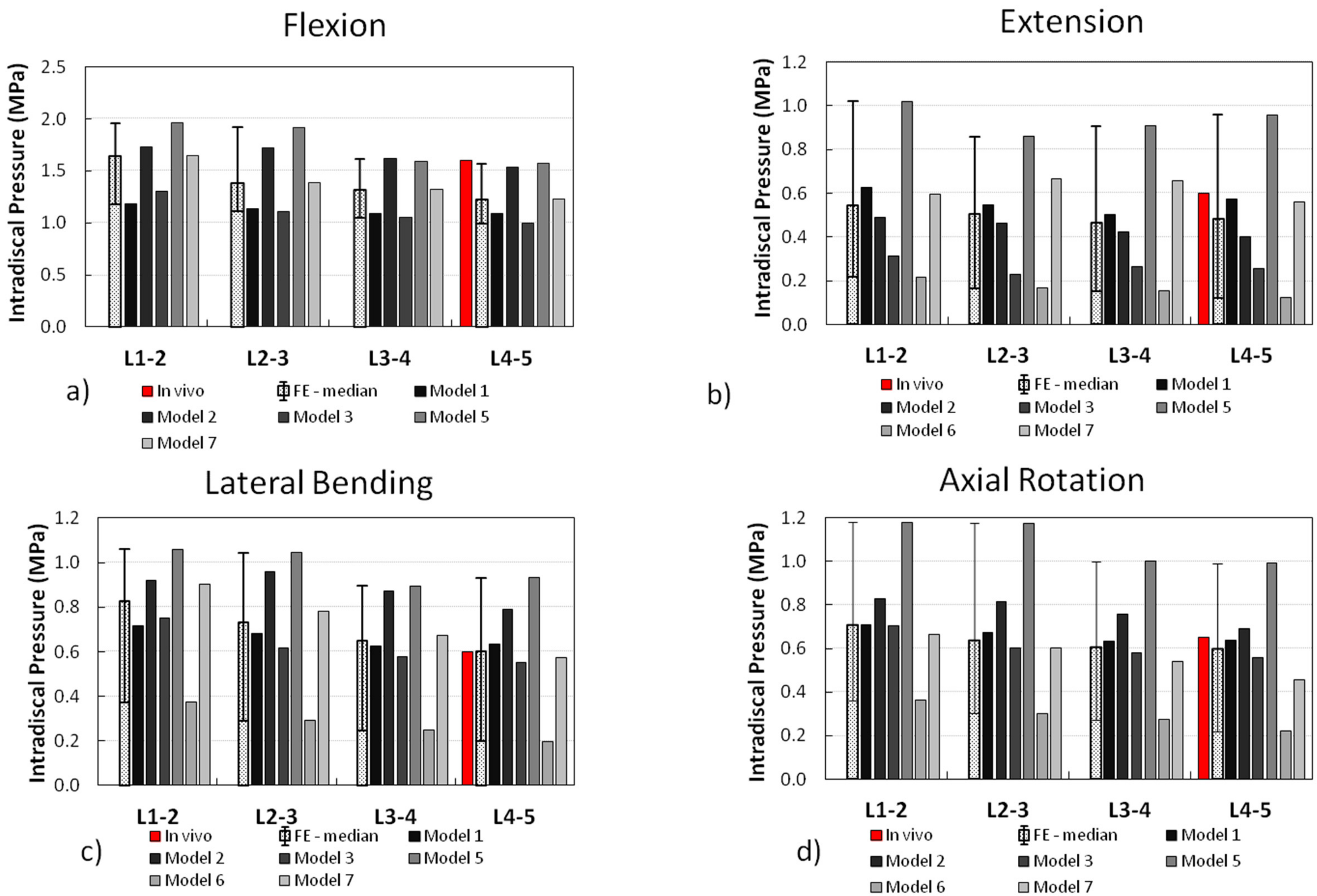

Figure 4: Comparison between predicted intradiscal pressures in different spinal levels for flexion (a), extension (b), lateral bending (c) and axial rotation (d) of up to six finite element models compared to *in vivo* measurements (red bars) by Wilke et al.(2001). The dotted bar represents the segmental median value of all finite element models and their range of results.

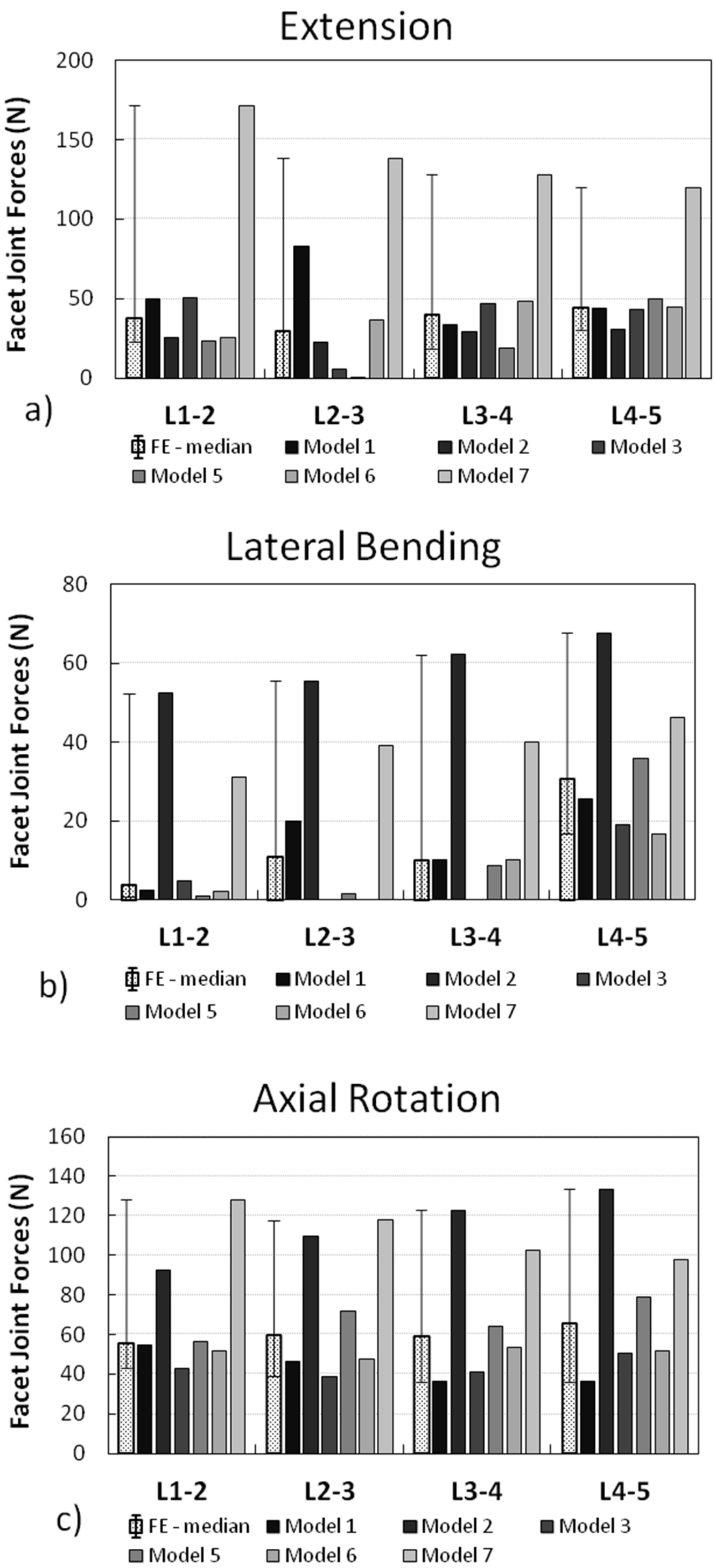

Figure 5): Predicted facet joint forces of six finite element models for the loading cases extension (a), lateral bending (b) and axial rotation (c). The dotted bar represents the segmental median value of all finite element models and their range of results.

4. Discussion

Over the last few decades, the finite element method has been used to investigate the biomechanical behavior of the lumbar spine. These FE models are usually based on only one specific or one idealized average subject with unique mechanical and geometrical characteristics. Thus, with a few exceptions (Little and Adam, 2013; Niemeyer et al., 2012), the effect of inter-subject variability in geometry has mostly not been accounted for in modeling efforts. In addition, the crucial role of individualized material properties has not been incorporated due to the lack of appropriate data, although image analysis and its future developments appear promising for providing in vivo material coefficients. In order to reduce these confounding effects, experimental measurements with sufficient sample size attempt to account for such variabilities, though they remain limited due to the availability of specimens, inaccessibility of regions of interest and experimental limitations. An improved insight into the impact of the material and geometrical diversity on the biomechanical behavior of the lumbar spine is essential for an enhanced understanding of spinal mechanics and patient care. This FE model study aimed to estimate the relative predictive power in using a number of published models when comparing to available limited measurements. Towards this goal, the results of eight FE models of the lumbar spine of different research centers were subjected to almost identical loading and boundary conditions. Under pure moment and compressive loading, the results showed that numerical predictions are in good agreement with in vitro measurements of IVR, but differ more from each other and from in vitro values for IDP and FJF. In support of our hypothesis, the median response of pooled predictions was in better agreement with reported measurements than the individual predictions. Under combined loads, in vivo measured values for IVR and IDP were predicted for extension, lateral bending and axial rotation (Fig. 3, 4).

Under pure moments, almost all models predicted RoMs that moderately differ from each other, and these data compared satisfactorily well with experimental median values. Interestingly, the numerical ranges of eight individual models fit the experimental observations well (Fig. 2a). However, the inter-model deviation in predictions increases for parameters, such as the FJF or IDP, that give insights into the internal loading conditions of the lumbar spine but which are difficult to validate with experimental measurements (Fig. 2c-d). However and interestingly, the median of all model predictions was always relatively close to the in vitro median values of the IVR, IDP and FJF indicating the improved capability of FE models when grouped together to predict the experimental results (Fig. 2). This is to a certain extent also true for the second part of this study despite the challenge in simulating maximum voluntary trunk rotations in different planes.

This study confirms that the employed combined loading modes of extension, lateral bending and axial rotation lead to the median predicted IDP values which are close to in vivo measurements (Fig. 4). Furthermore, except for flexion, the employed moments and forces lead to median segmental IVRs which are close to in vivo measurements, especially for axial rotation and lateral bending (Fig. 3). A bending moment of 7.5 Nm is evidently not sufficient to simulate the peak upper body flexion under maximal voluntary motion with segmental IVR of more than 10° as measured in vivo. For upper body flexion, a compression force of 1175 N yields IDP values slightly smaller to those measured by Wilke et al. (2001; 1.6 MPa), which was measured under maximal motion. Using the IDP and disc area measured by Wilke et al. (2001), the compressive force under 1.6 MPa in L4-5 can be estimated to approximately 1900 N (Dreischarf et al., 2013). Earlier compression estimations at L5-S1 of about 2200 N (Arjmand et al., 2010) and 2900 N (Bazrgari et al., 2008) may be due to the L5-S1 level rather than L4-5, subject weight and variation in peak flexion. The employed loading modes for extension, lateral bending and axial rotation can be used as a reference for a more physiologically-relevant simulation under maximal voluntary motion. Since there is no in vivo measurement of the FJF, the FJF predictions of the FE models cannot be verified.

Despite the aforementioned advantages of numerical models and their value e.g. as a comparative tool for investigating parameter sensitivity and modeling medical implants, these results emphasize the difficulty in confidently drawing biomechanical conclusions from a single FE model for a certain population. On the contrary, in vitro models are limited in providing valuable insights into how the lumbar spine functions and fails, but depending on the sample size, account for potential effects of inter-subject variability. If a model aims to predict the behavior of an average subject, it should incorporate average anatomical properties (Table 2; e.g. lumbar lordosis, disc area and disc height) and be validated for biomechanical parameters (e.g. IVR, IDP) to increase predictive confidence. For this, the sensitivity of input parameters with an important influence on the mechanical behavior (Lu et al., 1996; Meijer et al., 2011; Natarajan and Andersson, 1999; Niemeyer et al., 2012; Robin et al., 1994) such as the articular facet orientations (Niemeyer et al., 2012; Woldtvedt et al., 2011) or disc height and area is crucial for validation. Furthermore, the complex combination and interaction of several geometrical and material properties govern the response of a model under a certain load. To assist future research and to help new researchers in the field of spine biomechanics, the employed material properties and average geometrical values from all models are listed in Tables 1 and 2.

For the present study, it has to be noted that two models included also the most distal level L5-S1 and were constrained at the S1 level. This has an effect on the response of the adjacent segment L4-5. Furthermore, the models differ not only in values of certain material properties and laws (e.g. Young's modulus of cortical bone, ligaments, bony posterior elements), but also in representation of disc nucleus, disc annulus and facet articulations.

In light of high inter-subject variability, one must be cautious when generalizing predictions obtained from one deterministic model. A possible solution to provide robust information of one specific model is to use statistical methods, e.g. factorial and probabilistic designs, to assess the sensitivity and robustness of the model to variations in input parameters and their interactions. However, incorporating all the main geometric parameters of the lumbar spine into a statistical approach would require a fully parameterized model. The development of such a model, however, has proven to be notoriously difficult. One valid option might be to investigate a few subjects that are representative of the population's variability of interest. This gives an indication of the level of variability one may expect in model predictions. In this study, eight of those representative FE models developed during the last decades were, for the first time, combined and employed to estimate its median and range during pure and combined loading modes. This study confirms that by combining several distinct models, the median of individual numerical results can be used as an improved prediction in order to estimate the response of the lumbar spine. In combination with a sophisticated experimental database, the FE method is thus better able to develop its potential to enhance our understanding of the mechanics of the lumbar spine.

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2.8 Publication 8: Biomechanics of the L5-S1 Motion Segment after Total Disc Replacement –Influence of Iatrogenic Distraction, Implant Positioning and Preoperative Disc Height on the Range of Motion and Loading of Facet Joints.

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Abstract

Total disc replacement has been introduced to overcome negative side effects of spinal fusion. The amount of iatrogenic distraction, preoperative disc height and implant positioning have been considered important for surgical success. However, their effect on the postoperative range of motion (RoM) and loading of the facets merits further discussion.

A validated osteoligamentous finite element model of the lumbosacral spine was employed and extended with four additional models to account for different disc heights. An artificial disc with a fixed center of rotation (CoR) was implemented in L5-S1. In 4,000 simulations, the influence of distraction and the CoR's location on the RoM, facet joint forces (FJFs) and facet capsule ligament forces (FCLFs) was investigated.

Distraction substantially altered segmental kinematics in the sagittal plane by decreasing range of flexion (0.5° per 1mm of distraction), increasing range of extension (0.7°/mm) and slightly affecting complete sagittal RoM (0.2°/mm). The distraction already strongly increased the FCLFs during surgery (up to 230N) and in flexion (~12N/mm), with higher values in models with larger preoperative disc heights, and increased FJFs in extension. A more anterior implant location decreased the RoM in all planes. In most loading cases, a more posterior location of the implant's CoR increased the FJFs and FCLFs, whereas a more caudal location increased the FCLFs but decreased the FJFs.

The results of this study may explain the worse clinical results in patients with overdistraction after TDR. The complete RoM in the sagittal plane appears to be insensitive to detecting surgery-related biomechanical changes.

1. Introduction

Low back pain is a serious worldwide public health problem that affects approximately 80% of all adults at some point during their lives (Andersson, 1998). It is, among others, associated with degenerative disc diseases (DDDs; Luoma et al., 2000), which are frequently treated with spinal fusion if conservative treatment is unsuccessful. However, the treatment of lumbar DDDs with spinal fusion is highly controversial because it is associated with early and late complications, such as accelerated adjacent level degeneration (Levin et al., 2007). To avoid these negative side effects, motion-preserving technologies, such as lumbar total disc replacement (TDR), have been introduced as alternatives to spinal fusion.

