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The Potential of Individualized Musculoskeletal Models of the Torso for Systematic Analysis of Spinal Biomechanics

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Isn't every congress a spine congress?

- A. Martini, 2023

Thank you

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Finally, I would like to thank my family. My parents, Gerlinde and Schorsch, and my sister Franzi and Max for many years of support and a home that I am always happy to return to.

I don't want to end with the obligatory "thank you for putting up with me during this time". Fully aware that such a phase of life is accompanied by dry spells, frustration and doubts, which here and there even threaten to tip over into despair, it was first and foremost a wonderful and exciting time. And I owe that not only to the great working environment but also to a large extent to the many great people who have accompanied me in the last few years and hopefully will continue to do so for a long time. To mention everyone by name, including individual praise, would certainly go beyond the scope of this section and the risk of forgetting someone is just too high for me. I just want to say thank you for the many great hours spent making music together, partying, bathing in the Isar, theater and clown performances, simply eating well, and having serious and not so serious conversations.
Thank you!

Abstract

Chronic low back pain (CLBP) is a major global health issue associated to multiple causes, that make research on its origins and progression challenging. Spinal loading is often linked to degeneration and pain, but in vivo measurements are only feasible to a limited extent due to ethical reasons. Simulations with multibody models (MBS) are a non-invasive method make this data available for epidemiological studies on CLBP. However, generating models with the necessary degree of individualization to represent the biological diversity of an actual population usually involves time-consuming procedures. Therefore, most MBS models that can be found in the literature are generic, and thus, fail to capture real-life interindividual variability. To consider this variability in large cohorts, both, individualization of the models as well as automation of the modeling process is required. In this thesis, the potential of highly individualized multi-body torso model, automatically derived from CT data, will be evaluated.

After assessing the current state of the art of MBS models of the thoracolumbar spine (publication 1), a framework for automated generation of individualized torso models was developed using a pipeline for CT-based spine labeling and segmentation. Models included individual vertebral geometries, spinal alignment, and torso weight distribution. Model validation was carried out based on in vivo measurements of spinal loading and muscle activation in various static loading tasks (publication 2). Subsequently, a study was conducted to evaluate how model individualization affects spinal load estimation (publication 3). Additionally, the influence of individual morphological parameters, related to spinal alignment, torso weight, or muscle architecture was analyzed in a large and diverse patient cohort (n = 93).

Overall, simulations predicted spinal loading and muscle activity in close agreement with in vivo measurements. Different degrees of model individualization showed that effect sizes of individual parameters on spinal loads decreased, when more individual parameters were included. Torso weight had the strongest impact on compression forces, while lumbar lordosis was most determinant for anterior-posterior shear forces. Reduced muscle cross-section increased spinal loads, in particular in high-intensity loading tasks. The simulation results emphasize the importance of individualization when it comes to analyzing spinal loading mechanisms in large patient cohorts. They further show that such cohorts can be utilized to identify effects of both morphological and functional patient-specific characteristics in a diverse cohort. This thesis lays the foundation for the integration of individual loading patterns into large-scale studies, that will support a profound understanding of spinal biomechanics and CLBP.

Contents

1. Introduction

This thesis summarizes my work as a research assistant at the *Associate Professorship of Sports Equipment and Sports Materials* between 2017 and 2024. My research revolved around the mechanics of the human musculoskeletal system, with a particular focus on spinal biomechanics. The content of this thesis was created in cooperation with the Department of Diagnostic and Interventional Neuroradiology at Klinikum rechts der Isar. More precisely, as a part of the projects *iBack* and *iBack-epic*, funded by the European Research Counsil (ERC) and under the supervision of Prof. Dr. med. Jan S. Kirschke. During the *iBack* project with the full title "**I**ndividualized treatment planning in chronic **back** pain patients by advanced imaging and multi-parametric biomechanical models" quantitative imaging methods and a deep-learning based image processing pipeline were developed to automatically generate highly individualized musculoskeletal models of the spine from CT data of the torso. Based on these achievements, the ERC funded the follow-up project *iBack-epic* ("Biomechanical modeling and computational **i**maging to identify different causes of **back** pain in large **ep**idemiolog**ic**al studies") as part of the *ERC Consolidator Grant 2021*.

The first chapter gives concise insights into fundamentals, as well as the motivation and objectives of this work, followed by the methods used for modeling and simulation. The third chapter is devoted to the publications that were created as part of this work. In order to provide stringency, each publication can be assigned to one respective object introduced in chapter 1.2 and is briefly summarized. The main achievments and findings will be discussed in the fourth chapter with respect to the stated objectives and given limitations. Ultimately, this thesis will conclude glance into future perspectives. Full-text versions of the referenced publications are included in the appendix.

1.1 Motivation

Chronic low back pain (CLBP) is one of the major burdens on global health. According to the Global Burden of Disease Study, CLBP ranked first on a global scale for years lived with disability (YLDs) and sixth for disability-adjusted life years (DALYs) (Hoy et al., 2014; Murray et al., 2012) with an estimated prevalence of more than 800 million affected people worldwide by 2050 (Ferreira et al., 2023). Due to its multi-factorial nature, epidemiological analysis of its causes is challenging (Cholewicki et al., 2019). In the literature, correlations to a multitude of factors can be found (Andrade & Chen, 2022; Landmark et al., 2018; Tagliaferri et al., 2020), whose interrelations and causalities are manifold and difficult to untangle (Figure 1.1).

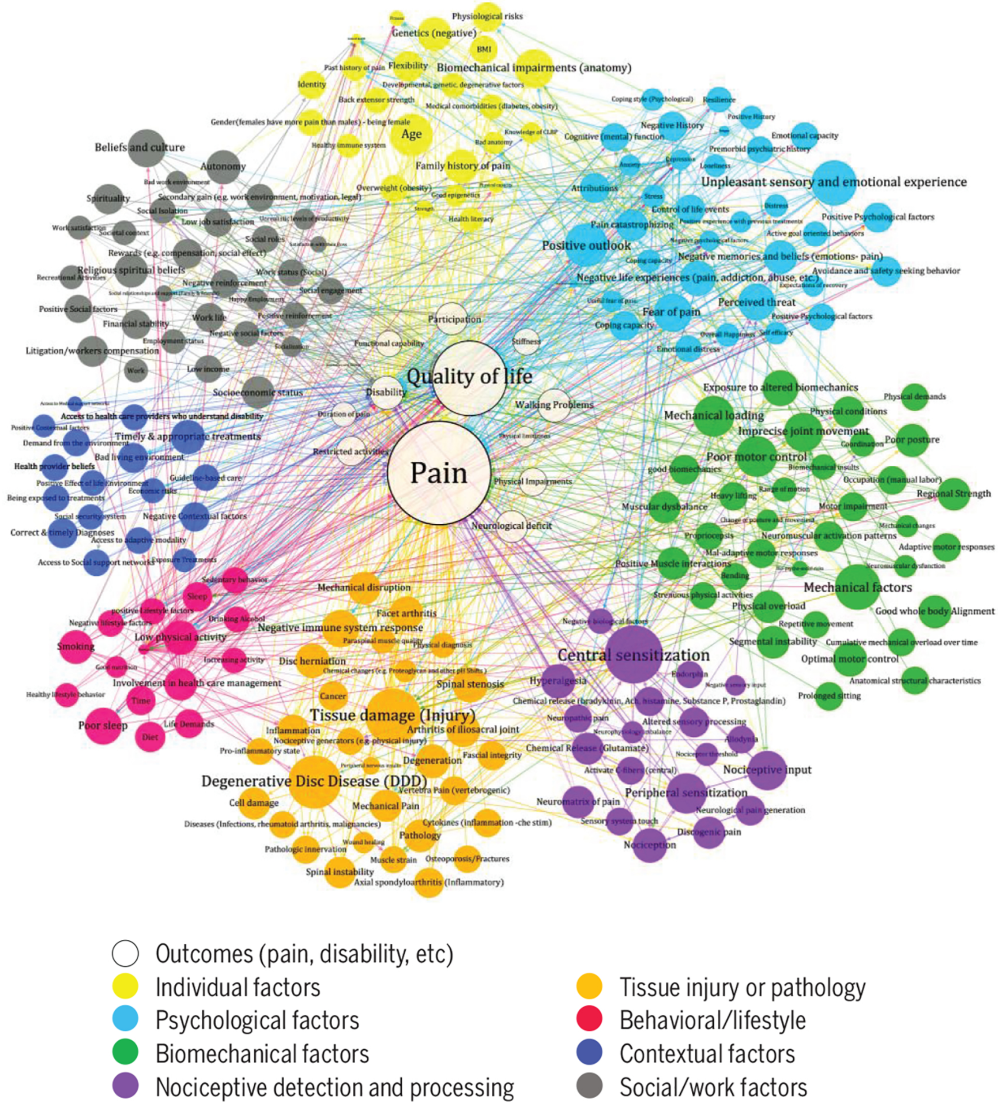

Figure 1.1: Overview of factors associated to various aspects of chronic low back pain and their interrelations. Reproduced with permission from (Cholewicki et al., 2019). Copyright ©Journal of Orthopaedic & Sports Physical Therapy®, Inc.

In accordance to the biopsychosocial model, introduced in 1977 by Engel (Engel, 1977), there is a vast consensus, that biological, psychological, and social factors need to be considered for a holistic and sustainable treatment of CLBP (Gatchel, 2004; Gatchel et al., 2007; Miaskowski et al., 2020; Tagliaferri et al., 2020). In the past, countless studies have attempted to extract the extent to which each aspect contributes to CLBP (Andrade & Chen, 2022; Battié et al., 2008, 2009; Bayartai et al., 2020; Dario et al., 2015; Livshits et al., 2011).

Although the definite role of biomechanics in pain generation and perpetuation is still controversial (Cholewicki et al., 2019), it is associated with a wide range of the parameters related to CLBP, in a sense that their causes or consequences can be related to morphological changes and altered loading within the musculoskeletal system. There is various evidence in the literature, that mechanical overloading contributes to pathogenic structural changes in the spine like degeneration of the intervertebral disc (IVD) (Cornaz et al., 2021; Fu et al., 2021; Gewiess et al., 2023) or facet joints (Zhao et al., 2023), which is often linked to back pain (Azril et al., 2023; Goode et al., 2022; Hira et al., 2021; Murata et al., 2023). However, chronic back pain is not always due to specific pathologies. In fact, a large proportion (80-95 %) of it cannot be explained by such findings, which is commonly referred to as non-specific CLBP (Maher et al., 2017; Tagliaferri et al., 2020).

The mechanisms of mechanical loading and the threshold to potentially pathological overloading are complex, and studies, that address this issue in the context of CLBP have lead to conflicted results. For example, the association with work-related physical activity is described numerous times in the literature (Murtezani et al., 2011). This however is contradicted by twin studies, whose results indicate, that exposure to physical loading could explain the variance in disc degeneration scores only to a minor extend in subjects with an identical genome (7 %) (Battié et al., 1995) and attribute up to 74 % of degenerative changes to genetic factors (Pincus et al., 2002; Sambrook et al., 1999). Based on these findings, Battié et al. concluded in 2008, that "the once commonly held view that disc degeneration is primarily a result of aging and "wear and tear" from mechanical insults and injuries was not supported by this series of studies. Instead, disc degeneration appears to be determined in great part by genetic influences" (Battié et al., 2009). This conclusion implies, that mechanical influences are detached from genetics, which is misleading, since the composition of spinal mechanics includes more aspects than externally imposed loading scenarios. Thus, internal subject-specific influencing factors, such as spinal alignment, body weight, tissue mechanics, or muscle morphology affect spinal loading and are strongly related to genetics (Dubois et al., 2012; Mikkola et al., 2009; Stone et al., 2015; Tiainen et al., 2009; Tian et al., 2017). Corresponding indications of correlations between these factors and spinal degeneration and back pain can be found in the literature (Danneels et al., 2000; Gibbons et al., 1997; Kalichman et al., 2010, 2017; Lee et al., 2011; Madhuchandra et al., 2023; Sponbeck et al., 2022; Tanaka et al., 2023), such as the correlation of back pain and spinal degeneration to sagittal alignment (Hira et al., 2021; Madhuchandra et al., 2023), or body mass index (BMI) (Elgaeva et al., 2020; Nitecki et al., 2023). Apart from these strictly morphological aspects of the passive torso, the role of the abdominal muscles in the onset and development of chronic back pain has been vastly studied for several years now (Cooley et al., 2022; Lee et al., 2011; Miki et al., 2020; Sponbeck et al., 2022; Z. Wang et al., 2022). Based on image data and questionnaires, these studies investigated potential correlations between muscle architecture parameters and subjects with and without CLBP. Common criteria to assess the respective conditions of paraspinal muscles are the physiological cross-sectional area (PCSA), muscle density, or muscular fat infiltration. Several studies have reported to find a decrease of muscle PCSA in patients with LBP compared to non-symptomatic controls (Danneels et al., 2000; Gibbons et al., 1997; Lee et al., 2011; Sponbeck et al., 2022), and spinal degeneration (Cooley et al., 2022; Miki et al., 2020), as well as muscle density and fat infiltration (Kalichman et al., 2017). The functional state of abdominal muscles plays a central role in preserving spinal stability (Z. Wang et al., 2022), which is one of the mechanisms associated with CLBP. Therapy aiming for lumbar stabilization has been reported to improve quality of life and functional outcome in patients with CLBP (Shaughnessy & Caulfield, 2004) and therefore, conservative therapy often incorporates specific exercise to strengthen abdominal muscles in order to increase spinal stability (Shaughnessy & Caulfield, 2004). While the effectiveness of such treatments has been subject to numerous studies, the exact effects of muscle architecture and accompanying functionality on spinal loading remain unclear (Maia et al., 2021).

Up to this point, we solely addressed the "bio"-part of the biopsychosocial perspective. In order to be able to clearly classify or exclude biomechanical influences on CLBP, it remains to be answered how known psychological and social risk factors influence the anatomical characteristics of those affected. Thus, recent studies have shown correlations between muscle strength and depression (Zhang et al., 2023) or between obesity and socioeconomic status (L. N. Anderson et al., 2022). However, these potential interactions receive little attention in large-scale epidemiological studies.

The complexity and ambiguity of associated causes indicate that there can be no universal solution for CLBP. The subject of pain is highly complex itself and physical induction is only one aspect of many. This makes it all the more important to understand its origins to develop therapeutic interventions, that sustainably improve the quality of life for the patient. In the past years, there have been repeated attempts for patient subgrouping to promote a development towards individualized therapy (Fersum et al., 2010; Langenmaier et al., 2019). However, such classification had shown to have only minor impact on the improvement of pain intensity and disability (Tagliaferri et al., 2022a). Commonly, these attempts are based on randomized clinical trials, neglecting individual loading patterns, since this information is not available in large sample sizes. To collect this data, experimental as well as numerical methods can be applied.

Experimental studies on spinal biomechanics can only be realized to a very limited extent for various reasons. In vitro studies under laboratory conditions allow quantitative controlled analyses of isolated structures of the spine. While they provide valuable insights into the passive mechanical properties of functional spine units (FSUs), IVDs, ligaments, or even the whole torso (Jokeit et al., 2023), they are not applicable when it comes to the investigation of biomechanics including active components. To collect such data of the musculoskeletal torso, in vivo measurements are required. However, the invasive character of those experimental methods via intradiscal pressure sensors (Sato et al., 1999; Takahashi et al., 2006; Wilke et al., 2001) or instrumented vertebral implants (Dreischarf et al., 2016a; Rohlmann et al., 2008) makes them unsuitable for clinical analysis. Due to ethical reasons, these studies cannot be carried out in large test groups without any indication for an invasive intervention. Therefore, they usually consider either single healthy individuals (Takahashi et al., 2006; Wilke et al., 2001) or subjects with a previous indication for vertebral body replacement (Rohlmann et al., 2008), e.g. due to fracture, which comes with additional fixation of the respective motion segment and therefore, interfering substantially with its mechanics. Thus, the generation of a database on natural spinal loading in a large diverse set of healthy patients is not feasible based on in vivo measurements.

Numerical models of the spine provide a non-invasive alternative to systematically assess spinal loading and reveal its underlying mechanisms. From the late 1960s to today, the number of publications on Scopus including such models of the spine increased from one to over 500 contributions per year. The improved accessibility to respective models via commercially or freely available software packages, as well as the continuing interest in the mechanics of the healthy and diseased spine, lead to ongoing research projects that constantly answer old questions while raising new ones at the same time.

Roughly, two methods for numerical biomechanical modeling can be distinguished. While finite element simulation is primarily suitable for the examination of deformation states and internal stresses in single flexible bodies, (Akhavanfar et al., 2018; El Ouaaid et al., 2016; Eskandari et al., 2019; Ghezelbash et al., 2016a; Little & Adam, 2015; Naserkhaki et al., 2016; Périé et al., 2002; Vergari et al., 2016), multibody models allow the consideration of biomechanics of the spine from a more comprehensive perspective and can take multiple aspects of mechanical loading into account (Dreischarf et al., 2016b; Gould et al., 2021; Knapik et al., 2022; Lerchl et al., 2023a) by simplifying mechanical systems to a combination of rigid bodies, connecting joints, and active and passive force elements. In biomechanics, body segments or single bones are commonly assumed to be rigid bodies, while connective tissue, such as ligaments or cartilage, is modeled as flexible force elements, representing elastic or viscous properties that enable the human body the balancing act between the necessary stability and sufficient flexibility. Hypothesizing, that conspicuous loading patterns might lead to changes of spinal biomechanics and potential overloading, numerous studies have been incorporating such models to investigate morphological factors such as sagittal alignment (Bruno et al., 2012; Müller et al., 2021), body weight (Akhavanfar et al., 2018; Ghezelbash et al., 2017) and its distribution (Acar & Grilli, 2002; Ghezelbash et al., 2017), or muscle morphology (Z. Wang et al., 2022).

Most multibody models are generic in nature and thus represent a strong simplification of biological complexity. In respective studies, single parameters are often varied systematically to investigate their effects on spinal loading (Akhavanfar et al., 2018; Bassani et al., 2019; Bruno et al., 2012, 2017; Galbusera et al., 2014; Müller et al., 2021). The advantage of this One-Factor-At-A-Time (OFAT) testing is that it supports an understanding of the effect of each individual parameter on the outcome or results of the simulation. By isolating one parameter while keeping others constant, researchers can observe how changes in that specific parameter influence the overall system or model. Contrasting this, a recent trend towards individualized models has emerged in the relevant literature (Banks et al., 2023; Burkhart et al., 2020; Fasser et al., 2021; Overbergh et al., 2020) in order to account for the inherent complexity of clinical practice, where each patient comes with an unique combination of influencing factors that leads to individual loading scenarios. In such systems with multiple inconsistent parameters that are suspected to interact with each other, multifactorial testing can help uncover these interactions and understand their combined effects.

For all the potential that individualized models hold, they also pose special challenges. The balancing act between sufficient model complexity and necessary simplifications is part of any modeling process, aiming to draw distinct conclusions from the obtained results while adequately considering all relevant aspects of the system to be modeled with respect to the posed research question. When multiple factors are changed simultaneously, interactions between the parameters can occur, leading to confounding effects. This can obscure the understanding of which specific parameters are driving changes in the system, induce bias, and carries the risk of error propagation. Consequently, it can be challenging to draw meaningful conclusions from such simulation results. However, oversimplified models can also lead to biased results, such as the overestimation of individual effects due to the neglect of other parameters and their interrelations. In short: the question of the right level of detail is crucial in biomechanical modeling.

Depending on the degree of individualization, patient-specific models can combine a multitude of parameters, that come with a high variability. Starting from individual geometries of single bones to anatomic superstructures, like spinal alignment, individual body weight and its distribution, muscle architecture and functionality, or highly individual mechanical properties of passive structures, like ligaments or IVDs, biological variability is manifold. The consideration of all these parameters in respective models would require vast and in-depth experimental investigations on multiple levels and might never be reached due to limited accessibility of the relevant information, especially considering in vivo subjects. However, state-of-the-art multimodal imaging can already supply a broad range of data to include in respective models for creation of digital copies of large patient cohorts, at least partially representing the diversity of an actual population. Only few studies are incorporating models derived from large patient cohorts (Ignasiak et al., 2023; Nguyen et al., 2024; K. Wang et al., 2023). Ignasiak et al. used their validated multibody model to investigate effects of sagittal alignment on postoperative changes in spinal loading after realignment in 205 patients (Ignasiak et al., 2023). Anderson et al. published a set of 250 models including individual height, weight, trunk muscle morphology, and spinal curvature from 125 males and 125 females from the Framingham Heart Study (D. Anderson et al., 2020). This dataset was used in several studies, investigating the role of paraspinal muscles (K. Wang et al., 2023), load-to-strength patterns for fracture prediction (Mokhtarzadeh et al., 2020), and possible complications following T10-Pelvis spinal fusion (Nguyen et al., 2024). All of those studies follow the same approach of using a validated generic model of the thoracolumbar spine (Bruno et al., 2015; Ignasiak et al., 2016) and scaling the individual parameters according to patient CTs. They don't involve bone and soft tissue segmentation for each patient and therefore, neglect individual variability of vertebral geometries and body weight distribution. However, some studies state that parameters, such as vertebral height or transverse process width influence lumbar loading notably and recommend to include these parameters in subject-specific modeling (Putzer et al., 2016).

Highly individualized modeling is usually time-consuming and therefore, respective models are often only available in limited sample sizes. However, in order to obtain meaningful and statistically relevant results, the analysis of large and diverse patient cohorts is essential. Due to diagnostic and clinical practice, as well as large population-based cohort studies (e.g. German National Cohort, UK Biobank), such datasets are available for scientific interest and during the past decade, developments in data analytics, especially in the field of artificial intelligence, have been providing promising tools to make these datasets accessible for further analysis and model generation (Sekuboyina et al., 2021). Apart from data pre-processing, it is inevitable to also automate modeling itself, in order to make these highly individualized models suitable for systematic studies on spinal biomechanics and clinical practice.

1.2 Objectives

The overarching aim of this work is to assess the potential of individualized musculoskeletal modeling for systematic analysis of spinal loading in a digital representation of a large diverse patient cohort. Therefore, an automated process for generation of multibody models based on CT data from the torso was set up and the potential and limitations of these models were evaluated. This can be broken down into the following four objectives.

I. **Assessment of the State of Research in Multi Body Modeling of the Thoracolumbar Spine**

   In order to keep up with state of the art research, it is necessary to engage with both, achievements of the past as well as recent developments in the particular field of interest. Thus, a comprehensive and accompanying analysis of existing work throughout the scientific process is required to assess the state of research, open limitations and challenges in current approaches in musculoskeletal modeling of the spine, as well as the potential of such approaches to address clinical questions.

II. **Automated Generation and Validation of Individualized Models**

   Based on automated segmentation of CT imaging, thoracolumbar vertebral geometries, and spinal alignment, as well as torso weight and its distribution will be derived and included in the highly individualized MBS models of the torso. To avoid the time-consuming manual modeling, the whole process should be automated. Created models should reflect the state of the art in biomechanical modeling and be validated based on in vivo data from the literature.

III. **Evaluation of the Effects of Model Individualization on Lumbar Load Estimation in Musculoskeletal Modeling of the Spine**

   One objective was to examine how different degrees of model individualization affect observed influences of various morphological parameters on spinal loading. It will be investigated, whether significant effects observable in generic models still stand, when model individualization is increased and whether changes in effect strength appear in the process. This will support a general understanding of the relevance of common practices in spine modeling and evaluate the potential of studies based on diverse patient cohorts for multivariate investigations on spinal biomechanics.

IV. **Analysis of Potential Effects of Morphological Characteristics on Spinal Loading Using Individualized Models**

   Based on a digital representation of a large diverse patient cohort, the effects of various individual parameters on spinal loading will be investigated. The aim is to analyze, whether loading patterns can be identified under consideration of variation in morphological parameters derived from medical imaging. Further, the predictive potential of these models should be assessed via manipulation of control variables and the resulting impact in lumbar loads.

2. Fundamentals

In this section, the basics of multibody simulation will be provided, followed by a short introduction to spinal biomechanics. For reasons of brevity, the focus will be on introducing relevant terminology, while concisely explaining mechanical core concepts, background information and important context.

2.1 Multibody Simulation

Multibody simulation (MBS) is a numerical method that is widely used for estimation of kinematics and kinetics of mechanical systems. In the classical notion, these systems are composed of rigid bodies that are interconnected via mechanical linkages like joints, constraints or connections (Figure 2.1).

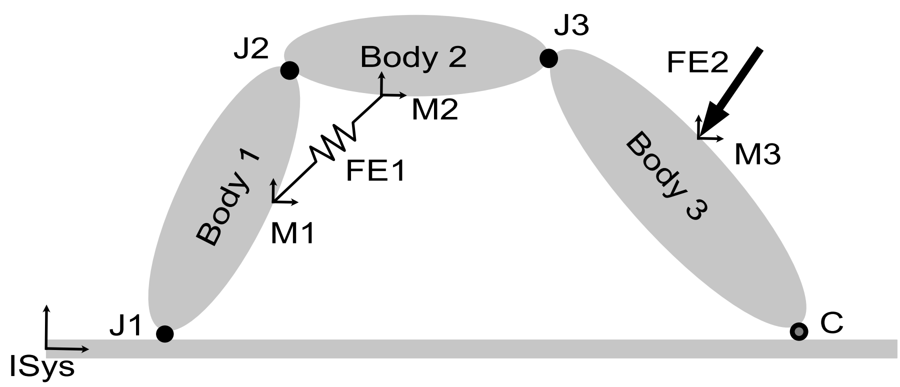

Figure 2.1: Schematic representation of a multibody system consisting of three bodies with respective joints (J), a constraint (C) and a force element (FE). Body-dependent position and orientation for joints, force elements or constraints are defined via markers (M).These can be defined in reference to the bodies (local coordinates) or the initial system (Isys) (global coordinates).

Thus, complicated mechanical phenomena are reduced to essential mechanisms, supporting a deep understanding of their dynamics from a comprehensive point of view. Joints define the respective degrees of freedom for each body in reference to either another body or a reference system. To each body, exactly one joint is assigned, which is enough to build an open kinematic chain, but not for closed loop systems. For those modeling tasks, constraints can be added to the model to provide the necessary boundary conditions. So called force elements represent a multitude of components that induce forces and torques to the system. These can show passive behavior, such as in contacts or spring-damper units, or apply loads actively in form of excitation. No masses are attributed to these force elements and therefore, inertia effects result from the mass properties of the bodies.

Positions and orientations in reference to the individual bodies or other reference systems are defined by local coordinate systems, in the following referred to as markers. These markers are utilized to define specific locations, for example for joints or attachment of force elements. The model's behavior over time can be described via states, which is a collective term for all time-dependent properties of the system. Dynamic states include variables that change over time and are therefore described using differential equations. Algebraic states represent boundary conditions and static constraints, that need to be satisfied at all times during the simulation.

There are two basic ways to introduce kinematics into the model: via a forward or via an inverse dynamic approach (Figure 2.2). In forward dynamics, models are actuated by intrinsic and extrinsic forces and moments to generate a desired kinematic behavior. In inverse dynamics, a predefined motion sequence is imposed to the model and internal forces and moments required to produce the observed movement are calculated (Ezati et al., 2019).

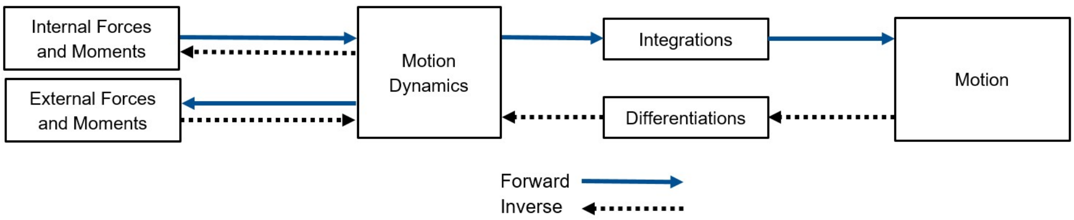

Figure 2.2: Dataflow for forward and inverse dynamic systems. Modified from Ezati et al. (2019).

Forward dynamic simulation can provide a comprehensive representation of the system's behavior over time including force, torque and motion trajectories. Therefore, complex interactions between different parts of the system, such as contact forces can be captured. However, to achieve accurate representation of the desired motion, in-depth knowledge on actuating forces and torques is required, which can be challenging or simply not feasible to measure in real-life biomechanical systems. Furthermore, forward dynamics usually come with high computational costs.

In comparison, inverse dynamic simulations tend to be computationally less intensive. However, the quality of their outcome is highly dependent on accurate kinematic data, as discrepancies can accumulate during simulation and lead to erroneous joint loads (Hatze, 2002). Additionally, in redundant systems (i.e. more actuators than degrees of freedom), this approach can only provide one possible solution from multiple possible ones and therefore, might lead to an inaccurate representation of the actual behavior of the system. This is commonly addressed by including mathematical optimization to find the optimal solution according to one or multiple predefined cost functions and constraints.

2.2 Biomechanics of the Spine

The spinal column is the central structure in the musculoskeletal system of humans and every other vertebrate. It can be divided into five sections: the cervical, thoracic, and lumbar spine, as well as the sacrum and coccyx. The caudally located sacrum and coccyx have eight to ten vertebrae, which are fused together, whereas the cervical, thoracic, and lumbar spine consists of seven, twelve, and five vertebrae, connected by IVDs, facet joints, paraspinal ligaments, and muscles (Figure 2.3), allowing for limited motion in between.

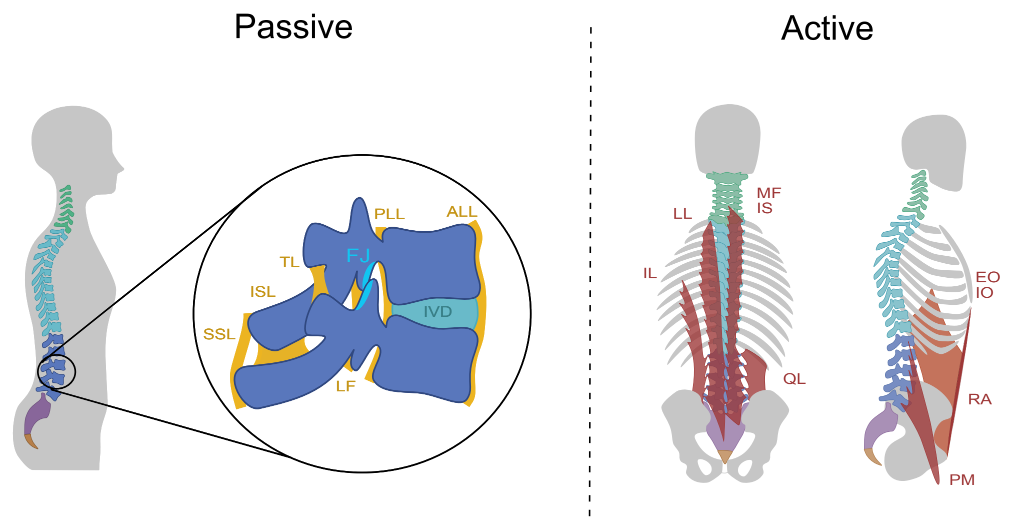

Figure 2.3: Passive and active structure of the musculoskeletal system of the spine. Left: Cervical (green), thoracal (turquoise), lumbar (blue), sacral (purple) spine and coccyx (orange) with detailed illustration of one functional spine unit (FSU) including two vertebrae, the IVD. facet joint (FJ) and paraspinal ligaments (supraspinous ligament (SSL), interspinous ligament (ISL), ligamentum flavum (LF), posterior and anterior longitudinal ligament (PLL, ALL) and intertransverse ligament (TL). Right: Abdominal muscles: iliocostalis lumborum (IL), longissimus thoracis pars lumborum (LL), interspinales lumborum (IS) and multifidus (MF), quadratus lumborum (QL), psoas major (PM), rectus abdominis (RA), and internal and external obliques (IO, EO))

The spine serves multiple functions, such as protection of the spinal cord, shock absorption, or structural support and stabilization of the torso, while enabling a variety of movements. The biomechanics of the healthy spine can best be explained on the basis of one motion segment, also called functional spine unit (FSU). It consists of two vertebral bodies, the connecting IVD, facet joints and the stabilizing ligaments. The microscopic composition of the IVD and the ligaments plays a key role in the mobility of the spine. Both structures have non-linear viscoelastic behavior, which supports the challenging balancing act between sufficient flexibility and the necessary stability.

Despite naturally different structural compositions due to varying requirements, IVDs, ligaments, and tendons are vastly assembled by the same basic components: water, directional and non-directional collagen fibers that induce stiffness and strength, Proteoglycane (PG), hydrophile macromolecules, mainly responsible for binding of water and collagen fibers, leading to viscous material properties, and elastin, elastic fibers enabling flexibility and recoiling ability in the tissue (Sharabi, 2022). Depending on their function in the musculoskeletal system, these components occur in different proportions, designs and arrangements and thus determine the mechanical properties of the respective tissue. Due to these shared basic components, one central characteristic feature can be found in all these structures: the J-shaped stress-strain behavior under uniaxial tension. In the unloaded state, the directed collagen fiber bundles show a wave form, commonly referred to as crimping (Baer et al., 1991; Sharabi, 2022). Under loading conditions, the tissue collagen fibers are thus first straightened, before they start carrying the load (Figure 2.4).