Several clinical studies have demonstrated satisfactory clinical results for monosegmental TDR, but these results were demonstrated only in carefully selected patients (Freeman and Davenport, 2006; Guyer et al., 2009; Siepe et al., 2014). Various contraindications have been identified for TDR (Chin, 2007; Huang et al., 2004; McAfee, 2004; Wong et al., 2007), and the success of TDR in the clinic has fallen short of its initial high expectations. In particular, the spino-pelvic alignment ('sagittal balance') is a key factor for surgical success (Mehta et al., 2012; Pellet et al., 2011; Roussouly et al., 2005). Strube and co-workers (2012) demonstrated that the sagittal profile types 1 and 4 from the classification proposed by Roussouly et al. (2005) represent a contraindication for lumbar TDR at L4-5 and L5-S1. Siepe et al. (2007, 2008) demonstrated that TDR in L4-5 is clinically superior to L5-S1 and that lumbar facet and/or iliosacral-joint-pain are the most common causes of unsatisfactory clinical results following TDR (e.g., indicated by clinical scores such as the "visual analogue scale" or the "Oswestry Disability Index"). They also showed that patients with a preoperative larger disc height reported significantly lower subjective patient satisfaction rates (Siepe et al., 2009). Aside from preoperative radiological parameters, in a combined clinical and computational study, Strube et al. (2013) and Rohlmann et al. (2013) emphasized that an iatrogenic posterior translation of L5 with respect to S1 followed by an increase in the facet capsule ligament forces as well as an overdistraction followed by an increase of lordosis in L5-S1 leads to inferior clinical outcomes. However, a crucial relationship between individual preoperative disc height, iatrogenic distraction, resultant postoperative biomechanical changes (segmental range of motion, RoM; facet joint loading) and resultant clinical results remains to be established.

Finite element (FE) models of the lumbar spine have been introduced to clarify these elementary biomechanical relationships (Chen et al., 2009; Chung et al., 2009; Le Huec et al., 2010; Rohlmann et al., 2009a; Rundell et al., 2012; Schmidt et al., 2012; Zander et al., 2009). These models can provide detailed insight into the segmental kinematics and loading of the facet joints (facet joint forces (FJFs) and facet capsule ligament forces (FCLFs)). Their detailed knowledge is clinically important to understand potential mechanical risk factors after TDR surgery. In several FE model studies, the biomechanical consequences of a TDR compared with the intact state were investigated and it was shown in line with *in vitro* experiments that TDR mainly increased the segmental RoM, particularly the range of extension (RoE; Chen et al., 2009; Chung et al., 2009; Goel et al., 2005; Wilke et al., 2012). The impact of surgery and patient-related factors, such as the amount of iatrogenic distraction, implant location or preoperative disc height, on the biomechanical outputs after TDR has been less frequently investigated (Le Huec et al., 2010; Schmidt et al., 2012); however, these factors may be decisive for optimal treatment and patient selection. Therefore, the specific postoperative consequence of a TDR, which is influenced by the combination of these three factors and their individual impact on the resultant RoM in all anatomical planes and loading of the facet joints, merits further discussion.

Thus, this FE model sensitivity study aims to determine the effect of the amount of iatrogenic segmental distraction, the individual disc height and the implant's location on the segmental RoM and facet joint loads after TDR using several different lumbar spinal geometries. The authors hypothesized that:

(1) the amount of distraction, preoperative disc height, and implant location substantially affect the segmental kinematics and

(2) an iatrogenic distraction substantially increases the facet joint loads.

2. Methods

2.1. FE models of the lumbosacral spine

A previously published symmetrical osteoligamentous FE model of the intact lumbosacral spine (L1-S1) was employed (Model 0; Fig. 1; Rohlmann et al., 2006a; Zander et al., 2001). The model was extensively validated using experimental data for the RoM, intradiscal pressure and FJFs (Heuer et al., 2007; Rohlmann et al., 2001; Wilson et al., 2006); furthermore, its predictions correspond well to those of other published FE models (Dreischarf et al., 2014). Based on this model, four additional models were created using the classification proposed by Roussouly et al. (2005) to account for the large anatomical variability in the sagittal alignment (Models 1-4; Fig. 1). The global geometrical dimensions of all models are given in Table 1.

Table 1: Geometrical characteristics of all employed finite element models.

	Model 0	Model 1	Model 2	Model 3	Model 4
Global lordosis	44°	51°	51°	60°	71°
Upper arc of lordosis	5.5°	22°	19°	22°	21°
Lower arc of lordosis	38.5°	29°	32°	38°	50°
L5-S1 lordosis (disc)	17°	22°	12°	14°	21°
L5-S1 mean disc height	8.8 mm	10.4 mm	7.5 mm	7.8 mm	9.3 mm

In brief, all models consist of seven distinct structural regions, namely cancellous bone, cortical bone, posterior bony elements, annulus fibrosus, nucleus pulposus, cartilaginous endplates and seven major spinal ligaments (Table 2). The ligaments were simulated by tension-only spring elements with nonlinear elastic behavior in accordance with the experimental measurements of Nolte et al. (1990). The nucleus was represented by an incompressible fluid. The annulus was assumed to be a composite of collagen fibers with non-linear tensile properties embedded in a matrix of ground substance. The fibers were arranged in concentric rings around the nucleus pulposus in a criss-cross pattern. The cancellous bone was modeled using a linear elastic transverse isotropic formulation, whereas the cortical bone and posterior bony structures were assumed to be linearly elastic and isotropic. The facet joints consisted of two frictionless curved articulating surfaces (Putz, 1976) covered with a thin cartilaginous layer and were simulated using a soft contact with an exponentially increasing contact pressure and decreasing contact gap (Sharma et al., 1995). Their anatomical orientation and location were selected in agreement with Panjabi et al. (1993) and Masharawi et al. (2004).

Table 2: Material properties and element types used for the different tissues.

Component	**Elastic modulus (MPa)**	**Poisson ratio (–)**	**Element type**	**References**
Cortical bone	10,000	0.30	8-Node Hex	Rohlmann et al. (2006b)
Cancellous bone (transverse isotropic)	200/140	0.45/0.315	8-Node Hex	Ueno and Liu (1987)
Posterior bony elements	3500	0.25	8-Node Hex	Shirazi-Adl et al. (1986)
Ground substance of annulus fibrosus	Hyperelastic, neo-Hoookean C_{10}=0.3448, D_1=0.3		8-Node Hex	Eberlein et al. (2001)
Fibres of annulus fibrosus	Non-linear and dependent on the distance from the disc centre		Rebar	Shirazi-Adl et al. (1986)
Ligaments	Non-linear		Connector elements	Nolte et al. (1990) Rohlmann et al. (2006b)
Cartilage of facet joint	Soft contact			Sharma et al. (1995)

2.2. FE model with a TDR in L5-S1

An artificial disc with a fixed center of rotation (CoR) similar to the ProDisc prosthesis was implemented in all five models at the L5-S1 level. The artificial disc was simulated by kinematically coupling adjacent vertebrae, which simulated an idealized frictionless sliding contact between articulating surfaces of the implant, as modeled in a previous study (Rohlmann et al., 2013). This coupling was realized with connector elements, which ensured that the nodes of the adjacent endplates remained within the limits allowed by the kinematics of the disc. In accordance with surgical guidelines (SYNTHES-Spine, 2006), the central part of the intervertebral disc, as well as the anterior and posterior longitudinal ligaments, were resected, and the cartilaginous endplates were removed, leaving only the lateral part of the annulus fibrosus intact (Fig. 1, A).

In the first simulation step, the disc space height of the L5-S1 segment was increased to account for an iatrogenic distraction during surgery (Fig. 1, B). The distraction of the segment places tension on the remaining ligaments and annulus fibrosus. Thus, the segment was subsequently allowed to adapt its lordosis (Fig. 1, D) in the second simulation step after the distraction and insertion of the implant (Fig. 1, C). The initial reference location of the artificial disc's CoR is shown in Figure 1 (C, D) and was selected in accordance with previous studies (e.g., Zander et al., 2009).

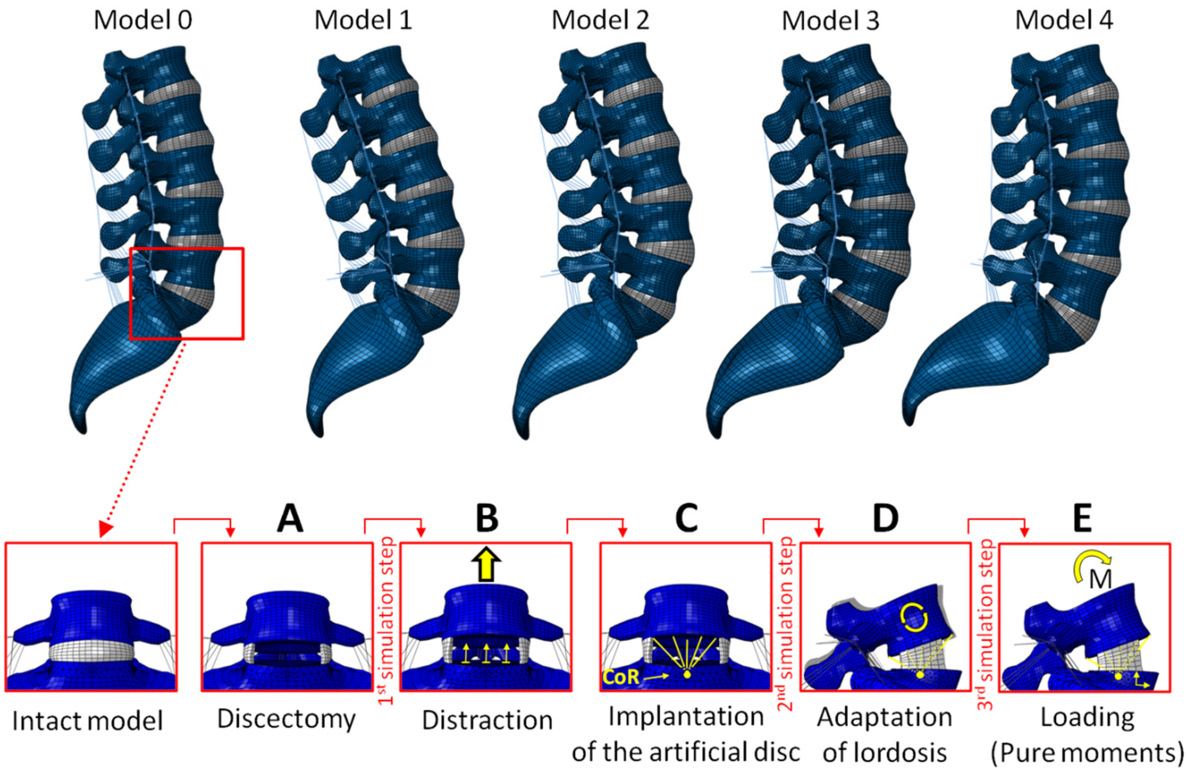

Figure 1: Finite element models of the lumbar spine employed in the present study (top). Procedure employed in this study (bottom): (A) Resection of the central part of the intervertebral disc, anterior and posterior longitudinal ligaments and the cartilaginous endplates; (B) 1st simulation step: iatrogenic distraction and (C) subsequent insertion of the implant; (D) 2nd simulation step: adaption of the segmental lordosis and (E) subsequent simulation of flexion, extension, lateral bending and axial rotation using pure moments (3rd step).

2.3. Boundary and loading conditions

The sacrum was rigidly fixed in all models. After distraction, implant insertion and adaptation of lordosis (first and second simulation steps), the models were subjected (third step) to pure moments of 7.5 Nm in flexion and extension, 7.8 Nm in lateral bending and 5.5 Nm in axial rotation, as recommended in the literature, to simulate maximal voluntary motion (Fig. 1, E; Dreischarf et al., 2011, 2012; Rohlmann et al., 2009b).

2.4. Sensitivity studies for the distraction and location of the CoR

Four sensitivity studies were performed as part of the present investigation, as shown in Table 3. Previous clinical studies emphasized the importance of iatrogenic distraction for surgical success (Strube et al., 2013). Therefore, the first sensitivity study was designed to exclusively analyze the elementary effects of an iatrogenic distraction in models with different disc heights on the FJFs, FCLFs and segmental RoM. To this end, the amount of iatrogenic distraction (ranging between 0 and 4 mm) and the spinal geometry (Models: 0-4) were uniformly randomized in 250 different samples (Latin hypercube sampling method; OptiSLang, Dynardo, Germany) for each of the four loading cases.

The location of the implant's CoR can vary due to individual anatomical characteristics, differences in implant design and surgical procedure variations. Therefore, three further sensitivity studies (studies 2-4; Table 3) were designed to investigate the effect of *an additional* variation of the position of the implant's CoR on the loading of the facet joints and the segmental kinematics. Thus, this effect was investigated in addition to the segmental distraction by separately varying the location of the CoR in all three anatomical directions in 250 samples:

- Anterior-posterior (AP) position: -3…+3 mm (negative values: posterior from the reference position; positive values: anterior),
- Caudal-cranial (CC) position: -3…+3 mm (negative values: caudal; positive values: cranial),
- Left-right (LR) position: -3…+3 mm (negative values: left from the central reference position; positive values: right).

Table 3: Study design and parameters considered in the sensitivity studies.

Sensitivity study	FE Model	Distraction	Location of CoR	Loading case
1	Model 0-4	0...4 mm	Central position (0 mm)	F, E, LB, AR
2	Model 0-4	0...4 mm	AP-Position: -3…+3 mm	F, E, LB, AR
3	Model 0-4	0...4 mm	CC-Position: -3…+3 mm	F, E, LB, AR
4	Model 0-4	0...4 mm	LR-Position: -3…+3 mm	F, E, LB, AR

Abbr.: AP (anterior-posterior), CC (caudal-cranial), LR (left-right), Flexion (F), Extension (E), Lateral bending (LB), Axial rotation (AR)

One thousand samples were simulated for each of the four sensitivity studies, resulting in 4,000 single FE simulations in the present study. The results were analyzed for each load case, and scatter diagrams were generated for each input-output combination. Linear regression analyses (linear regression model: $y=a \cdot x+b$; R^2: coefficient of determination) were performed between each combination of outputs (dependent variables, e.g., FJF) and input parameters (independent variables, e.g., the amount of iatrogenic distraction). The coefficient “a” (slope/gradient of the regression model) was calculated to identify the input-output sensitivity, which indicates the average change in the dependent variable (output, e.g., FJF) per unit change in the independent variable (input, e.g., distraction).

The FE software package ABAQUS (version 6.10; SIMULIA Inc., Providence, Rhode Island, USA) was used for all simulations.

3. Results

3.1. Sole distraction and subsequent adaptation of the segmental lordosis

In general, the intraoperative distraction places the spinal ligaments under tension. During sole distraction (1st step; Fig. 1, B), the FCLFs non-linearly increased up to approximately 230 N at a maximal distraction of 4 mm (Fig. 2, A). Subsequently, these forces in the posterior spinal ligaments created an extension bending moment, which passively increased segmental lordosis (2nd step, Fig. 1, D) by an average of 1.2° per 1 mm of distraction (Fig. 2, B). A deviation of the CoR to the left or right resulted in small intervertebral rotations of up to 0.8° in the coronal plane for maximal distraction.

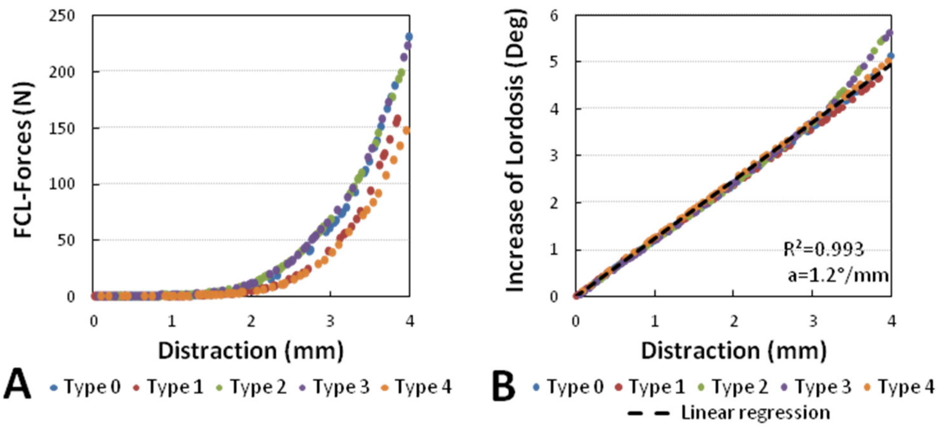

Figure 2: (A) Non-linear increase of the facet capsule ligament forces (FCLFs) in all models due to sole iatrogenic distraction (see Figure 1, B) and (B) subsequent adaptation of segmental lordosis after sole distraction (see Figure 1, D).

3.2. Flexion and extension

In all FE models, the range of flexion (RoF) and FCLFs were primarily affected by the amount of iatrogenic distraction (Fig. 3). The RoF was reduced by approximately 0.5° per 1 mm of distraction (i.e., ~0.5°/mm), and the FCLFs increased by ~12 N/mm. The effect of the implant position was small (Fig. 3). Models with a higher preoperative disc height (Models 1 and 4) predicted a larger RoF but experienced higher FCLFs. The FJFs were typically zero in flexion.

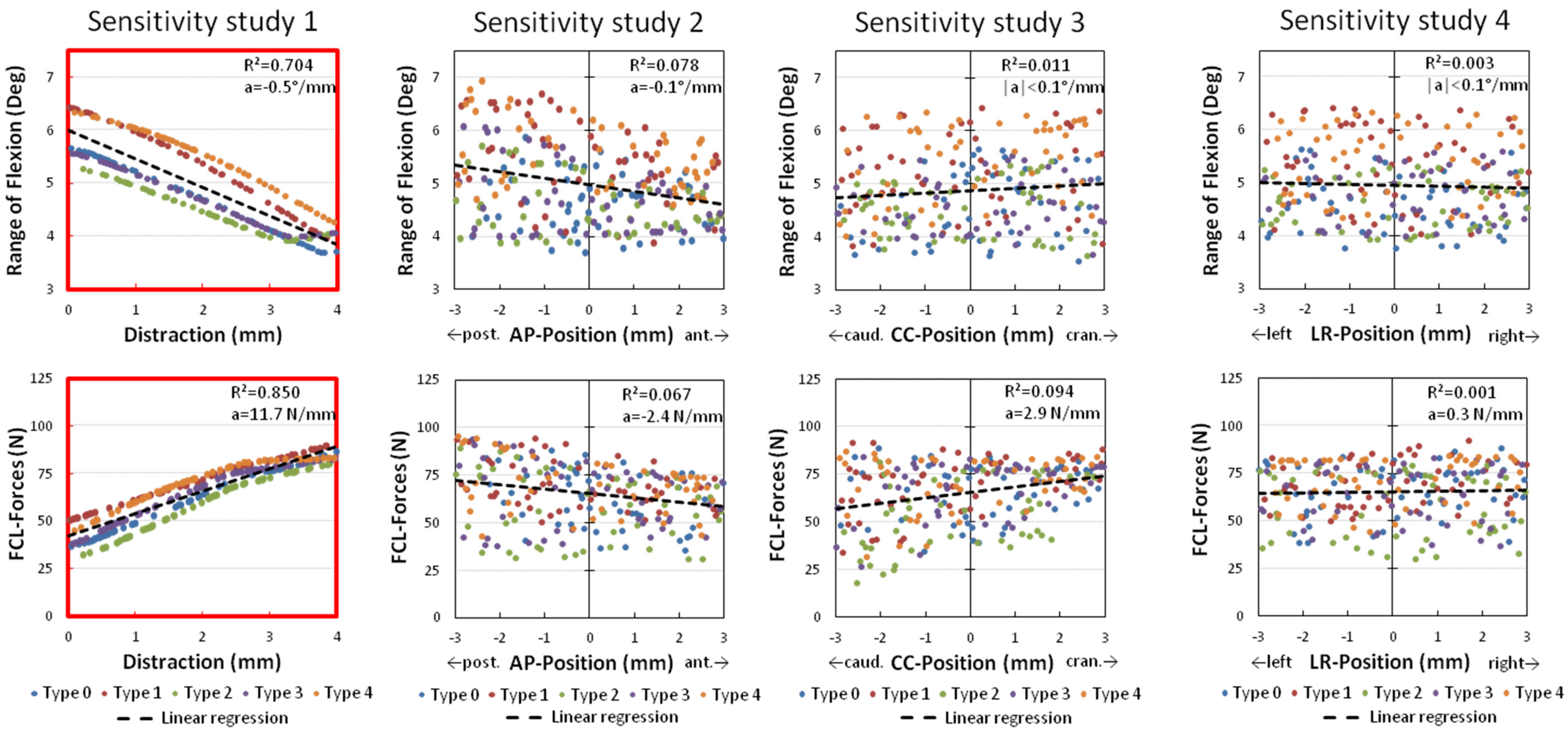

Figure 3: Flexion: Influence of the distraction (sensitivity study 1) and of the location of the center of rotation in the anterior-posterior (AP; sensitivity study 2), caudal-cranial (CC; sensitivity study 3) and left-right (LR; sensitivity study 4) directions on the range of flexion (above) and facet capsule ligament forces (FCLFs; below). The red frames highlight the factors with a large influence.

The RoE was primarily affected by the distraction and implant AP-position (Fig. 4). A distraction increased the resultant RoE by ~0.7°/mm, whereas a more anterior implant position reduced the RoE by ~0.4°/mm (Fig. 4). Similar to flexion, models with a higher preoperative disc height exhibited a higher RoE (Models 1 and 4). The FCLFs were considerably higher in extension than in flexion, but in contrast to flexion, the FCLFs were only slightly affected by the distraction; however, the location of the implant's CoR in the caudal-cranial direction affected the FCLFs. A caudal deviation increased the FCLFs by ~15 N/mm. Both the distraction of the segment and the implant location affected the FJFs. Increased distraction (~11 N/mm) and a more posterior (~7 N/mm) and/or cranial (~14 N/mm) implant location of the CoR resulted in higher FJFs.

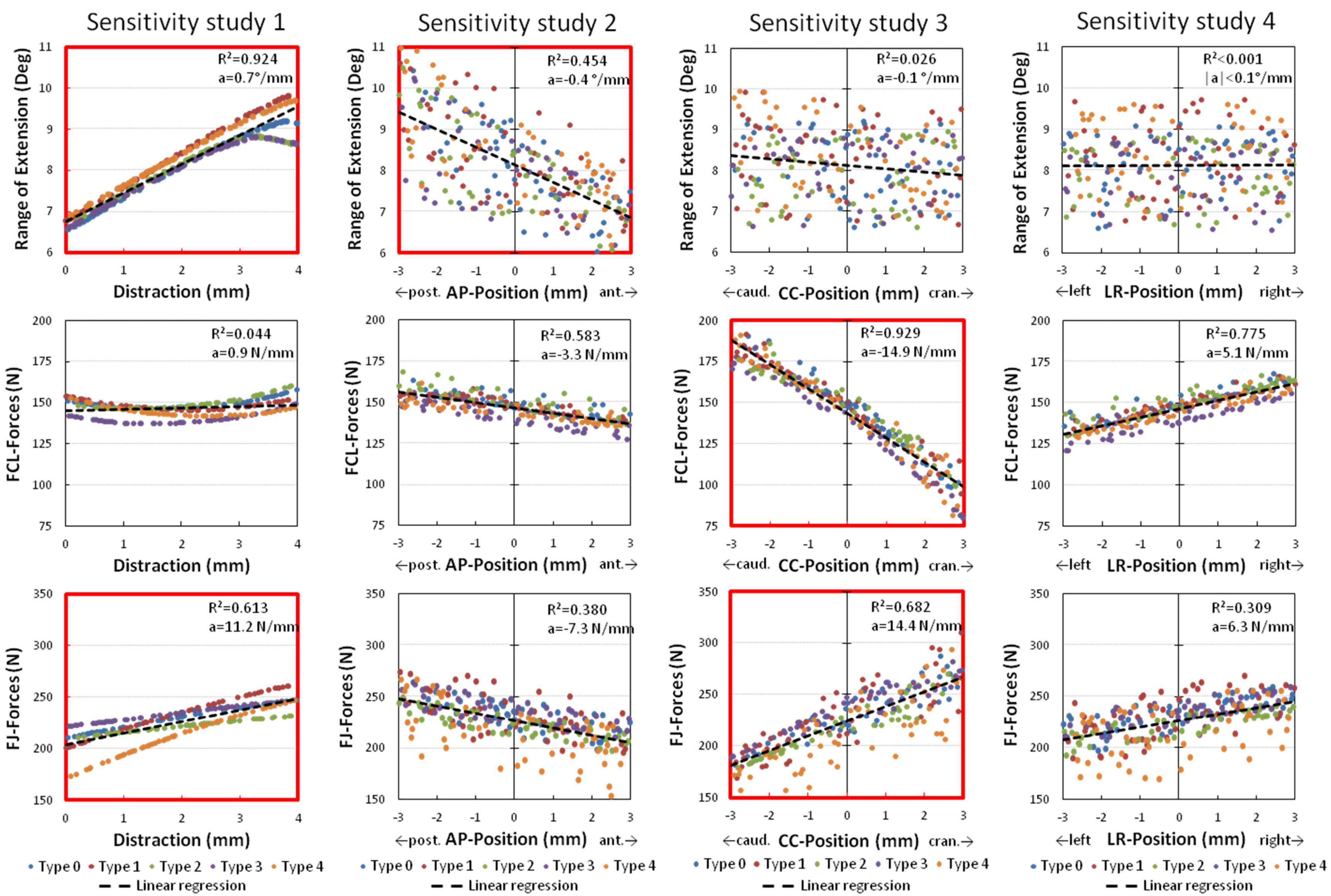

Figure 4: Extension: Influence of the distraction (sensitivity study 1) and of the location of the center of rotation in the anterior-posterior (AP; sensitivity study 2), caudal-cranial (CC; sensitivity study 3) and left-right (LR; sensitivity study 4) directions on the range of extension (top), facet capsule ligament forces (FCLFs; middle) and facet joint forces (FJFs; bottom). The red frames highlight the factors with a large influence.

Iatrogenic distraction only marginally affected the total RoM (~0.2°/mm), i.e., the sum of the RoF and RoE; however, the AP positioning of the CoR (Fig. 5) affected the total RoM. A more anterior CoR location reduced the overall RoM by ~0.6°/mm.

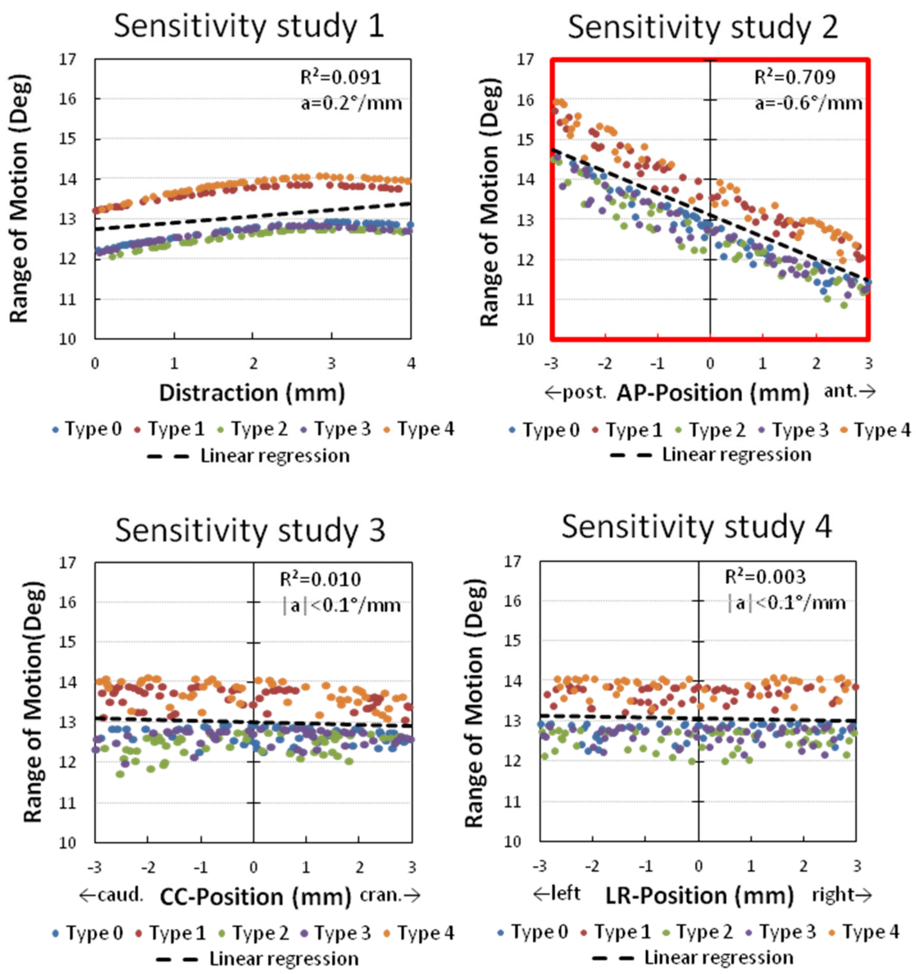

Figure 5: Flexion-Extension: Influence of the distraction (sensitivity study 1) and of the location of the center of rotation in the anterior-posterior (AP; sensitivity study 2), caudal-cranial (CC; sensitivity study 3) and left-right (LR; sensitivity study 4) directions on the range of motion in the sagittal plane (sum of the range of flexion and extension). The red frames highlight the factor with a large influence.

3.3. Lateral bending

The distraction (~0.1°/mm) and location of the implant only slightly affected the RoM during lateral bending (Fig. 6). The FE models with a higher preoperative disc height tended to exhibit a greater RoM.

The FCLFs were considerably higher for the ipsilateral (IL) side than for the contralateral (CL) side of the motion. A distraction of the segment decreased the FCLFs on the ipsilateral side (~10 N/mm) but slightly increased the FCLFs on the contralateral side (~2 N/mm). A more caudal position of the CoR (~7 N/mm) predicted higher FCLFs on the ipsilateral side.

Similar to the FCLFs, the FJFs were higher on the ipsilateral side than on the contralateral side. A distraction of the segment decreased the FJFs on the ipsilateral (~6 N/mm) but increased the FJFs on the contralateral side (~15 N/mm). A change in the CoR in the CC-direction exerted the largest effect on the FJF, resulting in higher forces on both sides with a more cranial position of the CoR (IL: ~9 N/mm; CL: ~9 N/mm).