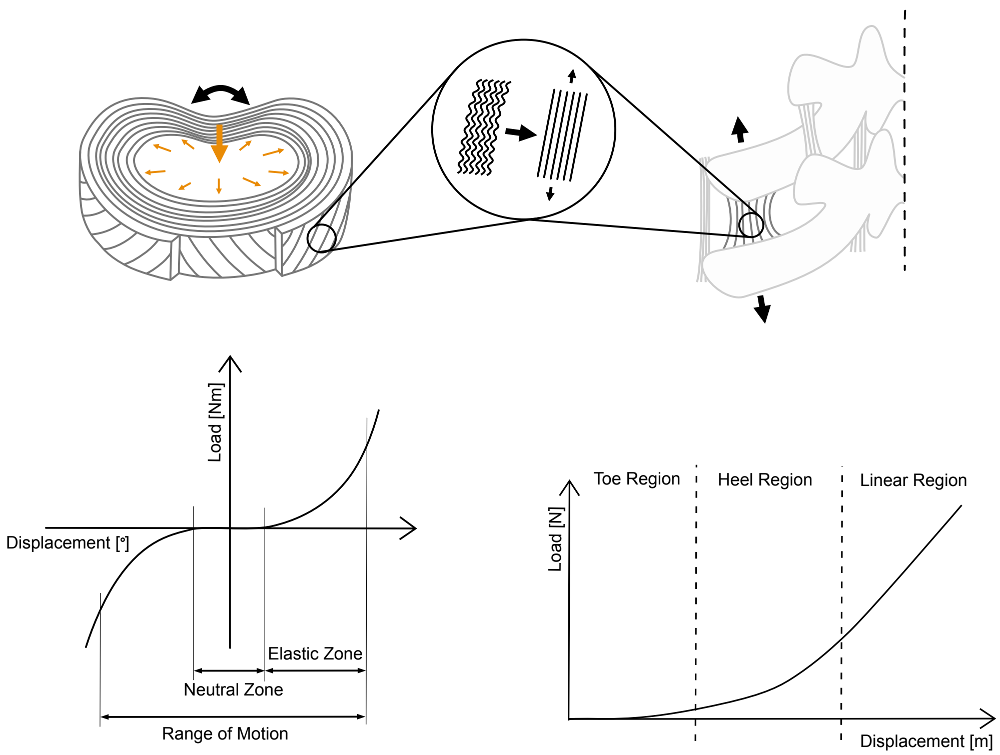

Figure 2.4: Behavior of collagen fibers in IVD (left) and ligaments (right) under loading. When the fibers are stretched, they are first smoothed (neutral zone, toe region) out of the crimped stat before they begin to absorb loads in the stretched state (elastic zone, heel region) and are stretched on a molecular level in the linear region.

The tissue therefore reacts with a minimal mechanical response to small deformations due to elastin and PGs in the matrix, enabling nearly free motion in the respective range, called the toe region for ligaments and neutral zone for IVDs respectively. In the subsequent heel region (ligaments) or elastic zone (IVDs), the straightened fiber bundles start to carry the imposed load, leading to fibril sliding and elongations and consequently, to increasing stiffness. This is followed by the linear region, where stretching and straightening of the structure of collagen fibers on a molecular level results in a linear mechanical response to applied deformation (Fratzl & Weinkamer, 2007).

Tendons and ligaments are responsible for energy-efficient load transfer from muscle to bones, and in between bones respectively. Being similar in structure, both are composed mainly of water (ca. 70 %) with unidirectional collagen fibers, grouped into fascicles and a matrix containing elastin and PGs. The fibers are highly aligned with the direction of tension and their shape shows the characteristic crimping in the unloaded state. The resulting non-linear viscoelastic behavior makes them optimally suited for tensile load transfer while preserving an adequate deformation capability, which is more pronounced in ligaments compared to tendons (De Santis et al., 2004).

In comparison, IVDs face a much more diverse set of load cases. Being mainly exposed to compression, they further need to cope with shear and rotational loading in all spatial directions. They are crucial for enabling flexion/extension, lateral bending, and axial rotation, while stabilizing the whole torso and preventing joint overloading. This complex requirement profile leads to a likewise complex composition, that is briefly explained in the following. The IVD is a heterogeneous tissue, consisting of the gelatinous nucleus pulposus (NP), surrounded by the collageneous annulus fibrosus (AF), which is connected via collagen fiber bundles to the adjacent vertebrae through a thin cartilaginous endplate (CEP) to the underlying bony endplate (Newell et al., 2017). The NP consists to a high amount of water (70 % - 90 %, decreasing with age), loose and non-directional collagen fibers, as well as proteoglycans (PG) (Antoniou et al., 1996). The AF is built from 15–25 concentric layers, called lamellae. Each lamella consists of collagen fiber bundles, with altering orientation $\pm$ 25–45° to the transverse plane between the layers. Under compression, this arrangement combined with the hydrostatic pressure of the NP enables the collagen fibers to be loaded in tension and thus, to exert resistance against deformation.

Therefore, the IVDs, as well as ligaments and tendons provide the necessary flexibility to allow the spine a wide range of motion, while having stabilizing effects to prevent overloading, which potentially will lead to injury or degeneration.

3. Methods

This chapter provides an overview of the methods used for model generation and simulation. The first section covers image data processing and derivation of relevant input data for model generation. The algorithms used during the steps elaborated in this section were primarily developed by other members of the *iBack* research group (Sekuboyina et al., 2021) and were therefore not subject of this doctorate. They are presented here for the sake of comprehensiveness. The following section briefly covers the process for modeling automation before introducing the general model setup with description on joint, ligament, IVD and muscle representation. Subsequently, the applied approach for muscle force estimation is elaborated, before the applied statistical methods are introduced. The content of this chapter has previously been published in a similar form in (Lerchl et al., 2022).

3.1 Image Data Processing

For the automated extraction of patient data from asynchronously phantom based calibrated CT image data (Kaesmacher et al., 2017), an automated deep learning based process for vertebrae segmentation and labeling (Sekuboyina et al., 2021) was utilized. Based on the segmentations of the vertebrae and corresponding subregions, points of interest (POIs) for muscle and ligament attachments, as well as intervertebral joint definitions were identified. In Figure 3.1 the whole process is illustrated.

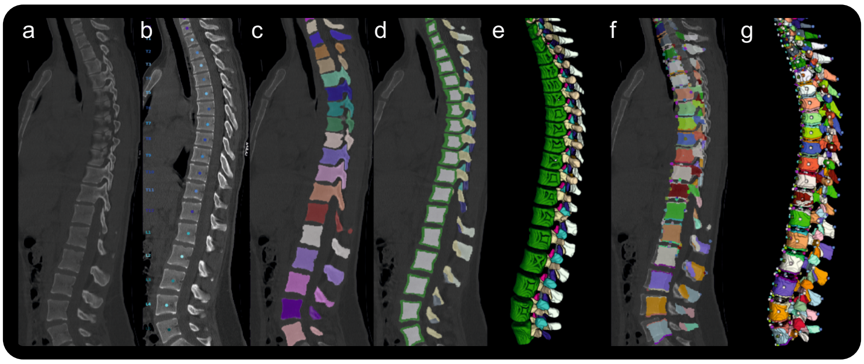

Figure 3.1: Pipeline overview from left to right; original data, vertebrae identification; vertebrae segmentation; subregion segmentation (cross section and 3D rendering); re-alignment in craniocaudal direction and calculation of points of interest; 3D rendering of the final dataset (Lerchl et al., 2022)©.

Briefly, three artificial neural networks (ANNs) were incorporated for spine detection, vertebra identification and labeling (b) as well as label-based segmentation of each vertebra (c). For each vertebra, centroids as well as segmentation masks for eleven subregions (d,e) were generated using a fourth ANN: vertebral body (further divided into cortex and the trabecular compartment), vertebral arch, spinous and transverse processes, as well as superior and inferior, left and right articular processes. For each subregion, the corresponding center of mass was calculated. To account for posture differences between supine position from CT scans and upright position, the centroids of the first thoracic and last lumbar vertebra were aligned vertically (f). The aligned image and segmentation masks were further used to calculate respective POIs (g).

Based on the segmentation, vertebral surface meshes were created using the marching cubes algorithm with the method according to Lewiner et al. (Lewiner et al., 2003) and were saved in a stereolithography (stl) format. In the next step, points for muscle and ligament attachment for each individual vertebra were defined. Therefore, the algorithm iterated over each vertebra, creating bounding boxes based on respective binary vertebra segmentations. Within each bounding box, POIs were defined under consideration of individual previously segmented subregions (Figure 3.2).

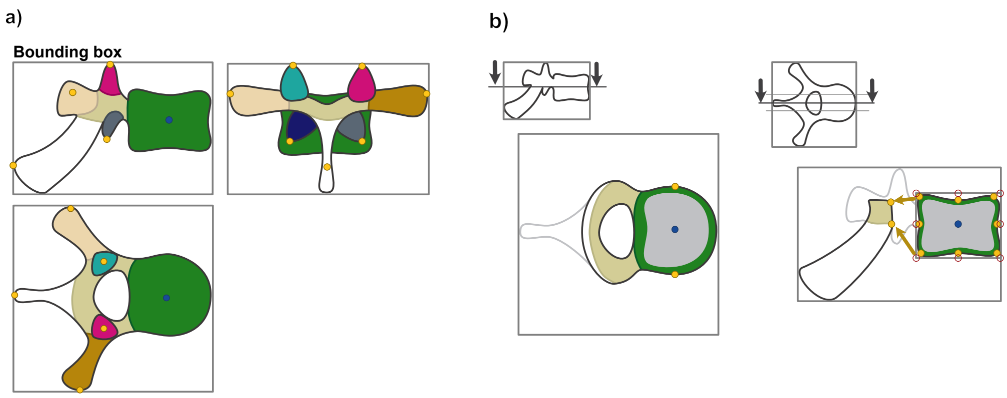

Figure 3.2: Calculation of points of interest. The vertebra is divided into subregions, which are further used to identify landmarks based on geometrical extreme values (a). Horizontal and auxiliary planes are inserted to identify points of interest of the vertebral body via a projection of the border points of a bounding box on the respective subregion (b) (Lerchl et al., 2022)©.

Therefore, the minimal and maximal coordinate values along the corresponding spatial axis on the surface of the respective subregion were incorporated to determine the most posterior, inferior, superior or lateral point on the surface. These points were considered to adequately represent local coordinates for ligaments and muscles attaching to bony landmarks, such as the spinous or transverse processes. From the centroid, the most lateral points on each side of the vertebral body were extracted. However, this approach was not feasible to determine POIs located in the central area anterior and posterior on the vertebral body, as well as the inside of the vertebral arch. In order to take into account the broad, flat course of the corresponding ligaments, three related points were defined at these areas. For this purpose, an auxiliary sagittal plane was set through the centroids of the vertebral body (Figure 3.2 b) with a normal defined by the connecting line between superior articular processes. In the sagittal sectional plane, a rectangle is fitted around the subregion of the vertebral body. Corner and center points of the rectangle border were then projected onto the surface by the shortest distance. Using a similar function, attachment points on the vertebral arch were determined via the minimal distance between the anterior border of its sectional plane and posterior points in the vertebral body. The plane was then shifted right and left by a third of the absolute distance to the respective articulate process and the process was repeated.

After assigning POIs to each vertebra individually, these points were used to define the location and orientation of intervertebral joints. The location was assumed to be the midpoint of the straight line connecting the central points of the lower and upper endplates of the two vertebrae representing one motion segment (Figure 3.3).

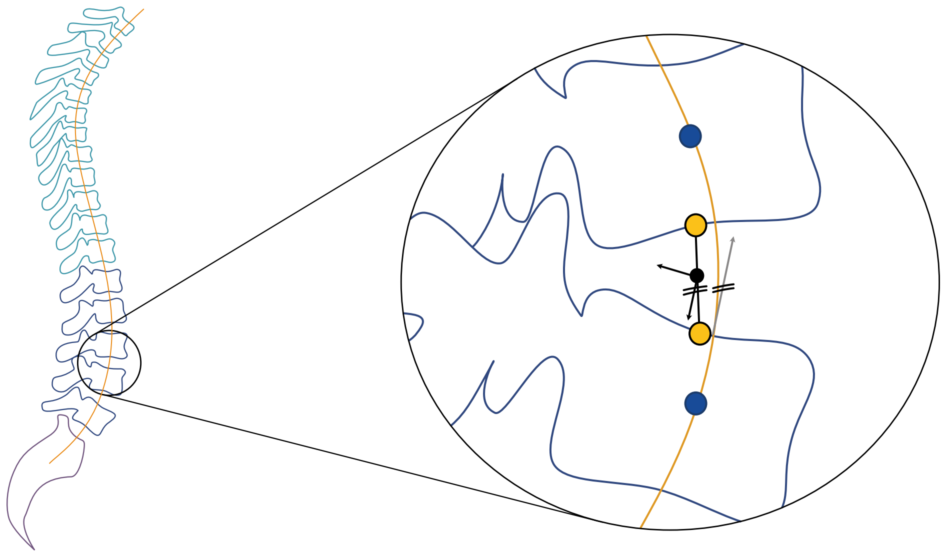

Figure 3.3: Determination of intervertebral joint location and orientation. The position of the joint is assumed to be the midpoint of the straight line connecting the central points of the endplates. Orientation of the marker is defined via the derivative of intersection of the spline interpolation of vertebral centroids.

To be able to differentiate clearly between compression and shear forces, marker orientation was calculated based on the upper endplate orientation of the inferior vertebra of the respective motion segment. Therefore, we used a spline interpolation connecting all vertebral body centroids, calculated its derivative at the intersection with the endplate, and declared this to be the direction of compression force.Its respective angles relative to the body reference system defined local marker orientation as cardan angles.

A segmentation mask for lung, fat and muscle/organ tissue was created based on typical CT intensity ranges to include individual torso weight distribution (Figure 3.4). Subsequently, the segmented tissue was assigned to the nearest vertebra depending on its minimal anterior-posterior distance. Thus, the torso weight was subdivided into segments for each vertebral level, defined as the range between center of rotations of each joint. For each segment, the algorithm calculated the respective center of mass and total weight of each segment corresponding to its individual tissue distribution. Average density was assumed to be 0.25 g/cm^3 for lung, 0.96 g/cm^3 for fat and 1.06 g/cm^3 for the remaining soft tissues (Akhavanfar et al., 2018; Pearsall et al., 1996).

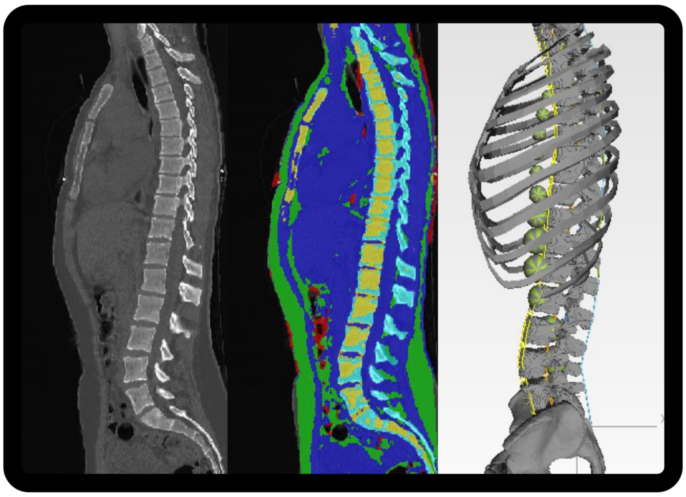

Figure 3.4: Tissue segmentation for fat (green) and muscular and organ tissue (blue). Lungs are not depicted in this view.

Coordinates, orientations and segment masses were written in a SubVar-file, a formatted text file, which serves as input for the MBS software Simpack (Dassault Systèmes, France), which was used for musculoskeletal modeling during this work. SubVars (Substitution Variables) are used for data parameterization in Simpack, so modeling data, such as marker coordinates are not assigned explicitly, but via the name of the SubVar.

3.2 Automation of Modeling

The Simpack scripting engine allows creating, investigating and modifying models, as well as controlling the Simpack solvers. Simpack scripting is based on the ECMAScript standard and was developed in QTScript, a scripting engine from the Qt framework for creating cross-platform applications. Being similar to JavaScript, it is an object orientated prototype-based language that includes Simpack specific classes to manage models and simulations. For the purpose of this work, a generic script (genScript.sjs) was created, including the architecture of the models as described in the following section. The script referred to the directories including the patient-specific information, namely the SubVar-file and individual geometries. After specifying the path to the patient data, a separate model for each patient was created.

The following chapter will provide a detailed description of model composition and simulation approaches.

3.3 Modeling

For modeling and simulation, the multibody simulation software Simpack (Versions 2022/2023x, Dassault systèmes, France) was used. According to a classical notion of multibody dynamics, mechanical systems are represented here as an arrangement of rigid bodies that are connected to each other via actuated or passive joints. Massless passive or active force elements are used to introduce forces or torques to the model according to their underlying physical laws or imposed excitation.

Models include the individual thoracolumbar spine and paraspinal soft tissue distribution with viscoelastic components representing ligaments and IVDs combined with generic bodies of the head–neck complex, ribcage, simplified upper extremities, and the pelvic-sacral region. These generic structures were individually scaled according to Winter et al. (2005), and equipped with relevant points for muscle insertion and integrated into the model. Intervertebral joints were modeled as actuated spherical joints to ensure necessary stability. Joints connecting the thoracic spine, head–neck and ribcage were fixated to form one rigid body. Segment masses for soft tissue were also linked rigidly to each vertebra according to the calculated centers of mass. Assigned masses for head-neck and simplified arms, were calculated relatively to the overall torso mass (Winter, 2005) and a density of 1.5 g/cm^3 was assumed for skeletal components (Akhavanfar et al., 2018; Pearsall et al., 1996). IVDs and spinal ligaments, were modeled as nonlinear, elastic force elements (Rupp et al., 2015; White, 2022), as only static load cases were considered. The following (Figure 3.5, equation 3.1) describes exemplary, how the IVDs were modeled for rotational displacement in flexion and extension. Modeling for lateral bending and axial rotation was done similarly. Specific data on stiffness and neutral zones of the IVDs were taken from (White, 2022).

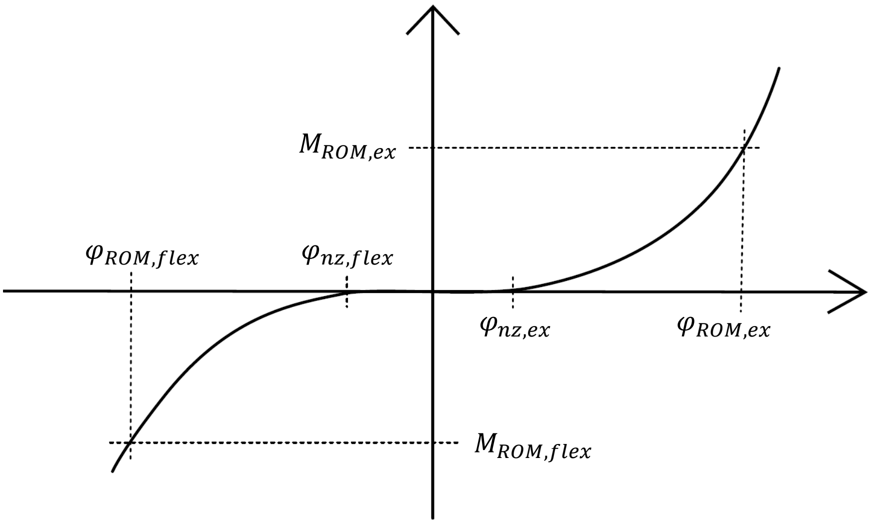

Figure 3.5: Typical load-deformation curve to describe the rotational stiffness of IVDs. The physiological range of motion (ROM) includes neutral zone (nz) and elastic zone (chapter 2.2).

$$M_{el}(\varphi) = \begin{cases} c_{flex}/(\varphi_{ROM,flex} - \varphi_{nz,flex}) * (\varphi - \varphi_{nz,flex})^2, & \text{for } \varphi \leq \varphi_{nz,flex} \\ 0, & \text{for } \varphi \leq \varphi_{nz,ex} \\ c_{ex}/(\varphi_{ROM,ex} - \varphi_{nz,ex}) * (\varphi - \varphi_{nz,ex})^2, & \text{for } \varphi > \varphi_{nz,ex} \end{cases} \tag{3.1}$$

$c_{flex/ex} = \frac{M_{ROM,flex/ex}}{\varphi - \varphi_{nz,flex/ex}}$, $c_{\text{flex/ex}}$: approximated linear stiffness in the elastic zone for flexion and extension, $M_{\text{ROM, flex/ex}}$: moment at the max. displacement within the range of motion, $\varphi_{nz,flex/ex}$: displacement at the end of the neutral zone

Focusing on sagittal loading and movement, the model included anterior and posterior longitudinal ligaments (ALL and PLL), flavum ligament (LF), interspinal ligament (ISL), and supraspinal ligament (SSL), while laterally located ligament were neglected. The characteristic force–length curve for the elastic behaviour of ligaments (Figure 4) shows a nonlinear toe region in the region of small deformations (A), followed by a linear elastic region before the final failure of the ligament (B). Inspired by the study of Rupp et al. (Rupp et al., 2015), their nonlinear force–length characteristics are described in equation 3.2.

Individual lengths for ligament segments were measured during the modeling process directly in the model during neutral position, which was considered as the posture derived directly from the CT. Based on the measured lengths, initial ligament lengths were calculated considering respective pre-strains according to the literature (Aspden, 1992; Nachemson & Evans, 1968; Robertson et al., 2013). The main difference to the mechanical law provided by Rupp et al. is that we take relative strain values for $l_{lig,\,A}$ and $l_{lig,\,B}$ instead of absolute elongations (Figure 3.6). This ensured uniform preloads within one ligamentous structure for the neutral position. Parameters for strains ϵ_A, ϵ_B and forces F_A and F_A at points A and B, are taken from the literature (Chazal et al., 1985).

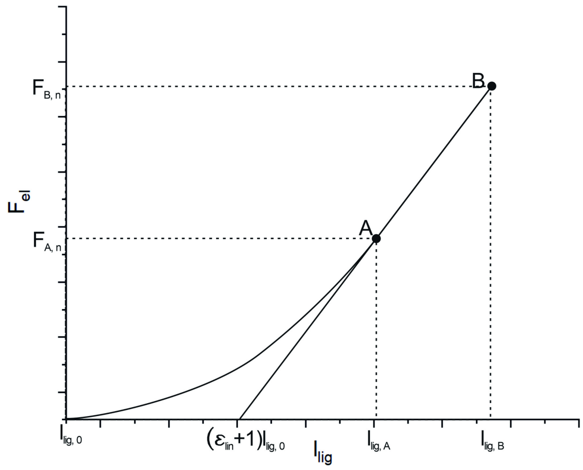

Figure 3.6: Typical force-length curve to describe the mechanical behaviour of ligaments. Transition from non-linear to linear regions are defined by l_A and F_A and F_B marks maximum force before failure occurs (Lerchl et al., 2022)[cc].

$$F_{el}(l_{lig}) = \begin{cases} 0, & \text{for } l_{lig} \leq l_{lig,0} \\ K_{nl}(l_{lig} - l_{lig,0})^{exp_{nll}}, & \text{for } l_{lig} \leq l_{lig,A} \\ F_{A,n} + K_{lin}(l_{lig} - l_{lig,A}), & \text{for } l_{lig} > l_{lig,A} \end{cases} \tag{3.2}$$

$l_{lig,0} = (1 - \epsilon_{pre})l_{neut}$, l_{neut}: individually measured length for each ligament segment in neutral position, ϵ_{pre}: individual pre-strain

$F_{A/B,n} = \frac{F_{A/B}}{n}$, n: number of parallel components for each ligament, F_A: ligament force at point A (same for B)

$l_{lig,A/B} = (1 + \epsilon_{A/B})l_{lig,0}$, l_A: length at point A and ϵ_A (same for B)

$K_{lin} = \frac{F_{B,n} - F_{A,n}}{l_{lig,B} - l_{lig,A}}$, K_{lin}: elastic stiffness in the linear region

$\epsilon_{lin} = \frac{F_{A,n}}{K_{lin} l_{lig,0}}$, ϵ_{lin}: strain at the intersection of the applied tangent from the linear region with the abscissa

$exp_{nll} = \frac{\epsilon_A}{\epsilon_{lin}}$, exp_{nll}: order of non-linearity of the toe region

$K_{nl} = \frac{F_{A,n}}{\left(\epsilon_A l_{lig,0}\right)^{exp_{nll}}}$, K_{nl}: individual factor that defines stretch/compression of the toe-region

Nine muscle groups of the lower back and abdomen were included, overall represented as 103 point-to-point actuators: rectus abdominis (RA), internal obliques (IO), external obliques (EO), psoas major (PM), quadratus lumborum (QL), multifidus (MF), longissimus thoracis pars lumborum (LTL), iliocostalis lumborum (IL) and the interspinales lumborum (IS) (Figure 3.7). LTL and IL together form the erector spinae (ES).

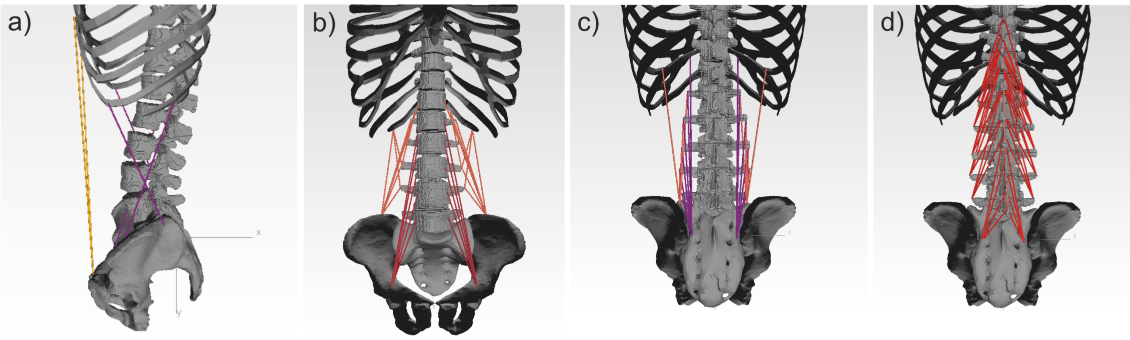

Figure 3.7: Musclegroups included in the model with: RA, EO, IO (a); QL,PM (b); ES consisting of LTL, IL (c); MF, IS (d) (Lerchl et al., 2022)©.

Muscles acting globally along the entire spinal column, RA, IO, and EO, as well as those muscle fascicles of LL, QL, and IL attached to the ribcage, were simplified each to one actuator per side. Muscles acting locally on the lumbar spine are modeled in detail based on attachment points taken from a cadaver study (Bayoglu et al., 2017). Muscle fascicles attached to the same subregion were combined and PCSA based on Christophy et al. (Christophy et al., 2012) were assigned to respective fascicles.

3.4 Muscle Force Estimation

Due to the redundancy of the system, it is not possible to clearly determine the acting muscle forces. Thus, an optimization approach was pursued that approximated the optimal solution based on an objective function and took into account defined constraints. Since Simpack does not provide such a function, a co-simulation with Matlab/Simulink (v2020b) was set up for this purpose (Figure 3.8). The SIMAT interface provided by Simulink enabled the data transfer between Matlab and Simpack.

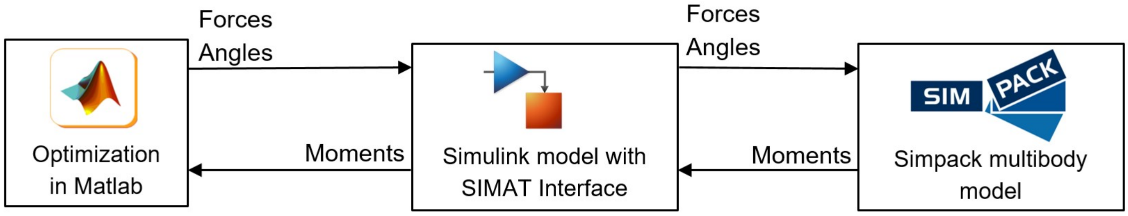

Figure 3.8: Workflow for co-simulation between Matlab/Simulink and Simpack for optimization based muscle force estimation.

The MBS model calculates necessary joint moments M to hold the imposed static positions, which are transferred to Matlab via a Simulink model, where muscle forces are calculated using a static optimization approach (Gagnon et al., 2001). In order to increase the chances of finding a global optimum, we used the globalsearch solver (Global Optimization Toolbox, Matlab 2020b) to solve the following optimization problem:

$$Minimize\left(CostFunktion = \sum_{i=1}^{n}\left(\frac{F_i}{PCSA_i}\right)^3\right) \tag{3.3}$$

subject to equality constraints

$$c_{eq} = \begin{pmatrix} M_{x,1} \\ \dots \\ M_{z,i} \end{pmatrix} = 0 \tag{3.4}$$

and bound constraints

$$0 \leq F_i \leq \sigma_{max} PCSA_i \tag{3.5}$$

Focusing on vertebral loading in the sagittal and frontal plane, equality constraints consider respective moments (x for frontal, z for sagittal) occurring in each lumbar intervertebral joint. Only active forces are taken into account neglecting the passive elastic behaviour of muscular tissues. To guarantee compliance with the equilibrium conditions for all load cases, maximal muscle stress (MMS) was set to 1 MPa (Beaucage-Gauvreau et al., 2019; Bruno et al., 2015; Favier et al., 2021). Applied flexion was assumed to be 40 % sacral rotation and 60% lumbar flexion (T. Liu et al., 2019) and distributed to the intervertebral joints according to (Christophy et al., 2012; Wong et al., 2006)

3.5 Statistical Methods

To draw meaningful conclusions from data including large cohorts and multiple parameters, it is essential to apply adequate methods for data analysis. The methods applied throughout this thesis will be briefly introduced in the following.

T-Distributed Stochastic Neighbor Embedding

T-distributed stochastic neighbor embedding (T-SNE) (Van der Maaten & Hinton, 2008) is a technique used for non-linear dimension reduction, pattern recognition and visualization of high-dimensional data. It maps high-dimensional data to a virtual two- or three-dimensional space, while preserving local similarities. Therefore, higher dimensional data is converted into a visualizable space while concisely containing the underlying information. In other words, similar data points are clustered closely, while those, that differ strongly are displayed with a matching distance. The process begins by calculating pairwise similarities between data points in the high-dimensional space. These similarities are measured using a Gaussian distribution centered at each point. The conditional probability that one point would pick another as its neighbor is calculated, and then symmetrized to ensure the similarities are mutual. In an iterative optimization process using gradient descent the positions of points in the low-dimensional space are updated to best match the high-dimensional similarities. The resulting low-dimensional map from T-SNE is typically easy to interpret, revealing clusters and patterns that may not be visible in the original high-dimensional space. This makes T-SNE a powerful tool for exploratory data analysis and understanding complex datasets. However, it is not suitable for quantitative analysis, as the data is represented in a virtual space, which serves for projection and is not directly interpretable in terms of the measure and scales of the underlying information. In the scope of this thesis, T-SNE allowed to evaluate trends in lumbar loading over all lumbar levels (dimensions), which were mapped to a two-dimensional space (chapter 4.1.3 and 4.2.1).

Linear Regression Models

Linear regression models are basic tools of statistical analysis for understanding the relationship between a dependent variable and one or more independent variables. The basic form of linear regression involves a single independent variable, where the model estimates the best-fit line through the data points by minimizing the sum of squared residuals (differences between observed and predicted values). This method is valuable for predicting outcomes and identifying trends, and provides insight into how changes in the independent variable affect the dependent variable. There are different types of linear regression models, the applicability of which depends on the respective research question and study design. Three types that were used during the work on this thesis are briefly presented below.

Multiple Regression

Multiple regression extends the framework of linear regression by including multiple independent variables, both categorical and continuous variables, to model their combined effects on a single dependent variable (Stolzenberg, 2004). This approach helps to understand the relative influence of each predictor and identify possible interactions between them. By considering multiple predictors, multiple regression provides a more comprehensive overview of the factors influencing the dependent variable. It allows for more accurate predictions and better control of confounding variables. This technique is widely used in various research areas to understand complex relations and create predictive models that take multiple factors into account simultaneously. Multiple regression was used in this work for evaluation of multiple morphological parameters in data without nested structure (chapter 4.1.3 and 4.2.1)

Analysis of Variance

In the context of linear regression, analysis of variance (ANOVA) is used to compare means of different groups by modeling a categorical independent variable (Stahle, Wold, et al., 1989). ANOVA divides the total variance observed in the dependent variable into components that are attributable to the independent variable(s) and the residual variance. This tests whether the mean values of different groups differ statistically significantly from each other. This method is particularly useful in experimental designs where the aim is to determine whether different treatments or conditions lead to different outcomes. For multiple comparison between the group means, Tukey's range test can be applied (Tukey, 1959). This test compares all pairs of groups and inherently controls the familywise error rate, which describes the probability of at least one false positive occurring in multiple comparisons. One-way ANOVA was used to evaluate trends for different muscle configurations without consideration of individual factors to evaluate general effects (chapter 4.2.2).