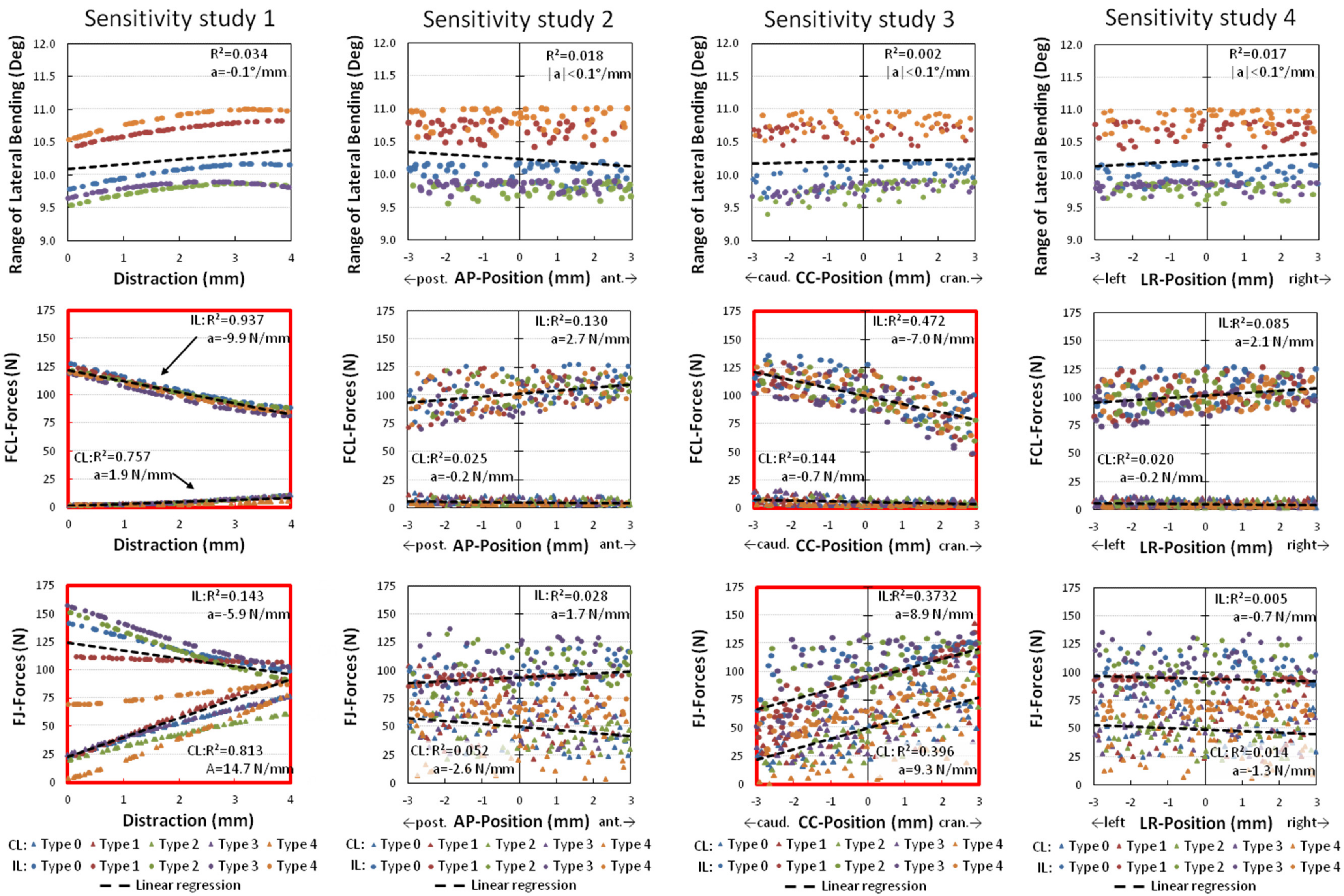

Figure 6: Lateral Bending: Influence of the distraction (sensitivity study 1) and of the location of the center of rotation in the anterior-posterior (AP; sensitivity study 2), caudal-cranial (CC; sensitivity study 3) and left-right (LR; sensitivity study 4) directions on the range of lateral bending (top), facet capsule ligament forces (FCLFs; middle) and facet joint forces (FJFs; bottom). The red frames highlight the factors with a large influence. "IL" indicates the ipsilateral side, and "CL" indicates the contralateral side.

3.4. Axial rotation

The distraction as well as the AP and CC positioning of the implant's CoR only slightly affected the RoM (Fig. 7). An increase in the distraction slightly increased the segmental RoM (~0.1°/mm), whereas a more anterior and/or cranial location of the CoR slightly reduced the segmental RoM (~0.1°/mm).

Iatrogenic distraction of the segment in all models (~4 N/mm) increased the FCLFs. A posterior implant position slightly affected the FCLFs, with more posterior locations exhibiting higher forces (~2 N/mm).

A distraction of the segment decreased (~5 N/mm) and a more posterior (~2 N/mm) or cranial (~2 N/mm) implant CoR increased the FJFs.

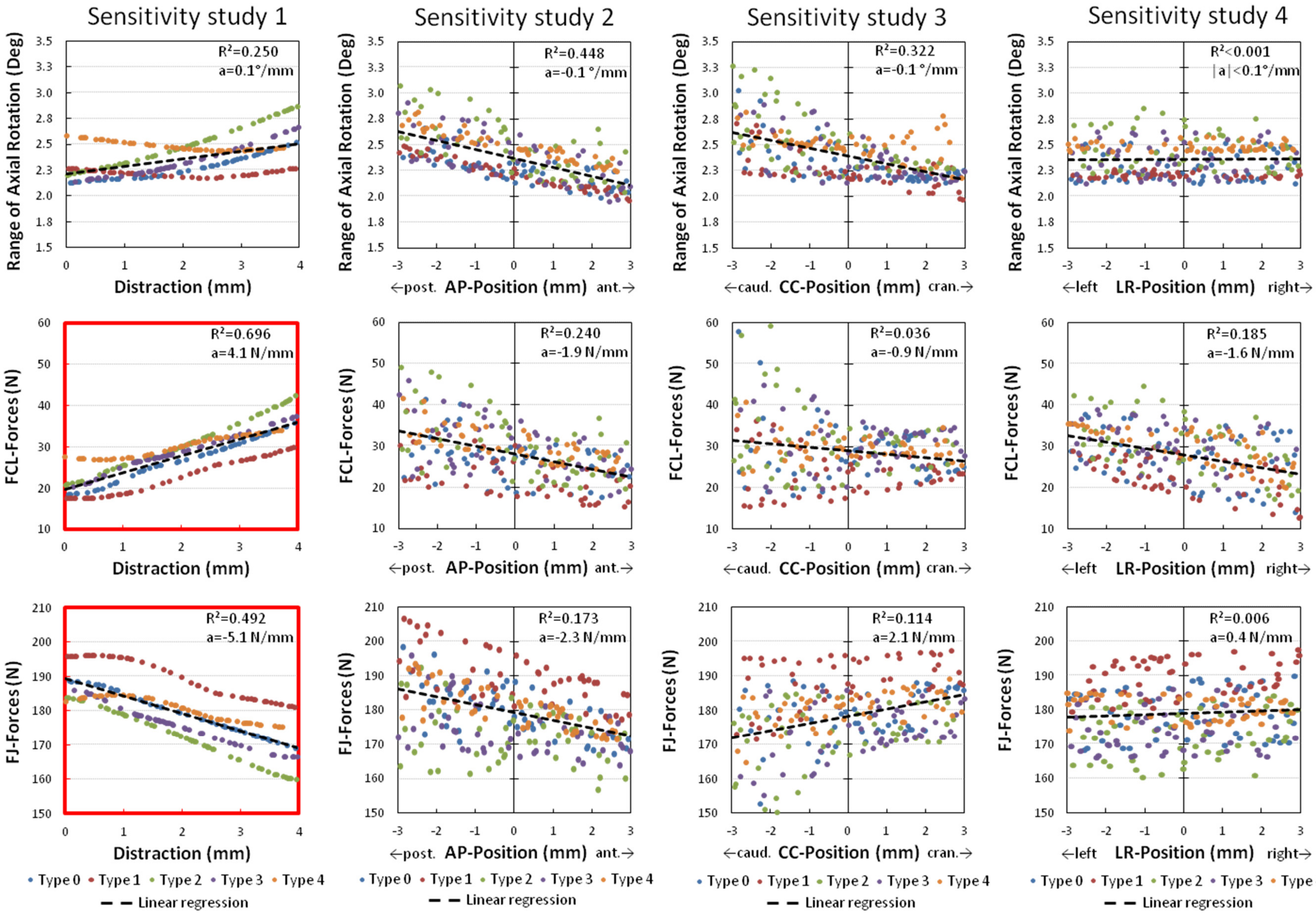

Figure 7: Axial Rotation: Influence of the distraction (sensitivity study 1) and of the location of the center of rotation in the anterior-posterior (AP; sensitivity study 2), caudal-cranial (CC; sensitivity study 3) and left-right (LR; sensitivity study 4) directions on the range of axial rotation (top), facet capsule ligament forces (FCLFs; middle) and facet joint forces (FJFs; bottom). The red frames highlight the factors with a large influence.

4. Discussion

The present finite element sensitivity study showed that the amount of iatrogenic distraction and the location of the implant's CoR specifically affect the resultant RoM and loading of the facet joints after TDR for each anatomical main plane. A greater distraction increases the RoM in extension and, to a lesser degree, in lateral bending and axial rotation but decreases the RoM in flexion. The distraction already strongly increased the FCLFs during surgery and in flexion, with higher values in models with larger preoperative disc heights and increased FJFs in extension. A more anterior implant location decreased the RoM in all planes. For most loading cases, a more posterior location of the implant's CoR increased the FJFs and FCLFs, whereas a more caudal location increased the FCLFs but decreased the FJFs. A deviation to the left or right tended to have the smallest effect on the output parameters. A higher preoperative disc height leads to larger RoM values.

The present study emphasizes the multifactorial relationship between the postoperative RoM and preoperative disc height as well as surgery-related changes. In particular, iatrogenic distraction oppositely affected the RoF and RoE, such that they balance each other out. A distraction increased the tension in the spinal ligaments (e.g., facet capsule ligaments), which more rigorously impeded motion in flexion. In contrast, a distraction increased the gap between articulating facet surfaces and decreased the facet joint articulation overlap (Liu et al., 2006), which facilitated motion in extension (as well as slightly during axial rotation and lateral bending). Accordingly, the clinical measurements of Leivseth et al. (2006) revealed that patients treated with TDR mainly exhibit a motion deficit in flexion at the index level, which might be the result of the change in RoF due to distraction, as shown in the present study. Thus, in accordance with our first hypothesis, a greater distraction substantially alters segmental kinematics and does not *per se* increase the overall stability of the segment in flexion-extension as well as in axial rotation and lateral bending, as previously supposed (Schmidt et al., 2012; Siepe et al., 2012). In addition to these substantial alterations in segmental kinematics, a sole iatrogenic distraction can result in high FCLFs during surgery and thus might harm these ligaments during the surgical intervention. In addition, a larger iatrogenic distraction increases the FCLFs in flexion and, to a lesser degree, during axial rotation. It also increases the FJFs in extension. These observed increases agree with our second hypothesis. Thus, these predicted high loads might explain the clinical results of Strube et al. (2013), who demonstrated that an iatrogenic overdistraction is significantly associated with clinical failure after TDR. Furthermore, Leivseth et al. (2006) showed that the amount of distraction is typically larger in L5-S1 than in L4-5, which might partially explain the unsatisfactory clinical results of a TDR in the lumbosacral segment L5-S1 (Siepe et al., 2008, 2007). The complete postoperative RoM in the sagittal plane (sum of the RoF and RoE) was measured in patients in several clinical studies, and a direct correlation with the resultant clinical outcome was investigated (e.g., Johnsen et al., 2013; Leivseth and Brinckmann, 2010; Leivseth et al., 2006; Siepe et al., 2009; Strube et al., 2013). However, the resultant complete RoM appears to be insensitive to detecting the elementary mechanical changes shown herein, in particular those due to the iatrogenic distraction (Johnsen et al., 2013).

The influence of the preoperative disc height on the outcome after of TDR is an on-going subject of debate; some authors argue that a preoperative more rigid and collapsed disc might compensate for the rotational instability of an artificial disc (e.g., Siepe et al., 2012). In the present study, FE models type 1 and 4 with higher preoperative disc heights and thus lower disc stiffnesses, predicted a larger average RoM, especially during flexion (Maquer et al., 2014). Due to this lower disc stiffness, the posterior spinal column experiences a higher load, which leads to larger FCLFs in flexion. This relationship might partly explain why the subjective patient satisfaction rate is significantly lower in patients with a greater preoperative disc height as well as why sagittal profile types 1 and 4 from Roussouly et al. (2005) result in worse clinical outcomes (Siepe et al., 2009; Strube et al., 2012). However, this effect might be confounded by an interrelation between the preoperative disc height and the resultant distraction because a higher disc height appears to require and thus might result in a reduced iatrogenic distraction. However, the combination of both (high preoperative disc height and additional large iatrogenic distraction) might lead to unsatisfactory clinical results.

Aside from the distraction, the location of the CoR of an artificial disc can affect the postoperative facet loading and segmental motion. The distance between the CoR and the resultant FJFs and/or FCLFs is mechanically decisive. For larger distances (e.g., an anterior position of the CoR during flexion, extension or rotation), the facets and capsule ligaments can more effectively balance the external loads due to the larger lever arm, which decreases the FJFs or FCLFs as well as the segmental rotations.

Although computational models may provide insight into the loading of spinal structures, they often suffer from several limitations, such as deterministic study designs with few selected calculations that use only one simplified spinal geometry (Dreischarf et al., 2014). To account for these general limitations, this study used a sensitivity approach that considered five different elementary geometries in several thousands of FE calculations to reveal the most important mechanical parameters that influence the results of TDR surgery. However, only one material composition (Table 1) was selected, although the material characteristics can vary between subjects and by the degree of degeneration. Furthermore, spinal ligaments were simplified as tension-only spring elements with nonlinear elastic behavior, although they show a viscoelastic behavior in experimental studies, which decreases part of the load over time (Troyer and Puttlitz, 2012). However, this simplification will not qualitatively alter the presented order of sensitivities. Biomechanical models are simplified reflections of complex biological systems, such as the lumbar spine, but can help to identify surgery-related mechanical risk factors. Nevertheless, these risk factors must be clinically evaluated and validated in patients. The amount of clinically occurring distraction and, in particular, the deviations of the CoR used in this study are unknown and are thus reasonably estimated for the current study. The employed distraction of a maximum of 4 mm was simulated starting from the initial intact disc height of the FE models. This approach agrees with that of Johnson et al. (2013) and Leivseth et al. (2006), who demonstrated that the insertion of a prosthesis (ProDisc II) considerably increases the disc height in L5-S1 by more than 3.5 mm compared with the normal intact disc height. This increase is even greater when compared with the degenerated disc height. Furthermore, simplified loading conditions (pure moments) were used, similarly to *in vitro* investigations (Wilke et al., 1998) without a follower compression force (Patwardhan et al., 1999). Due to the systematic change in the location of the CoR in the present study, the follower load would create artificial moments and thus an additional intersegmental rotation, depending on the misplacement of the CoR (Dreischarf et al., 2010), which would yield misleading results. Furthermore, potential load differences that arise, for instance, from different alignments of the lumbar spine were not considered.

In conclusion, this study emphasizes that an overdistraction of the segment increases the FCLFs during surgery as well as in flexion, and it also increases the FJFs in extension. Furthermore, an overdistraction considerably alters the segmental kinematics. However, these mechanical changes do not appear to affect the resultant complete RoM, i.e., the sum of the RoF and RoE in the sagittal plane. The resultant postoperative loading of the facet joints and the RoM are furthermore a multifactorial product of the location of the implant and the preoperative disc height. The results of the present study may explain the worse clinical results after TDR in patients with overdistraction as well as with higher preoperative disc heights (Siepe et al., 2009; Strube et al., 2012, 2013).

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3. Summary of results

Publication 1 – "In vivo loads during upper body bending"

This *in vivo* study on five patients with a telemeterized vertebral body replacement shows that forward bending of the upper body during upright standing substantially increases the spinal loads already present at smaller inclination angles. The flexion process thereby showed a characteristic inclination-load pattern, with an initial force increase until an average upper body inclination of approximately 33° (range: 32°-39°), resulting in an average force of 450 N (425-638 N). With ongoing flexion of the upper body, the measured implant force was constant, or even showed a slight decrease, until an average maximal inclination of 53° (44-66°). Maximal average force values of 565 N (450-770 N) were measured in all subjects when returning to the upright position. These results demonstrate that even during relatively small inclinations, lumbar spine loading is markedly high. This implies that bending is a potential mechanical risk factor for LBP when performed frequently. Furthermore, the measured inclination-load pattern allows for the validation of biomechanical models.

Publication 2 – "In vivo loads during different lifting techniques"

These *in vivo* results emphasize that lifting a weight from the ground can result in extraordinarily high loads of more than 1600 N in the anterior spinal column. Interestingly, the utilization of either the stoop or the squat lifting technique did not substantially affect the measured implant loads. Although patients followed the instructions and performed both techniques differently, with more knee bending and less upper body bending during squat lifting compared to stoop lifting, the resulting average load differences between both elementary techniques were found to be only 4%. However, inter-individual differences of 28% were found in the load ratio, with one subject showing 10% smaller loads and another subject showing 18% larger loads, on average, in squat lifting than in stoop lifting. Although the lifting technique did not influence the results on average, it could be demonstrated that the crate location slightly affected the loading, with an average of 14% smaller loads occurring when the weight was lifted laterally versus when lifting an identical weight in front of the body. From a biomechanical perspective, and in contrast to the common opinion, the here presented results do not advocate the stoop or squat lifting technique. Lifting in general resulted in the highest loads ever measured *in vivo* on a vertebral body replacement.

Publication 3 – "Age-related loss of lumbar spinal lordosis and mobility"

This study on a large asymptomatic cohort (n=323) demonstrates that with increasing age, the lumbar spine flattens and mobility in the sagittal plane decreases significantly. In detail, aging significantly affects total lumbar lordosis (reduction: ~20%, p<0.001) as well as the range of flexion (~12%, p<0.001) and extension (~31%, p<0.001) in the lumbar spine during a standardized choreography in upright standing, when comparing the oldest (>50 yrs) to the youngest (20-29 yrs) cohort. Furthermore, the process of aging characteristically differs between men and women and is level dependent. For the first time, it was shown in a large cohort that the lower part of the lumbar spine generally retains its lordosis and mobility over time, whereas lordosis and mobility are significantly reduced in the middle lumbar spine. Gender only affects the range of extension (p<0.001), with significantly larger values in females than in males. These results lay the groundwork for an improved understanding of age- and level-dependent spinal disorders and demonstrate the need for age-specific surgical treatments in order to achieve long-term clinical success.

Publication 4 –"Age- and gender-related alterations in the lumbo-pelvic rhythm"

This publication focused on the interplay between the lumbar spine and the pelvis during upper body flexion when standing upright (n=309). It was demonstrated that aside from the amount of lordosis, sacrum orientation is also significantly affected by aging (verticalization: ~30%, p<0.001). In contrast to the reduction in the lumbar range of flexion, the pelvic range of flexion increases (~30%, p=0.010) with aging, particularly in men, and this seems to compensate for the loss of lumbar spine mobility. These substantial changes resulted in a significant reduction of the L/P ratio (i.e., the change in lumbar lordosis relative to the change in pelvic orientation during the motion) with aging for full flexion as well as for the early part of the flexion motion. Furthermore, L/P ratios were significantly smaller in females than in males during middle and late flexion (p<0.001). These results emphasize that the currently employed functional clinical tests (e.g., the Schober test, fingertip-to-floor distance) appear insufficient for a sophisticated differential diagnosis that requires an age- and gender-specific functional assessment of the spinal and pelvic motion. Changes in the L/P ratio with aging also suggest an increase in spinal loading with increasing age.

Publication 5 – "Lumbar lordosis and motion in daily life"

Through long-term measurements (over 24 hours) of 208 asymptomatic subjects, this study demonstrated that lumbar lordosis is highly variable over the course of the day. It was thereby demonstrated for the first time that on average, lordosis is significantly smaller in daily life (8.0°, $p<0.001$) than in the clinically employed standing reference position, in which X-ray investigations are currently performed (33.0°). Furthermore, the ranges of flexion and extension, clinically determined during upper body bending in standing (short-term measurements), differed significantly from the corresponding values determined using long-term measurements in "real life". The range of flexion was significantly larger (20%, $p<0.001$) and the range of extension significantly smaller (13%, $p<0.001$) during the day than in the standard short-term evaluation. Moreover, it could be demonstrated that the effects of age and gender on lumbar lordosis and motion significantly differed between the short-term and long-term evaluations and resulted in opposite conclusions. Therefore, the clinically and biomechanically currently employed short-term investigations in standing must be questioned with respect to their applicability to daily life. These results provide a new, 24-hour perspective on lumbar lordosis and motion, which will help to improve surgical planning and raise the awareness of the mechanical challenges that implants and spinal structures face during the day.

Publication 6 – "Spinal mobility in daily life"

The actual number of spinal movements that occur during the day in the sagittal plane were measured in 208 study participants. The median number of spinal movements that altered the lumbar lordosis by more than 5° was determined to be approximately 4400 over the course of 24 hours; 66% of all determined movements caused lordosis changes ranging from 5°-10°. For instance, only 3% of all counted movements caused lordosis changes within a range of 20°-25°. Thus, substantial high numbers of movements causing smaller lordosis changes were measured, and only a small number of large movements were determined. On average, 50 movements during the day reached the full flexion range of motion. Large inter-individual differences were found. In most investigated movement classes, a significantly higher number of movements were detected in females than in males. The presented data further our basic understanding of daily human behavior and are highly relevant to realistic *in vitro* or *in silico* spinal implant testing.

Publication 7 – "Comparison of lumbar finite element models"

Using eight different, previously validated finite element models of the lumbar spine from international research groups, this study demonstrated that the pooled predictions of all these models were in better agreement with *in vitro* and *in vivo* reference measurements than individual models' results. Under standardized loads, almost all predicted lumbar motion values fell within the measured *in vitro* reference ranges. The differences in median values between the models and experimental results were only 2° for flexion-extension, 1° for lateral bending and 5° for axial rotation. Individual model predictions for facet joint forces or intradiscal pressure values exceeded the *in vitro* range; however, the median of all models again showed a good agreement with the experimental median values. Except for flexion loading, this was also true for combined loading modes simulating the *in vivo* situation. This study provides a detailed overview of the employed material properties as well as of all model geometries (e.g., lumbar lordosis) of the most-known international static finite element models of the lumbar spine to assist future research. Furthermore, this study emphasizes that the generalization of single finite element model predictions remains a concern. Future studies aiming to predict quantitative results should incorporate several representative models and statistical methods to improve the prediction and assessment of inter-subject variability.

Publication 8 – "Mechanical risk factors of a total disc replacement"

This probabilistic finite element study employed several representative lumbar spine morphologies in 4000 simulations and analyzed a total disc replacement. The investigation revealed the complex interplay of individual and surgery-related parameters (e.g., preoperative intervertebral disc height, iatrogenic distraction, implant location) with clinically essential postoperative outcomes (e.g., facet joint loading, segmental motion). The amount of iatrogenic distraction was thereby essential, as it substantially altered the segmental kinematics at the index level (e.g., in flexion) and considerably increased facet capsule ligament forces during surgery and for instance during postoperative flexion. However, the overall sagittal range of motion, which is usually clinically determined, was almost insensitive, particularly to the amount of distraction, during TDR. In addition, implant location specifically affected segmental motion and facet joint loading in a direction-dependent manner. The presented findings were verified by clinical observations, could biomechanically explain unsatisfactory results for patients with over-distraction and might assist surgeons in accounting for critical surgical parameters, such as implant position. Furthermore, the overall sagittal range of motion at the index level appeared to be insensitive to most surgery-related changes, which calls into question its clinical diagnostic value for a TDR.

4. Discussion

Low back pain is one of the most serious health care problems worldwide [1,3,4]. Due to the challenging demographic changes of an aging society, this problem will increase in industrialized countries. Today, the complexity and multifaceted causes of LBP result in a very demanding medical situation, which is often treated with insufficiently evidence-based therapeutic approaches. From biomechanical and clinical perspectives, the knowledge of risk factors for LBP, precise diagnoses that allow patient-specific treatment selection and the understanding of currently employed research tools and treatment options all remain incomplete. In clinical practice, this results in low therapeutic success rates and high revision surgery numbers and complication rates [98,99]. The loading of the lumbar spine as well as its individual shape and motion are recognized to play major medical roles for LBP patients and are thus key factors for improving patient-centered care. Therefore, the present dissertation investigated in detail the *in vivo* loading of the lumbar spine during the essential activities of upper body bending and lifting of heavy weights. Both activities are assumed to result in high loads and thus to be associated with LBP. Furthermore, the shape and motion of the lumbar spine and potential age- and gender-related changes were investigated in large cohorts using standard short-term choreographies as well as, for the first time, using long-term measurements in daily life. Finally, currently employed finite element models of the lumbar spine from several international research groups were, for the first time, directly evaluated and compared as a validation of a relevant clinical-biomechanical analysis. The overall insight gained was subsequently employed in a probabilistic finite element study to investigate in detail individual as well as surgery-related risk factors of a lumbar total disc replacement with the aim of directly improving the current clinical care of LBP patients.

Loading on the VBR during upper body bending in the sagittal plane

Although different epidemiological studies have concluded that frequent upper body bending and the lifting of heavy weights, in particular, are considered mechanical risk factors [11,12], the understanding of the spinal loading that occurs during these essential activities and of the factors influencing loading is still incomplete. One important reason for this lack of knowledge is the limited number of direct *in vivo* measurements that validly and objectively quantify the loading within the human body. Since Nachemson's early intradiscal pressure measurements [19,20], subsequent investigations by Wilke et al. [31,38], Sato et al. [39] and Takahashi et al.

[40] have examined upper body bending and demonstrated, in agreement with the results of the current dissertation, that this activity yields a substantial load increase with respect to standing. However, in most cases, only single IDP values were reported without detailed, continuous information of loading during the movement. Furthermore, the performed inclinations were small (e.g., Nachemson [19]), or no information of the subject's upper body inclination was reported in detail (e.g., Sato et al. [39]), which makes a comparison between different studies difficult. In addition, although IDP measurements give fundamental insight into the *in vivo* spinal loading of healthy, asymptomatic subjects, this procedure was limited by measuring only a few or a single subject (e.g., Wilke et al. [31]) and by allowing only single measurement sessions. This makes an assessment of the intra- and inter-individual load variations mostly impossible and thus limits the generalization of the results. Therefore, the present dissertation provides, for the first time, detailed load information that is based on more than 80 single measurements in standing collected during numerous measurement sessions. The gained results characterize the load pattern during the motion and emphasize that maximal loads in the anterior spinal column occur not necessarily at an upper body inclination angle of 90°, as usually expected [74,100], but already occur at intermediate flexion angles (32-39°) in vertebral body replacement (VBR) patients. This interesting finding may illustrate an important change in the stabilization mechanism of the upper body during motion, which is known as the "flexion-relaxation" phenomenon and was first reported by Floyd and Silver in 1951 [101]. Floyd and Silver, as well as subsequent investigators [101,102], could show that after a certain trunk inclination (approximately at 30-45°), the electromyograph (EMG) activity in specific global extensor muscles (e.g., iliocostalis or longissimus) decreases, despite the increase in the net external moment [100]. Thus, the upper body is progressively stabilized by passive spinal components with further flexion (e.g., passive muscle forces or ligament forces). Therefore, it can be speculated that structures, such as the thoracolumbar fascia or the supraspinous ligaments, may stabilize the trunk more effectively at higher inclinations with larger lever arms, resulting in smaller compressive forces. This might partly explain the typically measured inclination-load pattern in the present dissertation, with maximal forces already at an intermediate trunk inclination. The here presented findings (paragraph 2.1) are in disagreement with computational predictions, e.g., of kinematic-driven finite element models in asymptomatic subjects without LBP (Arjmand et al. [74], Hajihosseinali et al. [100]), which usually compute maximal compression forces at a

90° inclination, where the net-external moment is at its maximum. The here presented results can furthermore be compared with those of Takahashi et al. [40], who published continuous IDP values for three subjects, but only for small to intermediate inclinations. Two of the subjects showed a more linear and subsequently sinusoidal increase in intradiscal pressure, which is more comparable to the findings of the aforementioned computational studies [74][100]. However, although all three subjects had very similar anthropometrics, the third subject showed a loading curve with a near-maximal spinal loading at an early state of trunk flexion. These findings are more similar to the results of the present dissertation. These overall dissimilar loading curves could be explained by differences in the specific lumbo-pelvic rhythm during the flexion motion. Tafazzol et al. [72] already demonstrated that differences in the specific L/P ratio (i.e., the change in lumbar lordosis relative to the change in pelvic orientation during motion) can substantially change the amount of the aforementioned passive and active contribution to trunk stabilization and thus alter the resultant spinal loading. The current dissertation also presents an analysis of the lumbo-pelvic rhythm (paragraph 2.4), which also demonstrates that there is large inter-subject variability in the L/P ratio. Furthermore, due to posterior fixation, the L/P ratios of the measured VBR patients might also be different than those of healthy subjects, which could influence the spinal loading. These overall findings emphasize that even small, inconspicuous changes in the way in which an exercise is performed can substantially affect loading during the motion. A further explanation for the here presented loading curve might be an increase in passive load support of the abdomen or in the intraabdominal pressure at higher inclinations; however, these effects are still very controversially discussed in the literature [103–108].

The results presented in paragraph 2.1 might have important clinical and ergonomic consequences. They demonstrate that in daily life and during work-related activities, which frequently incorporate flexion movements, the spine is already highly loaded at small inclinations. This knowledge is also of particular importance for the prevention of injury in patients, especially directly after surgery, in order to avoid complications, such as implant subsidence or damage to the bony vertebral body. As a further consequence, the here presented information of loading at characteristic points of upper body inclination could serve as a basis for the validation of computational models, which play an increasingly important role in spinal biomechanics. Due to the complexity and invasiveness of *in vivo* measurements, several inverse static and dynamic computational models have recently been developed to predict spinal loading or muscle forces in relevant postures, e.g., for ergonomic, sports science or orthopedic purposes (e.g., [74,109,110]). However, as a basis for realistic simulations, these models require adequate validation [41,79]. As upper body bending is not only assumed to result in high spinal loads but also demonstrated to result in the largest range of motion of all the main anatomical planes [23], this particular exercise is frequently simulated and employed for the validation of computational models (e.g., [100,111]). The here presented inter- and intra-subject variations of the measured loads and inclinations could be used as realistic ranges for validation. Following this principle, in a further co-authored publication (Zander et al. [112]), which is not integrated in the current dissertation, it could indeed be demonstrated that load predictions of a frequently employed inverse dynamic model (AnyBody Technology, Aalborg, Denmark [110]), modified by the insertion of a VBR, agree well with *in vivo* measurements of a VBR. Furthermore, up to 88% of the *in vivo* inter- and intra-subject variability of the model could additionally be explained by the variation of patient body height and weight and the fraction of the force carried by the VBR. Therefore, the *in vivo* results presented in the current dissertation can increase the confidence in those models, which in turn can provide highly relevant information, such as on muscle forces, which are only at most partly or not measurable *in vivo* yet.