Linear Mixed-Effects Model

Linear mixed-effects models (LMM) further extend the scope of regression analysis by introducing random effects that account for variability within data clusters or groups that are not captured by fixed effects alone (Oberg & Mahoney, 2007). This is particularly useful in longitudinal studies or hierarchical data structures where observations are not independent. Mixed models allow for the inclusion of both fixed effects that are consistent across the population and random effects that vary at different levels of the data hierarchy. By integrating both types of effects, these models provide a robust framework for analyzing complex data, improving the accuracy of predictions and providing insights into both fixed and random sources of variability. This flexibility makes mixed models particularly suited for data with hierarchical, nested or repeated measurement structures. LMM was applied to evaluate changes due to different muscle configurations while taking the characteristics of each subject into account to evaluate the effects of reduced muscles for the individual (chapter 4.2.2).

4. Accomplishments

4.1 Peer-Reviewed Articles

This chapter provides an overview over the peer-reviewed articles, that were created in the context of this work. The respective publications can be assigned to the objectives 1-3, which were introduced in chapter 1.2.

4.1.1 Publication 1: Multibody Models of the Thoracolumbar Spine: A Review on Applications, Limitations, and Challenges

It goes without saying, that a comprehensive knowledge and understanding of existing work is an integral part of any profound scientific work. The insights I gained in this regard during my doctorate were summarized in the form of an extensive review of the state of research in the field of multibody models of the spine (objective I). Within the scope of this work, developments in common modeling methods and applications were addressed. Further, one central objective was the identification and discussion of limitations and challenges in state-of-the-art spine modeling. The manuscript was published after peer-review in January 2023 as part of the Special Issue on "Biomechanics-Based Motion Analysis" by the MDPI journal *Bioengineering* (Lerchl et al., 2023a)

Summary

We focused on studies using multibody models of the healthy, thoracolumbar spine published between 2013 and the end of 2022. A systematic search was carried out in PubMed and Scopus including the keywords "spine AND model AND ((multi AND body) OR musculoskeletal)" in November and December 2022. After filtering 2592 articles according to our inclusion and exclusion criteria, overall 81 musculoskeletal modeling studies were reviewed regarding their modeling approaches and their applications. Subsequently, we identified core limitations of state-of-the-art modeling, and discussed possible solutions in the process.

A large proportion of studies including multibody models of the torso are based on few original models, which were adapted, extended or manipulated according to the requirements of the respective study. Those original models were created using either the commercially available software AnyBody (AnyBody Technology A/S, Aalborg, Denmark) (de Zee et al., 2007; Ignasiak et al., 2016) or the open-source software OpenSim (Stanford, CA, USA) (Bruno et al., 2015; Christophy et al., 2012). Both platforms provided accessibility of these models, which enabled their adaption and further development even to researchers outside the respective original group.

We analyzed modeling approaches with respect to general model setup and kinematics, modeling of the passive viscoelastic components, scaling and individualization, and muscle force estimation. The majority of reviewed studies included models with five lumbar vertebrae usually combined with a rigid thoracic component. Few models include detailed representation of the thoracic spine and ribcage (Bayoglu et al., 2019; Bruno et al., 2015; Ignasiak et al., 2016). In most studies, intervertebral joints were simplified as spherical joints (3 rot. DOFs) (Christophy et al., 2012; Fasser et al., 2021), only few incorporate 6-DOF-joints (Ignasiak et al., 2016; Meng et al., 2015; Rupp et al., 2015; Senteler et al., 2016). Passive structures like paraspinal ligaments and IVDs were either neglected (Bruno et al., 2015; Christophy et al., 2012; de Zee et al., 2007; Fasser et al., 2021), combined in representative joint stiffness (Bayoglu et al., 2019; Favier et al., 2021; Malakoutian et al., 2018), or modeled explicitly (Guo et al., 2021; Khurelbaatar et al., 2015; Lerchl et al., 2022; Rupp et al., 2015).

Most multibody models are generic, vastly neglecting inter-individual variability. However, in the past years, an increasing number of studies have been published, putting an emphasis on the individualization of the models. Model adaption to individual characteristics can range from simple scaling of generic models regarding anthropometrics, to incorporation of bone geometry and muscle morphology derived from imaging data.

To account for muscular influence, usually a combination of inverse dynamics and static optimization is applied, which is assumed to be suited for static and low-dynamic scenarios (F. C. Anderson & Pandy, 2001). Depending on the used muscle model and research question, minimum fatigue, the sum of squared muscle forces or activation is amongst the criteria most commonly considered for the cost function. Only few models incorporate forward dynamics in combination with previously collected electromyography (EMG) data.

With regard to the application of existing models, a distinction was made between studies with a methodological, and biomechanical or clinical focus. Publications with a methodological focus include validation studies of new models as well as studies on specific model approaches for individual aspects, such as joint definitions or sensitivity analyses (Bassani et al., 2017; Bruno et al., 2015; Christophy et al., 2012; Dao et al., 2014; de Zee et al., 2007; Favier et al., 2021; Huynh et al., 2015; Khurelbaatar et al., 2015). Biomechanically focused studies, on the other hand, analyzed the mechanical impact of anthropometric and morphological characteristics (Bassani et al., 2019; Bruno et al., 2017; Müller et al., 2021), basic movements, such as flexion-extension (Bruno et al., 2017; Favier et al., 2021; Panero et al., 2021), walking or lifting (Beaucage-Gauvreau et al., 2020, 2021; Breloff & Chou, 2017; Ghiasi et al., 2016; Guo et al., 2021; M. Huang et al., 2016; H.-K. Kim & Zhang, 2017; J.-W. Kim et al., 2022; von Arx et al., 2021; Zaman et al., 2021; Zhu et al., 2017), as well as pathological and clinically relevant scenarios, as occurring in accidents (Valdano et al., 2022; Wei et al., 2022) or post-surgery (Bauer & Paulus, 2014; Fasser et al., 2022; Ignasiak, 2020; Kantelhardt et al., 2015), on spinal loads.

Apart from various modeling-specific limitations, such as commonly made simplifications in joint and muscle representation as well as the widely neglected impact of intra-abdominal pressure, we identified the provision of consistent data sets as a major challenge in biomechanical modeling. Particularly with respect to individualized modeling, this poses major challenges. Due to limited accessibility for in vivo investigation of biomechanics, for instance of mechanical properties of passive structures, comprehensive models of the torso need a combination of in vivo, in vitro, and population-based anthropometric data to adequately represent upper body mechanics. Thus, they are inevitably built from multiple sources and therefore, fail to depict specific individuals. To address this problem, new non-invasive methods are needed to collect the respective information. Engaging machine learning in medical imaging processing provides a promising perspective to derive patient-specific data, not only in terms of morphological parameters like bony shapes, but regarding information on mechanical states as well. That way, functional impairments due to degenerative changes, like IVD degeneration according to Pfirrmann (Pfirrmann et al., 2001) or fatty infiltration in muscles could be considered in individualized models.

CRediT Author Statement

Tanja Lerchl: conceptualization, writing - original draft preparation; **Kati Nispel:** writing - editing and review; **Thomas Baum:** writing - editing and review; **Jannis Bodden:** writing - editing and review, **Veit Senner:** writing - editing and review, supervision; **Jan S. Kirschke:** writing - editing and review, project administration, funding acquisition, supervision

Citation

Lerchl, T., Nispel, K., Baum, T., Bodden, J., Senner, V., and Kirschke, J. S. (2023). Multibody models of the thoracolumbar spine: a review on applications, limitations, and challenges. Bioengineering. 2023; 10(2):202. doi: doi.org/10.3390/bioengineering10020202

4.1.2 Publication 2: Validation of a Patient-Specific Musculoskeletal Model for Lumbar Load Estimation Generated by an Automated Pipeline From Whole Body CT

The purpose of this study was the introduction of a developed pipeline for automated generation of individualized multibody models, the validation of such models in static loading tasks, and the evaluation of their potential for systematic analysis of spinal loads under consideration of individual characteristics ((objective II)). The manuscript was published in *Frontiers in Bioengineering and Biotechnology* in July 2022 (Lerchl et al., 2022).

Summary

We combined CT derived patient-specific data including individual vertebral geometries, spinal alignment, as well as torso weight and its distribution with generic bodies for sacrum, pelvis, head-neck and simplified arms to create highly individualized models of the torso and validated them against data from in vivo studies in terms of obtained lumbar loading and estimated muscle forces. A detailed description on modeling and simulation can be found in chapter 3.3.

Based on CT data of two healthy individuals (1 M, 1 F), we created two individualized models and simulated various static loading tasks with and without additional weight, based on the load cases covered in the comparative in vivo studies: upright standing, 10°, 20°, and 30° flexion unloaded and with an additional weight of 10 kg, elevated arms, as well as lifting of 20 kg close to the chest and with stretched arms. Model validation was carried out based on experimental studies from the literature, measuring spinal loads at individual levels using an intradiscal pressure sensor in L4/L5 (Takahashi et al., 2006; Wilke et al., 2017) or instrumented implants for L1 (Rohlmann et al., 2008). Simulation results from the model of the healthy male subject (body height = 173 cm), similar in body height to subjects from comparative in vivo studies (avg. body height = 173.2 ± 4.4) (Rohlmann et al., 2008; Takahashi et al., 2006; Wilke et al., 2017) were compared to the experimental results from the respective study. Ligament strains were checked for physiological ranges and estimated ES forces were compared to measured EMG-signals (Takahashi et al., 2006). For better comparability, we normalized data from the simulations and measurements to upright standing and subsequently, compared simulation results to the measurements. For a proof-of-concept of the potential of individualized models for systematic investigation of spinal loading with respect to individual morphologic and anthropometric parameters, obtained results from both models were compared to each other and interpreted with respect to individual spinal alignment.

Ligament forces during simulation were mostly within a physiological range. Merely forces in the ligamentum flavum exceeded physiological maximums for moderate flexions of 30° initially, whereupon pre-strains were adjusted from 10 % to 5 %, which is still within the standard deviation of experimentally determined values (Nachemson & Evans, 1968). Muscle force estimations showed high correlation (r = 0.95) with in vivo EMG signals, and vertebral loading predictions were closely

matched (r = 0.98) with reported spinal load measurements. However, compression forces tended to be underestimated by up to 16 % in low- and moderate-intensity scenarios, like upright standing as well as loaded and unloaded flexion, while simulations overestimated high-intensity load cases involving 20 kg lifting by a maximum of 33 %. The interindividual comparison of both models showed noticeable differences in compression, anterior-posterior and lateral shear forces, which could be put into context with individual spinal alignment. For example, the thoracolumbar transition showed increased lateral shear forces for the female subject with mild thoracic scoliosis, as well as larger anterior-posterior shear forces in the lower lumbar region in accordance with a more pronounced lumbar lordosis.

Overall, we were able to predict spinal loads (r = 0.98) and muscle activity (r= 0.95) in close accordance with in vivo measurements, although some deviations occurred. Thus, simulations overestimated spinal loads during rather demanding lifting tasks (20 kg with stretched arms) by up to 33 %.

In conclusion, we introduced an automated pipeline for generation of patient-specific musculoskeletal models from CT data, incorporating individual anatomical details to estimate lumbar loads and muscle forces and validated the generated model. This provides a foundation for systematic analysis of large patient cohorts to identify biomechanical risk factors for spine diseases and to support a profound understanding of spinal biomechanics. Despite some limitations, the approach allows for detailed analysis of individual variations and for contributing valuable insights into personalized medical approaches for spine health.

CRediT Author Statement

Tanja Lerchl: conceptualization, methodology, validation, formal analysis, investigation, data curation, writing - original draft preparation, visualization; **Malek El Husseini**: methodology, software, writing - editing and review; **Amirhossein Bayat:** methodology, software, writing - editing and review; **Anjany Sekuboyina:** methodology, software, writing - editing and review; **Louis Hermann:** methodology, writing - editing and review; **Kati Nispel:** methodology, writing - editing and review; **Thomas Baum:** resources, writing - editing and review; **Maximilian T. Löffler:** resources, writing - editing and review; **Veit Senner:** writing - editing and review, supervision; **Jan S. Kirschke:** writing - editing and review, project administration, funding acquisition, supervision

Citation

Lerchl T, El Husseini M, Bayat A, Sekuboyina A, Hermann L, Nispel K, Baum T, Löffler MT, Senner V and Kirschke JS (2022) Validation of a Patient-Specific Musculoskeletal Model for Lumbar Load Estimation Generated by an Automated Pipeline From Whole Body CT. Front. Bioeng. Biotechnol. 10:862804. doi: 10.3389/fbioe.2022.862804

4.1.3 Publication 3: Musculoskeletal Spine Modeling in Large Patient Cohorts: How Morphological Individualization affects Lumbar Load Estimation

In this study, we investigated how different degrees of model individualization affect the observed effects of morphological factors on spinal loading by utilizing our validated pipeline for automated generation of highly individualized models of the torso (Lerchl et al., 2022) introduced in the previous chapter (objective III). The manuscript was published in *Frontiers in Bioenigneering and Biotechnology* in June 2024.

Summary

Incorporating our previously introduced pipeline (Chapter 3.1), we created models with different degrees of individualization based on CT data of 93 patients. In advance, a clinical professional assessed thoracic kyphosis and lumbar lordosis based on the respective CT for each patient. For each patient, three models were generated: one with both, individualized spine and body weight and distribution (Indiv), one with uniform spine but individualized body weight and distribution (uniSpine), and one with individualized spine but uniform body weight and distribution (uniTorso). With the resulting 279 models, simulations of four static loading tasks were carried out: upright standing, 30° flexion, and lifting of 10 kg close to the chest and with stretched arms.

Subsequently, we carried out statistical analyses of resulting lumbar compression and anterior-posterior shear forces to investigate their potential correlations with individualized parameters. For Indiv-models, these were thoracic kyphosis (TK), lumbar lordosis (LL), torso height (TH), torso weight (TW), and the center of mass of the torso weight in superior-inferior and anterior-posterior direction from the spinal column (CoM SI, CoM AP), for uniTorso-models only TK, LL, and TH, and for uniSpine-models only TW, CoM SI and CoM AP respectively. To check for cross-level patterns, we applied t-distributed stochastic neighbor embedding (T-SNE) to investigate overarching patterns over multiple dimensions, in our case lumbar levels (Van der Maaten & Hinton, 2008). Additionally, we performed multiple regression individually for all load cases and lumbar levels, and compared occurring influences of the investigated parameters on lumbar loads in terms of significance and effect strength depending on the degree of individualization of the respective model. That way, we aimed to assess, how simplification impacts observed correlations and their expression.

Load case-specific T-SNE showed concise clustering for compression and combined loading in semi-individualized models, while highly individualized models showed the same grouping, but with overlapping transitions between the groups. In other words, different load cases could lead to similar loading in individualized models, whereas in semi-individualized models, occurring loading could clearly be assigned to specific load cases. Merely, anterior-posterior shear forces in uniTorso-models showed comparable data scattering to the results from Indiv-models.

Results obtained from multiple regression for L4/L5 revealed, that TW had highly significant influence ($p < 0.001$) on compression for all load cases in both, semi- and highly individualized models. However, effect strength tended to decrease with increasing model individualization. For anterior-posterior shear forces, this observation was even more pronounced in loaded and unloaded upright standing. Regarding sagittal alignment, LL showed strongest significant effects ($p < 0.001$) on anterior-posterior shear forces with similar effect strengths, while respective effects on compression were only significant ($p < 0.05$) in uniTorso-models, but not in Indiv-models. In upright standing, TK showed significant unloading effects on compression forces, with decreasing effect strength when model individualization was increased. The evaluation of the coefficient of determination R^2 showed, that in uniSpine-models, multiple regression with only three independent variables (TW, CoM AP, CoM SI) was able to explain the variability in compression forces almost completely for all loadcases ($R^2 > 0.93$). In comparison, for uniTorso-models, the applied regression models showed poor to moderate fit ($R^2 < 0.47$). However, Indiv-models showed rather good fit for upright standing load cases ($R^2 > 0.7$). In all models, R^2 during 30° flexion, as well as for analysis of anterior-posterior shear forces in general were notably lower.

Overall, model individualization tended to show similar trends regarding the effects of single parameters, such as TW and LL on spinal loading when compared to semi-individualized models or the pertinent literature (Ghezelbash et al., 2016b; Hajihosseinali et al., 2015; Han et al., 2013; Müller et al., 2021). The observed decrease in effect strength and occasionally, even the loss of significance, however, indicate that the isolated consideration of simplified models holds the risk to overestimate the relevance of single parameters. Considering effects of TK, our results do not align with findings from the publications, stating that spinal compression forces increased with increasing TK (Bruno et al., 2012). One reason for this might be that characteristics like TK, which are varied in generic models in a targeted and isolated manner, are accompanied by other features in reality, such as an increased LL as well.

CRediT Author Statement

Tanja Lerchl: conceptualization, methodology, formal analysis, investigation, data curation, writing - original draft preparation, visualization; **Kati Nispel:** methodology, writing - editing and review; **Jannis Bodden:** methodology, writing - editing and review; **Anjany Sekuboyina:** methodology, software, writing - editing and review; **Malek El Husseini**: methodology, software, writing - editing and review; **Christian Fritzsche:** methodology, writing - editing and review; **Veit Senner:** writing - editing and review, supervision; **Jan S. Kirschke:** writing - editing and review, project administration, funding acquisition, supervision

Citation

Lerchl T, Nispel K, Bodden J, Sekuboyina A, El Husseini M, Fritzsche C, Senner V and Kirschke JS (2024), Musculoskeletal spine modeling in large patient cohorts: how morphological individualization affects lumbar load estimation. Front. Bioeng. Biotechnol. 12:1363081. doi: 10.3389/fbioe.2024.1363081

4.2 Additional Research

After evaluating, how the inclusion of various individual parameters affects the distinctiveness of results, the generated digital patient cohort was used to address clinically relevant questions (objective IV). Two studies examined the influence of (i) morphological parameters of the passive musculoskeletal system and (ii) the influence of altered muscle morphology on spinal loading in a diverse patient cohort. Both studies have been accepted for oral presentation at (i) *the 29th Congress of the European Society of Biomechanics 2024* and (ii) *the 29th Congress of the International Society of Biomechanics 2023*, respectively.

4.2.1 The Effect of Morphological Parameters of the Torso on Lumbar Loading in Large Patient Cohorts

Based on the results from highly individualized models of 93 patients introduced in the previous chapter, the effects of six parameters on lumbar loading were examined: thoracic kyphosis (TK), lumbar lordosis (LL), torso height (TH), torso weight (TW), anterior-posterior, and superior-inferior position of center of mass (CoM AP, CoM SI). The distinctive effects of each parameter were subsequently investigated in a multivariate qualitative and quantitative analysis. First, the parameters were checked for multicollinearities. T-distributed statistic neighbor embedding (T-SNE) was then applied to analyze the effects of applied load cases on all lumbar levels as well as to identify possible patterns across all load cases and lumbar levels. Subsequently, multiple regression was carried out to analyze effect sizes (β) and significance (p) of possible correlations between the investigated parameters and sagittal lumbar loading for each level and load case separately. To enable comparability of various parameters, independent variables were standardized and centered based on absolute values. This was particularly important for anterior-posterior shear forces to be able to distinguish between loading and unloading effects. Detailed information on modeling, simulation and applied statistical methods can be found in chapter 3.5.

Solely TH and CoM SI were highly correlated (r = 0.91). TW and CoM AP showed moderate correlation (r = 0.65). Remaining parameters showed low correlations (r = 0.04 - 0.35), indicating, that there is no pronounced multicollinearity within the set of parameters. Table 4.1 shows the respective correlation matrix.

Table 4.1: Correlation matrix of investigated morphological parameters.

	LL	**TK**	**TH**	**TW**	**CoM SI**	**CoM AP**
LL	1.00	0.36	-0.19	-0.22	-0.18	-0.34
TK	0.36	1.00	-0.26	-0.15	-0.22	0.04
TH	-0.19	-0.26	1.00	0.39	0.91	0.13
TW	-0.22	-0.15	0.39	1.00	0.35	0.65
CoM SI	-0.18	-0.22	0.91	0.35	1.00	0.05
CoM AP	-0.34	0.04	0.13	0.65	0.05	1.00

Investigating the effects of the simulated load cases showed distinct clusters for each load case in compression and combined loading, i.e. considering both, compression and anterior-posterior shear simultaneously. However, the clusters are adjacent to each other and show partial overlap between the individual scenarios, particularly between 30° flexion and lifting 10 kg with stretched arms (Figure 4.1 a, h). Looking solely at the results for anterior-posterior shear loading, the data points for each load case do not form such clear clusters. Only the results at 30° flexion differ considerably from those from upright postures. In contrast to observed clusters in compression and combined loading, it is noticeable that the corresponding cluster is formed at the maximum distance from the one assigned to 10 kg lifting with stretched arms, indicating that shear forces resulting from those scenarios differ strongly (Figure 4.1 o). T-SNE plots illustrating the effects of different morphological parameters across all loading cases showed a gradient based on lumbar lordosis on anterior-posterior shear forces, suggesting that this parameter is more crucial than the applied loading case (Figure 4.1 q). Such effects could not be observed for other parameters, although that slight gradients are emerging if results for different loading scenarios are considered separately. However, due to the limited sample size, detailed effects for each load case as well as for each lumbar level were investigated via multiple regression analysis.

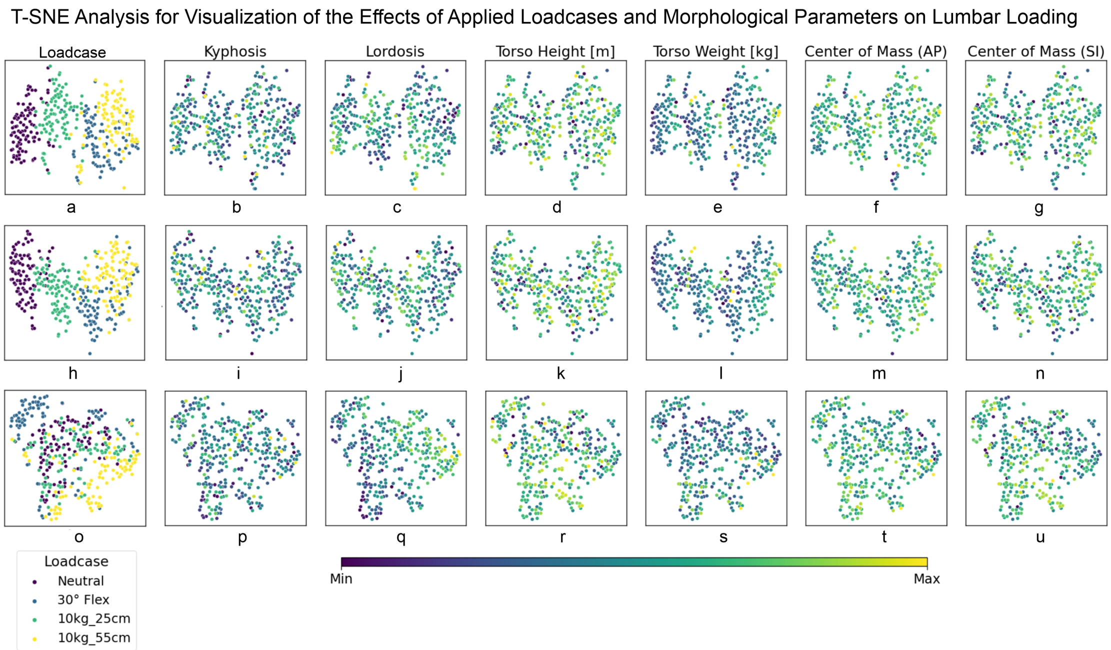

Figure 4.1: T-SNE analysis across all lumbar levels in various loadcases. Adapted from (Lerchl et al., 2024)©

Multiple regression for each load case and lumbar level showed highly significant ($p < 0.001$) strong correlations of the body weight and compression forces ($\beta > 0.6$) over all levels and load cases. The strongest significant effects increasing anterior shear force could be detected for LL with a more pronounced effect in the lower lumbar spine ($\beta \approx$ - 0.5, $p < 0.001$). TK could be associated with moderate significant effects ($\beta < 0.5$) leading to unloading in the lower lumbar spine and increased loading in the upper region. A comparatively superior located center of mass leads to significant decrease in shear loading in the lumbar spine for all load cases. Generally, in 30° flexion, only few other significant correlations could be detected, mainly for TW on compression. R^2 values ranged for loaded and unloaded standing from 0.6 to 0.9, but decreased to 0.4 for 30° flexion.

Significant correlations for different parameters on lumbar loading could be identified using individualized models derived from a large diverse patient cohort. However, the obtained R^2 values indicate, that the given variability can only partially be explained by the investigated parameters. Especially during flexion, a considerable proportion of the influencing factors remains unaddressed by the analyses carried out. For example, effects of passive structures, which, in combination with individual vertebral geometries, lead to additional loading, were not taken into account in our analysis. A comprehensive analysis of the underlying patient data is therefore necessary to do justice to the complexity at hand.

4.2.2 The Role of Spinal Muscles for Lumbar Load Estimation in Large Patient Cohorts

The previously introduced dataset was incorporated to investigate the influence of altered muscle morphology of the Erector Spinae (ES) and Multifidus Muscle (MF) on spinal loading under consideration of inter-individual variability.

For abdominal muscle force estimation, we used a combination of inverse dynamics and static optimization (global search, fmincon, Matlab). The cost function was defined as the sum of cubed muscle stress and maximum muscle stress was set to 1 MPa (Chapter 3.4). PCSA of single fascicles of ES and MF were each set to 0 %, 30 %, and 50 % (Figure 4.2), similar to the study design of Wang et al. (K. Wang et al., 2023), who carried out a musculoskeletal modeling study on the role of MF on lumbar loading.

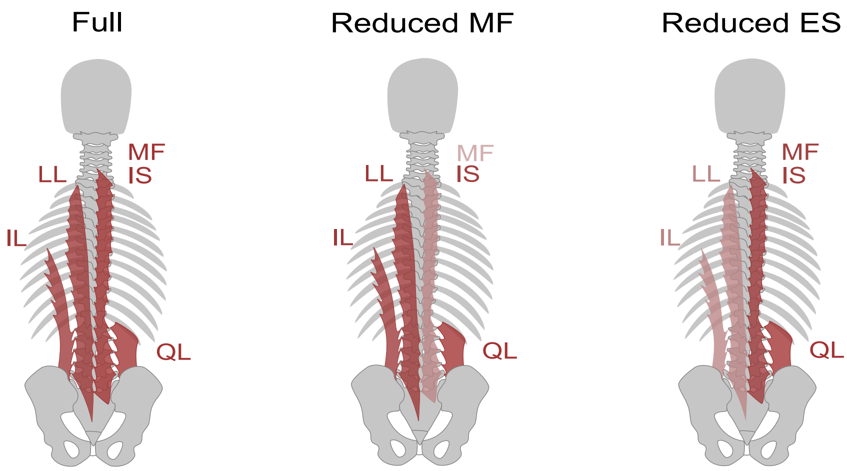

Figure 4.2: Different muscle configurations applied in this study. Respective muscle groups were reduced to 0 %, 30 % and 50 % of the and spinal loads were compared to results from simulations with full muscle architecture.

After simulation, the number of failed optimizations for models with different muscle configuration were compared. Failed optimizations mean in this case, that the equilibrium conditions could not be met. Subsequently, results were filtered with respect to failed optimizations and changes in lumbar loading for remaining cases were investigated. In a first step, one-way ANOVA with Tukey's range test was carried out to analyze the occurring effects without accounting for subject specific characteristics. Additionally, linear mixed effects models with the subject ID defined as random effect and muscle configuration as categorical fixed effects were applied to investigate the effects of reduced muscle PCSA under consideration of subject-specific characteristics. Finally, results from both methods were compared to evaluate (i) the effects of reduced muscle PCSA on spinal loading, as well as (ii) whether consideration of individual characteristics affects significance and strength of observed effects.

During most demanding load cases (30° flex and loaded standing with stretched arms), optimization could not meet equilibrium conditions in all simulations with reduced muscle PCSA, reaching up to 97% for fully eliminated multifidus muscle (MF0). An increase in failed optimization could be detected in simulations for those loadcases in simulations with altered muscle PCSA compared to full muscle architecture. Overall, reducing multifidus PCSA lead to more failed optimizations compared to simulations with reduced ES PCSA (Figure 4.3).

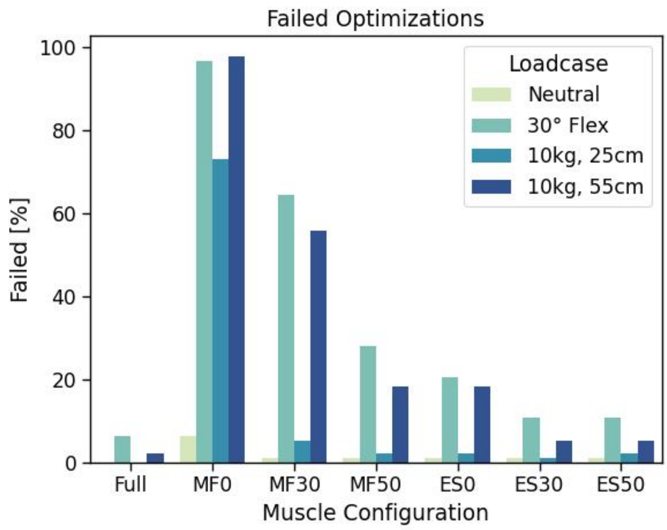

Figure 4.3: Optimizations, that could not meet equilibirum conditions, for different muscle configurations. Multifidus (MF) and erector spinae (ES) muscles were reduced to 0%, 30%, and 50%, indicated by the numbers in the abbreviations.

Before applying ANOVA and LMM analysis, cases with failed optimizations were removed from the results. Due to consequently strongly reduced number of successful simulations with MF0 and MF30, the respective results will not be addressed in the following.

For compression forces, ANOVA with pairwise Tukey's range test showed no significant effects of reduced muscle PCSA compared to full muscle architecture in upright standing loadcases. The only exception here showed complete elimination of ES (ES0) in upright standing while lifting 10kg with stretched arms in the upper lumbar region, where a significant increase up to 240 N in loading of the upper lumbar spine could be detected. However, when applying LMM, significant effects of almost all muscle configurations could be found in neutral standing, but mainly with marginal effects of 20-40 N increase of compression loads in the upper levels, and even slightly unloading in the L5/S1 level. Solely during upright standing while lifting 10kg with stretched arms, a more evident increase of up to 300 N could be detected in models with completely eliminated ES in L1/L2. In comparison to the other scenarios, the most striking results were seen at 30° flexion, both in the general and in the patient-specific evaluation. As such, the ANOVA also showed significant increase in loading for all levels and muscle configurations, with more pronounced effects for reduced ES (up to 560 N) in the upper region, and for reduced MF (up to 478 N) in the lower lumbar region. Similarly, LMM showed the strongest effects for reduced ES in the upper region (up to 740N in L1/L2) and for MF50 in lower region (ca. 450 N).

Regarding anterior-posterior shear forces, similarly to the observations in compressive changes, ANOVA hardly showed significant effects for upright standing. LMM however revealed significant, but also a marginal increase by ca. 15 N for reduced ES and MF in the upper, and for reduced ES in the lower region. In both cases of loaded upright standing, reduced ES led to decreased loading in the upper lumbar spine (up to 136 N) and increased loading in the lower lumbar spine. In all upright standing scenarios, effects were negligible in the mid-lumbar region. For 30° flexion, both, ANOVA and LMM showed a significant increase by up to 90 N for reduced ES in the upper lumbar region. In the lower lumbar region, a significant increase of 78 N could be detected for MF50 in the lower region when applying LMM.

The obtained results underline the relevance of taking patient-specific characteristics into account when analyzing muscular influences on spinal loads. While one-way ANOVA often showed no significant effects of different muscle configurations, these could be demonstrated using a mixed-effects model, which takes individualization of the models into account. Furthermore, our results indicate that the loss of functional muscle cross sectional area, e.g. due to muscle atrophy or intramuscular fat, leads to increased spinal loading with a pronounced effect on anterior-posterior shear forces. Our study therefore emphasizes the relevance of paraspinal musculature for spinal stability under consideration of patient-specific characteristics, such as associated malalignment (Müller et al., 2021) to prevent potentially pathological overload.

5. Discussion

The presented work evaluates the potential of individualization in torso modeling for biomechanical analysis of lumbar loading. The key perspective is to close the gap regarding the inclusion of individual loading patterns in large-scale multidimensional studies on risk factors of CLBP and spinal degeneration. In the process, the following goals were achieved:

I. The development of a pipeline for automated generation of highly individualized models of the torso including individual vertebral geometries, spinal alignment, torso weight and torso weight distribution

II. The validation of the highly individualized model based on in vivo studies from the literature

III. Evaluation of the effects of individualization on lumbar load estimation based on a large diverse patient cohort

IV. Evaluation of morphological effects of the passive and active musculoskeletal system of the spine based on a large diverse patient cohort

The obtained results indicate, that the incorporation of highly individualized models can support a profound understanding of influences and interrelations of complex in vivo spinal loading, while reducing the risk to derive apparent correlations from studies using generic models, which fail to capture this very complexity. The following shall provide a detailed discussion of the obtained results in the context of the pertinent literature and objectives stated in chapter 1.2.

During the validation study (Lerchl et al., 2022), the presented model achieved simulation results in good agreement with experimental data regarding relative compression forces in static loading tasks and muscle activity. Overall, simulations tended to underestimate lumbar load by up to 16 %.