In addition to the aforementioned consequences, the here presented *in vivo* measurements are particularly interesting in terms of more-realistic implant testing as well as biomechanical analysis in *in vitro* investigations. The results of this dissertation deliver a complete biomechanical picture of upper body bending as an essential activity by providing loads measured *in vivo* and by measuring the number of spinal movements (paragraph 2.6), the spinal curvature and the range of motion in the sagittal plane during daily life (paragraph 2.5). This knowledge is important for *in vitro* tests that aim to reveal the actual causes of implant or tissue failure in patients and can help to improve the relevance and closeness to reality of those tests. Currently, *in vitro* testing is based mainly on the application of a single pure moment (mostly 7.5 Nm) without an additional physiological compression force [113,114]. Alternatively, a hybrid protocol (displacement/angle controlled) for the application of predefined rotations is also employed [115]. It has to be clearly noted that these testing procedures have the advantage of offering reliable and standardized testing and thus enable comparisons among testing laboratories. However, as shown in the present dissertation, the lumbar spine is constantly highly loaded during flexion exercises, in particular, and it is submitted to multiple different posture changes during the day (paragraph 2.5 and 2.6). Specifically, the quantification of spinal movements in paragraph 2.6 demonstrated that when extrapolating the presented measurement data to 1 year, more than 1,000,000 movements with changes in lordosis between 5-10° and approximately 8000 movements larger than 45° occur in human beings on average. This might be of interest as a basis for fatigue tests, e.g., of motion-preserving implants or fusion devices. Furthermore, the results presented in paragraph 2.5 highlight that the spine is on average in a much more flexed position than usually assumed during current *in vitro* investigations. This indicates a substantially different working point during the day and thus a different average loading of implants as well as of adjacent spinal structures than usually assumed. Moreover, different radiological studies, such as those by Pearcy et al. [23], Plamondon et al. [116], Dvorak et al. [117] or Steffen et al. [118], measured the total and segmental rotations during full flexion in standing, short-term measurements, which serve as important reference values for those implant tests. The results of the present dissertation, however, indicate that particularly during flexion, the actual range of motion during the day is significantly larger than these reference values in standing. This implies that the overall loading scenario *in vivo* during the day is more demanding than usually assumed. Therefore, all these limitations call into question the meaningfulness and expressiveness of current *in vitro* tests in spinal biomechanics with respect to actual daily situations.

Loading on the VBR during stoop and squat lifting

In addition to frequent upper body bending as a potential risk factor for LBP, the results of the present dissertation confirm that lifting heavy weights results in a considerable spinal loading of more than 1600 N, even in the upper lumbar spine at level L1. This loading might even be higher in the lower lumbar spine, where maximal loads are usually assumed to occur at L5-S1. This exceptionally high loading during lifting is generally in accordance with the literature. Early studies of Nachemson and Elfström [33] showed that the largest IDP values of several different investigated activities were determined during lifting. In a comparison study of more than 1,000 different activities, Rohlmann et al. [119] previously demonstrated that lifting resulted in the highest loads of all the investigated activities. In addition, Wilke et al. [31,38] investigated several activities of daily living and also confirmed that lifting resulted in the highest spinal loads. Therefore, during recent decades, various factors that might affect loading during lifting have been investigated (e.g., lifting speed [120,121], load-splitting [45], gender [122], lifting technique [43,123,124], size of the weight [46], and mental processing [125], among others). Thereby, potential load differences between stoop and squat lifting were in the focus of research and very controversially discussed [43,44,47,123]. Nevertheless, the common assumption that smaller spinal loads occur during squat lifting is largely the accepted consensus and has thus become integrated in recommendations in back schools as well as in work-related ergonomic guidelines [48][49]. However, in 1999, van Dieen et al. [43] concluded in a highly regarded review of 27 different studies, which usually employed model estimations of spinal compression forces or net-moment measurements, that both techniques result in similar spinal loads. This is in agreement with the here presented *in vivo* measurements. Although patients performed the two lifting techniques substantially different from each other, as confirmed by the measurements of upper body inclination and knee bending, the resultant forces differed on average by only 4%. Therefore, based on this biomechanical study, neither of the two here presented lifting techniques can clearly be favored with respect to smaller spinal loads. However, in agreement with early findings of Andersson et al. [37], the current results additionally indicate that the position of the weight appears to be more important for spinal loads than the employed lifting technique. In the current investigation, the crate was usually close to the toe tips and thus clearly in front of the body. In a few additional *in vivo* measurements, the crate was placed directly between the feet close to the body. This resulted in a load relief, which might explain the measurement results of Wilke et al. [38], who found approximately 35% smaller IDP values during squat lifting than during stoop lifting. Thus, in general, the anterior-posterior distance appears to be highly important and should be minimized to reduce spinal loading during lifting. Moreover, the inter-subject variability must be emphasized, as differences in the load ratio of up to 28% were observed (Patient 4 (WP4) vs. Patient 5 (WP5)). These differences may partly be explained by the individual accomplishment of the lifting exercise, as indicated by the differences and the variability in the achieved upper body inclination and knee-bending angle, which result from each patient's individual levels of fitness, coordination and flexibility. Differences could also be caused by factors, such as lifting speed, which slightly differed among subjects and measurement sessions and was not controlled or standardized [120,121]. During the measurements, except for the introduction into stoop and squat lifting, few further instructions were given to the patients because the aim was to measure a real-life situation, which is obviously characterized by non-standardized lifting procedures. In agreement with van Dieen et al. [43], those variations have to be considered an integral part of the lifting technique in the workplace or in daily life. This argument is essential for an evidence-based and robust recommendation of a certain lifting technique, which is assumed to result in smaller spinal loads. However, such a robust recommendation cannot be given for stoop or squat lifting based on the here presented results. Furthermore, it has to be clearly noted that in this *in vivo* study, only the *implant loading* on a VBR as a measure of the spinal loading is reported. For an overall recommendation of a specific lifting technique and for the goal of preventing LBP in general, the overall occupational safety situation as well as for instance the frequency of the lifting exercises, which are performed in a certain time period, are also decisive. Moreover, a subject's individual constitution and the specific working environment have to be considered. Only an integral approach considering all these factors can result in a better understanding of the etiology of LBP.

General limitations of *in vivo* measurements with a telemeterized VBR

The here presented *in vivo* measurements (paragraphs 2.1. and 2.2) provide a unique insight into spinal loading directly determined within a human body in various measurement sessions as well as in different subjects. However, as a general limitation of those *in vivo* studies, the small number of patients did not allow a sophisticated inferential statistical analysis. Yet, as an advantage over *in vivo* intradiscal pressure measurements, robust results based on numerous sessions can be provided and the intra-subject variability can be assessed. All measurements that were performed over recent years via a telemeterized VBR were characterized by a large intra- and inter-subject variability. This is in agreement with telemeterized implant measurements in other main anatomical joints, e.g., the hip or the knee [126,127], and with the few IDP measurement studies that included several subjects [39]. Aside from the aforementioned differences in the performance of the here investigated activities (e.g., the amount of upper body inclination), this variability arises from anatomical (e.g., differences in lumbar lordosis, thoracic kyphosis, pelvic morphology, material characteristics), diurnal (e.g., load history of spinal structures) and anthropometric variations (e.g., body height, weight, body mass index) among subjects and measurement sessions. Contrary to IDP measurements, which are usually performed in the non-degenerated intervertebral discs of healthy volunteers [31], the here presented findings are based on measurements in *patients* that were at an older age. Due to this reason, as well as to the generally very labor-intensive measurements and the required measurement equipment (e.g., inductive coil, antenna), it was not possible to additionally employ more sophisticated motion capture techniques on the subjects' backs (e.g., Vivon analysis), although these would have allowed more accurate determinations of parameters such as the upper body inclination angle. However, the assessment of each patient's kinematics from the videotaped images served only as an addition to the accurate load measurements to demonstrate the expected differences in lifting execution and to describe characteristic points during the flexion motion with an acceptable accuracy. Furthermore, it clearly has to be noted that due to the implantation of the VBR as well as the posterior fixation system, several spinal segments become fused; thus, the spinal loading and motion of the patients is altered compared with those of young, asymptomatic subjects [36,128]. The complete spinal loading is therefore not transferred via the VBR but is shared in the implant complex with the remaining vertebral body and the posterior fixation system. However, in a recent finite element study, Zander et al. [129] estimated that more than 82% of the total compressive force is transferred via the VBR and only 6% and 12% by the remaining bone and the fixation system. Moreover, due to the large and very stiff implants employed in the here present *in vivo* studies and the small amount of bone between the pedicel screws and implant relative to that in the computational study (evaluated by available patient X-rays), it appears reasonable that the overall majority of the loading is transferred via the VBR. However, the exact load distribution in a specific patient is unknown, externally unquantifiable and potentially dependent on the fusion process after surgery. This individual internal load sharing might therefore influence the loading curves during the motion. Moreover, due to the rigid and large implants and the internal fixateurs, a moment transmission at the fused segments is possible. This requires smaller moment compensation by the muscle apparatus, which in turn might result in a smaller local spinal loading in comparison to the healthy state with deformable intervertebral discs. This relationship was recently demonstrated using an inverse dynamic computational model in another co-authored study (Zander et al. [112]). Furthermore, it has to be emphasized that the *in vivo* VBR measurements were performed in the upper (vertebral body L1; patient 1-4 (WP1 to WP4)) and middle (L3; patient 5 (WP5)) lumbar spine. A quantitative comparison of the results with IDP measurements in healthy subjects is therefore difficult, as these measurements were usually performed more caudally at spinal levels L3-L4 or L4-L5 (e.g., [31,39]). The absolute forces measured on a VBR are of direct value for implant testing. However, due to all the aforementioned limitations, the absolute forces in a distinct measurement session are generally difficult to interpret and to compare between patients. Therefore, only the “load ratio” between different activities in a certain session or the load changes due a patient’s activity was employed, calculated and compared. Several studies have already shown that this approach results in good agreements with corresponding IDP measurements for various activities [130]. Furthermore, this procedure has already been employed to identify essential parameters that affect spinal loading during different key activities, such as sitting or standing [131,132]. Therefore, the here presented measurements performed in various sessions and in five patients provide a robust insight into differences in spinal loading among essential activities/postures (e.g., between different lifting techniques or different points during upper body bending), which was the main goal of these studies.

Age- and gender-related changes of spinal shape and motion in short- and long-term measurements

The second part of the present dissertation focused on the *shape and motion* of the lumbar spine as complementary characteristics to lumbar spine *loading*. In the first study on particularly age-related changes of spinal shape and motion (paragraph 2.3), the standing position and upper body bending were investigated. This assessment in standing was in accordance with the standard procedure, in which X-ray measurements are performed in clinical studies [21,27]. The ranges of motion in the sagittal plane are here quantitatively determined between three static positions: upright standing, standing flexed and standing extended [23,116]. Furthermore, these positions have been the focus of various previous research studies that also employed non-invasive measurement techniques to analyze the shape and motion of the lumbar spine (e.g., [133,134]). In agreement with several previously published studies, it could be shown that lumbar lordosis and spinal motion are significantly affected by aging, resulting in less lordosis and mobility in older males and females [62,66,135,136]. This process of aging is more continuous in females than in males, who demonstrated a discontinuous loss of lordosis during standing in their fourth decade of life. This discontinuous aging process might therefore be an important reason why some studies, which did not include a young reference cohort (<30 years), could not detect any age-related changes [67,137]. Furthermore, in all the investigated age groups, a large inter-subject variability was present. Therefore, from a statistical point of view, the investigated cohort size should be adequate to achieve a sufficient statistical power to detect the here presented effects of aging. In agreement with the majority of previous studies, no significant difference in total lumbar lordosis in a standing position between men and women was detected [51,62,137,138]. In addition to these results for total lumbar lordosis and motion, the here presented investigation reveals a more detailed description of the specific location of the age-related changes. It could be demonstrated that the loss of lordosis and mobility occurs mainly in the middle lumbar spine and less in the thoraco-lumbar and lumbo-sacral transitions. An intensive literature review revealed that only one radiological study of a small cohort by Gelb et al. [62] investigated age-related changes in all segmental lumbar levels and could support our findings. Their results confirm a significant loss of lordosis only at L3-4 ($p<0.05$), in the middle of the lumbar spine. Only a trend was observed in the adjacent segments (L2-3, L4-5; $0.05<p\leq0.1$). Furthermore, the lowest lumbar spine segment, L5-S1, showed no significant changes with aging ($p>0.25$), in agreement with the results of the present dissertation. These findings have important implications, in particular for the lower lumbar spine, which have been shown to be highly mechanically loaded [31,139]. Beyond this, the present study indicates that this lower part retains its lordosis and mobility with increasing age. Thus, at older ages, a relatively large part of the entire flexion motion arises from the lower lumbar spine. This emphasizes the demanding mechanical environment of the lower lumbar spine, which might be an important contributor to the prevalent degenerative changes in this part of the spine [29,30]. Furthermore, the presented age-related loss of lordosis might have important implications for different surgical treatments, e.g., for the reconstruction of the standing sagittal alignment after surgery. Currently, the amount of lordosis is thereby estimated by the individual amount of pelvic incidence, as a morphological parameter, which is assumed to be independent from age (e.g., lumbar lordosis=pelvic incidence +/-9°) [140]. However, the here presented physiological loss of lordosis with aging, which also occurs in asymptomatic volunteers, suggests that an adequate and patient-specific reconstruction must consider the individual age of the patient. Reference values or classification systems of the sagittal alignment, such as that presented by Roussouly et al. [21], obtained from young healthy volunteers are therefore not representative for the aged and degenerated lumbar spines of older patients.

The aforementioned analysis of lumbar lordosis and motion in a *standing position* is in accordance with the current clinical practice and represents a state-of-the-art analysis of lumbar spine shape and motion. The entire concept of the spinal “sagittal balance” is based on these standard X-ray measurements [54,57,141]. The standing position is assumed to be a representative and reproducible standard posture, and lumbar lordosis is assessed as a simple scalar value [21,27]. Postoperative, “well-balanced” lumbar lordosis, which is in accordance with the standing reference values of asymptomatic subjects, is assumed to be important for clinical success and therefore essential for numerous instrumented surgical procedures [142,143]. However, the presented long-term measurements of daily activities in the current dissertation (paragraph 2.5) demonstrate for the first time that this static radiological perspective is a strong simplification of what occurs during daily life. Actual lumbar lordosis during the day is not a constant characteristic but is instead not only highly variable but also considerably smaller, on average, than lordosis clinically assessed in standing. On average, the lumbar spine demonstrated a lordosis value in only 9% of the day, which was similar to the clinically assessed and employed value in standing. The clinically used radiological “snapshot” of lordosis in standing differs therefore substantially from the everyday occurrence of the lumbar spine. The reason for this discrepancy might be the dominantly sedentary lifestyle in industrialized countries [144][75]. Daily life and work-related activities frequently take place in sitting postures, which results in approximately 7–9 hours of sitting a day [75]. In another co-authored publication and in agreement with the literature, we could show that the sagittal alignment in sitting is characterized by a strong reduction of lumbar lordosis compared with standing [145], which thus explains the significantly smaller average lordosis observed during the day. This might have important implications for the current surgical practice that, on the contrary, usually aims at achieving a postoperatively balanced profile of a standing subject. The current paradigm of a balanced standing alignment could thus result in a paradoxical clinical situation after surgery, with an iatrogenically corrected part following the standing example and the remaining spino-pelvic alignment following an average sedentary posture. In particular, after the use of multi-level instrumentation, this might result in additional mechanical stresses in the transition region between the treated and untreated spinal levels. Depending on the magnitude of these stresses, this might be an important cause of long-term clinical failure. The findings of the present dissertation therefore emphasize the difficulty of using the standing posture as the main reference position for surgical interventions and question the meaningfulness of standing classification systems, as their alignment represents only a minor fraction of the daily spinal configuration. A radiological analysis of the spinal alignment in a sitting posture might be more representative of the daily alignment and should therefore additionally be clinically considered [146].

Aside from the substantial differences between the actual daily alignment and the clinically assessed and employed standing alignment, the results presented in paragraph 2.5 also question the current clinical and research practices of collecting short-term measurements for the evaluation of spinal motion and the investigation of age-and gender-related influences. This is reflected by significantly different and conflicting results between the here presented short- and long-term measurements. While aging significantly reduced lordosis in the short-term measurements in standing, this effect was substantially smaller and insignificant for the average lordosis values assessed over 24 hours. Furthermore, significant differences between men and women in the extent of lordosis were demonstrated only in the long-term evaluation and not in the standing assessment. Additionally, the results demonstrate that the determined values of the ranges of motion in the sagittal plane during standard upper body bending differed significantly from the actual values in "real life." These overall findings are generally in agreement with related research in other medical fields, such as cardiology (e.g., Holter monitoring for heart activity) or neurology (e.g., long-term electroencephalography), in which it has already been demonstrated that the assessments of patients' parameters can vary considerably between short- and long-term clinical evaluations and measurements. The presented results therefore confirm for the first time that a valid analysis of spinal shape and motion requires a combination of a standardized short-term measurement and a long-term assessment in daily life.

Age- and gender-related differences in the lumbo-pelvic rhythm

Although the presented short-term evaluations are limited in their explanatory power for the characterization of actual daily lordosis or maximal ranges of motion, they still might be valuable for monitoring a patient´s healing process during rehabilitation or for a specific differential diagnosis of LBP patients. Toward the latter aim, numerous studies have investigated the complex motion pattern of upper body bending in order to characterize and differentiate healthy motion patterns from those of different LBP patients [14,16,58,147]. A detailed understanding of this elementary motion in the sagittal plane appears especially important, as the results of this dissertation clearly emphasize that upper body bending in the sagittal plane can strongly increase spinal loads already at small inclinations (paragraph 2.1). This appears to be particularly essential, as small flexion movements are very frequently performed during the day, as demonstrated in paragraph 2.6. In agreement with the findings of previous studies [72], the here presented results reveal that upper body bending is characterized by a complex interplay between pelvic and lumbar spine motion. The initial motion at a smaller inclination is thereby dominated by changes in the lumbar spine, whereas the later motion at a higher inclination is dominantly accomplished by changes in pelvic rotation. For the first time, the findings of paragraph 2.4 clearly highlight significant differences in the motion patterns of the two genders, with larger L/P ratios occurring in males than in females. Although no systematic analysis of the effect of gender on the L/P ratio exists in the literature, studies containing only men (e.g., Porter and Wilkinson [148]: 17 males; L/P ratio: 1.18) reported larger L/P ratios than studies including both genders in their study design (e.g., Esola et al. [70]; 13 males, 8 females; L/P ratio of 0.61). Therefore, these findings indirectly support the here presented results. Furthermore, for the first time, it was clearly demonstrated that aging significantly affects the interplay between pelvic and lumbar spine motion. The aging process in the lumbar spine, which is characterized by a loss of intervertebral disc height, results in a loss of lumbar spine mobility, which appears to be compensated for by an increased mobility of the pelvis. These findings are essential for attaining an improved differential diagnosis in clinical examinations or for optimizing physiotherapy. In the case of an overall motion deficit, current standard, non-invasive practices, such as the measurement of the fingertip-to-floor distance [149], cannot determine whether the deficit arises from the pelvis or from the lumbar spine. On the contrary, the frequently employed Schober test [150] measures only the mobility of the lumbar spine. However, a profound and meaningful analysis of a patient's mobility with the aim of a targeted and thus more promising therapy choice should incorporate a gender- and age-specific differentiation and analysis of the pelvic and spinal motion components. The here presented results can thus be used as reference values and can be compared to non-specific or specific LBP patients in future research.

In addition to the analysis of the spino-pelvic posture and motion and its relevance, e.g., for LBP-diagnosis, the here shown age-related changes also have valuable implications for the resultant spinal loading. As mentioned above, Tafazzol and co-workers [72] demonstrated in a kinematics-driven, musculoskeletal finite element model that a change in the L/P ratio can substantially affect the resultant spinal loading during the flexion motion process. Their model predicted that compared to a larger L/P ratio, a smaller L/P ratio decreases the contribution of the passive spinal components to the stabilization of the trunk. For a specific upper body inclination, this results in an increase of the spinal loading for smaller L/P ratios. This increase was even more pronounced at small inclination angles. However, especially for these smaller inclination angles (i.e., early flexion phase), the L/P ratios were most dominantly decreased with aging. This suggests a higher loading of the lumbar spine at an older age than at a younger age during an identical upper body inclination. Furthermore, the aforementioned presented *in vivo* measurements with a VBR during upper body flexion (paragraph 2.1) clearly reveal that high spinal loads already occur at smaller inclination angles and not necessarily at peak flexion. Furthermore, it was confirmed that these smaller flexion movements occur frequently during the day, even at an older age (paragraph 2.6). The findings of the present dissertation highlight that with aging, not only do spinal posture and motion change significantly, but as a consequence, so does spinal loading. This might be an important factor and explanatory approach for the higher risk of LBP at an older age.

Limitations of back shape measurement techniques in assessing lumbar spine shape and motion

The measurements presented here (paragraph 2.3-2.6) of the spino-pelvic alignment, mobility and motion were performed in a large asymptomatic cohort. All investigated volunteers were free from acute low back pain and had no low back pain within six months prior to the measurements. In addition, the subjects had no history of spinal surgery. Therefore, from an ethical perspective, an intensive radiological measurement of this large asymptomatic cohort would not have been feasible. In addition, from a scientific perspective, a radiological evaluation does not allow the assessment of spinal shape and motion in daily life, but only in a standardized standing posture. These considerations and limitations have led to the further development, validation and utilization of a non-invasive, back shape measuring system (Epionics SPINE System) in the present dissertation. Several customized routines were developed and employed to evaluate the data of this non-invasive and non-radiative measurement alternative for assessing lumbar spine curvature and mobility in standing and daily life. The system was systematically evaluated and validated for motion analysis in the sagittal plane. To evaluate the static accuracy and repeatability of the system, several sensor strips were previously systematically applied onto well-defined arcs with seven predefined curvatures ranging between 0° and 12.5° for flexion and extension of the sensor strips. In a correlation analysis, it could be shown that the measurements correlated significantly and highly with the predefined arcs ($r>0.98$, [151]). In addition, unpublished data by the manufacturer demonstrated that the segmental angles showed absolute differences of less than 0.5°. Furthermore, the test-retest reliability was assessed for these static measurements on two different days by measuring 10 repetitions on seven different arcs. All the determined intraclass correlation coefficients (ICCs) were larger than 0.98 [151]. Thus, although the system can be regarded as accurate and reliable, it must first be noted that the system measures the shape of the back and does not directly measure the shape of the spine. However, several studies, e.g., by Guermarzi et al. [152], Stokes et al. [153] and Adams et al. [154], have already demonstrated that spinal shape and mobility and corresponding measurements obtained by assessing the shape of the back are significantly and highly correlated with each other (e.g., Guermazi et al. [152]: r=0.86; Adams et al. [154]: r=0.91). In own preliminary studies, these significant correlations between X-ray and back shape measurements were confirmed only for subjects with a BMI<26 kg/m², which limited the current investigations to subjects with normal weights. In an ongoing comparison study with established non-invasive back shape measurement systems, such as the MediMouse system (Idiag AG, Switzerland) and the Formetric III (rasterstereography, Diers International GmbH, Germany), a significant correlation with the here employed system could additionally be confirmed for the investigated back shape parameters. The results of these well-established, non-invasive back shape measurement systems have previously been shown to be correlated with corresponding X-ray measurements (e.g., [152]). Therefore, the employed non-invasive approach of the present dissertation offers an ethical and harmless alternative to radiological measurements and further allows, for the first time, a valid perspective of spinal lordosis and lumbar spine motion in daily life. However, it has to be clearly emphasized that those non-invasive measurement approaches can certainly not replace X-ray measurements in clinical practice. A radiological examination enables a clear analysis of the bony spinal structures, potential vertebral fractures as well as the spinal curvature in the sagittal *and* coronal plane. The here presented measurements are limited to the assessment of spinal shape and motion only in the sagittal plane. However, as shown by the here presented corresponding *in vivo* measurements, changes in the sagittal plane result in substantial load changes in the lumbar spine and are thus biomechanically and ergonomically considered to be essential. Unpublished data, as well as measurements by Wilke et al. [31,38] or Nachemson [33], confirmed that load increases are most pronounced when subjects bend the upper body in the sagittal plane. Only smaller load changes were measured with a VBR during axial rotation or lateral bending. Nevertheless, future research might also investigate the motion that occurs during lateral bending as well as axial rotation, which is assumed to specifically load the facet joints in the posterior region of the spine; these investigations were not possible with the current approach. It also must be noted that the presented approach concentrated on the analysis of the clinically essential lumbar spine and did not assess changes elsewhere, e.g., in the thoracic spine, where however only small motions occur [134].

Comparison of currently employed finite element models of the lumbar spine and their limitations

Previous studies and the results of the present dissertation emphasize that the shape and motion of the lumbar spine and the resultant loading are characterized by a high inter-subject variability. This variability has important consequences not only for a subject-specific treatment but also for related applied research, particularly computational model studies that aim to evaluate or optimize treatment options for LBP patients. Considering the aforementioned studies and the present dissertation, the current practice of computational model studies, which are usually based on one specific finite element model with a single spinal shape and material composition (e.g., [81,82,84]), appear to strongly oversimplify the analysis of an inhomogeneous patient cohort. The here presented comparative finite element model study (paragraph 2.7) is thus a direct and inevitable consequence that translates the aforementioned results into the field of biomechanical computational studies. The presented findings clearly reveal, for the first time, that most employed finite element models predict results within the *in vitro* (e.g., [155,156]) or *in vivo* (e.g., [23,31,38]) reference ranges and thus usually confirm their validity and the general high research quality in this field. However, the *pooled* median of the predicted rotations, intradiscal pressure values or facet joint forces of all models were usually in better agreement with the reference values than were *single* model predictions. Furthermore, the compilation of several models with different spinal shapes more realistically assessed the inter-subject variability of corresponding *in vitro* tests. This was particularly the case under standardized loads for the predicted intervertebral rotations in all main anatomical planes. However, for parameters such as the intradiscal pressure or the facet joint forces, which are more difficult to measure *in vitro* and are thus more difficult to validate, the predicted ranges exceeded the experimental references. In agreement with the argument made by Viceconti et al. [41] or Oreskes et al. [42], this highlights the importance of a comprehensive validation of computational models in order to attain meaningful and clinically relevant simulations. However, the validation of current models is still limited, as only a few complex experimental studies exist that would allow such a detailed validation [157,158]. Thus, future research must concentrate on providing a more sophisticated experimental basis. Furthermore, the results underline the difficulty in confidently drawing biomechanical conclusions from one specific finite element model with respect to a certain population. Therefore, due to the high inter-subject variability, one must be cautious when generalizing results from single models. A more profound computational analysis should thus use statistical approaches (e.g., probabilistical study design) that allow a convincing assessment of the sensitivity of model inputs (e.g., material composition, implant dimensions and locations) and the robustness of model outputs (e.g., segmental motion, intradiscal pressure). Furthermore, future finite element model studies should include at least several representative model geometries that can represent a population's variability.

Analysis of a lumbar total disc replacement

On the basis of the aforementioned comparative investigation and following its recommendations, the last computational biomechanical study of this dissertation investigated a total disc replacement (TDR) in a probabilistic study design, employing five different spinal geometries in more than 4000 single finite element (FE) simulations. This study aimed to overcome some of the crucial limitations of current FE model studies, which were discussed above, to systematically reveal biomechanical risk factors for the TDR intervention. By demonstrating the complex, multifactorial interrelation of the spinal geometry, implant location and amount of iatrogenic distraction on the one hand and the postoperative RoM and facet joint loading on the other hand, the results presented here provide biomechanical explanations for the current complex and disappointing clinical treatment situation after a TDR. In particular, the amount of iatrogenic distraction appears to be essential for surgical success, as it already strongly increases the facet capsule ligament forces (FCLFs) during the intervention, which might simultaneously harm these ligaments. Furthermore, a distraction increases facet capsule ligament forces in flexion and in axial rotation, as well as facet joint forces (FJFs) during extension. In a previously co-authored combined computational and clinical study, it could be shown that the loading of the facet capsule is essential for surgical success after TDR [96,97]. This is in accordance with investigations performed by Siepe et al. [159,160], who demonstrated that facet joint pain is a major source of postoperative problems after TDR. The here presented findings can thus biomechanically explain the clinical results of Strube et al. [96], who demonstrated in a clinical investigation that compared to a small distraction, a large iatrogenic distraction results in inferior clinical findings. Moreover, further investigations by Siepe and co-workers [160] clearly demonstrated inferior clinical results in the spinal level L5-S1 compared with L4-L5. However, Leivseth et al. [161] showed that the spinal segment L5-S1 experiences a larger distraction on average than the segment L4-L5 during TDR. The crucial impact of the distraction on the facet joint loading, as shown in the present dissertation, might therefore also partly explain this level dependence of the clinical outcome after TDR. In addition to the loading of the facets, the here presented results emphasize that distraction oppositely affects the RoF and RoE, such that they balance each other. A larger distraction increases the pretension in the posterior ligaments, which thus impede motion during flexion. On the contrary, a distraction increases the gap in the facet joints, which enables larger motion during extension [162]. These predicted results are in agreement with those of clinical studies by Leivseth et al. [161], who demonstrated that TDR patients exhibit a motion deficit usually during flexion. Moreover, these results call into question the current clinical practice (e.g.: [161,163–165]) of assessing the complete RoM (i.e., the sum of RoF and RoE) and correlating it with clinical outcome. However, although a distraction can substantially change the loading in the facet joints and the segmental motion at the index level, the complete RoM is largely insensitive to these changes. This calls into question the value of using the complete segmental RoM for the clinical diagnosis after a TDR. Aside from iatrogenic distraction, the results also reveal the important roles of individual spinal shape and implant location in surgical success. Thereby, spinal shape configurations (Types 1 and 4, according to Roussouly et al. [21]) with a higher preoperative disc height and therefore smaller disc stiffness [166] were predicted to have larger RoM values, particularly during flexion. However, this increase in motion was also accompanied by larger FCLFs. This important interrelation might explain the inferior clinical outcomes in patients with profile types 1 and 4 [59] versus types 2 and 3, as well as in patients with greater preoperative disc heights, as demonstrated by Siepe et al. [165]. This effect might be confounded by a smaller amount of distraction in patients with a larger preoperative disc height. However, these interrelations strongly suggest that the combination of both a pronounced distraction in patients with a large preoperative disc height would result in clearly inferior clinical results. Indeed, in another co-authored retrospective clinical study submitted for publication, it could be clinically verified that these types of patients suffer from significantly and considerably worse clinical results and should not undergo TDR surgery. Therefore, these findings allow a more objective preoperative selection of appropriate patients for TDR and help to optimize the surgical intervention with the aim of increasing clinical success. During the intervention, the surgeon should also evaluate the exact implant location, as it also affects loading and segmental motion. In general, the distance between the center of rotation of the artificial disc and the facet joints is important; this lever arm modulates the effectiveness of the FJFs or FCLFs when balancing an external load. In future research, this essential distance should be evaluated in an additional radiological study to further improve patient selection prior to implantation.

Although the presented FE sensitivity study accounted for five spinal curvatures in 4000 single calculations, there are still important limitations that must be discussed here. One main simplification in current finite element model studies is the utilization of simplified loading modes. In this study, only pure moments were employed, in accordance with the recommendation for standard *in vitro* testing [113,167,168]. However, the present study did not employ standard loads of 7.5 Nm in all planes, as is usually recommended [114], but instead used optimized loads from previously published studies to ensure an optimal agreement with *in vivo* spinal kinematics during maximal voluntary motion [169,170]. Furthermore, a compressive follower load, as suggested by Patwardhan et al. [171] and Shirazi Adl et al. [172], was not considered in this study, in accordance with previous studies that investigated a TDR in the lumbar spine (e.g., [97]). A follower load was not employed because it would have induced artificial moments and thus unstandardized additional intervertebral rotations, depending on the systematic alteration of the location of the implant. This would have yielded misleading results that would have been difficult to interpret. Furthermore, the employed amount of iatrogenic distraction of 4 mm was simulated with respect to the initial intact disc height. This amount was found in previously published studies by Johnson et al. [164] and Leivseth et al. [161], who demonstrated that the distraction after TDR in L5-S1 can be larger than 3.5 mm with respect to the normal disc height. However, in clinical practice, the amount of distraction is larger because the preoperative degenerated disc height is usually taken as the reference. This study employed validated FE models in a probabilistic study to investigate a TDR as a frequently employed surgical treatment. Future research should further concentrate on posterior dynamic implants or fusion devises to also optimize these surgical approaches.