There are several aspects, that need to be considered to be able to reflect on these observations adequately. First, we need to take a close look on the basis for assessment of the validity of the models. There are only few studies in the literature, that provide data for model validation from in vivo studies (Rohlmann et al., 2008; Takahashi et al., 2006; Wilke et al., 2001). In their study on validation of muskuloskeletal models of the spine, Fasser et al. claimed that they tended to overestimate lumbar loads when compared to experimental data published by Rohlmann et al. in 2008 (Fasser et al., 2021). During these experimental studies, spinal loads were measured using instrumented implants, which consisted of a vertebrae replacement and additional spinal fixators, that were assumed to lead to a reduced load on the implant (Bruno et al., 2017; Fasser et al., 2021; Han et al., 2012). Since such stabilization is not included in the respective models, this might explain the observed discrepancies. These models however neglect the influence of passive tissue like the IVD or ligaments. Recent studies have shown, that the inclusion of these structures in musculoskeletal modeling of the spine results in compression force reduction (Meszaros-Beller et al., 2023b), due to load absorption leading to decreased muscle stress. Having accounted for these effects in the presented model can therefore be one reason, why the results underestimated relative loading. We further neglected the effects of co-contraction and intra-abdominal pressure, which become more evident with increased intensity of the loading scenario. The effects of the IAP on spinal loading are still controversial. While the prevailing assumption in the past was, that it contributes to unloading of the spine by creating a counter-torque during flexion and therefore supporting the ES, the theory that the activation of the abdominal muscles increases the compression on the IVDs and generally stabilizes the spine has also become established. The simulations carried out showed the largest deviation (ca. 33%) in reference to the underlying experimental data for lifting 20 kg with stretched arms in front of the chest. One possible reason for this could be that in reality, the subject would be likely to lean backwards during lifting to compensate for the additional anterior weight (Kimura et al., 2001), reducing the occurring moment and therefore, necessary muscle forces. Furthermore, we neglected the intra-abdominal pressure, which is reported to have an unloading effect on the spine, especially in high-intensity loading scenarios (Hodges et al., 2001; Stokes et al., 2010). Another major limitation is the assumption of fixed centers of rotation, whereas the physiological center of rotation migrates considerably posteriorly during inclination movement (Aiyangar et al., 2017; Z. Liu et al., 2016). This could be one explanation for increased posterior ligament forces.

To investigate the influence of model simplification on obtained correlations between morphological parameters and sagittal loading, a study was conducted that compared such potential correlations from models with different degrees of individualization. Based on a patient cohort including 93 individuals, models were created with either both, individualized spine, and torso weight distribution, or combining individualized spines with uniform torso weights and vice versa. The objective of the study, was to evaluate how the inclusion of various individual parameters affects significance and effect strength of respective correlations. Our results showed that even though similar influences could be detected throughout all degrees of individualization, single effects tended to decrease with increased model individualization. For example, torso weight could be identified as most pronounced influence on spinal loading in general, which is in accordance to findings from other studies (Ghezelbash et al., 2016b; Hajihosseinali et al., 2015; Han et al., 2013). However, although the increase in the number of patient-specific parameters led to a similar trend, it was considerably less pronounced, in particular regarding anterior-posterior shear forces, where LL was most determinant.

While the observed effects of LL (decreasing compression, increasing anterior shear) are in accordance to the literature (Müller et al., 2021), observed effects of TK did not support findings from published studies, that are stating that spinal compression forces increased with increasing TK, with most pronounced effects in the thoracolumbar and lumbar region (Bruno et al., 2012). In our study, no significant correlation between TK and compression could be found for the T12/L1 level for both Indiv- and uniTorso models, while significant unloading effects were detected for L4/L5. Apart from the effect of posture on lumbar loads, which was additionally stated by Bruno et al. (Bruno et al., 2012), one reason for this discrepancy could be that increased TK might also be correlated with other morphological factors, such as increased LL. Due to this potential correlation, muscle activity and geometric determined changes in lumbar loads will occur, which could not be assessed using generic models, where changes in TK are specifically induced without including other possible influences that might come along. To check for such a correlation, we performed linear regression analysis resulting in a moderate significant correlation between LL and TK ($\beta = 0.4$) but a low R^2 (0.16), indicating that only a small part of the variability of thoracic TK can be correlated to LL. The study thus shows that significant effects could be identified despite the consideration of multiple parameters. At the same time, it emphasizes the effect that simplification can have on observed effect strengths and the conclusions derived from them.

Nevertheless, it is not clear whether a high degree of individualization also leads to more realistic results. This would require in vivo data that take into account the diversity of large cohorts. As already addressed in the introduction, the collection of such data is associated with invasive methods that cannot be implemented on a large scale. The basis for model validation is therefore limited to a few individuals, which consequently can only be compared with individual models. However, there are several indications in the literature that model individualization in biomechanics leads to more accurate and realistic results (Akhundov et al., 2022; Davico et al., 2022; Meszaros-Beller et al., 2023a). Davico et al. published a study in 2022 that explored the influence of individualization in neuromusculoskeletal knee models of children (Davico et al., 2022). Based on experimentally derived data, models with different degrees of neuromusculoskeletal individualization were developed and simulated muscle and joint reaction forces were evaluated regarding physiological plausibility. In this context, the authors concluded, that individualization of musculoskeletal anatomy and muscle activation patterns had the largest overall effect. Furthermore, a study on the effect of individualization regarding lower-limb kinematics, kinetics and muscle activity stated, that model individualization can especially be beneficial, when investigating populations with large inter-individual variability (Akhundov et al., 2022). These findings combined with the fact that chronic back pain cannot be assigned to a uniform group of patients suggests that taking into account the inherent diversity of the affected population is a promising approach.

Highly individualized models of 93 patients served as a basis for studies to evaluate the influence of (i) morphological parameters and (ii) muscle architecture. The motivation was to evaluate their potential for diagnostics (i) and therapeutic interventions (ii), such as targeted muscle building, for instance within a conventional therapy.

Regarding the influence of morphological parameters on spinal loading, strong effects could be identified for torso weight on compression force. Our findings are thus consistent with the connection of obesity and spinal degeneration with back pain, vastly described in the literature (Dario et al., 2015; Jain & Berven, 2019;

Nahorna & Baur, 2023; Shiri et al., 2019). However, when it comes to anterior-posterior shear loading, the influence of torso weight appears to be considerably less determinant compared to the effect of lumbar lordosis. Spinal shear forces have been correlated to spinal degeneration in the past. Yet, overweight and obesity is still more prevalent when it comes to risk assessment for back pain and degeneration. It is often stated in the literature, that female subjects bear a higher risk to suffer from CLBP. There can be various reasons for this observation. Apart from hormonal characteristics that might influence tissue properties, anatomic parameters such as body height and body weight distribution can be associated to sex. However, in our study torso height and weight distribution hardly showed any significant effects, which is in accordance with Marras et al., who experimentally evaluated the dependence of spinal loading on sex and stated, that the differences under controlled lifting tasks could primarily be assigned to the body weight (Marras et al., 2002).

Investigating the influence of back muscle morphology on spinal loading, the strong reduction of muscle PCSA led to a high number of failed optimizations. Failed optimizations mean in this case, that the equilibrium conditions could not be met. In other words, the muscles were not capable to produce the necessary moment for the respective loading scenario. Transferring this to in vivo situations, in this case more stress would be put on passive structures like the IVDs or facet joints. Most evident was this observation for reduced MF muscle. This indicates, that this muscle group shows higher relevance for spinal stabilization compared to ES. The importance of the MF muscle is widely discussed in the literature (Cooley et al., 2022). The results further showed significantly increased loading in both, compression and anterior-posterior shear forces. A strong reduction of ES had a slightly stronger effects on shear loading in the upper lumbar spine, while MF influence was more pronounced regarding compression forces for the lower lumbar spine. In the view of the fact, that several studies can be found in the literature, that state atrophy of both ES and MF in patients with spinal degeneration, the discussed results fit well. It is still controversial, if muscle atrophy results from spinal degeneration or is the cause of it. Applying our approach to longitudinal studies in the future could address this very question in a sense by analyzing conspicuous loading patterns regarding later occurring muscle atrophy.

Current Limitations

Despite the close agreement with in vivo data, the present model also comes with a number of limitations, of which several are evident in a large proportion of existing models in the literature.

Center of Rotation

Starting with the assumption of a spherical joint with fixed center of rotation within the IVD, it needs to be pointed out that this represents a rough approximation of in vivo kinematics of the intervertebral joint. In fact, the center of rotation migrates superiorly and posteriorly with increased trunk flexion during movement of the spine, and recent studies have shown that the definition of the center of rotation shows a remarkable effect on the mechanical response of the disc (Allais et al., 2023). In other words, instead of a combination of flexion and compression occurring in vivo, models perform pure flexion. The widely used simplification of this complex process, leads to unphysiological FSU kinematics, that can result in overestimation of ligament strain and therefore, induce higher forces on the spine due to passive structures. To account for this, models were introduced that incorporate flexible bodies such as beam elements into rigid body models and thus soften the boundary between FEM and MBS models (Heidari et al., 2022; Khoddam-Khorasani et al., 2020). Alternatively, joints could be equipped with six degrees of freedom while being stabilized solely by viscoelastic passive structures, namely the IVD, ligaments and facet joints. Thus, a realistic representation of the FSU motion would be provided, but lead to new challenges when it comes to muscle force estimation. During static optimization, the solver searches for the optimal solution to meet equilibrium conditions at one specific time step. In this process, the position of the respective joints are predefined leading to zero degrees of freedom to provide stable boundary conditions for the solver. Otherwise, model instability would prevent convergence. Introducing six degrees of freedom, dynamic optimization could be applied, considering the time history of the movement of interest and accounting for stabilizing effects. However, this is accompanied by a massive increase of computational cost, as elaborated already in chapter 2.1. Another approach would be to predefine joint positions in all six degrees of freedom for static optimization, demanding the respective trajectories, that are highly dependent on the properties of the stabilizing components and individual kinematics. To obtain this data, utilizing inverse kinematics based on motion capturing data is one commonly pursued option, but needs individual kinematic data.

Mechanical Properties of Soft Tissue

Further, the developed model in its current state neglects a number of parameters, that can be related to mechanical loading of the spine and might therefore be crucial in loading pattern recognition in large patient cohorts. Our data do not yet allow any quantitative patient-specific statements to be made on the mechanical properties of passive tissues such as IVDs and ligaments. Respective information can currently only be determined with the help of in vitro studies (Ashton-Miller & Schultz, 1997;

Heuer et al., 2007; Panjabi et al., 1976; Pintar et al., 1992; White, 2022), which requires the isolation of the structure of interest to mount them in respective testing machines. In order to obtain consistent datasets for biomechanical models, noninvasive methods must be developed to determine these parameters in large subject cohorts. The combination of experimental studies, multimodal imaging, and ANNs could be a possible solution to increase the level of model individualization beyond its anthropometric and musculoskeletal characteristics. Thus, the individual mechanical condition of functional components can be evaluated partly on the basis of imaging data. For instance, according to the Pfirrmann scale, a potential degradation of the IVD can be determined via the height and signal intensity from MRI data (Pfirrmann et al., 2001). Correlating this degradation with the mechanical alteration of the IVDs (Foltz et al., 2017), this can be used to consider the individual mechanical state of connective tissue in future approaches. Training ANNs with this data will provide large, more diverse datasets for individualized multibody models.

Torso Weight Distribution

Furthermore, it is necessary to critically reflect on the vastly made simplification to assign the torso weight level-wise to the respective vertebrae. While this assumption supports an easy and fast integration of individual body weight and its paraspinal distribution, it does not account for the in-vivo composition of visceral organs and subcutaneous fat. Thus, a complex network of connective tissue runs through the abdomen, attaching organs, muscles and fatty components to the skeletal system. How exactly the corresponding loads are transferred to the spine is not yet fully understood and is currently still the subject of research. Although it is questionable whether the detailed integration of individual organs and the associated connective tissue in musculoskeletal models is expedient, a better understanding of internal passive force transmission and the corresponding consideration in modeling can lead to more realistic loading scenarios. Wasserthal et al. published the *total segmentator* in 2023, a machine learning-based toolbox for automated segmentation of multiple organs from CT data (Wasserthal et al., 2023). This toolbox provides the opportunity for time-efficient integration of a detailed representation of abdominal components and thus, to investigate various approaches in a controlled sensitivity analysis.

Muscle Modeling

Our models incorporate generic muscles at the moment. However, our study presented at the *29th Congress of the International Society of Biomechanics* has shown, that altering muscle morphology can lead to changes in spinal loading (Lerchl et al., 2023b). Thus, even in simple muscle models like the one applied in this work, the consideration of individual muscle architecture in terms of individual PCSA or fat infiltration can influence the simulation results. Both, reduced PCSA as well as fat infiltration in back muscles have been correlated to CLBP and spinal degeneration in previous studies (Y. Huang et al., 2022). These parameters can be derived from imaging data and therefore should be included in individualized models.

One major limitation related to muscle modeling is that muscles are modeled as simple point-to-point actuators acting on a straight line between origin and insertion of the respective fascicle. Especially considering multiarticulate muscles, this leads to errors, e.g. when taking differences in spinal alignment into account. For example, in models with a pronounced LL, this point-to-point line of action can lead to lever arms that are considerably larger compared to models that redirect muscle fascicles along the spine. In the future, this should be addressed by including additional path points along the spine to ensure realistic lines of action and consequently, to realistic lever arms. Such methods are already established in several models available in the literature (Bruno et al., 2015; Ignasiak et al., 2016), but were neglected in this study due to software-related limitations. Apart from that, optimization approaches usually do not account for stabilizing effects, such as co-contraction, as this contradicts the minimization assumption of muscle activation for the load case of interest. For static or low-dynamic cases, antagonist activation will be eliminated for the sake of the "optimal solution". However, particularly in high intensity scenarios, such as heavy lifting, these effects will strongly effect lumbar loads and should not be neglected.

Validation Data

One general problem in biomechanical modeling is, that invasive experimental studies on spinal loading for model validation are rare and are not widely feasible due to ethical reasons (Chapter 1). Accordingly, even consistently constructed models cannot ultimately be validated against data pertaining to the individual in question. Apart from the general problem this poses in terms of model validity, this is particularly evident for individualized models. In the future, incorporating clinical data from longitudinal studies in numerical simulation and data analysis can support the evaluation of model validity in large patient cohorts. Unfortunately, there are hardly any such large-scale studies, but data from clinical diagnostics with appropriate follow-up examinations can serve as a first basis for this.

6. Future Perspectives

Multibody models of the spine have been an integral part of biomechanical research for several decades now. They can help to understand the basic mechanisms of spinal loading and degeneration or how surgical treatment will affect biomechanics. It is one "golden rule" in modeling and simulation, that each model should be as simple as possible, and as complex as necessary. However, it is precisely adequate simplification that requires a profound understanding of the system to be modeled in order to preserve validity considering the respective research question. Regarding the mechanics of the musculoskeletal system, the spine represents undoubtedly one of the most challenging substructures due to the multi-layered functions and requirements, to which it is exposed.

Despite the remarkable achievements of the past decades, there is still a long road ahead. The limitations discussed in the previous chapter need to be addressed in order to eliminate known bias induced by methodically conditioned compromises. In the following, a brief outlook on potential steps to come shall be provided.

There are several questionable assumptions commonly made, when it comes to abstracting spinal biomechanics. One is the widely used simplification of torso weight distribution as level-wisely attached masses. To evaluate the validity of this approach, sensitivity analyses should be carried out for different degrees of detail regarding the attachment of organs and fatty components to the skeletal system using tools for automated organ segmentation (Wasserthal et al., 2023) integration in respective models. In respective studies, the automation of model generation will be beneficial as well and support the understanding of mechanics induced by biological components beyond the musculoskeletal system. A similar approach can be found in the literature for evaluation of the relevance of implemented muscles on joint reaction forces (Benemerito et al., 2022).

Other model-related limitations, such as the simplification of the intervertebral joint with a fixed center of rotation need to be critically reflected in order to meet the demands of individual mechanics of the spine. Although the importance of the center of rotation has already been the subject of corresponding analyses in the past, the influence of the individual was also only marginally considered here. Recent advances in automated model creation and simulation from imaging data can be used to investigate individual kinematics and, if necessary, integrate them into corresponding models. In this context, detailed representation of the IVD as a finite-element model could be combined with multibody models of the whole torso. Thus, providing the necessary ground truth and subsequently employing machine learning algorithms, it is even conceivable that this information could be derived directly from imaging data at one point. The intention of this perspective is to predefine joint kinematics, which could be applied in the context of inverse dynamics.

While the inclusion of individual muscle characteristics like individual PCSA or percentage of fat infiltration can directly be derived from imaging data, mechanical properties of passive structures can currently only be determined with the help of in vitro studies (Ashton-Miller & Schultz, 1997; Heuer et al., 2007; Panjabi et al., 1976; Pintar et al., 1992; White, 2022), which require the isolation of the structure of interest to mount them in respective testing machines. In order to obtain consistent datasets for biomechanical models, noninvasive methods must be developed to determine these parameters in large subject cohorts. The combination of experimental studies, multimodal imaging, and ANNs could be a possible solution to increase the level of model individualization beyond its anthropometric and musculoskeletal characteristics. Thus, the individual mechanical condition of functional components can be evaluated partly on the basis of imaging data. For instance, according to the Pfirrmann scale, a potential degradation of the IVD can be determined via the height and signal intensity from MRI data (Pfirrmann et al., 2001). Correlating this degradation with the mechanical alteration of the IVDs (Foltz et al., 2017), this can be used to consider the individual mechanical state of connective tissue in future approaches. Training ANNs with this data will provide large, more diverse datasets for individualized multibody models.

Heading towards the implementation of individualized models of the spine in large-scale epidemiological studies, provides a promising opportunity for a profound analysis of the risk factors for CLBP and spinal degeneration. Thus, other influencing factors apart from the strictly physiological perspective (Waddell, 1987) can be considered and analysed from a biomechanical perspective. Large-scale population based studies (German National Cohort, UK Biobank) provide comprehensive datasets to take psychosocial factors into account and to investigate respective interrelations between the disciplines. Integrating biomechanical simulations based on such datasets can help identify possible loading patterns and correlate them to respective biological, psychological and social factors. Considering this information could help to subgroup patients with and without chronic back pain. In 2022, Tagliaferri et al. utilized machine learning algorithmy to subgroup patients with CLBP based on psychosocial, brain and physical factors (Tagliaferri et al., 2022b). Including loading patterns in such an analysis would allow the investigation from a more comprehensive perspective.

In a perfect world, we would at some point be able to create a digital twin of every individual and could generate reliable estimations of spinal loading taking into account all relevant characteristics. The obtained model would provide the necessary information to assess the individual risk of each patient to develop CLBP or spinal degeneration, and even support physicians in choosing the most suitable and sustainable treatment strategy. While this currently remains an utopian vision, the rapid pace of technological progress is providing almost daily new tools to help us to understand the biomechanics of the healthy and pathological spine, sharpen our focus on the essentials and thus, to bring us a step-by-step closer to this goal.

Bibliography

Acar, B. S., & Grilli, S. L. (2002). Distributed body weight over the whole spine for improved inference in spine modelling. *Computer Methods in Biomechanics & Biomedical Engineering*, *5*(1), 81–89. https://doi.org/10.1080/10255840290008079

Aiyangar, A., Zheng, L., Anderst, W., & Zhang, X. (2017). Instantaneous centers of rotation for lumbar segmental extension in vivo. *Journal of biomechanics*, *52*, 113–121. https://doi.org/10.1016/j.jbiomech.2016.12.021

Akhavanfar, M. H., Kazemi, H., Eskandari, A. H., & Arjmand, N. (2018). Obesity and spinal loads; a combined mr imaging and subject-specific modeling investigation. *Journal of biomechanics*, *70*, 102–112. https://doi.org/10.1016/j.jbiomech.2017.08.009

Akhundov, R., Saxby, D. J., Diamond, L. E., Edwards, S., Clausen, P., Dooley, K., Blyton, S., & Snodgrass, S. J. (2022). Is subject-specific musculoskeletal modelling worth the extra effort or is generic modelling worth the shortcut? *PloS one*, *17*(1), e0262936. https://doi.org/10.1371/journal.pone.0262936

Allais, R., Capart, A., Da Silva, A., & Boiron, O. (2023). Biomechanical consequences of the intervertebral disc centre of rotation kinematics during lateral bending and axial rotation. *Scientific Reports*, *13*(1), 3172. https://doi.org/10.1038/s41598-023-29551-7

Anderson, D., Mokhtarzadeh, H., Allaire, B., Burkhart, K., & Bouxsein, M. (2020). *Subject-specific spine models for 250 individuals from the Framingham Heart Study*. https://doi.org/10.7910/DVN/SJ5MVM

Anderson, F. C., & Pandy, M. G. (2001). Static and dynamic optimization solutions for gait are practically equivalent. *Journal of biomechanics*, *34*(2), 153–161. https://doi.org/10.1016/S0021-9290(00)00155-X

Anderson, L. N., Fatima, T., Shah, B., Smith, B. T., Fuller, A. E., Borkhoff, C. M., Keown-Stoneman, C. D., Maguire, J. L., & Birken, C. S. (2022). Income and neighbourhood deprivation in relation to obesity in urban dwelling children 0–12 years of age: A cross-sectional study from 2013 to 2019. *J Epidemiol Community Health*, *76*(3), 274–280. https://doi.org/10.1136/jech-2021-216455

Andrade, F. C. D., & Chen, X. S. (2022). A biopsychosocial examination of chronic back pain, limitations on usual activities, and treatment in brazil, 2019. *Plos one*, *17*(6), e0269627. https://doi.org/10.1371/journal.pone.0269627

Antoniou, J., Steffen, T., Nelson, F., Winterbottom, N., Hollander, A. P., Poole, R. A., Aebi, M., Alini, M., et al. (1996). The human lumbar intervertebral disc: Evidence for changes in the biosynthesis and denaturation of the extracellular matrix with growth, maturation, ageing, and degeneration. *The Journal of clinical investigation*, *98*(4), 996–1003. https://doi.org/DOI:10.1172/JCI118884

Ashton-Miller, J. A., & Schultz, A. B. (1997). Biomechanics of the human spine. *Basic orthopaedic biomechanics*, *2*, 353–385.

Aspden, R. M. (1992). Review of the functional anatomy of the spinal ligaments and the lumbar erector spinae muscles. *Clinical Anatomy*, *5*(5), 372–387. https://doi.org/10.1002/ca.980050504

Azril, Huang, K.-Y., Hobley, J., Rouhani, M., Liu, W.-L., & Jeng, Y.-R. (2023). Correlation of the degenerative stage of a disc with magnetic resonance imaging, chemical content, and biomechanical properties of the nucleus pulposus. *Journal of Biomedical Materials Research Part A*, *111*(7), 1054–1066. https://doi.org/10.1002/jbm.a.37490

Baer, E., Cassidy, J. J., & Hiltner, A. (1991). Hierarchical structure of collagen composite systems: Lessons from biology. *Pure and Applied Chemistry 33rd*, *63*(7), 961–973. https://doi.org/10.1351/pac199163070961

Banks, J. J., Alemi, M. M., Allaire, B. T., Lynch, A. C., Bouxsein, M. L., & Anderson, D. E. (2023). Using static postures to estimate spinal loading during dynamic lifts with participant-specific thoracolumbar musculoskeletal models. *Applied Ergonomics*, *106*, 103869. https://doi.org/10.1016/j.apergo.2022.103869

Bassani, T., Casaroli, G., & Galbusera, F. (2019). Dependence of lumbar loads on spinopelvic sagittal alignment: An evaluation based on musculoskeletal modeling. *PloS one*, *14*(3), e0207997. https://doi.org/10.1371/journal.pone.0207997

Bassani, T., Stucovitz, E., Qian, Z., Briguglio, M., & Galbusera, F. (2017). Validation of the anybody full body musculoskeletal model in computing lumbar spine loads at l4l5 level. *Journal of biomechanics*, *58*, 89–96. https://doi.org/10.1016/j.jbiomech.2017.04.025

Battié, M. C., Videman, T., Kaprio, J., Gibbons, L. E., Gill, K., Manninen, H., Saarela, J., & Peltonen, L. (2009). The twin spine study: Contributions to a changing view of disc degeneration. *The Spine Journal*, *9*(1), 47–59. https://doi.org/10.1016/j.spinee.2008.11.011

Battié, M. C., Videman, T., Levälahti, E., Gill, K., & Kaprio, J. (2008). Genetic and environmental effects on disc degeneration by phenotype and spinal level: A multivariate twin study. *Spine*, *33*(25), 2801–2808. https://doi.org/10.1097/brs.0b013e31818043b7

Battié, M. C., Videman, T., Gibbons, L. E., Fisher, L. D., Manninen, H., & Gill, K. (1995). Determinants of lumbar disc degeneration: A study relating lifetime exposures and magnetic resonance imaging findings in identical twins. *Spine*, *20*(24), 2601–2612.

Bauer, S., & Paulus, D. (2014). Analysis of the biomechanical effects of spinal fusion to adjacent vertebral segments of the lumbar spine using multi body simulation. *International Journal of Simulation: Systems, Science and Technology*, *15*(2), 1–7. https://doi.org/10.5013/IJSSST.a.15.02.01

Bayartai, M.-E., Ferreira, P. H., Pappas, E., Pinheiro, M. B., Dambadarjaa, B., Khuyagbaatar, E., & Sullivan, J. (2020). Genetic and environmental effects on lumbar posture, flexibility and motion control in healthy adults. *Musculoskeletal Science and Practice*, *50*, 102253. https://doi.org/10.1016/j.msksp.2020.102253

Bayoglu, R., Galibarov, P. E., Verdonschot, N., Koopman, B., & Homminga, J. (2019). Twente spine model: A thorough investigation of the spinal loads in a complete and coherent musculoskeletal model of the human spine. *Medical engineering & physics*, *68*, 35–45. https://doi.org/10.1016/j.medengphy.2019.03.015

Bayoglu, R., Geeraedts, L., Groenen, K. H. J., Verdonschot, N., Koopman, B., & Homminga, J. (2017). Twente spine model: A complete and coherent dataset for musculo-skeletal modeling of the lumbar region of the human spine. *Journal of biomechanics*, *53*, 111–119. https://doi.org/10.1016/j.jbiomech.2017.01.009

Beaucage-Gauvreau, E., Brandon, S. C., Robertson, W. S., Fraser, R., Freeman, B. J., Graham, R. B., Thewlis, D., & Jones, C. F. (2020). A braced arm-to-thigh (batt) lifting technique reduces lumbar spine loads in healthy and low back pain participants. *Journal of Biomechanics*, *100*, 109584. https://doi.org/10.1016/j.jbiomech.2019.109584

Beaucage-Gauvreau, E., Brandon, S. C., Robertson, W. S., Fraser, R., Freeman, B. J., Graham, R. B., Thewlis, D., & Jones, C. F. (2021). Lumbar spine loads are reduced for activities of daily living when using a braced arm-to-thigh technique. *European Spine Journal*, *30*(4), 1035–1042. https://doi.org/https://doi.org/10.1007/s00586-020-06631-0

Beaucage-Gauvreau, E., Robertson, W. S. P., Brandon, S. C. E., Fraser, R., Freeman, B. J. C., Graham, R. B., Thewlis, D., & Jones, C. F. (2019). Validation of an opensim full-body model with detailed lumbar spine for estimating lower lumbar spine loads during symmetric and asymmetric lifting tasks. *Computer Methods in Biomechanics and Biomedical Engineering*, *22*(5), 451–464. https://doi.org/10.1080/10255842.2018.1564819

Benemerito, I., Montefiori, E., Marzo, A., & Mazzà, C. (2022). Reducing the complexity of musculoskeletal models using gaussian process emulators. *Applied Sciences*, *12*(24), 12932. https://doi.org/10.3390/app122412932

Breloff, S. P., & Chou, L.-S. (2017). Three-dimensional multi-segmented spine joint reaction forces during common workplace physical demands/activities of daily living. *Biomedical Engineering - Applications, Basis and Communications*, *29*(4). https://doi.org/10.4015/S1016237217500259

Bruno, A. G., Anderson, D. E., D'Agostino, J., & Bouxsein, M. L. (2012). The effect of thoracic kyphosis and sagittal plane alignment on vertebral compressive loading. *Journal of Bone and Mineral Research*, *27*(10), 2144–2151. https://doi.org/10.1002/jbmr.1658

Bruno, A. G., Bouxsein, M. L., & Anderson, D. E. (2015). Development and validation of a musculoskeletal model of the fully articulated thoracolumbar spine and rib cage. *Journal of biomechanical engineering*, *137*(8), 081003. https://doi.org/10.1115/1.4030408

Bruno, A. G., Burkhart, K., Allaire, B., Anderson, D. E., & Bouxsein, M. L. (2017). Spinal loading patterns from biomechanical modeling explain the high incidence of vertebral fractures in the thoracolumbar region. *Journal of Bone and Mineral Research*, *32*(6), 1282–1290. https://doi.org/10.1002/jbmr.3113

Burkhart, K., Grindle, D., Bouxsein, M. L., & Anderson, D. E. (2020). Between-session reliability of subject-specific musculoskeletal models of the spine derived from optoelectronic motion capture data. *Journal of biomechanics*, *112*, 110044. https://doi.org/10.1016/j.jbiomech.2020.110044

Chazal, J., Tanguy, A., Bourges, M., Gaurel, G., Escande, G., Guillot, M., & Vanneuville, G. (1985). Biomechanical properties of spinal ligaments and a histological study of the supraspinal ligament in traction. *Journal of biomechanics*, *18*(3), 167–176. https://doi.org/10.1016/0021-9290(85)90202-7

Cholewicki, J., Breen, A., Popovich Jr, J. M., Reeves, N. P., Sahrmann, S. A., Van Dillen, L. R., Vleeming, A., & Hodges, P. W. (2019). Can biomechanics research lead to more effective treatment of low back pain? a point-counterpoint debate. *journal of orthopaedic & sports physical therapy*, *49*(6), 425–436. https://doi.org/10.2519/jospt.2019.8825

Christophy, M., Faruk Senan, N. A., Lotz, J. C., & O'Reilly, O. M. (2012). A musculoskeletal model for the lumbar spine. *Biomechanics and modeling in mechanobiology*, *11*(1-2), 19–34. https://doi.org/10.1007/s10237-011-0290-6

Cooley, J. R., Jensen, T. S., Kjaer, P., Jacques, A., Theroux, J., & Hebert, J. J. (2022). Spinal degeneration is associated with lumbar multifidus morphology in secondary care patients with low back or leg pain. *Scientific Reports*, *12*(1), 14676. https://doi.org/10.1038/s41598-022-18984-1

Cornaz, F., Widmer, J., Farshad-Amacker, N. A., Spirig, J. M., Snedeker, J. G., & Farshad, M. (2021). Biomechanical contributions of spinal structures with different degrees of disc degeneration. *Spine*, *46*(16), E869–E877. https://doi.org/10.1097/brs.0000000000003883

Danneels, L. A., Vanderstraeten, G., Cambier, D. C., Witvrouw, E. E., De Cuyper, H. J., & Danneels, L. (2000). Ct imaging of trunk muscles in chronic low back pain patients and healthy control subjects. *European spine journal*, *9*, 266–272. https://doi.org/10.1007/s005860000190

Dao, T. T., Pouletaut, P., Charleux, F., Lazáry, Á., Eltes, P., Varga, P. P., & Tho, Marie Christine Ho Ba. (2014). Estimation of patient specific lumbar spine muscle forces using multi-physical musculoskeletal model and dynamic mri. In *Knowledge and systems engineering* (pp. 411–422). Springer. https://doi.org/10.1007/978-3-319-02821-7_36

Dario, A. B., Ferreira, M. L., Refshauge, K. M., Lima, T. S., Ordonana, J. R., & Ferreira, P. H. (2015). The relationship between obesity, low back pain, and lumbar disc degeneration when genetics and the environment are considered: A systematic review of twin studies. *The spine journal*, *15*(5), 1106–1117. https://doi.org/10.1016/j.spinee.2015.02.001

Davico, G., Lloyd, D. G., Carty, C. P., Killen, B. A., Devaprakash, D., & Pizzolato, C. (2022). Multi-level personalization of neuromusculoskeletal models to estimate physiologically plausible knee joint contact forces in children.