This dissertation investigated spinal loading occurring during several hundred measurement sessions of upper bending and lifting of weights, which are assumed to be risk factors for low back pain. The resultant load changes in these activities were systematically analyzed and demonstrated. Using a non-invasive measurement tool, spinal shape and motion was investigated in several hundred subjects, and in particular, differences between short- and long-term measurements and age- and gender-related variations were revealed. The overall *in vivo* perspective gained from all these analyses and measurement results of spinal loading, shape and motion, which is characterized by a high degree of inter-subject variability, was subsequently compared with the current scientific practice of computational modeling in spinal biomechanics. Although great advances have been made during recent decades in the field of computational biomechanics, in light of the high inter-subject variability and the difficulties of thorough validation, the generalization of a single model to a patient cohort remains limited. However, as shown in the investigation of an artificial disc, this limitation might be overcome with several representative models in large probabilistic studies. The implications and consequences of this dissertation for current clinical practices, ergonomics and for basic spinal biomechanical research are explained in further detail in the discussion sections of all eight publications. It is the strong hope of the author of this dissertation that the presented biomechanical results will stimulate further research in this field and improve the current care of low back pain patients. However, as the Australian low back pain researcher P. R. Wilson stated in 1995:

> *"Despite the scientific advances being made, it must be remembered that the back is a part of a person, who has a psyche, and who is part of a family and society"* [173].

Therefore, the biomechanical approach of this dissertation is thus only one piece for an improved understanding of the lumbar spine and of low back pain. All the pieces related to different research fields, such as biomechanics, clinical research, ergonomics, public health, psychology, biology and neurology, must be combined into an integral therapeutic approach in the future to significantly reduce the tremendous burden of the low back.

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6. Statutory declaration

I hereby declare that I have authored this thesis independently, that I have not used other than the declared sources / resources, and that I have explicitly marked all material, which has been quoted either literally or by content from the used sources. This PhD thesis has not been submitted for conferral of degree elsewhere.

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Eidesstattliche Erklärung

Hiermit versichere ich, dass ich die vorliegende Arbeit selbstständig verfasst und keine anderen als die angegebenen Quellen und Hilfsmittel benutzt habe. Alle Ausführungen, die anderen veröffentlichten oder nicht veröffentlichten Schriften wörtlich oder sinngemäß entnommen wurden, habe ich kenntlich gemacht.

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Ort, Datum Unterschrift

7. Declaration to the contribution of the publications

In vivo implant forces acting on a vertebral body replacement during upper body flexion.
Dreischarf M, Albiol L, Zander T, Arshad R, Graichen F, Bergmann G, Schmidt H, Rohlmann A.
Journal of Biomechanics. 2015 Feb 26;48(4):560-5. Impact factor (2015): 2.431
Contribution in detail: *idea, organization and conception of the research for this publication, literature review, data ascertainment, data analyses and interpretation, descriptive statistical analysis, writing of the publication, accomplishment of the review process.*

In vivo loads on a vertebral body replacement during different lifting techniques.
Dreischarf M, Rohlmann A, Graichen F, Bergmann G, Schmidt H.
Journal of Biomechanics 2016 Apr 11;49(6):890-5. Impact factor (2015): 2.431
Contribution in detail: *idea, organization and conception of the research for this publication, literature review, data ascertainment, data analyses and interpretation, descriptive statistical analysis, writing of the publication, accomplishment of the review process.*

Age-related loss of lumbar spinal lordosis and mobility - a study of 323 asymptomatic volunteers.
Dreischarf M, Albiol L, Rohlmann A, Pries E, Bashkuev M, Zander T, Duda GN, Druschel C, Putzier M, Schmidt H.
PLOS ONE 2014 Dec 30;9(12):e116186. Impact factor (2014): 3.234
Contribution in detail: *idea, organization and conception of the research for this publication, literature review, further development of the measurement tool, validation of the measurement system, data analyses and interpretation, descriptive and inferential statistical analysis, writing of the publication, accomplishment of the review process.*

The effects of age and gender on the lumbopelvic rhythm in the sagittal plane in 309 subjects.
Pries* E, **Dreischarf* M**, Bashkuev M, Putzier M, Schmidt H.
(*The authors contributed equally to this work.)
Journal of Biomechanics 2015 Sep 18;48(12):3080-7. Impact factor (2015): 2.431
Contribution in detail - *In cooperation with Esther Pries: idea, organization and conception of the research for this publication, literature review, further development of the analysis tools, validation of the measurement system, data analyses and interpretation, descriptive and inferential statistical analysis, writing of the publication, accomplishment of the review process.*

Measurement of the number of lumbar spinal movements in the sagittal plane in a 24-hour period.
Rohlmann A, Consmüller T, **Dreischarf M**, Bashkuev M, Disch A, Pries E, Duda GN, Schmidt H.
European Spine Journal 2014 Nov;23(11):2375-84. Impact factor: 2.066
Contribution in detail: assistance in literature review, data interpretation, descriptive and inferential statistical analysis, helping in writing the manuscript and in accomplishing the review process.

Differences between clinical "snap-shot" and "real-life" assessments of lumbar spine alignment and motion - What is the "real" lumbar lordosis of a human being?
Dreischarf M, Pries E, Bashkuev M, Putzier M, Schmidt H.
Journal of Biomechanics 2016 Mar 21;49(5):638-44. Impact factor (2015): 2.431
Contribution in detail: *idea, organization and conception of the research for this publication, literature review, further development of the analysis tools, validation of the measurement system,*

data analyses and interpretation, descriptive and inferential statistical analysis, writing of the publication, accomplishment of the review process.

Comparison of eight published static finite element models of the intact lumbar spine: predictive power of models improves when combined together.
Dreischarf M, Zander T, Shirazi-Adl A, Puttlitz CM, Adam CJ, Chen CS, Goel VK, Kiapour A, Kim YH, Labus KM, Little JP, Park WM, Wang YH, Wilke HJ, Rohlmann A, Schmidt H.
Journal of Biomechanics 2014 Jun 3;47(8):1757-66. Impact factor (2015): 2.431
Contribution in detail: *idea, organization and conception of the research for this publication, literature review, gathering simulation results from all participating research groups, FE-model validation and adaptation of the FE model, lumbar spine FE simulations, data analyses and interpretation, descriptive statistical analysis, writing of the publication, accomplishment of the review process.*

Biomechanics of the L5-S1 motion segment after total disc replacement - Influence of iatrogenic distraction, implant positioning and preoperative disc height on the range of motion and loading of facet joints.
Dreischarf M, Schmidt H, Putzier M, Zander T.
Journal of Biomechanics 2015 Sep 18;48(12):3283-91. Impact factor (2015): 2.431
Contribution in detail: *idea, organization and conception of the research for this publication, literature review, FE model development and performing FE simulation, FE-model validation, data analyses and interpretation, descriptive statistical analysis, clinical verification and translation, writing of the publication, accomplishment of the review process.*

8. Curriculum vitae

9. List of publications (2013-2016)

2016 Arshad R, Zander T, **Dreischarf M**, Schmidt H.: *Influence of lumbar spine rhythms and intra-abdominal pressure on spinal loads and trunk muscle forces during upper body inclination.*
Med Eng Phys. 2016 Apr;38(4):333-8.

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J Biomech. 2016 Apr 11;49(6):833-45.

Bashkuev M, Vergroesen PP, **Dreischarf M**, Schilling C, van der Veen AJ, Schmidt H, Kingma I: *Intradiscal pressure measurements: A challenge or a routine?*
J Biomech. 2016 Apr 11;49(6):864-8.

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Schmidt H, Schilling C, Reyna AL, Shirazi-Adl A, **Dreischarf M**: *Fluid-flow dependent response of intervertebral discs under cyclic loading: On the role of specimen preparation and preconditioning.*
J Biomech. 2016 Apr 11;49(6):846-56.

2015 Pries E, **Dreischarf M**, Bashkuev M, Putzier M, Schmidt H: *The effects of age and gender on the lumbopelvic rhythm in the sagittal plane in 309 subjects.*
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J Biomech. 2015 Sep 18;48(12):3283-91.

Pries E, **Dreischarf M**, Bashkuev M, Schmidt H: *Application of a novel spinal posture and motion measurement system in active and static sitting.*
Ergonomics. 2015;58(9):1605-10.

Zander T, **Dreischarf M**, Schmidt H, Bergmann G, Rohlmann A: *Spinal loads as influenced by external loads: A combined in vivo and in silico investigation.* J Biomech. 2015 Feb 26;48(4):578-84.

Dreischarf M, Albiol L, Zander T, Arshad R, Graichen F, Bergmann G, Schmidt H, Rohlmann A: *In vivo implant forces acting on a vertebral body replacement during upper body flexion.*
J Biomech. 2015 Feb 26;48(4):560-5.

2014 **Dreischarf M**, Albiol L, Rohlmann A, Pries E, Bashkuev M, Zander T, Duda GN, Druschel C, Putzier M, Schmidt H: *Age-related loss of lumbar spinal lordosis and mobility - a study of 323 asymptomatic volunteers.*
PLOS ONE 2014 Dec 30;9(12):e116186.

Rohlmann A, Consmüller T, **Dreischarf M**, Bashkuev M, Disch A, Pries E, Duda GN, Schmidt H: *Measurement of the number of lumbar spinal movements in the sagittal plane in a 24-hour period.*
Eur Spine J. 2014 Nov;23(11):2375-84.

Likhitpanichkul M, **Dreischarf M**, Illien-Junger S, Walter BA, Nukaga T, Long RG, Sakai D, Hecht AC, Iatridis JC: *Fibrin-genipin adhesive hydrogel for annulus fibrosus repair: performance evaluation with large animal organ culture, in situ biomechanics, and in vivo degradation tests.*
Eur Cell Mater. 2014 Jul 18; 28:25-37.

Dreischarf M, Zander T, Shirazi-Adl A, Puttlitz CM, Adam CJ, Chen CS, Goel VK, Kiapour A, Kim YH, Labus KM, Little JP, Park WM, Wang YH, Wilke HJ, Rohlmann A, Schmidt H: *Comparison of eight published static finite element models of the intact lumbar spine: predictive power of models improves when combined together.*
J Biomech. 2014 Jun 3;47(8):1757-66.

Rohlmann A, **Dreischarf M**, Zander T, Graichen F, Bergmann G: *Loads on a vertebral body replacement during locomotion measured in vivo.*
Gait Posture 2014 Feb;39(2):750-5.

2013 Rohlmann A, **Dreischarf M**, Zander T, Graichen F, Strube P, Schmidt H, Bergmann G: *Monitoring the load on a telemeterised vertebral body replacement for a period of up to 65 months.*
Eur Spine J. 2013 Nov;22(11):2575-81.

Strube P, Hoff EK, Schmidt H, **Dreischarf M**, Rohlmann A, Putzier M: *Parameters influencing the outcome after total disc replacement at the lumbosacral junction. Part 2: distraction and posterior translation lead to clinical failure after a mean follow-up of 5 years.*
Eur Spine J. 2013 Oct;22(10):2279-87.

Schmidt H, Bashkuev M, **Dreischarf M**, Rohlmann A, Duda G, Wilke HJ, Shirazi-Adl A: *Computational biomechanics of a lumbar motion segment in pure and combined shear loads.*
J Biomech. 2013 Sep; 46(14):2513-21.

Rohlmann A, Lauterborn S, **Dreischarf M**, Schmidt H, Putzier M, Strube P, Zander T: *Parameters influencing the outcome after total disc replacement at the lumbosacral junction. Part 1: misalignment of the vertebrae adjacent to a total disc replacement affects the facet joint and facet capsule forces in a probabilistic finite element analysis.*
Eur Spine J. 2013 Oct;22(10):2271-8.

Srbinoska H, **Dreischarf M**, Consmüller T, Bergmann G, Rohlmann A: *Correlation between back shape and spinal loads.*
J Biomech. 2013 Jul;46(11):1972-5.

Dreischarf M, Rohlmann A, Zhu R, Schmidt H, Zander T: *Is it possible to estimate the compressive force in the lumbar spine from intradiscal pressure measurements?* A finite element evaluation.
Med Eng Phys. 2013 Sep; 35(9):1385-90.

Zhu R, Zander T, **Dreischarf M**, Duda GN, Rohlmann A, Schmidt H: *Considerations when loading spinal finite element models with predicted muscle forces from inverse static analyses.*
J Biomech. 2013 Apr;46(7):1376-8.

10. Selected conference presentations (2013-2016)

2015 **Dreischarf M**, Pries E, Bashkuev M, Putzier M, Schmidt H: *Klinische Kurzzeitanalysen spiegeln die komplexe Form und Beweglichkeitder Lendenwirbelsäule im Alltag nur unzureichend wider: Langzeitmessungen an 208 Probanden.*
9. Jahrestagung der Deutschen Gesellschaft für Biomechanik. 06.-08. Mai 2015, Bonn.

2014 **Dreischarf M**, Albiol L, Rohlmann A, Pries E, Strube P, Druschel C, Putzier M, Schmidt H: *Die lokale und globale Form der Lendenwirbelsäule ist alters- und geschlechtsabhängig – In vivo Untersuchung an 323 asymptomatischen Probanden.*
Deutscher Kongress für Orthopädie und Unfallchirurgie. 28.-31. Oktober 2014, Berlin.

Dreischarf M, Zander T, Shirazi-Adl A, Puttlitz C, Wilke HJ, Rohlmann A, Schmidt H: Comparison of eight published lumbar finite element models.
7th World Congress of Biomechanics. July 6-11 2014, Boston, USA.

2013 **Dreischarf M**, Rohlmann A, Albiol L, Zander T, Bashkuev M, Pries E, Druschel C, Putzier M, Schmidt H: *Die lokale und globale Form der Lendenwirbelsäule ist alters- und geschlechtsabhängig und beeinflusst die lumbale Beweglichkeit – Eine in vivo Untersuchung an 398 Probanden.*
8. Jahrestagung der Deutschen Wirbelsäulengesellschaft. 5.-7. Dezember 2013, Frankfurt.

Dreischarf M, Rohlmann A, Lauterborn S, Schmidt H, Putzier M, Strube P, Zander T: *Influence of a vertebral misalignment after total disc replacement on fact joint forces, capsule tensile forces and clinical outcome.*
19th Congress of the European Society of Biomechanics, 25-28 August 2013, Patras, Greece.

Dreischarf M, Rohlmann A, Lauterborn S, Schmidt H, Putzier M, Strube P, Zander T: *Eine Fehlstellung der Wirbelkörper nach Implantation einer künstlichen Bandscheibe beeinflusst der OP-Erfolg.*
8. Jahrestagung der Deutschen Gesellschaft für Biomechanik. 15.-17. Mai 2013, Neu-Ulm.

11. Awards

2014 ***„Reisestipendium der Deutschen Gesellschaft für Biomechanik (DGfB)"***
Dreischarf, M

2013 ***„Clinical Biomechanics Award" of the European Society of Biomechanics***
Dreischarf M, Rohlmann A, Lauterborn S, Schmidt H, Putzier M, Strube P, Zander T: *"Influence of a vertebral misalignment after total disc replacement on fact joint forces, capsule tensile forces and clinical outcome."*
19th Congress of the European Society of Biomechanics, Patras Greece

„Georg-Schmorl-Preis" of the German Spine **Society**
Rohlmann A., **Dreischarf M**, Zander T, Graichen F, Strube P, Schmidt H, Bergmann G: *„Monitoring the load on a telemeterised vertebral body replacement for a period of up to 65 months." Eur Spine J Nov;22(11):2575-81.*

„Travel Award" of the European Society of Biomechanics
Dreischarf, M

2012 ***„Promotionsstipendium der Studienstiftung des deutschen Volkes"***
Dreischarf, M