Biomechanics and Modeling in Mechanobiology, *21*(6), 1873–1886. https://doi.org/10.1007/s10237-022-01626-w

De Santis, R., Sarracino, F., Mollica, F., Netti, P. A., Ambrosio, L., & Nicolais, L. (2004). Continuous fibre reinforced polymers as connective tissue replacement. *Composites Science and Technology*, *64*(6), 861–871. https://doi.org/10.1016/j.compscitech.2003.09.008

de Zee, M., Hansen, L., Wong, C., Rasmussen, J., & Simonsen, E. B. (2007). A generic detailed rigid-body lumbar spine model. *Journal of biomechanics*, *40*(6), 1219–1227. https://doi.org/10.1016/j.jbiomech.2006.05.030

Dreischarf, M., Rohlmann, A., Graichen, F., Bergmann, G., & Schmidt, H. (2016a). In vivo loads on a vertebral body replacement during different lifting techniques. *Journal of biomechanics*, *49*(6), 890–895. https://doi.org/10.1016/j.jbiomech.2015.09.034

Dreischarf, M., Shirazi-Adl, A., Arjmand, N., Rohlmann, A., & Schmidt, H. (2016b). Estimation of loads on human lumbar spine: A review of in vivo and computational model studies. *Journal of biomechanics*, *49*(6), 833–845. https://doi.org/10.1016/j.jbiomech.2015.12.038

Dubois, L., Ohm Kyvik, K., Girard, M., Tatone-Tokuda, F., Pérusse, D., Hjelmborg, J., Skytthe, A., Rasmussen, F., Wright, M. J., Lichtenstein, P., et al. (2012). Genetic and environmental contributions to weight, height, and bmi from birth to 19 years of age: An international study of over 12,000 twin pairs. *PLOS one*, *7*(2), e30153. https://doi.org/10.1371/journal.pone.0030153

El Ouaaid, Z., Shirazi-Adl, A., & Plamondon, A. (2016). Effects of variation in external pulling force magnitude, elevation, and orientation on trunk muscle forces, spinal loads and stability. *Journal of biomechanics*, *49*(6), 946–952. https://doi.org/10.1016/j.jbiomech.2015.09.036

Elgaeva, E. E., Tsepilov, Y., Freidin, M. B., Williams, F. M., Aulchenko, Y., & Suri, P. (2020). Issls prize in clinical science 2020. examining causal effects of body mass index on back pain: A mendelian randomization study. *European Spine Journal*, *29*, 686–691. https://doi.org/10.1007/s00586-019-06224-6

Engel, G. L. (1977). The need for a new medical model: A challenge for biomedicine. *Science*, *196*(4286), 129–136. https://doi.org/10.1126/science.847460

Eskandari, A. H., Arjmand, N., Shirazi-Adl, A., & Farahmand, F. (2019). Hypersensitivity of trunk biomechanical model predictions to errors in image-based kinematics when using fully displacement-control techniques. *Journal of biomechanics*, *84*, 161–171. https://doi.org/10.1016/j.jbiomech.2018.12.043

Ezati, M., Ghannadi, B., & McPhee, J. (2019). A review of simulation methods for human movement dynamics with emphasis on gait. *Multibody System Dynamics*, *47*(3), 265–292. https://doi.org/10.1007/s11044-019-09685-1

Fasser, M.-R., Gerber, G., Passaplan, C., Cornaz, F., Snedeker, J. G., Farshad, M., & Widmer, J. (2022). Computational model predicts risk of spinal screw loosening in patients. *European Spine Journal*, 1–11. https://doi.org/10.1007/s00586-022-07187-x

Fasser, M.-R., Jokeit, M., Kalthoff, M., Gomez Romero , David A., Trache, T., Snedeker, J. G., Farshad, M., & Widmer, J. (2021). Subject-specific alignment and mass distribution in musculoskeletal models of the lumbar spine. *Frontiers in Bioengineering and Biotechnology*, *9*, 745. https://doi.org/10.3389/fbioe.2021.721042

Favier, C. D., Finnegan, M. E., Quest, R. A., Honeyfield, L., McGregor, A. H., & Phillips, A. T. M. (2021). An open-source musculoskeletal model of the lumbar spine and lower limbs: A validation for movements of the lumbar spine. *Computer Methods in Biomechanics and Biomedical Engineering*, 1–16. https://doi.org/10.1080/10255842.2021.1886284

Ferreira, M. L., de Luca, K., Haile, L. M., Steinmetz, J. D., Culbreth, G. T., Cross, M., Kopec, J. A., Ferreira, P. H., Blyth, F. M., Buchbinder, R., et al. (2023). Global, regional, and national burden of low back pain, 1990–2020, its attributable risk factors, and projections to 2050: A systematic analysis of the global burden of disease study 2021. *The Lancet Rheumatology*, *5*(6), e316–e329. https://doi.org/10.1016/s2665-9913(23)00098-x

Fersum, K. V., Dankaerts, W., O'sullivan, P., Maes, J., Skouen, J. S., Bjordal, J. M., & Kvåle, A. (2010). Integration of subclassification strategies in randomised controlled clinical trials evaluating manual therapy treatment and exercise therapy for non-specific chronic low back pain: A systematic review. *British journal of sports medicine*, *44*(14), 1054–1062. https://doi.org/10.1136/bjsm.2009.063289

Foltz, M. H., Kage, C. C., Johnson, C. P., & Ellingson, A. M. (2017). Noninvasive assessment of biochemical and mechanical properties of lumbar discs through quantitative magnetic resonance imaging in asymptomatic volunteers. *Journal of biomechanical engineering*, *139*(11). https://doi.org/10.1115/1.4037549

Fratzl, P., & Weinkamer, R. (2007). Nature's hierarchical materials. *Progress in materials Science*, *52*(8), 1263–1334. https://doi.org/10.1016/j.pmatsci.2007.06.001

Fu, F., Bao, R., Yao, S., Zhou, C., Luo, H., Zhang, Z., Zhang, H., Li, Y., Yan, S., Yu, H., et al. (2021). Aberrant spinal mechanical loading stress triggers intervertebral disc degeneration by inducing pyroptosis and nerve ingrowth. *Scientific reports*, *11*(1), 772. https://doi.org/10.1038/s41598-020-80756-6

Gagnon, D., Larivière, C., & Loisel, P. (2001). Comparative ability of emg, optimization, and hybrid modelling approaches to predict trunk muscle forces and lumbar spine loading during dynamic sagittal plane lifting. *Clinical biomechanics*, *16*(5), 359–372. https://doi.org/10.1016/S0268-0033(01)00016-X

Galbusera, F., Brayda-Bruno, M., Costa, F., & Wilke, H.-J. (2014). Numerical evaluation of the correlation between the normal variation in the sagittal alignment of the lumbar spine and the spinal loads. *Journal of Orthopaedic Research*, *32*(4), 537–544. https://doi.org/10.1002/jor.22569

Gatchel, R. J. (2004). Comorbidity of chronic pain and mental health disorders: The biopsychosocial perspective. *American Psychologist*, *59*(8), 795. https://doi.org/10.1037/0003-066x.59.8.795

Gatchel, R. J., Peng, Y. B., Peters, M. L., Fuchs, P. N., & Turk, D. C. (2007). The biopsychosocial approach to chronic pain: Scientific advances and future directions. *Psychological bulletin*, *133*(4), 581. https://doi.org/10.1037/0033-2909.133.4.581

Gewiess, J., Eglauf, J., Soubrier, A., Grad, S., Alini, M., Peroglio, M., & Ma, J. (2023). The influence of intervertebral disc overloading on nociceptor calcium flickering. *Jor Spine*, *6*(3), e1267. https://doi.org/10.1002%2Fjsp2.1267

Ghezelbash, F., Shirazi-Adl, A., Arjmand, N., El-Ouaaid, Z., & Plamondon, A. (2016a). Subject-specific biomechanics of trunk: Musculoskeletal scaling, internal loads and intradiscal pressure estimation. *Biomechanics and modeling in mechanobiology*, *15*(6), 1699–1712. https://doi.org/10.1007/s10237-016-0792-3

Ghezelbash, F., Shirazi-Adl, A., Arjmand, N., El-Ouaaid, Z., Plamondon, A., & Meakin, J. R. (2016b). Effects of sex, age, body height and body weight on spinal loads: Sensitivity analyses in a subject-specific trunk musculoskeletal model. *Journal of biomechanics*, *49*(14), 3492–3501. https://doi.org/10.1016/j.jbiomech.2016.09.026

Ghezelbash, F., Shirazi-Adl, A., Plamondon, A., Arjmand, N., & Parnianpour, M. (2017). Obesity and obesity shape markedly influence spine biomechanics: A subject-specific risk assessment model. *Annals of biomedical engineering*, *45*, 2373–2382. https://doi.org/10.1007/s10439-017-1868-7

Ghiasi, M. S., Arjmand, N., Boroushaki, M., & Farahmand, F. (2016). Investigation of trunk muscle activities during lifting using a multi-objective optimization-based model and intelligent optimization algorithms. *Medical and Biological Engineering and Computing*, *54*(2-3), 431–440. https://doi.org/10.1007/s11517-015-1327-2

Gibbons, L. E., Latikka, P., Videman, T., Manninen, H., & Battié, M. C. (1997). The association of trunk muscle cross-sectional area and magnetic resonance image parameters with isokinetic and psychophysical lifting strength and static back muscle endurance in men. *Clinical Spine Surgery*, *10*(5), 398–403.

Goode, A. P., Hu, D., George, S. Z., Schwartz, T. A., Kraus, V. B., Huebner, J. L., Cleveland, R. J., Taylor, K. A., Jordan, J. M., & Golightly, Y. M. (2022). Biomarker clusters differentiate phenotypes of lumbar spine degeneration and low back pain: The johnston county osteoarthritis project. *Osteoarthritis and cartilage open*, *4*(3), 100270. https://doi.org/10.1016/j.ocarto.2022.100270

Gould, S. L., Cristofolini, L., Davico, G., & Viceconti, M. (2021). Computational modelling of the scoliotic spine: A literature review. *International Journal for Numerical Methods in Biomedical Engineering*, e3503. https://doi.org/10.1002%2Fcnm.3503

Guo, J., Guo, W., & Ren, G. (2021). Embodiment of intra-abdominal pressure in a flexible multibody model of the trunk and the spinal unloading effects during static lifting tasks. *Biomechanics and Modeling in Mechanobiology*, *20*(4), 1599–1626. https://doi.org/10.1007/s10237-021-01465-1

Hajihosseinali, M., Arjmand, N., & Shirazi-Adl, A. (2015). Effect of body weight on spinal loads in various activities: A personalized biomechanical modeling approach. *Journal of biomechanics*, *48*(2), 276–282. https://doi.org/10.1016/j.jbiomech.2014.11.033

Han, K.-S., Rohlmann, A., Zander, T., & Taylor, W. R. (2013). Lumbar spinal loads vary with body height and weight. *Medical engineering & physics*, *35*(7), 969–977. https://doi.org/10.1016/j.medengphy.2012.09.009

Han, K.-S., Zander, T., Taylor, W. R., & Rohlmann, A. (2012). An enhanced and validated generic thoraco-lumbar spine model for prediction of muscle forces. *Medical engineering & physics*, *34*(6), 709–716. https://doi.org/10.1016/j.medengphy.2011.09.014

Hatze, H. (2002). The fundamental problem of myoskeletal inverse dynamics and its implications. *Journal of biomechanics*, *35*(1), 109–115. https://doi.org/10.1016/S0021-9290(01)00158-0

Heidari, E., Arjmand, N., & Kahrizi, S. (2022). Comparisons of lumbar spine loads and kinematics in healthy and non-specific low back pain individuals during unstable lifting activities. *Journal of Biomechanics*, *144*, 111344. https://doi.org/10.1016/j.jbiomech.2022.111344

Heuer, F., Schmidt, H., Klezl, Z., Claes, L., & Wilke, H.-J. (2007). Stepwise reduction of functional spinal structures increase range of motion and change lordosis angle. *Journal of biomechanics*, *40*(2), 271–280. https://doi.org/10.1016/j.jbiomech.2006.01.007

Hira, K., Nagata, K., Hashizume, H., Asai, Y., Oka, H., Tsutsui, S., Takami, M., Iwasaki, H., Muraki, S., Akune, T., et al. (2021). Relationship of sagittal spinal alignment with low back pain and physical performance in the general population. *Scientific Reports*, *11*(1), 20604. https://doi.org/10.1038/s41598-021-00116-w

Hodges, P. W., Cresswell, A. G., Daggfeldt, K., & Thorstensson, A. (2001). In vivo measurement of the effect of intra-abdominal pressure on the human spine. *Journal of biomechanics*, *34*(3), 347–353. https://doi.org/10.1016/s0021-9290(00)00206-2

Hoy, D., March, L., Brooks, P., Blyth, F., Woolf, A., Bain, C., Williams, G., Smith, E., Vos, T., Barendregt, J., et al. (2014). The global burden of low back pain: Estimates from the global burden of disease 2010 study. *Annals of the rheumatic diseases*, *73*(6), 968–974. https://doi.org/10.1136/annrheumdis-2013-204428

Huang, M., Hajizadeh, K., Gibson, I., & Lee, T. (2016). Analysis of compressive load on intervertebral joint in standing and sitting postures. *Technology and Health Care*, *24*(2), 215–223.

Huang, Y., Wang, L., Zeng, X., Chen, J., Zhang, Z., Jiang, Y., Nie, L., Cheng, X., & He, B. (2022). Association of paraspinal muscle csa and pdff measurements with lumbar intervertebral disk degeneration in patients with chronic low back pain. *Frontiers in Endocrinology*, *13*, 792819. https://doi.org/10.3389/fendo.2022.792819

Huynh, K., Gibson, I., Jagdish, B., & Lu, W. (2015). Development and validation of a discretised multi-body spine model in lifemod for biodynamic behaviour simulation. *Computer methods in biomechanics and biomedical engineering*, *18*(2), 175–184.

Ignasiak, D. (2020). A novel method for prediction of postoperative global sagittal alignment based on full-body musculoskeletal modeling and posture optimization. *Journal of Biomechanics*, *102*, 109324. https://doi.org/10.1016/j.jbiomech.2019.109324

Ignasiak, D., Behm, P., Mannion, A. F., Galbusera, F., Kleinstück, F., Fekete, T. F., Haschtmann, D., Jeszenszky, D., Zimmermann, L., Richner-Wunderlin, S., et al. (2023). Association between sagittal alignment and loads at the adjacent segment in the fused spine: A combined clinical and musculoskeletal modeling study of 205 patients with adult spinal deformity. *European Spine Journal*, *32*(2), 571–583. https://doi.org/10.1007/s00586-022-07477-4

Ignasiak, D., Dendorfer, S., & Ferguson, S. J. (2016). Thoracolumbar spine model with articulated ribcage for the prediction of dynamic spinal loading. *Journal of biomechanics*, *49*(6), 959–966. https://doi.org/10.1016/j.jbiomech.2015.10.010

Jain, D., & Berven, S. (2019). Effect of obesity on the development, management, and outcomes of spinal disorders. *JAAOS-Journal of the American Academy of Orthopaedic Surgeons*, *27*(11), e499–e506. https://doi.org/10.5435/jaaos-d-17-00837

Jokeit, M., Cornaz, F., Calek, A.-K., Harshbarger, C., Snedeker, J. G., Farshad, M., & Widmer, J. (2023). Multilevel contribution of passive structures in the spine–a cadaveric stepwise reduction study on the torso. *4th International Workshop on Spine Loading and Deformation*, 32–33. https://doi.org/10.1016/j.bas.2023.102375

Kaesmacher, J., Liebl, H., Baum, T., & Kirschke, J. S. (2017). Bone mineral density estimations from routine multidetector computed tomography: A comparative study of contrast and calibration effects. *Journal of computer assisted tomography*, *41*(2), 217. https://doi.org/10.1097%2FRCT.0000000000000518

Kalichman, L., Carmeli, E., Been, E., et al. (2017). The association between imaging parameters of the paraspinal muscles, spinal degeneration, and low back pain. *BioMed research international*, *2017*. https://doi.org/10.1155%2F2017%2F2562957

Kalichman, L., Kim, D. H., Li, L., Guermazi, A., & Hunter, D. J. (2010). Computed tomography–evaluated features of spinal degeneration: Prevalence, intercorrelation, and association with self-reported low back pain. *The spine journal*, *10*(3), 200–208. https://doi.org/10.1016/j.spinee.2009.10.018

Kantelhardt, S., Hausen, U., Kosterhon, M., Amr, A., Gruber, K., & Giese, A. (2015). Computer simulation and image guidance for individualised dynamic spinal stabilization. *International Journal of Computer Assisted Radiology and Surgery*, *10*(8), 1325–1332. https://doi.org/10.1007/s11548-014-1138-1

Khoddam-Khorasani, P., Arjmand, N., & Shirazi-Adl, A. (2020). Effect of changes in the lumbar posture in lifting on trunk muscle and spinal loads: A combined in vivo, musculoskeletal, and finite element model study. *Journal of biomechanics*, *104*, 109728. https://doi.org/10.1016/j.jbiomech.2020.109728

Khurelbaatar, T., Kim, K., & Kim, Y. H. (2015). A cervico-thoraco-lumbar multibody dynamic model for the estimation of joint loads and muscle forces. *Journal of Biomechanical Engineering*, *137*(11). https://doi.org/10.1115/1.4031351

Kim, H.-K., & Zhang, Y. (2017). Estimation of lumbar spinal loading and trunk muscle forces during asymmetric lifting tasks: Application of whole-body musculoskeletal modelling in opensim. *Ergonomics*, *60*(4), 563–576. https://doi.org/10.1080/00140139.2016.1191679

Kim, J.-W., Eom, G.-M., & Kwon, Y.-R. (2022). Analysis of maximum joint moment during infant lifting-up motion. *Technology and Health Care*, (Preprint), 1–10. https://doi.org/10.3233/thc-151100

Kimura, S., Steinbach, G. C., Watenpaugh, D. E., & Hargens, A. R. (2001). Lumbar spine disc height and curvature responses to an axial load generated by a compression device compatible with magnetic resonance imaging. *Spine*, *26*(23), 2596–2600. https://doi.org/10.1097/00007632-200112010-00014

Knapik, G. G., Mendel, E., Bourekas, E., & Marras, W. S. (2022). Computational lumbar spine models: A literature review. *Clinical Biomechanics*, *100*, 105816. https://doi.org/10.1016/j.clinbiomech.2022.105816

Landmark, T., Dale, O., Romundstad, P., Woodhouse, A., Kaasa, S., & Borchgrevink, P. C. (2018). Development and course of chronic pain over 4 years in the general population: The hunt pain study. *European Journal of Pain*, *22*(9), 1606–1616. https://doi.org/10.1002/ejp.1243

Langenmaier, A.-M., Amelung, V. E., Karst, M., Krauth, C., Püschner, F., Urbanski, D., Schiessl, C., Thoma, R., & Klasen, B. (2019). Subgroups in chronic low back pain patients–a step toward cluster-based, tailored treatment in inpatient standard care: On the need for precise targeting of treatment for chronic low back pain. *GMS German Medical Science*, *17*. https://doi.org/10.3205/000275

Lee, H. I., Song, J., Lee, H. S., Kang, J. Y., Kim, M., & Ryu, J. S. (2011). Association between cross-sectional areas of lumbar muscles on magnetic resonance imaging and chronicity of low back pain. *Annals of rehabilitation medicine*, *35*(6), 852. https://doi.org/10.5535%2Farm.2011.35.6.852

Lerchl, T., El Husseini, M., Bayat, A., Sekuboyina, A., Hermann, L., Nispel, K., Baum, T., Löffler, M. T., Senner, V., & Kirschke, J. S. (2022). Validation of a patient-specific musculoskeletal model for lumbar load estimation generated by an automated pipeline from whole body ct. *Frontiers in Bioengineering and Biotechnology*, *10*. https://doi.org/10.3389/fbioe.2022.862804

Lerchl, T., Nispel, K., Baum, T., Bodden, J., Senner, V., & Kirschke, J. S. (2023a). Multibody models of the thoracolumbar spine: A review on applications, limitations, and challenges. *Bioengineering*, *10*(2), 202. https://doi.org/10.3390/bioengineering10020202

Lerchl, T., Nispel, K., Bodden, J., Sekuboyina, A., El Husseini, M., Fritzsche, C., Senner, V., & Kirschke, J. S. (2024). Musculoskeletal spine modeling in large patient cohorts: How morphological individualization affects lumbar load estimation. *Frontiers in Bioengineering and Biotechnology*, *12*, 1363081. https://doi.org/10.3389/fbioe.2024.1363081

Lerchl, T., Nispel, K., Senner, V., & Kirschke, J. S. (2023b). The role of spinal muscles for lumbar loads during static loading tasks in large patient cohorts: A musculoskeletal modeling study. *29th Congress of the International Society of Biomechanics*.

Lewiner, T., Lopes, H., Vieira, A. W., & Tavares, G. (2003). Efficient implementation of marching cubes' cases with topological guarantees. *Journal of graphics tools*, *8*(2), 1–15. https://doi.org/10.1080/10867651.2003.10487582

Little, J. P., & Adam, C. J. (2015). Geometric sensitivity of patient-specific finite element models of the spine to variability in user-selected anatomical landmarks. *Computer Methods in Biomechanics and Biomedical Engineering*, *18*(6), 676–688. https://doi.org/10.1080/10255842.2013.843673

Liu, T., Khalaf, K., Adeeb, S., & El-Rich, M. (2019). Effects of lumbo-pelvic rhythm on trunk muscle forces and disc loads during forward flexion: A combined musculoskeletal and finite element simulation study. *Journal of biomechanics*, *82*, 116–123. https://doi.org/10.1016/j.jbiomech.2018.10.009

Liu, Z., Tsai, T.-Y., Wang, S., Wu, M., Zhong, W., Li, J.-S., Cha, T., Wood, K., & Li, G. (2016). Sagittal plane rotation center of lower lumbar spine during a dynamic weight-lifting activity. *Journal of biomechanics*, *49*(3), 371–375. https://doi.org/10.1016/j.jbiomech.2015.12.029

Livshits, G., Popham, M., Malkin, I., Sambrook, P. N., MacGregor, A. J., Spector, T., & Williams, F. M. (2011). Lumbar disc degeneration and genetic factors are the main risk factors for low back pain in women: The uk twin spine study. *Annals of the rheumatic diseases*, *70*(10), 1740–1745. https://doi.org/10.1136/ard.2010.137836

Madhuchandra, P., Pawankumar, K., Santhosh, G. S., & Raju, K. (2023). Predictability of degenerative disc disease by lumbar sagittal alignment on conventional radiograph in comparison with cross-sectional magnetic resonance imaging. *Journal of Orthopaedic Diseases and Traumatology*, *6*(1), 106–110. https://doi.org/10.4103/jodp.jodp_79_22

Maher, C., Underwood, M., & Buchbinder, R. (2017). Non-specific low back pain. *The Lancet*, *389*(10070), 736–747. https://doi.org/10.1016/s0140-6736(16)30970-9

Maia, L. B., Amarante, L. G., Vitorino, D. F., Mascarenhas, R. O., Lacerda, A. C. R., Lourenco, B. M., & Oliveira, V. C. (2021). Effectiveness of conservative therapy on pain, disability and quality of life for low back pain in pregnancy: A systematic review of randomized controlled trials. *Brazilian Journal of Physical Therapy*, *25*(6), 676–687. https://doi.org/10.1016/j.bjpt.2021.06.007

Malakoutian, M., Street, J., Wilke, H.-J., Stavness, I., Fels, S., & Oxland, T. (2018). A musculoskeletal model of the lumbar spine using artisynth–development and validation. *Computer Methods in Biomechanics and Biomedical Engineering: Imaging & Visualization*, *6*(5), 483–490. https://doi.org/10.1080/21681163.2016.1187087

Marras, W. S., Davis, K. G., & Jorgensen, M. (2002). Spine loading as a function of gender. *Spine*, *27*(22), 2514–2520. https://doi.org/10.1097/00007632-200211150-00017

Meng, X., Bruno, A. G., Cheng, B., Wang, W., Bouxsein, M. L., & Anderson, D. E. (2015). Incorporating six degree-of-freedom intervertebral joint stiffness in a lumbar spine musculoskeletal model-method and performance in flexed postures. *Journal of biomechanical engineering*, *137*(10), 101008. https://doi.org/10.1115/1.4031417

Meszaros-Beller, L., Hammer, M., Riede, J. M., Pivonka, P., Little, J. P., & Schmitt, S. (2023a). Effects of geometric individualisation of a human spine model on load sharing: Neuro-musculoskeletal simulation reveals significant differences in ligament and muscle contribution. *Biomechanics and Modeling in Mechanobiology*, *22*(2), 669–694. https://doi.org/10.1007/s10237-022-01673-3

Meszaros-Beller, L., Hammer, M., Schmitt, S., & Pivonka, P. (2023b). Effect of neglecting passive spinal structures: A quantitative investigation using the forward-dynamics and inverse-dynamics musculoskeletal approach. *Frontiers in Physiology*, *14*, 1135531.

Miaskowski, C., Blyth, F., Nicosia, F., Haan, M., Keefe, F., Smith, A., & Ritchie, C. (2020). A biopsychosocial model of chronic pain for older adults. *Pain Medicine*, *21*(9), 1793–1805. https://doi.org/10.1093/pm/pnz329

Miki, T., Fujita, N., Takashima, H., & Takebayashi, T. (2020). Associations between paraspinal muscle morphology, disc degeneration, and clinical features in patients with lumbar spinal stenosis. *Progress in Rehabilitation Medicine*, *5*, 20200015. https://doi.org/10.2490%2Fprm.20200015

Mikkola, T. M., Sipilä, S., Rantanen, T., Sievänen, H., Suominen, H., Tiainen, K., Kaprio, J., Koskenvuo, M., Kauppinen, M., & Heinonen, A. (2009). Muscle cross-sectional area and structural bone strength share genetic and environmental effects in older women. *Journal of Bone and Mineral Research*, *24*(2), 338–345. https://doi.org/10.1359/jbmr.081008

Mokhtarzadeh, H., Anderson, D. E., Allaire, B. T., & Bouxsein, M. L. (2020). Patterns of load-to-strength ratios along the spine in a population-based cohort to evaluate the contribution of spinal loading to vertebral fractures. *Journal of Bone and Mineral Research*, *36*(4), 704–711. https://doi.org/10.1002/jbmr.4222

Müller, A., Rockenfeller, R., Damm, N., Kosterhon, M., Kantelhardt, S. R., Aiyangar, A. K., & Gruber, K. (2021). Load distribution in the lumbar spine during modeled compression depends on lordosis. *Frontiers in Bioengineering and Biotechnology*, *9*. https://doi.org/10.3389/fbioe.2021.661258

Murata, S., Hashizume, H., Tsutsui, S., Oka, H., Teraguchi, M., Ishomoto, Y., Nagata, K., Takami, M., Iwasaki, H., Minamide, A., et al. (2023). Pelvic compensation accompanying spinal malalignment and back pain-related factors in a general population: The wakayama spine study. *Scientific Reports*, *13*(1), 11862. https://doi.org/10.1038/s41598-023-39044-2

Murray, C. J., Vos, T., Lozano, R., Naghavi, M., Flaxman, A. D., Michaud, C., Ezzati, M., Shibuya, K., Salomon, J. A., Abdalla, S., et al. (2012). Disability-adjusted life years (dalys) for 291 diseases and injuries in 21 regions, 1990–2010: A systematic analysis for the global burden of disease study 2010. *The lancet*, *380*(9859), 2197–2223. https://doi.org/10.1016/S0140-6736(12)61689-4

Murtezani, A., Ibraimi, Z., Sllamniku, S., Osmani, T., & Sherifi, S. (2011). Prevalence and risk factors for low back pain in industrial workers. *Folia medica*, *53*(3), 68–74. https://doi.org/10.2478/v10153-011-0060-3

Nachemson, A. L., & Evans, J. H. (1968). Some mechanical properties of the third human lumbar interlaminar ligament (ligamentum flavum). *Journal of biomechanics*, *1*(3), 211–220. https://doi.org/10.1016/0021-9290(68)90006-7

Nahorna, A., & Baur, H. (2023). The relevance of identifying the biomechanical and functional effects of abdominar obesity on activities of daily living in individuals with low back pain. *Current Issues in Sport Science (CISS)*, *8*(2), 067–067. https://doi.org/10.36950/2023.2ciss067

Naserkhaki, S., Jaremko, J. L., & El-Rich, M. (2016). Effects of inter-individual lumbar spine geometry variation on load-sharing: Geometrically personalized finite element study. *Journal of biomechanics*, *49*(13), 2909–2917. https://doi.org/10.1016/j.jbiomech.2016.06.032

Newell, N., Little, J. P., Christou, A., Adams, M. A., Adam, C., & Masouros, S. (2017). Biomechanics of the human intervertebral disc: A review of testing techniques and results. *Journal of the mechanical behavior of biomedical materials*, *69*, 420–434. https://doi.org/10.1016/j.jmbbm.2017.01.037

Nguyen, A. Q., Rodriguez, C., Kumar, R., Gupta, S., Anderson, D., & Saifi, C. (2024). Biomechanical analysis of complications following t10-pelvis spinal fusion: A population based computational study. *Journal of Biomechanics*, 111969. https://doi.org/10.1016/j.jbiomech.2024.111969

Nitecki, M., Shapiro, G., Orr, O., Levitin, E., Sharshevsky, H., Tzur, D., Twig, G., & Shapira, S. (2023). Association between body mass index and nonspecific recurrent low back pain in over 600,000 healthy young adults. *American Journal of Epidemiology*, *192*(8), 1371–1378. https://doi.org/10.1093/aje/kwad102

Oberg, A. L., & Mahoney, D. W. (2007). Linear mixed effects models. *Topics in biostatistics*, 213–234. https://doi.org/10.1007/978-1-59745-530-5_11

Overbergh, T., Severijns, P., Beaucage-Gauvreau, E., Jonkers, I., Moke, L., & Scheys, L. (2020). Development and validation of a modeling workflow for the generation of image-based, subject-specific thoracolumbar models of spinal deformity. *Journal of Biomechanics*, *110*. https://doi.org/10.1016/j.jbiomech.2020.109946

Panero, E., Digo, E., Ferrarese, V., Dimanico, U., & Gastaldi, L. Multi-segments kinematic model of the human spine during gait. In: 2021. https://doi.org/10.1109/MeMeA52024.2021.9478594

Panjabi, M. M., Brand Jr, R., & White 3rd, A. (1976). Mechanical properties of the human thoracic spine as shown by three-dimensional load-displacement curves. *JBJS*, *58*(5), 642–652.

Pearsall, D. J., Reid, J. G., & Livingston, L. A. (1996). Segmental inertial parameters of the human trunk as determined from computed tomography. *Annals of biomedical engineering*, *24*(2), 198–210. https://doi.org/10.1007/BF02667349

Périé, D., Sales De Gauzy, J., & Hobatho, M. C. (2002). Biomechanical evaluation of cheneau-toulouse-munster brace in the treatment of scoliosis using optimisation approach and finite element method. *Medical & biological engineering & computing*, *40*(3), 296–301. https://doi.org/10.1007/BF02344211

Pfirrmann, C. W., Metzdorf, A., Zanetti, M., Hodler, J., & Boos, N. (2001). Magnetic resonance classification of lumbar intervertebral disc degeneration. *spine*, *26*(17), 1873–1878. https://doi.org/10.1097/00007632-200109010-00011

Pincus, T., Burton, A. K., Vogel, S., & Field, A. P. (2002). A systematic review of psychological factors as predictors of chronicity/disability in prospective cohorts of low back pain. *Spine*, *27*(5), E109–E120. https://doi.org/10.1097/00007632-200203010-00017

Pintar, F. A., Yoganandan, N., Myers, T., Elhagediab, A., & Sances Jr, A. (1992). Biomechanical properties of human lumbar spine ligaments. *Journal of biomechanics*, *25*(11), 1351–1356. https://doi.org/10.1016/0021-9290(92)90290-h

Putzer, M., Ehrlich, I., Rasmussen, J., Gebbeken, N., & Dendorfer, S. (2016). Sensitivity of lumbar spine loading to anatomical parameters. *Journal of biomechanics*, *49*(6), 953–958. https://doi.org/10.1016/j.jbiomech.2015.11.003

Robertson, D. J., von Forell, G. A., Alsup, J., & Bowden, A. E. (2013). Thoracolumbar spinal ligaments exhibit negative and transverse pre-strain. *Journal of the mechanical behavior of biomedical materials*, *23*, 44–52. https://doi.org/10.1016/j.jmbbm.2013.04.004

Rohlmann, A., Graichen, F., Kayser, R., Bender, A., & Bergmann, G. (2008). Loads on a telemeterized vertebral body replacement measured in two patients. *Spine*, *33*(11).

Rupp, T. K., Ehlers, W., Karajan, N., Günther, M., & Schmitt, S. (2015). A forward dynamics simulation of human lumbar spine flexion predicting the load sharing of intervertebral discs, ligaments, and muscles. *Biomechanics and modeling in mechanobiology*, *14*(5), 1081–1105. https://doi.org/10.1007/s10237-015-0656-2

Sambrook, P. N., MacGregor, A. J., & Spector, T. D. (1999). Genetic influences on cervical and lumbar disc degeneration: A magnetic resonance imaging study in twins. *Arthritis & Rheumatism: Official Journal of the American College of Rheumatology*, *42*(2), 366–372. https://doi.org/10.1002/1529-0131(199902)42:2%3C366::aid-anr20%3E3.0.co;2-6

Sato, K., Kikuchi, S., & Yonezawa, T. (1999). In vivo intradiscal pressure measurement in healthy individuals and in patients with ongoing back problems. *Spine*, *24*(23), 2468. https://doi.org/10.1097/00007632-199912010-00008

Sekuboyina, A., Husseini, M. E., Bayat, A., Löffler, M., Liebl, H., Li, H., Tetteh, G., Kukačka, J., Payer, C., Štern, D., et al. (2021). Verse: A vertebrae labelling and segmentation benchmark for multi-detector ct images. *Medical image analysis*, *73*, 102166. https://doi.org/10.1016/j.media.2021.102166

Senteler, M., Weisse, B., Rothenfluh, D. A., & Snedeker, J. G. (2016). Intervertebral reaction force prediction using an enhanced assembly of opensim models. *Computer Methods in Biomechanics and Biomedical Engineering*, *19*(5), 538–548. https://doi.org/10.1080/10255842.2015.1043906

Sharabi, M. (2022). Structural mechanisms in soft fibrous tissues: A review. *Frontiers in Materials*, *8*, 793647. https://doi.org/10.3389/fmats.2021.793647

Shaughnessy, M., & Caulfield, B. (2004). A pilot study to investigate the effect of lumbar stabilisation exercise training on functional ability and quality of life in patients with chronic low back pain. *International journal of rehabilitation research*, *27*(4), 297–301. https://doi.org/10.1097/00004356-200412000-00007

Shiri, R., Falah-Hassani, K., Heliövaara, M., Solovieva, S., Amiri, S., Lallukka, T., Burdorf, A., Husgafvel-Pursiainen, K., & Viikari-Juntura, E. (2019). Risk factors for low back pain: A population-based longitudinal study. *Arthritis care & research*, *71*(2), 290–299. https://doi.org/10.1002/acr.23710

Sponbeck, J., Moody, M., Mitchell, U., Neves, C., & Johnson, A. (2022). Multifidus muscle cross-sectional area adaptations over two volleyball seasons and one off-season in athletes with and without low back pain. *Journal of Back and Musculoskeletal Rehabilitation*, *35*(5), 1135–1142. https://doi.org/10.3233/bmr-210234

Stahle, L., Wold, S., et al. (1989). Analysis of variance (anova). *Chemometrics and intelligent laboratory systems*, *6*(4), 259–272. https://doi.org/10.1016/0169-7439(89)80095-4

Stokes, I. A., Gardner-Morse, M. G., & Henry, S. M. (2010). Intra-abdominal pressure and abdominal wall muscular function: Spinal unloading mechanism. *Clinical biomechanics*, *25*(9), 859–866. https://doi.org/10.1016/j.clinbiomech.2010.06.018

Stolzenberg, R. M. (2004). Multiple regression analysis. *Handbook of data analysis*, 165–208.

Stone, M. A., Osei-Bordom, D.-C., Inman, R. D., Sammon, C., Wolber, L. E., & Williams, F. M. (2015). Heritability of spinal curvature and its relationship to disc degeneration and bone mineral density in female adult twins. *European Spine Journal*, *24*, 2387–2394. https://doi.org/10.1007/s00586-014-3477-6

Tagliaferri, S. D., Miller, C. T., Owen, P. J., Mitchell, U. H., Brisby, H., Fitzgibbon, B., Masse-Alarie, H., Van Oosterwijck, J., & Belavy, D. L. (2020). Domains of chronic low back pain and assessing treatment effectiveness: A clinical perspective. *Pain Practice*, *20*(2), 211–225. https://doi.org/10.1111/papr.12846

Tagliaferri, S. D., Mitchell, U. H., Saueressig, T., Owen, P. J., Miller, C. T., & Belavy, D. L. (2022a). Classification approaches for treating low back pain have small effects that are not clinically meaningful: A systematic review with meta-analysis. *journal of orthopaedic & sports physical therapy*, *52*(2), 67–84. https://doi.org/10.2519/jospt.2022.10761

Tagliaferri, S. D., Wilkin, T., Angelova, M., Fitzgibbon, B. M., Owen, P. J., Miller, C. T., & Belavy, D. L. (2022b). Chronic back pain sub-grouped via psychosocial, brain and physical factors using machine learning. *Scientific reports*, *12*(1), 15194. https://doi.org/10.1038/s41598-022-19542-5

Takahashi, I., Kikuchi, S.-i., Sato, K., & Sato, N. (2006). Mechanical load of the lumbar spine during forward bending motion of the trunk-a biomechanical study. *Spine*, *31*(1), 18–23. https://doi.org/10.1097/01.brs.0000192636.69129.fb

Tanaka, Y., Miyagi, M., Inoue, G., Hori, Y., Inage, K., Murata, K., Fujimaki, H., Kuroda, A., Yokozeki, Y., Inoue, S., et al. (2023). Muscle strength rather than appendicular skeletal muscle mass might affect spinal sagittal alignment, low back pain, and health-related quality of life. *Scientific Reports*, *13*(1), 9894. https://doi.org/10.1038/s41598-023-37125-w

Tiainen, K., Sipila, S., Kauppinen, M., Kaprio, J., & Rantanen, T. (2009). Genetic and environmental effects on isometric muscle strength and leg extensor power followed up for three years among older female twins. *Journal of Applied Physiology*, *106*(5), 1604–1610. https://doi.org/10.1152/japplphysiol.91056.2008

Tian, X., Xu, C., Wu, Y., Sun, J., Duan, H., Zhang, D., Jiang, B., Pang, Z., Li, S., & Tan, Q. (2017). Genetic and environmental influences on pulmonary function and muscle strength: The chinese twin study of aging. *Twin Research and Human Genetics*, *20*(1), 53–59. https://doi.org/10.1017/thg.2016.97

Tukey, J. W. (1959). A quick compact two sample test to duckworth's specifications. *Technometrics*, *1*(1), 31–48. https://doi.org/10.1080/00401706.1959.10489847

Valdano, M., Asensio-Gil, J. M., Jiménez-Octavio, J. R., Cabello-Reyes, M., Vasserot-Tolmos, R., & López-Valdés, F. J. Parametric analysis of the effect of crs seatback angle in dummy measurements in frontal impacts. In: *2022-September*. 2022, 519–531.

Van der Maaten, L., & Hinton, G. (2008). Visualizing data using t-sne. *Journal of machine learning research*, *9*(11).

Vergari, C., Courtois, I., Ebermeyer, E., Bouloussa, H., Vialle, R., & Skalli, W. (2016). Experimental validation of a patient-specific model of orthotic action in adolescent idiopathic scoliosis. *European Spine Journal*, *25*(10), 3049–3055. https://doi.org/10.1007/s00586-016-4511-7

von Arx, M., Liechti, M., Connolly, L., Bangerter, C., Meier, M. L., & Schmid, S. (2021). From stoop to squat: A comprehensive analysis of lumbar loading among different lifting styles. *Frontiers in bioengineering and biotechnology*, *9*. https://doi.org/10.3389/fbioe.2021.769117

Waddell, G. (1987). 1987 volvo award in clinical sciences: A new clinical model for the treatment of low-back pain. *Spine*, *12*(7), 632–644. https://doi.org/10.1097/00007632-198709000-00002

Wang, K., Deng, Z., Chen, X., Shao, J., Qiu, L., Jiang, C., & Niu, W. (2023). The role of multifidus in the biomechanics of lumbar spine: A musculoskeletal modeling study. *Bioengineering*, *10*(1), 67. https://doi.org/10.3390/bioengineering10010067

Wang, Z., Zhao, Z., Han, S., Hu, X., Ye, L., Li, Y., & Gao, J. (2022). Advances in research on fat infiltration and lumbar intervertebral disc degeneration. *Frontiers in Endocrinology*, *13*, 1067373. https://doi.org/10.3389%2Ffendo.2022.1067373

Wasserthal, J., Breit, H.-C., Meyer, M. T., Pradella, M., Hinck, D., Sauter, A. W., Heye, T., Boll, D. T., Cyriac, J., Yang, S., et al. (2023). Totalsegmentator: Robust segmentation of 104 anatomic structures in ct images. *Radiology: Artificial Intelligence*, *5*(5). https://doi.org/10.48550/arXiv.2208.05868

Wei, W., Evin, M., Bailly, N., & Arnoux, P.-J. (2022). Biomechanical evaluation of back injuries during typical snowboarding backward falls. *Scandinavian*

Journal of Medicine and Science in Sports. https://doi.org/10.1111/sms.14254

White, A. A. (2022). *Clinical biomechanics of the spine*. Lippincott Williams & Wilkins. https://books.google.de/books?id=kc3DAAAACAAJ

Wilke, H.-J., Herkommer, A., Werner, K., & Liebsch, C. (2017). In vitro analysis of the segmental flexibility of the thoracic spine. *PLoS one*, *12*(5), e0177823.

Wilke, H.-J., Neef, P., Hinz, B., Seidel, H., & Claes, L. (2001). Intradiscal pressure together with anthropometric data – a data set for the validation of models. *Clinical biomechanics*, *16*, S111–S126. https://doi.org/10.1016/S0268-0033(00)00103-0

Winter, D. A. (2005). *Biomechanics and motor control of human movement* (3. ed.). Wiley. https://doi.org/10.1002/9780470549148

Wong, K. W. N., Luk, K. D. K., Leong, J. C. Y., Wong, S. F., & Wong, K. K. Y. (2006). Continuous dynamic spinal motion analysis. *Spine*, *31*(4). https://doi.org/10.1097/01.brs.0000199955.87517.82

Zaman, R., Xiang, Y., Cruz, J., & Yang, J. (2021). Three-dimensional asymmetric maximum weight lifting prediction considering dynamic joint strength. *Proceedings of the Institution of Mechanical Engineers, Part H: Journal of Engineering in Medicine*, *235*(4), 437–446. https://doi.org/10.1177/0954411920987035

Zhang, F., Yu, Y., Wang, H., Zhang, Y., Bai, Y., Huang, L., & Zhang, H. (2023). Association between handgrip strength and depression among chinese older adults: A cross-sectional study from the china health and retirement longitudinal study. *BMC geriatrics*, *23*(1), 299. https://doi.org/10.1186/s12877-023-04034-6

Zhao, J., Li, C., Qin, T., Jin, Y., He, R., Sun, Y., Liu, Z., Wu, T., Duan, C., Cao, Y., et al. (2023). Mechanical overloading-induced mir-325-3p reduction promoted chondrocyte senescence and exacerbated facet joint degeneration. *Arthritis Research & Therapy*, *25*(1), 54. https://doi.org/10.1186/s13075-023-03037-3

Zhu, X. Y., Kim, H. K., & Zhang, Y. (2017). Development of an enhanced musculoskeletal model for simulating lumbar spine loading during manual lifting tasks. *Lecture Notes in Computer Science (including subseries Lecture Notes in Artificial Intelligence and Lecture Notes in Bioinformatics)*, *10286 LNCS*, 229–237. https://doi.org/10.1007/978-3-319-58463-8_20

Appendix

Publications

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Review

Multibody Models of the Thoracolumbar Spine: A Review on Applications, Limitations, and Challenges

Tanja Lerchl, Kati Nispel, Thomas Baum, Jannis Bodden, Veit Senner and Jan S. Kirschke

Special Issue

Biomechanics-Based Motion Analysis

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Review

Multibody Models of the Thoracolumbar Spine: A Review on Applications, Limitations, and Challenges

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Abstract: Numerical models of the musculoskeletal system as investigative tools are an integral part of biomechanical and clinical research. While finite element modeling is primarily suitable for the examination of deformation states and internal stresses in flexible bodies, multibody modeling is based on the assumption of rigid bodies, that are connected via joints and flexible elements. This simplification allows the consideration of biomechanical systems from a holistic perspective and thus takes into account multiple influencing factors of mechanical loads. Being the source of major health issues worldwide, the human spine is subject to a variety of studies using these models to investigate and understand healthy and pathological biomechanics of the upper body. In this review, we summarize the current state-of-the-art literature on multibody models of the thoracolumbar spine and identify limitations and challenges related to current modeling approaches.

Keywords: musculoskeletal multibody dynamics; spinal biomechanics; spinal alignment; spinal loading; muscle force computation; thoracolumbar spine; biomechanical model

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1. Introduction

Chronic back pain is one of the major health issues worldwide. Though general risk factors such as occupation, obesity or anthropometric parameters could be identified in the past years [1], the specification of individual biomechanical indicators for the prediction of symptoms and chronicity is challenging, as it requires an in-depth knowledge of spinal kinematics and resulting loads. Even though experimental methods are essential to help build this knowledge, they come with limitations. In vitro studies can help understand segment mechanics but are not applicable when it comes to the investigation of complex in vivo biomechanics of the whole torso [2]. The invasive character of the in vivo measurement of these parameters via intradiscal pressure sensors [3,4] or instrumented vertebral implants [5,6] makes these methods unsuitable for clinical analysis. Computational, biomechanical models can provide a valuable alternative when it comes to the estimation of spinal loads. There are two approaches for the numerical analysis of spinal loading. While finite element models (FEM) hold the potential to investigate internal stress states in flexible bodies and their underlying or resulting deformation, multibody models (multibody system, MBS) can help analyze mechanical loads on the musculoskeletal system at a holistic level. Breaking the system down to its essential mechanical components, classic MBS models incorporate rigid bodies connected by joints and, depending on the respective research question, force elements representing flexible structures such as intervertebral discs (IVD), ligaments, cartilage, and other connective tissue. This way, MBS models represent a valuable tool to increase a profound understanding of healthy and pathological biomechanics. Gould et al. published a review on FEM and MBS models of the healthy and scoliotic spine in 2021 [7]. Focusing on the latter one, the authors state that their review provides solely a brief overview on MBS models of the healthy spine and refer the reader to the review on MBS modeling of the cervical spine by Alizadeh et al. [8] and the review by Dreischarf et al. on in vivo studies and computational models, published in 2016 [9].

The wide range of applications, improved technical capabilities, and increasing knowledge of spinal biomechanics, which answer old questions and raise new ones, mean that the demand for high-quality MBS models is not abating. As a consequence, the number of published models is increasing every year providing new opportunities and insight.

In recent years, models have been introduced that extend the classic notion of a multibody or musculoskeletal models. These models incorporate flexible bodies such as beam elements into rigid body models and thus soften the boundary between FEM and MBS models [10,11]. However, within the scope of this work, we want to review the developments in the field of multibody models of the healthy thoracolumbar spine, focusing on classical rigid body models. Hereby, we shed light on common modeling methods and applications, as well as identify and discuss related limitations and challenges in state-of-the-art spine modeling.

2. Methods

To generate a list of potentially relevant publications, a systematic search was carried out in PubMed and Scopus in November and December 2022. The search included the keywords "spine AND model AND ((multi AND body) OR musculoskeletal)". Excluding results prior to 2013 left 1288 publications on PubMed and 1304 on Scopus. However, relevant citations in the articles were also included, if they were published before 2013. Subsequently, duplicates were removed by identical PubMedIDs and titles. Remaining articles were then filtered by title and abstract and the full text eventually analyzed. Publications were excluded if they featured at least one of the following topics:

- Finite element modeling;
- Models of the cervical spine;
- Models without muscle incorporation;
- Models of the scoliotic spine;
- Models of the nonhuman spine;
- Studies with a medical scope other than biomechanics.

Inclusion criteria were set to

- Musculoskeletal models;
- Multibody models;
- Models of the thoracolumbar spine;
- Models of the healthy spine.

We analyzed the remaining studies systematically according to the represented modeling methods and applications and identified existing limitations and challenges.

3. Multibody Modeling of the Healthy Spine

After filtering a total of 2592 articles, 81 articles remained, which were included in this review. Focusing on extensive musculoskeletal models of the thoracolumbar spine, we discuss models with reduced complexity, such as abstracted models [12–16], skeletal models neglecting muscular effects [17,18] or models of the lumbar spine [19–29] only in passing.

Overall, our literature review revealed that a large proportion of published studies was based on a few original models [30–33]. Due to the accessibility of these models via the commercially available software AnyBody (AnyBody Technology A/S, Aalborg, Denmark) [30,33] or the open-source software OpenSim [31,32,34], numerous studies can be found that used, modified, and extended these models, beyond the boundaries of the respective research groups as well [35–58]. Apart from these widely reused models, further original models can be found in the literature using alternative software [59–64]. Table 1 provides an overview of the original models found and subsequent studies associated with them.

Table 1. Overview of original models of the musculoskeletal thoracolumbar spine and related modeling methods. Semi-individualized models are those that contain both individualized and generic musculoskeletal components. Joint definitions include potentially assigned constraints.

Reference	Included Segments	Joint Definition	Generic/Indiv.	Passive Force Elements	Muscle Model and Force Estimation	Software	Related Studies
de Zee et al. [30]	Pelvis, sacrum, L1-L5, thorax	3 rot. DOFs (IV)	Generic	-	Act., ID, SO	AnyBody	[33,35,36,39,44,45,47,65]
Christophy et al. [31]	Pelvis, sacrum L1-L5, thorax	3 rot. DOFs (IV)	Generic	-	Hill type	OpenSim	[37,40,41,46,48–53]
Bruno et al. [32]	Pelvis, sacrum T1-L5, ribs, sternum, upper limbs, head–neck	3 rot. DOFs (IV) 1 rot. DOFs (CV)	Generic	-	Hill type, ID, SO	OpenSim	[38,42,43,54–58]
Ignasiak et al. [33]	Pelvis, sacrum T1-L5, ribs, sternum head–neck	6 rot. DOFs (IV) 1 rot. DOFs (CV/CT) 3 rot. DOFs (CS I) 6 rot. DOFs (CS II-X)	Generic	CS, CT, CV, IV joint (lin.)	Act., ID, FSK [66], SO	AnyBody	[39,67,68]
Lerchl et al. [59]	Pelvis, sacrum, L1-L5, thorax, upper limbs, head–neck	3 rot. DOFs (IV)	Semi-indiv.	Lig. (nonlin.) IVD (nonlin.)	Actuators, ID, SO	Simpack	-
Favier et al. [69]	Lower limbs pelvis, sacrum, L1-L5, thorax (3 segments), upper limbs, head–neck	3 rot. DOFs (IV)	Semi-indiv.	Joint (lin.)	Hill type, IK, ID, SO	OpenSim	-
Malakoutian et al. [60]	Pelvis, sacrum, L1-L5, thorax, humeri	6 DOFs (IV)	generic	Joint, IAP	Hill type, FD-assisted SO	AriSynth	[70]
Rupp et al. [61]	Pelvis, sacrum, L1-L5, thorax	6 DOFs (IV)	Generic	Lig. (nonlin.) IVD (nonlin.)	Hill type, FD	In-house	-
Fasser et al. [62]	Pelvis, sacrum, L1-L5, thorax	3 rot. DOFs (IV)	Semi-indiv.	-	Hill type, IK, ID, SO	Matlab	[71]
Bayoglu et al. [72]	Pelvis, sacrum, C1-L5, ribs, sternum, skull (3 segments), shoulder (3 Segments)	3 rot. DOFs (IV) 6 DOFs (CS) 1 DOF (CV/CT)	Individ.	Joint (lin.)	Act., ID, SO	AnyBody	[73–75]
Huynh et al. [63]	Full-body, C1-L5	3 rot. DOFs (IV)	Generic	Lig. (lin.) IVD (lin.), IAP	IK, ID, SO	LifeMOD	[76]
Khurelbaatar et al. [64]	Pelvis, sacrum, C1-L5, ribs, sternum, upper limbs, head	6 DOFs (IV/CS), 3 rot. DOFs (CV)	Semi-indiv. (bones)	Lig. (nonlin.), IVD (nonlin.), CS cartilage (lin.), facet joints	Act., ID, SO	RECURDYN	-
Guo et al. [77]	Pelvis, sacrum, C1-L5, ribs, sternum, upper limbs, head	6 DOFs (IV)	Generic	Lig. (nonlin.), IVD (lin.), facet joints, IAP	Hill type, ALE, FD	OpenSim	-

The definition of the abbreviations can be found at the end of this article.

3.1. General Model Setup and Kinematics

In the past two decades, simplified models of the whole torso with a detailed lumbar spine were developed to investigate lumbar loads [30,31,59,61,69]. One of the first generic models for lumbar load estimation was introduced by de Zee et al. in 2007 [30], which comprised seven rigid bodies for the pelvis including the sacrum, five lumbar vertebrae, and one lumped segment representing the thoracic spine including the rib cage and cervical spine. The model anatomy was based on publications by Hansen et al. [78] and Bodguk et al. [79]. De Zee defined intervertebral joints as spherical joints with their respective center of rotation (COR) located in the intersection of the instantaneous axis of rotation and the midsagittal plane according to Pearcy and Bodguk [80]. A total of 154 actuators representing muscle fascicles for the erector spinae (ES), rectus abdominis (RA), internal obliques (IO), external obliques (EO), psoas major (PM), quadratus lumborum (QL), and multifidus (MF) were implemented in the model either as a straight line between insertion and origin or, in order to mimic more realistic lines of action, redirected using so-called via points or wrapping surfaces [30].

Inspired by de Zee's model, Christophy et al. published a generic multibody model of the lumbar spine in 2012 [31], incorporating a more detailed muscle architecture regarding the latissimus dorsi (LD) and the MF muscle. Using the open-source software OpenSim [34], the model has been widely used and extended in the past years [31,37,40,41,48–52,81,82]. In recent years, other models with simplified thorax have been published [59,61,69].

Favier et al. published a full-body model with a detailed lumbar spine in 2021 [69]. The model was created in OpenSim and included in total 20 rigid bodies including the head–neck, three-segment thoracic and cervical spine (spherical joints in T7-T8 and C7-T1), five lumbar vertebrae, pelvis with sacrum, as well as upper and lower extremities. The model incorporated a total of 538 muscle actuators for the lower limbs and lumbar spine [69].

Lerchl et al. introduced a pipeline for the semiautomated generation of individualized MBS models with a detailed lumbar spine created in the commercial multibody modeling software Simpack (Dassault Systèmes, France) in 2022 [59]. Based on CT data, the models included individual vertebrae T1-L5 with a fused thoracic part and rib cage and spherical lumbar intervertebral joints, and generic segments for the head–neck, pelvis, sacrum, and simplified arms. A total number of 103 actuators representing the muscles of the lower back were incorporated [59].

Research devoted to the loading of the thoracic spine is less common and therefore, only few models incorporating a detailed thoracic spine and rib cage can be found in the literature [32,33,72]. As opposed to musculoskeletal models with a rigid thorax, these models allow a comprehensive analysis of spinal loading for load cases involving thoracic movement. Based on the generic model of the lumbar spine by de Zee et al. [30], Ignasiak et al. introduced a musculoskeletal model of the thoracolumbar spine with a detailed articulated rib cage [33]. Ignasiak et al. extended the model by individual rigid bodies of 12 vertebrae, 10 pairs of ribs, and a sternum. Intervertebral thoracic joints were defined as six-DOF joints and lumbar joints, originally modeled as spherical joints [30], were also modified, respectively. Costovertebral (CV) and costotransverse (CT) joints were defined as revolute joints with the rotation axis in the frontal direction and all joints between the ribs and the sternum were modeled with six DOFs, except the first pair, which were modeled as spherical joints. The model was validated against in vivo data and used in follow-up studies [33,39,67,68].

A comprehensive model of the upper body including 60 segments (vertebrae, ribs, skull, sternum, hyoid, thyrohyoid, clavicles, scapulas, humeri, sacrum, and pelvis) created in AnyBody was published by Bayoglu et al. in 2019 [72].

Based on the lumbar spine model of Christophy et al. [31], Bruno et al. developed and validated a fully articulated model of the thoracolumbar spine in OPENSIM including individual vertebrae, ribs, and sternum [32]. Like Christophy's model, the thoracolumbar model of Bruno et al. has been widely used and adapted since its publication [32,43,54,56–58,83,84].

In biomechanical MBS modeling, intersegmental connections are usually implemented as joints with defined DOFs, which can either be defined directly in the joint or are implemented as constraints, limiting the joint's effective degrees of freedom to its relevant components. It is common practice to model intervertebral joints as spherical joints allowing rotation around three spatial axes [31,62]. Few models exist, that defined intervertebral joints with six DOFs, additionally accounting for translational motion [33,37,41,61]. The centers of rotation are located either in the geometrical center of the IVD [33,59,62] or in the instantaneous axis of rotation according to Pearcy and Bodguk [30,31,69,80]. CV joints are modeled as pin joints rotating around the vector between the costovertebral and costotransverse joints [32,33,72] or spherical joints [64] and CS joints as six DOFs [33,64,72]. Depending on the simulation approach (Section 3.4), kinematic data have been most commonly assigned to the respective DOFs according to findings from our own experimental studies or the literature (Section 3.3). This way, model kinematics are usually described using relative minimum coordinates. However, for inverse kinematic approaches, absolute coordinates are assigned to the end link of the kinematic chain. Providing stable boundary conditions for the mechanical analyses, the models are usually connected to the inertial frame of reference and therefore leaving the head–neck complex as the end link of the open kinematic chain. Upper-body weight is either combined and included in the center of mass of the lumped thoracic body [61], distributed according to the literature [85,86] or derived from patient-specific CT or MRI data and distributed levelwise along the thoracolumbar spine [59,62].

3.2. Passive (Visco)elastic Components

Various approaches have been taken regarding the modeling of viscoelastic structures that passively stabilize the spine, such as IVD, spinal ligaments, or the (cartilage) tissue of the thorax. The modeling approach can vary both in the level of detail and in the mechanical characteristics considered. Thus, some models neglect the effects of these components entirely [30–32,62], whereas others combine them partially or completely into one single stabilizing element per joint [60,69,72], or even integrate individual components explicitly [59,61,64,77]. The majority of approaches simplify the mechanical properties of connective tissue to linear elastic force elements, which produce corresponding forces and moments exclusively depending on their deformation. In multibody models, such material behavior is described via spring elements with constant stiffness for the corresponding DOFs. Only a few models incorporate the nonlinear mechanical behavior of biological passive structures [87]. However, modeling these components as purely elastic does not account for viscous effects that influence the mechanical response as a function of the deformation rate, also known as damping behavior. A detailed nonlinear viscoelastic modeling of IVDs and spinal ligaments, such as the anterior and posterior longitudinal ligament, the flavum ligament, as well as the interspinal and supraspinal ligament, can be found in only a few models [59,61]. The respective parameters are usually taken from in vitro studies available in the literature [88–92].

To examine thoracic loads, models require an appropriate force transmission from the rib cage to the thoracic spine in addition to intervertebral passive structures. In this context, costosternal (CS), costotransverse (CT) and costovertebral (CV) articulations are a central issue. Commonly, these connections are constrained and modeled as linear elastic elements according to the resulting DOFs. Stiffness parameters are usually taken from in vitro studies or adapted from previously published in silico studies. Bruno et al. included point-to-point actuators, which were placed between the ends of the ribs and the sternum (ribs 1–7) or between the ends of adjacent ribs (ribs 8–10) to represent forces transmitted by costal cartilage. As a result of a sensitivity analysis, forces generated by the actuators were set to 1000 N allowing the costal cartilage to provide a high supporting force to the end of the ribs [32].

Mechanical properties are usually incorporated either directly from mechanical testing, such as ligament tensile tests [88,93] or by simulating in vitro protocols, such as stepwise reduction studies, where individual connective structures are gradually removed from functional biological units, such as the FSU or the rib cage, while measuring the mechanical properties of the units after every resection [89,94,95]. However, due to the high level of intra- and interindividual variability regarding the mechanical characteristics of biological materials, the resulting parameters usually come with high standard deviations [96].

3.3. Scaling and Individualization

Spinal loading is highly dependent on a variety of subject-specific characteristics, such as spinal alignment, anthropometry, body weight distribution, or kinematics. While finite element models exist that account for individual characteristics [97–104], multibody models are predominantly generic in nature. In the past years, an increasing number of studies have been published, putting an emphasis on the individualization of the models [54,55,58,59,62].

A wide range of MBS models are based on measurements available in respective databases, e.g., in the OpenSim database (https://simtk.org/projects/osimdatabase, accessed on 27 December 2022). To gain reliable insights for the examined load cases, it is important to match the subject characteristics to the investigated kinematics as congruently as possible. It is common scientific practice to use available data based on measurements of bone geometries derived from imaging data or cadaver studies of individuals and scale and adapt the relevant parameters to the desired anthropometry depending on the characteristics of the studied target group. The need to make use of various sources in this regard makes it essential to be clear about the underlying data sets, in order to draw meaningful conclusions from simulation results. Thus, segment masses and body weight distribution and simplified kinematics are usually taken from the literature [85,86,105]. Some studies include experimental data collection of kinematics to scale the existing model appropriately [45,51,83] and include muscle activity from electromyography (EMG) measurement to drive the model [52]. This usually does not incorporate individual bone geometries, muscle morphology, or the mechanical properties of viscoelastic components.

However, the neglect or only limited consideration of interindividual variation makes these models poorly suitable for a detailed subject-specific analysis. Models based on coherent datasets regarding bone geometry, anthropometry, and muscle architecture, and kinematics are rare in the literature. Bayoglu et al. built a model based on extensive measurements of one cadaver, incorporating general kinematic data from the literature [72–74]. Dao et al. published a patient-specific model based on CT and MRI data [20] of the lumbar spine. Bruno et al. used their generic model [32] for the investigation of the impact of the integration of subject-specific properties [42]. Therefore, they incorporated CT-based measurements of trunk anatomy, such as spinal alignment and muscle morphology, indicating the relevance of considering these factors [42]. Based on this publication, Banks et al. investigated lumbar load in a patient-specific MBS model using CT data and marker-based motion capturing to combine individual musculoskeletal geometry and coherent kinematics [58]. However, the individualization of those models usually involves a time-consuming, manual, or semiautomated process which requires expert knowledge. To the best of our knowledge, only two publications can be found that deal with the topic of automating the individualization of MBS models [59,62].

Fasser at al. used annotated bi-planar radiography images (EOS imaging, Paris, France) for the automated generation of semi-subject-specific MBS models of the torso. The models included individual size and the alignment of bony structures as well as an individual body mass distribution. In the process, 112 and 109 points were marked in the frontal and sagittal plane, respectively, and converted into 3D coordinates. The body mass distribution was determined using the individual body contour of the imaging data. Individual bone geometries, muscle morphology, and passive elements were not included in the model. [62]

Based on the use of artificial neural networks (ANN), Lerchl et al. introduced a pipeline for the automated segmentation of vertebrae [106] and soft tissue of the torso, as well as the generation of the points of interest defining muscles and ligaments' attachment points and the location and orientation of intervertebral joints. All data were derived from CT imaging and the model generation required minimal manual interaction, making it suitable for the analysis of large patient cohorts. However, the individual characteristics of the muscles and connective tissue could not yet be integrated in the process [59].

3.4. Muscle Force Estimation

A mechanical analysis with multibody systems can follow two approaches, which define the necessary input data. Forward dynamic simulations (FD) require kinetic data to drive the model to generate specific kinematics. This usually means that muscle forces are applied directly or indirectly to the model to produce a desired motion. This is contrasted with the idea of inverse dynamic simulations(ID), which use kinematic data as input to calculate the required kinetic data. Thus, joint kinematics during as specific movement is imposed to the model and necessary joint moments and therefore, associated muscle forces are calculated. However, having more control variables, namely, muscle fascicles, than DOFs, the human musculoskeletal system is redundant. This leads to an infinite number of solutions for each load case. In order to determine the most suitable solutions, a mathematical optimization is a commonly used method. Numerous algorithms are available to find the optimal solution. Hereby, depending on the chosen algorithm, control variables, namely, muscle activation, excitation, or forces are varied in a deterministic or stochastic way until some given optimality criteria and constraints are met. Most commonly, a combination of inverse dynamics and static optimization (SO) is used [30,32,45], sometimes including inverse kinematics (IK) to determine individual joint kinematics [62,63,69]. The inverse dynamic simulation provides joint moments necessary to generate the simulated movement. Subsequently, the static optimization solves the redundancy problem for each time frame sequentially under the consideration of meeting equilibrium conditions.

In MBS models of the spine, muscles of interest are usually modeled as multiple fascicles, which comprehensively consider the respective lines of action (Section 3.1). Individual fascicles are modeled either as simple force actuators or, more complex, as Hill type muscles [107]. The classic muscle model according to Hill comprises serial and parallel elastic elements, representing passive elastic properties of the muscle–tendon complex as well as a contractile element representing the active component, namely, the function of myofilaments. This element can include muscle-specific characteristics, such as the force–length and force–velocity relationship as well as activation dynamics. Depending on how far these dynamics are taken into account, the muscle excitation, activation, or force can drive the model and therefore represent control variables for optimization routines. Detailed definitions of muscle-specific dynamics can be found in the literature [108,109].

4. Applications of MBS Models

MBS models can be used to address a wide range of questions. There are numerous publications devoted to the evaluation of methods in numerical modeling, including sensitivity analyss or validation studies. Furthermore, validated models can help to gain valuable insights into biomechanically or clinically relevant load cases. However, depending on the investigated load case and subject collective, model extensions, and modifications are usually necessary. Table 2 provides an overview of the most relevant studies using existing models to address specific research questions.

Table 2. Overview of representative studies using available original models to address methodological or biomechanical research questions.

Study	Focus	Modifications	Original Model
Actis et al. [48]	Methodological Validation for flexion, extension, lateral bending, axial rotation for participants with and without transtibial amputation	model extension by lower body [110], muscle strength [32], and body mass distribution [86] inclusion of experimental protocol for EMG and kinematic data collection	[31]
Arshad et al. [38]	Biomechanical Influence of spinal rhythm and IAP on lumbar loads during trunk inclination	Adapted spinal rhythm, inclusion of ligaments, IVD, and IAP	[30]
Arx et al. [83]	Biomechanical Lumbar loading during different lifting styles	Integration of measured kinematic data	[32]

Table 2. *Cont.*

Study	Focus	Modifications	Original Model
Banks et al. [58]	Biomechanical Comparison of static and dynamic vertebral loading during lifting patient-specific models in an older study population	CT-based individualization and integration of patient-specific kinematic data	[32]
Bassani et al. [45]	Methodological Model validation for various loading tasks via spinopelvic rhythm and IDP according to [4]	Integration of kinematic data	[30]
Bassani et al. [47]	Biomechanical Effect of spinopelvic sagittal alignment on lumbar loads	Variation of spinal alignment based on four parameters	[30].
Bayoglu et al. [75]	Methodological Sensitivity of muscle and IV disc force computations to variations in muscle attachment sites	Variation of the location of muscle insertion	[72]
Raabe et al. [40]	Biomechanical Jogging biomechanics	Combination with full-body model by [111]	[31]
Beaucage-Gauvreau et al. [49–51]	Biomechanical Effects of lifting techniques on lumbar loads	Adjust all spinal joints with 3 DOFs and inclusion of kinematic data from motion capturing during lifting	[31,40]
Burkhart et al. [54]	Methodological Reliability of optoelectronic motion capturing for subject-specific spine model generation	Combination with model of lower limbs [110]	[32]
Malakoutian et al. [70]	Methodological Effect of muscle parameters on spinal loading	Variation of biomechanical parameters of paraspinal muscles	[60]
Senteler et al. [41]	Methodological Joint reaction forces for flexion and lifting	Combination with models of upper limbs and neck, IV joints set to 6 DOFs, added passive lin. joint stiffness	[31]
Meng et al. [37]	Methodological Force-motion coupling in 6-DOF joint	6 DOFs (IV), added 6-DOF stiffness	[31]
Molinaro et al. [52]	Biomechanical Effects of throwing technique solid waste collection occupation on lumbar loads	Incorporation of collected kinematics and EMG data, EMG-assisted muscle force estimation and SO	[49]
Schmid et al. [56]	Methodological Validation of a thoracolumbar model for children and adolescents	Combination with model of the lower limbs [112], scaling to anthropometry of children and adolescents	[32]
Schmid et al. [57]	Methodological Feasibility of a skin-marker based method for spinal alignment modeling	Reduction of muscle architecture, implementation of skin-marker derived alignment	[56]
Wang et al. [84]	Methodological Implementation of a physiological FSU	Adaption of IV joints to represent passive properties of a physiological FSU	[32]
Overbergh et al. [55]	Methodological Workflow for generation of an image-based (CT), subject-specific thoracolumbar model of spinal deformity	Addition of kinematic coupling constraints, personalization of bone geometries, alignment, IV joint definitions and kinematics	[32]
Han et al. [36]	Methodological Effect of centers of rotation on spinal loads and muscle forces in total disc replacement of lumbar spine	Ligaments and facet joints added, altering location of CoR	[30]
Zhu et al. [46]	Biomechanical Effects of lifting techniques on lumbar loads	Combining with models of upper and lower limbs, 6-DOF IV joint, integration of a customized marker set	[31]
Kuai et al. [44]	Biomechanical Influence of disc herniation on kinematics of the spine and lower limbs	Integration of kinematic data from patients with lumbar disc herniation	[30]
Senteler et al. [113]	Methodological Sensitivity of intervertebral joint forces to CoR location	Altering location of CoR	[41]

4.1. Studies with Methodological Focus

Various publications can be found in the literature evaluating and validating new approaches in MBS modeling [19,30–32,45,63,64,69]. For the purpose of validating these approaches, it is common scientific practice to compare simulation results with existing results from in vivo or in vitro measurements. Of note, those comparisons are mainly relative, as few in vivo measurements are available and exact boundary conditions are hard to control. Frequently used in vivo studies to validate results on spinal loading from simulation are intradiscal pressure measurements [4,114]. Estimated muscle forces are usually compared to EMG measurements from one's own experimental studies [48] or the literature [59].

Apart from evaluating the validity of the modeling approach, the simulation results of generated MBS models can be used to validate novel methods in data processing regarding the derivation of both relevant modeling data from imaging [19–21] and kinematic data motion capture [54]. Due to the usually extensive effort connected to the processing of individual data, recent publications have focused on the automation of the process [59,62].

Simplifications are an integral part of any model and have to be taken into consideration when it comes to the interpretation of the results. To understand and evaluate their influence, MBS models have been used to systematically investigate common assumptions, such as the reduction of complex mechanics of the functional spine unit (FSU) [37,115]. Further, the sensitivity of the model accuracy to assumed positions of intervertebral centers of rotation [23,36] or muscle insertions [75] have been analyzed. Rockenfeller et al. investigated the effect of muscle- or torque-driven centrodes using an MBS model of the lumbar spine.

Furthermore, a systematic model-based analysis can help standardize clinical procedures, such as the classification of spinal shapes [116] or to define boundary conditions for experimental protocols [24].

4.2. Studies with Biomechanical or Clinical Focus

Validated models are used to comprehensively investigate biomechanical and clinical aspects of a wide range from routine scenarios to nonphysiological, or even traumatic events.

The relevance of low-dynamic everyday or work-related activities for the general population, as well as their experimental accessibility, make these scenarios among the most studied in biomechanical simulations. Therefore, numerous models exist that deal with the mechanical effects of lifting [12,13,25,46,76,77,82], everyday activities such as walking, flexion, extension, or lateral bending [15,43,69] or work-related situations such as high-frequency axial loading [17,18]. In this context, different lifting techniques were evaluated [50,51,83,117]. Accident situations were investigated by Wei et al. [16] for snowboarding and for frontal impact by Valdano et al. [14]. Incorporating noncritical higher dynamics, Raabe et al. combined a generic model of the lumbar spine [31] with a model of the lower limbs [111] to analyze the biomechanics of jogging [40]. Studies investigating specific kinematic boundary conditions usually involve an experimental setup to collect kinematic data in a healthy adult population [46,47,52,58,83]. Comparably few studies target more vulnerable populations, such as amputees [48,53] or children [27,56], who used validated models of adults and scales them according to the literature to match the average anthropometric data of children.

Regarding the influence of healthy anatomical and anthropometric and anatomical characteristics, biomechanical modeling have been used to determine the effect of spinal alignment [28,43,47], to gain insight into load sharing of passive structures of the FSU [22], the effect of ligament stiffness [65] or muscle strengthening [118].

Furthermore, MBS models can help to understand and treat pathological developing or surgically induced pathological biomechanics. Kuai et al. analyzed the impact of disc herniation on the kinetics of the spine and lower extremities during everyday activities [44].

Surgical interventions always represent a major intervention in the natural biomechanics of the musculoskeletal system. Thus, several studies on the effects of spinal fusion can be found in the literature [29,71,119]. The resulting kinematic effects of spinal fusion were investigated by Ignasiak et al., who proposed a method for the prediction of a full-body sagittal alignment including reciprocal changes as a reaction to spinal fusion [68].

5. Limitations and Challenges

It is in the nature of numerical models that they come with limitations. One of the great challenges is to keep the balance between necessary accuracy and reasonable complexity. This requires not only in-depth knowledge of the object to be modeled but also the corresponding data from experimental studies and the appropriate technical solutions for implementation. During our literature research, we were able to identify several core limitations that could be found in a wide range of MBS models of the spine and the related challenges when it came to addressing these limitations.

5.1. Database

Any model can only be as good as its input data. In the context of biomechanical models, this comprises bony geometry, anthropometry, muscle architecture, the mechanical parameters of viscoelastic components and kinematic data. Due to the necessary measurements to determine these parameters, it is currently not possible to build models based on fully consistent datasets. While anthropometric and kinematic data can be determined via noninvasive measures in biomechanics labs, such as marker-based motion capturing, the derivation of bony geometries, muscle architecture, and a detailed distribution of soft tissue usually need medical imaging or are performed in cadaver studies. However, the mechanical properties of viscoelastic components such as ligaments or the IVD can currently only be determined with the help of in vitro studies, which require the isolation of the structure of interest to mount them in respective testing machines. Consequently, these measurements are also usually performed with specimens from cadaver studies and highly dependent on the experimental conditions.

In the past years, more studies including widely individualized models were published [55,59,62]. However, even these models can only offer a limited customization.

In order to obtain consistent data sets for biomechanical models, alternative, noninvasive methods must be developed to determine these parameters in large subject cohorts. Here, the combination of experimental studies, multimodal imaging, and ANNs could be a possible solution to increase the level of model individualization beyond its anthropometric and skeletal characteristics. Thus, the individual mechanical condition of functional components can be evaluated partly on the basis of imaging data. For instance, according to the Pfirrmann scale, a potential degradation of the IVD can be determined via the height and signal intensity from MRI data [120]. Correlating this degradation with the mechanical alteration of IVD [121], this can be used to consider the individual mechanical state of connective tissue, when it is implemented in respective models. Training ANNs with these data will provide large, more diverse datasets for individualized multibody models.

Furthermore, invasive experimental studies on spinal loading for model validation are rare and are not widely feasible due to ethical reasons. Accordingly, even consistently constructed models cannot ultimately be validated against data pertaining to the individual in question. Additionally, the high level of variability in mechanical properties of biological materials as mentioned in Section 3.2, and therefore, the integration of parameters with high standard deviations inevitably leads to models containing inaccuracies. Depending on the complexity of the model, these inaccuracies can accumulate and further blur the generated results. It is necessary to be aware of existing inconsistencies and imprecision when interpreting simulation results in order not to draw incorrect conclusions.

5.2. Joint Definition

Intervertebral connections are a complex combination of the IVD, ligaments, facet joints, and articulated capsules. Depending on the applied load, this leads to complicated kinematics in which the instantaneous center of rotation migrates in the course of the motion [122]. However, in the vast majority of spine models, intervertebral joints are simplified to spherical joints allowing three rotational DOFs around a fixed center of rotation. The sensitivity of this assumption has been subject to several in silico studies [23,113,123], indicating that the effect of this assumption on the calculated muscle forces and spinal loading should not be neglected. Detailed modeling requires six degrees of freedom and the consideration of appropriate stabilizing structures, the validity of which depends primarily on the definition of their mechanical parameters (Section 5.1). There are some models to be found in the literature incorporating such detailed representation of intervertebral connection [22], mainly focusing on load sharing in passive structures.

Larger data sets could also help to better understand intervertebral dynamics in order to develop corresponding valid modeling approaches. As already mentioned in Section 5.1, the combination of imaging, machine learning for process automation, and in vitro studies can contribute to progress.

5.3. Intra-Abdominal Pressure

The stabilizing influence of intra-abdominal pressure (IAP) on the spine has been widely studied [124,125]. However, only a few MBS models consider its effects [38,60,63,70,77]. In consequence, spinal loads in lifting tasks or the inclination of the upper body are assumed to be overestimated in the MBS modeling of the spine. Arshad et al. observed a decrease of up to 514 N in lumbar compression force and 279 N in global muscle force due to the inclusion of intra-abdominal pressure [38]. These results indicated that it was necessary to consider the effects of IAP to obtain reliable quantitative results on spinal loads.

5.4. Muscle Modeling and Muscle Force Estimation

A valid representation of relevant muscles is crucial to gain meaningful findings on the biomechanics of the spine. Most of the models contain a detailed muscle architecture consisting of multiple fascicles spanning between origin and insertion according to the literature. Deploying modeling components, that are usually defined as point-to-point force elements, can lead to nonphysiological lever arms depending on the imposed movement. De Zee's model used so-called via points to redirect the lines of action of the modeled long muscle fascicles along the rib cage and thus create more realistic lines of action compared to simple straight lines [30]. However, this approach came with an increased computational cost, making it only conditionally suited for a systematic analysis of large participant cohorts.

Another aspect that has to be critically discussed is the applied muscle model. While simple force actuators are considered sufficient for a static investigation, high-dynamic load situations require the consideration of activation and contraction dynamics. This requires an in-depth knowledge of the characteristics of individual muscle morphology such as optimal fiber length, physiological cross-sectional area (PCSA), or pennation angle. Again, the need for subject-specific solutions is evident, as muscle morphology is highly dependent on the individual.

The vast majority of currently published models use a combination of inverse dynamics and static optimization for muscle force calculation. This approach provides a sufficient accuracy in static and quasi-static simulations but is dependent on the defined cost function, constraints, and used algorithm. Most commonly used are criteria for minimum fatigue [126], or the sum of squared muscle strength [127] or activation [34], and the maximum muscle stress is defined as the upper-bound constraint, which is usually set to 100 MPa [32,49,59] to guarantee that equilibrium conditions are met reliably. However, this value does not correspond to a physiological value [49]. Furthermore, SO neglects cocontraction, which incorporates the activation of the antagonist in addition to the agonist stabilizing the respective joint and therefore increasing muscle activation. This is in contradiction to the idea of static optimization, which aims at minimizing the defined cost function (e.g., muscle activation) [128]. In high-dynamic load cases, where the role of cocontraction is more evident, this leads to an underestimation of spinal loading.

One way to address this problem is to use dynamic optimization (DO). In contrast to static optimization, the entire time history of the motion under investigation is taken into account [128]. Integrating the respective criteria in the optimization objective, stabilizing effects such as cocontraction can come into play [25]. However, this method comes with a massive increase of computational cost [129]. Another possibility would be to train models with the help of artificial intelligence. However, such training requires large quantities of data, which is not possible due to the still widely manual and therefore time-consuming process of modeling [128]. Anderson et al. compared both approaches for the simulation of normal gait in 2001, stating that both provided equivalent results for low-dynamic simulations [129]. A similar comparison was made by Morrow et al. for wheelchair propulsion, noticing significant differences in estimated muscle activations [130]. Keeping in mind that wheelchair propulsion comprises higher dynamics than normal gait, these findings indicate that the validity of the chosen approach was largely dependent on the investigated load case.

6. Conclusions

Multibody models are a powerful tool to gain insight into the healthy and pathological musculoskeletal system. They can promote a general understanding of the pathobiomechanics of a large set of medical impairments and might even be able to support diagnostics and therapy planning in the future. Although simplifications and assumptions are an integral part of any model, it is essential to look closely at the implications of these assumptions, potential interactions, and possible solutions. Modern technology holds the potential to provide some of these solutions. Thus, artificial intelligence and state-of-the-art medical imaging can provide the necessary extensive data basis to systematically investigate critical parameters to derive appropriate solutions. These technical approaches coupled with a distinct awareness of existing limitations will lead us towards a growing, more profound understanding of musculoskeletal mechanics.

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Abbreviations

The following abbreviations are used in this manuscript:

MBS	Multibody system
FEM	Finite element method
DOF	Degree of freedom
FSU	Functional spine unit
IAP	Intra-abdominal pressure
EMG	Electromyography
COR	Center of rotation
IVD	Intervertebral disc
IV	Intervertebral
CS	Costosternal
CV	Costovertebral
CT	Costotransversal
FD	Forward dynamic
ID	Inverse dynamic
IK	Inverse kinematic
SO	Static optimization
DO	Dynamic optimization
ANN	Artificial neural network
ALE	Arbitrary Langrangian–Eulerian

References

1. Murtezani, A.; Ibraimi, Z.; Sllamniku, S.; Osmani, T.; Sherifi, S. Prevalence and risk factors for low back pain in industrial workers. *Folia Med.* **2011**, *53*, 68–74. [CrossRef]
2. Fu, L.; Ma, J.; Lu, B.; Jia, H.; Zhao, J.; Kuang, M.; Feng, R.; Xu, L.; Bai, H.; Sun, L.; et al. Biomechanical effect of interspinous process distraction height after lumbar fixation surgery: An in vitro model. *Proc. Inst. Mech. Eng. Part H J. Eng. Med.* **2017**, *231*, 663–672. [CrossRef]
3. Sato, K.; Kikuchi, S.; Yonezawa, T. In vivo intradiscal pressure measurement in healthy individuals and in patients with ongoing back problems. *Spine* **1999**, *24*, 2468. [CrossRef]
4. Wilke, H.J.; Neef, P.; Hinz, B.; Seidel, H.; Claes, L. Intradiscal pressure together with anthropometric data—A data set for the validation of models. *Clin. Biomech.* **2001**, *16*, S111–S126. [CrossRef] [PubMed]
5. Dreischarf, M.; Rohlmann, A.; Graichen, F.; Bergmann, G.; Schmidt, H. In vivo loads on a vertebral body replacement during different lifting techniques. *J. Biomech.* **2016**, *49*, 890–895. [CrossRef] [PubMed]
6. Rohlmann, A.; Graichen, F.; Kayser, R.; Bender, A.; Bergmann, G. Loads on a Telemeterized Vertebral Body Replacement Measured in Two Patients. *Spine* **2008**, *33*, 1170–1179. [CrossRef]
7. Gould, S.L.; Cristofolini, L.; Davico, G.; Viceconti, M. Computational Modelling of the Scoliotic Spine: A Literature Review. *Int. J. Numer. Methods Biomed. Eng.* **2021**, *37*, e3503. [CrossRef] [PubMed]
8. Alizadeh, M.; Knapik, G.G.; Mageswaran, P.; Mendel, E.; Bourekas, E.; Marras, W.S. Biomechanical musculoskeletal models of the cervical spine: A systematic literature review. *Clin. Biomech.* **2020**, *71*, 115–124. [CrossRef]
9. Dreischarf, M.; Shirazi-Adl, A.; Arjmand, N.; Rohlmann, A.; Schmidt, H. Estimation of loads on human lumbar spine: A review of in vivo and computational model studies. *J. Biomech.* **2016**, *49*, 833–845. [CrossRef]
10. Heidari, E.; Arjmand, N.; Kahrizi, S. Comparisons of lumbar spine loads and kinematics in healthy and non-specific low back pain individuals during unstable lifting activities. *J. Biomech.* **2022**, *144*, 111344. [CrossRef] [PubMed]
11. Khoddam-Khorasani, P.; Arjmand, N.; Shirazi-Adl, A. Effect of changes in the lumbar posture in lifting on trunk muscle and spinal loads: A combined in vivo, musculoskeletal, and finite element model study. *J. Biomech.* **2020**, *104*, 109728. [CrossRef] [PubMed]
12. Breloff, S.P.; Chou, L.S. Three-dimensional multi-segmented spine joint reaction forces during common workplace physical demands/activities of daily living. *Biomed. Eng.-Appl. Basis Commun.* **2017**, *29*, 1750025. [CrossRef]
13. Zaman, R.; Xiang, Y.; Cruz, J.; Yang, J. Three-dimensional asymmetric maximum weight lifting prediction considering dynamic joint strength. *Proc. Inst. Mech. Eng. Part H J. Eng. Med.* **2021**, *235*, 437–446. [CrossRef] [PubMed]
14. Valdano, M.; Asensio-Gil, J.M.; Jiménez-Octavio, J.R.; Cabello-Reyes, M.; Vasserot-Tolmos, R.; López-Valdés, F.J. Parametric Analysis of The Effect of CRS Seatback Angle in Dummy Measurements in Frontal Impacts. In Proceedings of the IRCOBI Conference 2022, Porto, Portugal, 14–16 September 2022; Volume 2022, pp. 519–531.
15. Panero, E.; Digo, E.; Ferrarese, V.; Dimanico, U.; Gastaldi, L. Multi-segments kinematic model of the human spine during gait. In Proceedings of the 2021 IEEE International Symposium on Medical Measurements and Applications (MeMeA), Lausanne, Switzerland, 23–25 June 2021. [CrossRef]
16. Wei, W.; Evin, M.; Bailly, N.; Arnoux, P.J. Biomechanical evaluation of Back injuries during typical snowboarding backward falls. *Scand. J. Med. Sci. Sport.* **2022**, 1–11. [CrossRef]

17. Valentini, P.P.; Pennestrì, E. An improved three-dimensional multibody model of the human spine for vibrational investigations. *Multibody Syst. Dyn.* **2016**, *36*, 363–375. [CrossRef]
18. Low, L.; Newell, N.; Masouros, S. A Multibody Model of the Spine for Injury Prediction in High-Rate Vertical Loading. In Proceedings of the IRCOBI Conference 2022, , Porto, Portugal, 14–16 September 2022.
19. Dao, T.T.; Pouletaut, P.; Charleux, F.; Lazáry, Á.; Eltes, P.; Varga, P.P.; Tho, M.C.H.B. Estimation of patient specific lumbar spine muscle forces using multi-physical musculoskeletal model and dynamic MRI. In *Knowledge and Systems Engineering*; Springer International, Basel, Switzerland, 2014; pp. 411–422.
20. Dao, T.T.; Pouletaut, P.; Charleux, F.; Lazáry, Á.; Eltes, P.; Varga, P.P.; Tho, M.C.H.B. Multimodal medical imaging (CT and dynamic MRI) data and computer-graphics multi-physical model for the estimation of patient specific lumbar spine muscle forces. *Data Knowl. Eng.* **2015**, *96*, 3–18. [CrossRef]
21. Dao, T.T.; Pouletaut, P.; Lazáry, Á.; Tho, M.C.H.B. Multimodal Medical Imaging Fusion for Patient Specific Musculoskeletal Modeling of the Lumbar Spine System in Functional Posture. *J. Med. Biol. Eng.* **2017**, *37*, 739–749. [CrossRef]
22. Abouhossein, A.; Weisse, B.; Ferguson, S.J. A multibody modelling approach to determine load sharing between passive elements of the lumbar spine. *Comput. Methods Biomech. Biomed. Eng.* **2011**, *14*, 527–537. [CrossRef]
23. Abouhossein, A.; Weisse, B.; Ferguson, S.J. Quantifying the centre of rotation pattern in a multi-body model of the lumbar spine. *Comput. Methods Biomech. Biomed. Eng.* **2013**, *16*, 1362–1373. [CrossRef] [PubMed]
24. Borrelli, S.; Putame, G.; Pascoletti, G.; Terzini, M.; Zanetti, E.M. In Silico Meta-Analysis of Boundary Conditions for Experimental Tests on the Lumbar Spine. *Ann. Biomed. Eng.* **2022**, *50*, 1243–1254. [CrossRef]
25. Ghiasi, M.S.; Arjmand, N.; Boroushaki, M.; Farahmand, F. Investigation of trunk muscle activities during lifting using a multi-objective optimization-based model and intelligent optimization algorithms. *Med Biol. Eng. Comput.* **2016**, *54*, 431–440. [CrossRef] [PubMed]
26. Bauer, S.; Hausen, U.; Gruber, K. Effects of individual spine curvatures—A comparative study with the help of computer modelling. *Biomed. Tech. Biomed. Eng.* **2012**, *57* (Suppl. 1), 132–135. [CrossRef] [PubMed]
27. Bauer, S.; Wasserhess, C.; Paulus, D. Quantification of loads on the lumbar spine of children with different body weight—A comparative study with the help of computer modelling. *Biomed. Tech.* **2014**, *59*, S913–S916.
28. Müller, A.; Rockenfeller, R.; Damm, N.; Kosterhon, M.; Kantelhardt, S.R.; Aiyangar, A.K.; Gruber, K. Load Distribution in the Lumbar Spine During Modeled Compression Depends on Lordosis. *Front. Bioeng. Biotechnol.* **2021**, *9*, 661258. [CrossRef] [PubMed]
29. Kantelhardt, S.; Hausen, U.; Kosterhon, M.; Amr, A.; Gruber, K.; Giese, A. Computer simulation and image guidance for individualised dynamic spinal stabilization. *Int. J. Comput. Assist. Radiol. Surg.* **2015**, *10*, 1325–1332. [CrossRef]
30. de Zee, M.; Hansen, L.; Wong, C.; Rasmussen, J.; Simonsen, E.B. A generic detailed rigid-body lumbar spine model. *J. Biomech.* **2007**, *40*, 1219–1227. [CrossRef]
31. Christophy, M.; Faruk Senan, N.A.; Lotz, J.C.; O'Reilly, O.M. A musculoskeletal model for the lumbar spine. *Biomech. Model. Mechanobiol.* **2012**, *11*, 19–34. [CrossRef]
32. Bruno, A.G.; Bouxsein, M.L.; Anderson, D.E. Development and Validation of a Musculoskeletal Model of the Fully Articulated Thoracolumbar Spine and Rib Cage. *J. Biomech. Eng.* **2015**, *137*, 081003. [CrossRef]
33. Ignasiak, D.; Dendorfer, S.; Ferguson, S.J. Thoracolumbar spine model with articulated ribcage for the prediction of dynamic spinal loading. *J. Biomech.* **2016**, *49*, 959–966. [CrossRef]
34. Delp, S.L.; Anderson, F.C.; Arnold, A.S.; Loan, P.; Habib, A.; John, C.T.; Guendelman, E.; Thelen, D.G. OpenSim: Open-source software to create and analyze dynamic simulations of movement. *IEEE Trans. Bio-Med. Eng.* **2007**, *54*, 1940–1950. [CrossRef]
35. Han, K.S.; Zander, T.; Taylor, W.R.; Rohlmann, A. An enhanced and validated generic thoraco-lumbar spine model for prediction of muscle forces. *Med. Eng. Phys.* **2012**, *34*, 709–716. [CrossRef] [PubMed]
36. Han, K.S.; Kim, K.; Park, W.M.; Lim, D.S.; Kim, Y.H. Effect of centers of rotation on spinal loads and muscle forces in total disk replacement of lumbar spine. *Proc. Inst. Mech. Eng. Part H J. Eng. Med.* **2013**, *227*, 543–550. [CrossRef]
37. Meng, X.; Bruno, A.G.; Cheng, B.; Wang, W.; Bouxsein, M.L.; Anderson, D.E. Incorporating Six Degree-of-Freedom Intervertebral Joint Stiffness in a Lumbar Spine Musculoskeletal Model-Method and Performance in Flexed Postures. *J. Biomech. Eng.* **2015**, *137*, 101008. [CrossRef] [PubMed]
38. 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**, *38*, 333–338. [CrossRef] [PubMed]
39. Ignasiak, D.; Ferguson, S.J.; Arjmand, N. A rigid thorax assumption affects model loading predictions at the upper but not lower lumbar levels. *J. Biomech.* **2016**, *49*, 3074–3078. [CrossRef]
40. Raabe, M.E.; Chaudhari, A.M. An investigation of jogging biomechanics using the full-body lumbar spine model: Model development and validation. *J. Biomech.* **2016**, *49*, 1238–1243. [CrossRef]
41. Senteler, M.; Weisse, B.; Rothenfluh, D.A.; Snedeker, J.G. Intervertebral reaction force prediction using an enhanced assembly of OpenSim models. *Comput. Methods Biomech. Biomed. Eng.* **2016**, *19*, 538–548. [CrossRef]
42. Bruno, A.G.; Mokhtarzadeh, H.; Allaire, B.T.; Velie, K.R.; De Paolis Kaluza, M.C.; Anderson, D.E.; Bouxsein, M.L. Incorporation of CT-based measurements of trunk anatomy into subject-specific musculoskeletal models of the spine influences vertebral loading predictions. *J. Orthop. Res. : Off. Publ. Orthop. Res. Soc.* **2017**, *35*, 2164–2173. [CrossRef]

43. Bruno, A.G.; Burkhart, K.; Allaire, B.; Anderson, D.E.; Bouxsein, M.L. Spinal loading patterns from biomechanical modeling explain the high incidence of vertebral fractures in the thoracolumbar region. *J. Bone Miner. Res.* **2017**, *32*, 1282–1290. [CrossRef]
44. Kuai, S.; Zhou, W.; Liao, Z.; Ji, R.; Guo, D.; Zhang, R.; Liu, W. Influences of lumbar disc herniation on the kinematics in multi-segmental spine, pelvis, and lower extremities during five activities of daily living. *BMC Musculoskelet. Disord.* **2017**, *18*, 1–13. [CrossRef]
45. Bassani, T.; Stucovitz, E.; Qian, Z.; Briguglio, M.; Galbusera, F. Validation of the AnyBody full body musculoskeletal model in computing lumbar spine loads at L4L5 level. *J. Biomech.* **2017**, *58*, 89–96. [CrossRef] [PubMed]
46. Zhu, X.Y.; Kim, H.K.; Zhang, Y. Development of an enhanced musculoskeletal model for simulating lumbar spine loading during manual lifting tasks. *Lect. Notes Comput. Sci. (Incl. Subser. Lect. Notes Artif. Intell. Lect. Notes Bioinform.)* **2017**, *10286*, 229–237. [CrossRef]
47. Bassani, T.; Casaroli, G.; Galbusera, F. Dependence of lumbar loads on spinopelvic sagittal alignment: An evaluation based on musculoskeletal modeling. *PLoS ONE* **2019**, *14*, e0207997. [CrossRef] [PubMed]
48. Actis, J.A.; Honegger, J.D.; Gates, D.H.; Petrella, A.J.; Nolasco, L.A.; Silverman, A.K. Validation of lumbar spine loading from a musculoskeletal model including the lower limbs and lumbar spine. *J. Biomech.* **2018**, *68*, 107–114. [CrossRef] [PubMed]
49. Beaucage-Gauvreau, E.; Robertson, W.S.P.; Brandon, S.C.E.; Fraser, R.; Freeman, B.J.C.; Graham, R.B.; Thewlis, D.; Jones, C.F. Validation of an OpenSim full-body model with detailed lumbar spine for estimating lower lumbar spine loads during symmetric and asymmetric lifting tasks. *Comput. Methods Biomech. Biomed. Eng.* **2019**, *22*, 451–464. [CrossRef]
50. Beaucage-Gauvreau, E.; Brandon, S.C.; Robertson, W.S.; Fraser, R.; Freeman, B.J.; Graham, R.B.; Thewlis, D.; Jones, C.F. A braced arm-to-thigh (BATT) lifting technique reduces lumbar spine loads in healthy and low back pain participants. *J. Biomech.* **2020**, *100*, 109584. [CrossRef]
51. Beaucage-Gauvreau, E.; Brandon, S.C.; Robertson, W.S.; Fraser, R.; Freeman, B.J.; Graham, R.B.; Thewlis, D.; Jones, C.F. Lumbar spine loads are reduced for activities of daily living when using a braced arm-to-thigh technique. *Eur. Spine J.* **2021**, *30*, 1035–1042. [CrossRef]
52. Molinaro, D.D.; King, A.S.; Young, A.J. Biomechanical analysis of common solid waste collection throwing techniques using OpenSim and an EMG-assisted solver. *J. Biomech.* **2020**, *104*, 109704. [CrossRef]
53. Honegger, J.D.; Actis, J.A.; Gates, D.H.; Silverman, A.K.; Munson, A.H.; Petrella, A.J. Development of a multiscale model of the human lumbar spine for investigation of tissue loads in people with and without a transtibial amputation during sit-to-stand. *Biomech. Model. Mechanobiol.* **2021**, *20*, 339–358. [CrossRef]
54. Burkhart, K.; Grindle, D.; Bouxsein, M.L.; Anderson, D.E. Between-session reliability of subject-specific musculoskeletal models of the spine derived from optoelectronic motion capture data. *J. Biomech.* **2020**, *112*, 110044. [CrossRef]
55. Overbergh, T.; Severijns, P.; Beaucage-Gauvreau, E.; Jonkers, I.; Moke, L.; Scheys, L. Development and validation of a modeling workflow for the generation of image-based, subject-specific thoracolumbar models of spinal deformity. *J. Biomech.* **2020**, *110*, 109946. [CrossRef] [PubMed]
56. Schmid, S.; Burkhart, K.A.; Allaire, B.T.; Grindle, D.; Anderson, D.E. Musculoskeletal full-body models including a detailed thoracolumbar spine for children and adolescents aged 6–18 years. *J. Biomech.* **2020**, *102*, 109305. [CrossRef]
57. Schmid, S.; Connolly, L.; Moschini, G.; Meier, M.L.; Senteler, M. Skin marker-based subject-specific spinal alignment modeling: A feasibility study. *J. Biomech.* **2022**, *137*, 111102. [CrossRef]
58. Banks, J.J.; Alemi, M.M.; Allaire, B.T.; Lynch, A.C.; Bouxsein, M.L.; Anderson, D.E. Using static postures to estimate spinal loading during dynamic lifts with participant-specific thoracolumbar musculoskeletal models. *Appl. Ergon.* **2023**, *106*, 103869. [CrossRef] [PubMed]
59. Lerchl, T.; El Husseini, M.; Bayat, A.; Sekuboyina, A.; Hermann, L.; Nispel, K.; Baum, T.; Löffler, M.T.; Senner, V.; Kirschke, J.S. Validation of a Patient-Specific Musculoskeletal Model for Lumbar Load Estimation Generated by an Automated Pipeline From Whole Body CT. *Front. Bioeng. Biotechnol.* **2022**, *10*, 862804. [CrossRef]
60. Malakoutian, M.; Street, J.; Wilke, H.J.; Stavness, I.; Fels, S.; Oxland, T. A musculoskeletal model of the lumbar spine using ArtiSynth–development and validation. *Comput. Methods Biomech. Biomed. Eng. Imaging Vis.* **2018**, *6*, 483–490. [CrossRef]
61. Rupp, T.K.; Ehlers, W.; Karajan, N.; Günther, M.; Schmitt, S. A forward dynamics simulation of human lumbar spine flexion predicting the load sharing of intervertebral discs, ligaments, and muscles. *Biomech. Model. Mechanobiol.* **2015**, *14*, 1081–1105. [CrossRef]
62. Fasser, M.R.; Jokeit, M.; Kalthoff, M.; Gomez Romero, D.A.; Trache, T.; Snedeker, J.G.; Farshad, M.; Widmer, J. Subject-Specific Alignment and Mass Distribution in Musculoskeletal Models of the Lumbar Spine. *Front. Bioeng. Biotechnol.* **2021**, *9*, 745. [CrossRef]
63. Huynh, K.; Gibson, I.; Jagdish, B.; Lu, W. Development and validation of a discretised multi-body spine model in LifeMOD for biodynamic behaviour simulation. *Comput. Methods Biomech. Biomed. Eng.* **2015**, *18*, 175–184. [CrossRef]
64. Khurelbaatar, T.; Kim, K.; Kim, Y.H. A cervico-thoraco-lumbar multibody dynamic model for the estimation of joint loads and muscle forces. *J. Biomech. Eng.* **2015**, *137*, 111001. [CrossRef]
65. Putzer, M.; Auer, S.; Malpica, W.; Suess, F.; Dendorfer, S. A numerical study to determine the effect of ligament stiffness on kinematics of the lumbar spine during flexion. *BMC Musculoskelet. Disord.* **2016**, *17*, 1–7. [CrossRef] [PubMed]

66. Andersen, M.S.; Damsgaard, M.; Rasmussen, J. Force-dependent kinematics: A new analysis method for non-conforming joints. In Proceedings of the XIII International Symposium on Computer Simulation in Biomechanics, Leuven, Belgium, 30 June–2 July 2011.
67. Ignasiak, D.; Valenzuela, W.; Reyes, M.; Ferguson, S.J. The effect of muscle ageing and sarcopenia on spinal segmental loads. *Eur. Spine J.* **2018**, *27*, 2650–2659. [CrossRef]
68. Ignasiak, D. A novel method for prediction of postoperative global sagittal alignment based on full-body musculoskeletal modeling and posture optimization. *J. Biomech.* **2020**, *102*, 109324. [CrossRef]
69. Favier, C.D.; Finnegan, M.E.; Quest, R.A.; Honeyfield, L.; McGregor, A.H.; Phillips, A.T.M. An open-source musculoskeletal model of the lumbar spine and lower limbs: A validation for movements of the lumbar spine. *Comput. Methods Biomech. Biomed. Eng.* **2021**, *24*, 1310–1325. [CrossRef] [PubMed]
70. Malakoutian, M.; Sanchez, C.A.; Brown, S.H.; Street, J.; Fels, S.; Oxland, T.R. Biomechanical properties of paraspinal muscles influence spinal loading—A musculoskeletal simulation study. *Front. Bioeng. Biotechnol.* **2022**, *10*, 852201. [CrossRef] [PubMed]
71. Fasser, M.R.; Gerber, G.; Passaplan, C.; Cornaz, F.; Snedeker, J.G.; Farshad, M.; Widmer, J. Computational model predicts risk of spinal screw loosening in patients. *Eur. Spine J.* **2022**, *31*, 2639–2649. [CrossRef]
72. Bayoglu, R.; Galibarov, P.E.; Verdonschot, N.; Koopman, B.; Homminga, J. Twente Spine Model: A thorough investigation of the spinal loads in a complete and coherent musculoskeletal model of the human spine. *Med. Eng. Phys.* **2019**, *68*, 35–45. [CrossRef]
73. Bayoglu, R.; Geeraedts, L.; Groenen, K.H.J.; Verdonschot, N.; Koopman, B.; Homminga, J. Twente spine model: A complete and coherent dataset for musculo-skeletal modeling of the lumbar region of the human spine. *J. Biomech.* **2017**, *53*, 111–119. [CrossRef]
74. Bayoglu, R.; Geeraedts, L.; Groenen, K.H.J.; Verdonschot, N.; Koopman, B.; Homminga, J. Twente spine model: A complete and coherent dataset for musculo-skeletal modeling of the thoracic and cervical regions of the human spine. *J. Biomech.* **2017**, *58*, 52–63. [CrossRef]
75. Bayoglu, R.; Guldeniz, O.; Verdonschot, N.; Koopman, B.; Homminga, J. Sensitivity of muscle and intervertebral disc force computations to variations in muscle attachment sites. *Comput. Methods Biomech. Biomed. Eng.* **2019**, *22*, 1135–1143. [CrossRef]
76. Huang, M.; Hajizadeh, K.; Gibson, I.; Lee, T. Analysis of compressive load on intervertebral joint in standing and sitting postures. *Technol. Health Care* **2016**, *24*, 215–223. [CrossRef] [PubMed]
77. Guo, J.; Guo, W.; Ren, G. Embodiment of intra-abdominal pressure in a flexible multibody model of the trunk and the spinal unloading effects during static lifting tasks. *Biomech. Model. Mechanobiol.* **2021**, *20*, 1599–1626. [CrossRef] [PubMed]
78. Hansen, L.; de Zee, M.; Rasmussen, J.; Andersen, T.B.; Wong, C.; Simonsen, E.B. Anatomy and biomechanics of the back muscles in the lumbar spine with reference to biomechanical modeling. *Spine* **2006**, *31*, 1888–1899. [CrossRef] [PubMed]
79. Bogduk, N. *Clinical Anatomy of the Lumbar Spine and Sacrum*; Elsevier Health Sciences: Amsterdam, The Netherlands, 1997.
80. Pearcy, M.J.; Bogduk, N. Instantaneous axes of rotation of the lumbar intervertebral joints. *Spine* **1988**, *13*, 1033–1041. [CrossRef]
81. Byrne, R.M.; Aiyangar, A.K.; Zhang, X. Sensitivity of musculoskeletal model-based lumbar spinal loading estimates to type of kinematic input and passive stiffness properties. *J. Biomech.* **2020**, *102*, 109659. [CrossRef]
82. Kim, H.K.; Zhang, Y. Estimation of lumbar spinal loading and trunk muscle forces during asymmetric lifting tasks: Application of whole-body musculoskeletal modelling in OpenSim. *Ergonomics* **2017**, *60*, 563–576. [CrossRef]
83. von Arx, M.; Liechti, M.; Connolly, L.; Bangerter, C.; Meier, M.L.; Schmid, S. From Stoop to Squat: A comprehensive analysis of lumbar loading among different lifting styles. *Front. Bioeng. Biotechnol.* **2021**, *9*, 769117. [CrossRef]
84. Wang, W.; Wang, D.; De Groote, F.; Scheys, L.; Jonkers, I. Implementation of physiological functional spinal units in a rigid-body model of the thoracolumbar spine. *J. Biomech.* **2020**, *98*, 109437. [CrossRef]
85. Pearsall, D.J.; Reid, J.G.; Livingston, L.A. Segmental inertial parameters of the human trunk as determined from computed tomography. *Ann. Biomed. Eng.* **1996**, *24*, 198–210. [CrossRef]
86. Winter, D.A. *Biomechanics and Motor Control of Human Movement*; Wiley, Weilheim, Germany, 2009.
87. Fung, Y.C. *Biomechanics: Mechanical Properties of Living Tissues*; Springer Science & Business Media: Luxemburg, 2013.
88. Pintar, F.A.; Yoganandan, N.; Myers, T.; Elhagediab, A.; Sances, A., Jr. Biomechanical properties of human lumbar spine ligaments. *J. Biomech.* **1992**, *25*, 1351–1356. [CrossRef]
89. Heuer, F.; Schmidt, H.; Klezl, Z.; Claes, L.; Wilke, H.J. Stepwise reduction of functional spinal structures increase range of motion and change lordosis angle. *J. Biomech.* **2007**, *40*, 271–280. [CrossRef] [PubMed]
90. Ashton-Miller, J.A.; Schultz, A.B. Biomechanics of the human spine. *Basic Orthop. Biomech.* **1997**, *2*, 353–385.
91. Panjabi, M.M.; Brand, R., Jr.; White, A., 3rd. Mechanical properties of the human thoracic spine as shown by three-dimensional load-displacement curves. *JBJS* **1976**, *58*, 642–652. [CrossRef]
92. White, A.A. *Clinical Biomechanics of the Spine*; Lippincott Williams & Wilkins: Philadelphia, PA, USA, 2022.
93. Myklebust, J.B.; Pintar, F.; Yoganandan, N.; Cusick, J.F.; Maiman, D.; Myers, T.J.; Sances, A., Jr. Tensile strength of spinal ligaments. *Spine* **1988**, *13*, 526–531. [CrossRef]
94. Liebsch, C.; Graf, N.; Appelt, K.; Wilke, H.J. The rib cage stabilizes the human thoracic spine: An in vitro study using stepwise reduction of rib cage structures. *PLoS ONE* **2017**, *12*, e0178733. [CrossRef]
95. Wilke, H.J.; Grundler, S.; Ottardi, C.; Mathew, C.E.; Schlager, B.; Liebsch, C. In vitro analysis of thoracic spinal motion segment flexibility during stepwise reduction of all functional structures. *Eur. Spine J.* **2020**, *29*, 179–185. [CrossRef]
96. Cook, D.; Julias, M.; Nauman, E. Biological variability in biomechanical engineering research: Significance and meta-analysis of current modeling practices. *J. Biomech.* **2014**, *47*, 1241–1250. [CrossRef]

97. Akhavanfar, M.H.; Kazemi, H.; Eskandari, A.H.; Arjmand, N. Obesity and spinal loads; a combined MR imaging and subject-specific modeling investigation. *J. Biomech.* **2018**, *70*, 102–112. [CrossRef]
98. El Ouaaid, Z.; Shirazi-Adl, A.; Plamondon, A. Effects of variation in external pulling force magnitude, elevation, and orientation on trunk muscle forces, spinal loads and stability. *J. Biomech.* **2016**, *49*, 946–952. [CrossRef]
99. Eskandari, A.H.; Arjmand, N.; Shirazi-Adl, A.; Farahmand, F. Hypersensitivity of trunk biomechanical model predictions to errors in image-based kinematics when using fully displacement-control techniques. *J. Biomech.* **2019**, *84*, 161–171. [CrossRef]
100. Ghezelbash, F.; Shirazi-Adl, A.; Arjmand, N.; El-Ouaaid, Z.; Plamondon, A. Subject-specific biomechanics of trunk: Musculoskeletal scaling, internal loads and intradiscal pressure estimation. *Biomech. Model. Mechanobiol.* **2016**, *15*, 1699–1712. [CrossRef] [PubMed]
101. Little, J.P.; Adam, C.J. Geometric sensitivity of patient-specific finite element models of the spine to variability in user-selected anatomical landmarks. *Comput. Methods Biomech. Biomed. Eng.* **2015**, *18*, 676–688. [CrossRef] [PubMed]
102. Naserkhaki, S.; Jaremko, J.L.; El-Rich, M. Effects of inter-individual lumbar spine geometry variation on load-sharing: Geometrically personalized Finite Element study. *J. Biomech.* **2016**, *49*, 2909–2917. [CrossRef] [PubMed]
103. Périé, D.; Sales De Gauzy, J.; Hobatho, M.C. Biomechanical evaluation of Cheneau-Toulouse-Munster brace in the treatment of scoliosis using optimisation approach and finite element method. *Med. Biol. Eng. Comput.* **2002**, *40*, 296–301. [CrossRef] [PubMed]
104. Vergari, C.; Courtois, I.; Ebermeyer, E.; Bouloussa, H.; Vialle, R.; Skalli, W. Experimental validation of a patient-specific model of orthotic action in adolescent idiopathic scoliosis. *Eur. Spine J.* **2016**, *25*, 3049–3055. [CrossRef]
105. Wong, K.W.N.; Luk, K.D.K.; Leong, J.C.Y.; Wong, S.F.; Wong, K.K.Y. Continuous Dynamic Spinal Motion Analysis. *Spine* **2006**, *31*, 414–419. [CrossRef]
106. Sekuboyina, A.; Husseini, M.E.; Bayat, A.; Löffler, M.; Liebl, H.; Li, H.; Tetteh, G.; Kukačka, J.; Payer, C.; Štern, D. VerSe: A vertebrae labelling and segmentation benchmark for multi-detector CT images. *arXiv* **2020**, arXiv:2001.09193.
107. Hill, A.V. The heat of shortening and the dynamic constants of muscle. *Proc. R. Soc. London. Ser. B-Biol. Sci.* **1938**, *126*, 136–195.
108. Thelen, D.G. Adjustment of muscle mechanics model parameters to simulate dynamic contractions in older adults. *J. Biomech. Eng.* **2003**, *125*, 70–77. [CrossRef]
109. Millard, M.; Uchida, T.; Seth, A.; Delp, S.L. Flexing computational muscle: Modeling and simulation of musculotendon dynamics. *J. Biomech. Eng.* **2013**, *135*, 021005. [CrossRef]
110. Delp, S.L.; Loan, J.P.; Hoy, M.G.; Zajac, F.E.; Topp, E.L.; Rosen, J.M. An interactive graphics-based model of the lower extremity to study orthopaedic surgical procedures. *IEEE Trans. Biomed. Eng.* **1990**, *37*, 757–767. [CrossRef]
111. Hamner, S.R.; Seth, A.; Delp, S.L. Muscle contributions to propulsion and support during running. *J. Biomech.* **2010**, *43*, 2709–2716. [CrossRef]
112. Anderson, F.C.; Pandy, M.G. A dynamic optimization solution for vertical jumping in three dimensions. *Comput. Methods Biomech. Biomed. Eng.* **1999**, *2*, 201–231. [CrossRef] [PubMed]
113. Senteler, M.; Aiyangar, A.; Weisse, B.; Farshad, M.; Snedeker, J.G. Sensitivity of intervertebral joint forces to center of rotation location and trends along its migration path. *J. Biomech.* **2018**, *70*, 140–148. [CrossRef] [PubMed]
114. Takahashi, I.; Kikuchi, S.i.; Sato, K.; Sato, N. Mechanical load of the lumbar spine during forward bending motion of the trunk-a biomechanical study. *Spine* **2006**, *31*, 18–23. [CrossRef] [PubMed]
115. Wang, Q.D.; Guo, L.X. Biomechanical role of osteoporosis in the vibration characteristics of human spine after lumbar interbody fusion. *Int. J. Numer. Methods Biomed. Eng.* **2020**, *36*, e3402. [CrossRef]
116. Rockenfeller, R.; Müller, A. Augmenting the Cobb angle: Three-dimensional analysis of whole spine shapes using Bézier curves. *Comput. Methods Programs Biomed.* **2022**, *225*, 107075. [CrossRef]
117. Kim, J.W.; Eom, G.M.; Kwon, Y.R. Analysis of maximum joint moment during infant lifting-up motion. *Technol. Health Care* **2022**, *30*, S441–S450. [CrossRef]
118. Nowakowska-Lipiec, K.; Michnik, R.; Linek, P.; Myśliwiec, A.; Jochymczyk-Woźniak, K.; Gzik, M. A numerical study to determine the effect of strengthening and weakening of the transversus abdominis muscle on lumbar spine loads. *Comput. Methods Biomech. Biomed. Eng.* **2020**, *23*, 1287–1296. [CrossRef]
119. Bauer, S.; Paulus, D. Analysis of the biomechanical effects of spinal fusion to adjacent vertebral segments of the lumbar spine using multi body simulation. *Int. J. Simulation: Syst. Sci. Technol.* **2014**, *15*, 1–7. [CrossRef]
120. Pfirrmann, C.W.; Metzdorf, A.; Zanetti, M.; Hodler, J.; Boos, N. Magnetic resonance classification of lumbar intervertebral disc degeneration. *Spine* **2001**, *26*, 1873–1878. [CrossRef]
121. Foltz, M.H.; Kage, C.C.; Johnson, C.P.; Ellingson, A.M. Noninvasive assessment of biochemical and mechanical properties of lumbar discs through quantitative magnetic resonance imaging in asymptomatic volunteers. *J. Biomech. Eng.* **2017**, *139*, 111002. [CrossRef]
122. Bogduk, N.; Macintosh, J.E.; Pearcy, M.J. A universal model of the lumbar back muscles in the upright position. *Spine* **1992**, *17*, 897–913. [CrossRef] [PubMed]
123. Aiyangar, A.; Zheng, L.; Anderst, W.; Zhang, X. Instantaneous centers of rotation for lumbar segmental extension in vivo. *J. Biomech.* **2017**, *52*, 113–121. [CrossRef]
124. Daggfeldt, K.; Thorstensson, A. The mechanics of back-extensor torque production about the lumbar spine. *J. Biomech.* **2003**, *36*, 815–825. [CrossRef] [PubMed]

125. Hodges, P.W.; Cresswell, A.G.; Daggfeldt, K.; Thorstensson, A. In vivo measurement of the effect of intra-abdominal pressure on the human spine. *J. Biomech.* **2001**, *34*, 347–353. [CrossRef] [PubMed]
126. Rasmussen, J.; Damsgaard, M.; Voigt, M. Muscle recruitment by the min/max criterion—A comparative numerical study. *J. Biomech.* **2001**, *34*, 409–415. [CrossRef]
127. Crowninshield, R.D.; Brand, R.A. A physiologically based criterion of muscle force prediction in locomotion. *J. Biomech.* **1981**, *14*, 793–801. [CrossRef]
128. Ezati, M.; Ghannadi, B.; McPhee, J. A review of simulation methods for human movement dynamics with emphasis on gait. *Multibody Syst. Dyn.* **2019**, *47*, 265–292. [CrossRef]
129. Anderson, F.C.; Pandy, M.G. Static and dynamic optimization solutions for gait are practically equivalent. *J. Biomech.* **2001**, *34*, 153–161. [CrossRef]
130. Morrow, M.M.; Rankin, J.W.; Neptune, R.R.; Kaufman, K.R. A comparison of static and dynamic optimization muscle force predictions during wheelchair propulsion. *J. Biomech.* **2014**, *47*, 3459–3465. [CrossRef] [PubMed]

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Validation of a Patient-Specific Musculoskeletal Model for Lumbar Load Estimation Generated by an Automated Pipeline From Whole Body CT

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Background: Chronic back pain is a major health problem worldwide. Although its causes can be diverse, biomechanical factors leading to spinal degeneration are considered a central issue. Numerical biomechanical models can identify critical factors and, thus, help predict impending spinal degeneration. However, spinal biomechanics are subject to significant interindividual variations. Therefore, in order to achieve meaningful findings on potential pathologies, predictive models have to take into account individual characteristics. To make these highly individualized models suitable for systematic studies on spinal biomechanics and clinical practice, the automation of data processing and modeling itself is inevitable. The purpose of this study was to validate an automatically generated patient-specific musculoskeletal model of the spine simulating static loading tasks.

Methods: CT imaging data from two patients with non-degenerative spines were processed using an automated deep learning-based segmentation pipeline. In a semi-automated process with minimal user interaction, we generated patient-specific musculoskeletal models and simulated various static loading tasks. To validate the model, calculated vertebral loadings of the lumbar spine and muscle forces were compared with *in vivo* data from the literature. Finally, results from both models were compared to assess the potential of our process for interindividual analysis.

Results: Calculated vertebral loads and muscle activation overall stood in close correlation with data from the literature. Compression forces normalized to upright standing deviated by a maximum of 16% for flexion and 33% for lifting tasks. Interindividual comparison of compression, as well as lateral and anterior–posterior shear forces, could be linked plausibly to individual spinal alignment and bodyweight.

Conclusion: We developed a method to generate patient-specific musculoskeletal models of the lumbar spine. The models were able to calculate loads of the lumbar spine for static activities with respect to individual biomechanical properties, such as spinal alignment, bodyweight distribution, and ligament and muscle insertion points. The process is automated to a large extent, which makes it suitable for systematic investigation of spinal biomechanics in large datasets.

Keywords: musculoskeletal multibody dynamics, spinal biomechanics, patient-specific, lumbar alignment, automated model generation, spinal loading, muscle force computation, chronic back pain

1 INTRODUCTION

Chronic back pain is considered a major burden for patients and healthcare systems worldwide. Though general risk factors, such as occupation, obesity, or anthropometric parameters, could be identified in the past years (Murtezani et al., 2011), specification of individual indicators for the prediction of symptoms and chronicity is challenging. The invasive character of *in vivo* measurement via intradiscal pressure sensors (Sato et al., 1999; Wilke et al., 2001) or instrumented vertebral implants (Rohlmann et al., 2008; Dreischarf et al., 2016) makes these methods unsuitable for clinical analysis. Computational biomechanical models can provide a valuable alternative when it comes to the estimation of spinal loads. However, biomechanics of the human spine are subject to a variety of influencing factors, such as spinal alignment, body weight distribution, the function of muscles, degeneration of connective tissues, and other preconditions of the musculoskeletal system. Due to the highly individual character of these factors, as many of them as possible should be considered during the modeling process to generate meaningful biomechanical models of the spine. The assessment of relevance to accounting for biological variation in biomedical engineering regarding modeling was the subject of several studies (Cook et al., 2014; Bruno et al., 2017; Akhavanfar et al., 2018; Iyer et al., 2018).

Biomechanical models have been widely used to gain insights into healthy and pathological biomechanics of the spine. While finite element models exist that account for individual characteristics (Akhavanfar et al., 2018; El Ouaaid et al., 2016; Eskandari et al., 2019; Ghezelbash et al., 2016; Little and Adam, 2015; Naserkhaki et al., 2016; Périé et al., 2002; Vergari et al., 2016), multibody models are predominantly generic or focus on specific pathologies such as adolescent idiopathic scoliosis (Jalalian et al., 2017; Petit et al., 2004). The neglect or only limited consideration of interindividual variation makes these models poorly suited for a detailed subject-specific analysis. In recent years, several such models were published (Delp et al., 2007; Christophy et al., 2012; Bruno et al., 2015; Actis et al., 2018; Favier et al., 2021; Bassani et al., 2019; de Zee et al., 2007; Han et al., 2012; Kim and Zhang, 2017; Liu et al., 2019). These generic models are often based on average anthropometric data (Bassani et al., 2019; de Zee et al., 2007; Han et al., 2012; Kim and Zhang, 2017; Liu et al., 2019) or detailed models based on cadaver studies (Bayoglu et al., 2017a; b, 2019). The necessary input to create accurate, individualized models can be provided by imaging data (Senteler et al., 2014; Dao et al., 2015; Dao et al., 2015; Hajihosseinali et al., 2015; Bruno et al., 2017; Favier et al., 2021). A study recently published by Fasser et al. introduced a pipeline for the generation of semi-individualized multi-body models of the spine based on manually annotated EOS imaging data (Fasser et al., 2021). In general, individualization of biomechanical models usually involves a time-consuming, manual or semi-automated process, which requires expert knowledge and therefore, makes it poorly suited for clinical applications.

On the way to integration of patient-specific numerical models in clinical practice, Zadpoor et al. identified two key parameters: accuracy and cost-effectiveness (Zadpoor and Weinans, 2015). While the aspect of accuracy can be covered by using imaging data (Blemker et al., 2007), the aspect of cost-effectiveness should be addressed by automating involved processes to a large extent. In 2021, Cina et al. published a deep learning process to identify landmarks for vertebral corners from radiographs (Cina et al., 2021). To this date, automated approaches for modeling from medical imaging are rare in the literature. In 2021, Caprara et al. introduced the first automated pipeline for the generation of patient-specific finite element models of the functional spine unit using a combination of deep learning, statistical, and FE methods on 3D CT scans (Caprara et al., 2021). To the best of our knowledge, a similar approach for multi-body modeling does not exist in the literature.

We established the first framework for a fully automated pipeline to derive individual biomechanical models from imaging data for the estimation of spinal loads to determine functional anthropometric parameters. The objective of this study is the validation of a musculoskeletal model of the torso with subject-specific spinal geometries and soft tissue distribution.

2 METHODS

Input data for the automated modeling process were derived from a deep learning-based pipeline for automated vertebrae segmentation and extraction of spinal characteristics from CT scans. We incorporated a detailed muscle architecture for the lumbar region, simulated various static activities, and compared estimated muscle forces and vertebral loading with *in vivo* data from the literature. Finally, an interindividual analysis of two models derived from two datasets served as proof of concept for

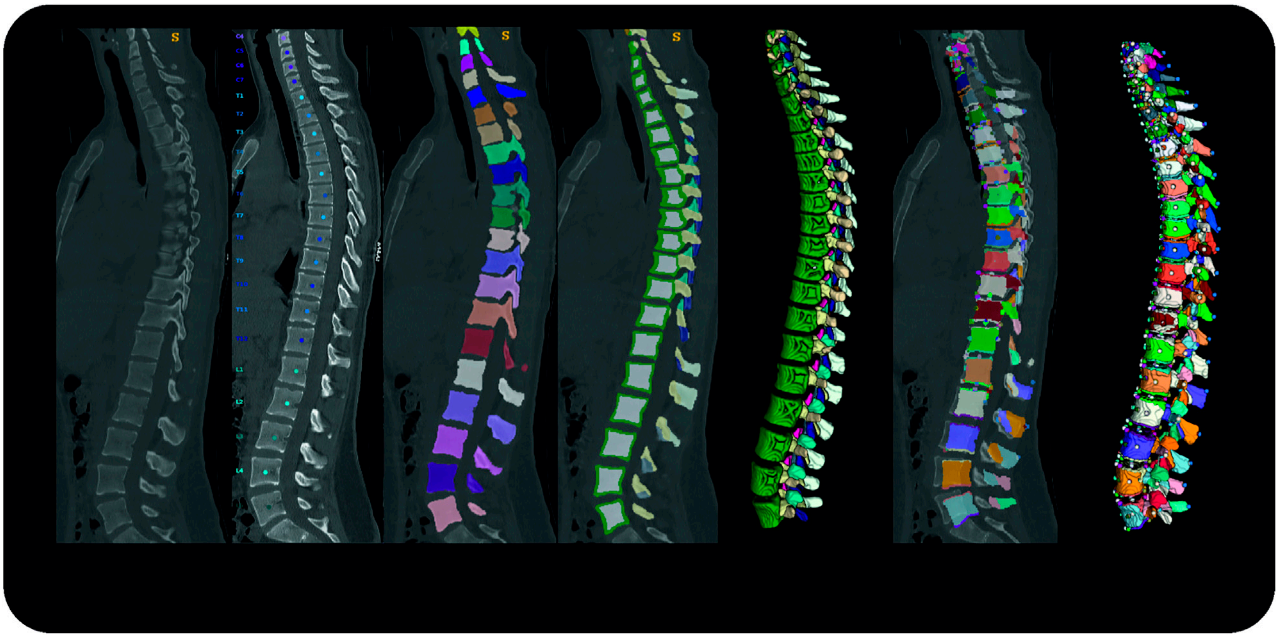

FIGURE 1 | Pipeline Overview from left to right; original data, vertebrae identification; vertebrae segmentation; subregion segmentation (cross-section and 3D rendering); re-alignment in craniocaudal direction and calculation of points of interest; 3D rendering of the final dataset.

the potential of our process to systematically investigate individual spinal loading.

2.1 Automated Extraction of Spinal Geometries and Points of Interest

The processing and extraction of patient data described in the following section were executed from asynchronously phantom-based calibrated CT image data (Kaesmacher et al., 2017). We labeled and segmented vertebrae using an automated deep learning-based process for vertebrae segmentation, which is described in detail elsewhere (Sekuboyina et al., 2020). In brief, three artificial neural networks (ANNs) are used to 1) detect the spine, 2) identify and label each vertebra as well as 3) segment each vertebra based on the label. The latter two steps were reviewed by a radiologist and could potentially be corrected. For each vertebra, centroids, as well as segmentation masks for eleven subregions, were generated using a fourth ANN: vertebral body (further divided into the cortex and the trabecular compartment), vertebral arch, spinous process, as well as transverse processes. Before calculating necessary points of interest, the centroids of the first thoracic and last lumbar vertebra were aligned vertically to account for posture differences between supine from CT scans and upright position. Thereafter, these data were used to calculate relevant points for muscle and ligament attachments. **Figure 1** shows the overall process.

Subsequently, we defined points of interest for each individual vertebra. Therefore, the algorithm iterated over each vertebra, creating bounding boxes based on its binary segmentations. Corresponding to those bounding boxes, individual subregion segmentations were used to define landmarks for muscle and ligament attachment points by geometrical extreme values as shown in **Figure 2A**. Thus, depending on the subregion, the most posterior, inferior, superior, or lateral point on the surface was determined by its minimal and maximal coordinate values along the corresponding spatial axis. Based on centroid positions, auxiliary sagittal and horizontal planes were set through the vertebral body to extract its attachment points (**Figure 2B**). In the horizontal sectional plane, the most lateral points on each side of the vertebral body were extracted. In the sagittal sectional plane, a rectangle is fitted around the subregion of the vertebral body. The corner and center points of the rectangle border were then projected onto the surface by the shortest distance. Using a similar function, attachment points on the vertebral arch were determined via the minimal distance between the anterior border of its sectional plane and posterior points in the vertebral body. The plane was then shifted right and left and the process was repeated.

We assumed the location of the intervertebral joint to be the midpoint of the straight line connecting the central points of the lower and upper endplates of the two vertebrae representing one motion segment (**Figure 3**). We used a spline interpolation of all vertebral body centroids to define intervertebral joint orientation by calculating the spline derivative at the intersection with the upper endplate of the inferior vertebra.

To account for individual torso weight distribution, a segmentation mask for lung, fat, and muscle/organ tissue was created based on typical CT intensity ranges. Subsequently, the segmented tissue was assigned to the nearest vertebra depending

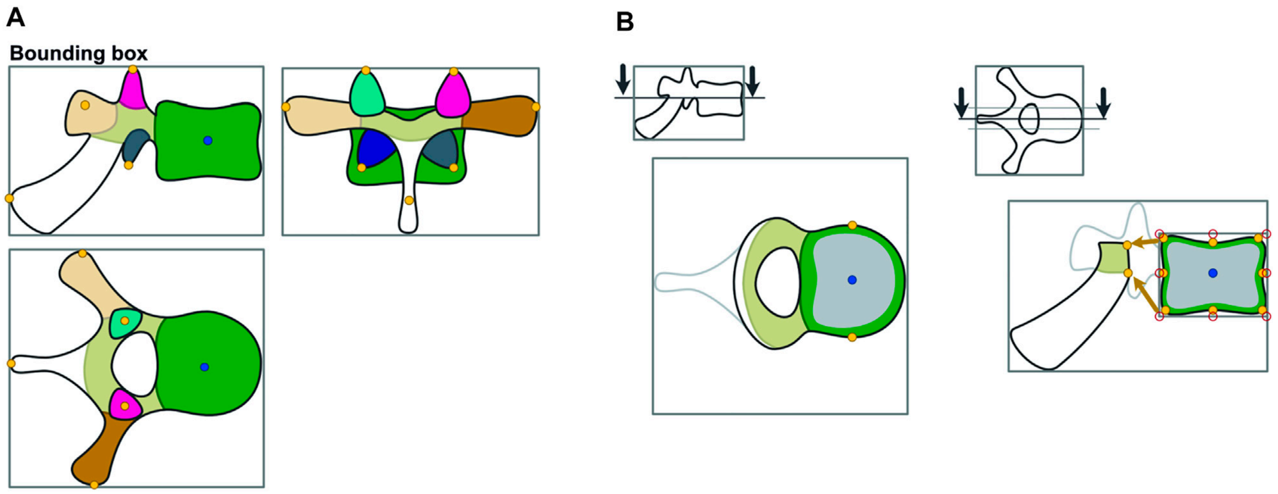

FIGURE 2 | Calculation of points of interest. The vertebra is divided in subregions, which are used further to identify landmarks based on geometrical extreme values **(A)**. Horizontal and auxiliary planes are inserted to identify points of interest of the vertebral body via a projection of the border points of a bounding box on the respective subregion **(B)**.

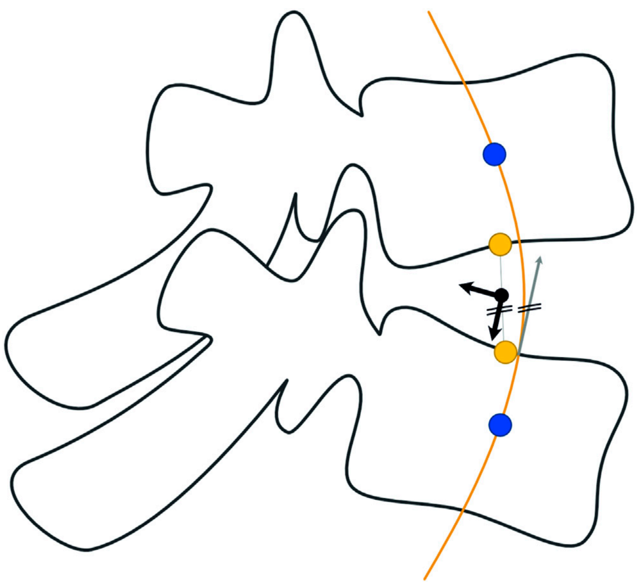

FIGURE 3 | Determination of intervertebral joint location and orientation. The position of the joint is assumed to be the midpoint of the straight line connecting the central points of the endplates. Orientation of the marker is defined via the derivative of intersection of the spline interpolation of vertebral centroids.

on its minimal anterior–posterior distance. Thus, the torso weight was subdivided into segments for each vertebral level. For each segment, the algorithm calculated its center of mass and total weight corresponding to its individual tissue distribution. We assume to have an average density of 0.25 g/cm^3 for the lung, 0.96 g/cm^3 for fat, and 1.06 g/cm^3 for the remaining soft tissues (Pearsall et al., 1996; Akhavanfar et al., 2018).

2.2 Individualized Musculoskeletal Model of the Thoracolumbar Spine

The automated modeling of the thoracolumbar spine with generic bodies of the head–neck complex, ribcage, simplified upper extremities, and the pelvic-sacral region is carried out using the multibody simulation software SIMPACK (Dassault systèmes, France). The thoracolumbar spine includes individual information on vertebrae T1-L5, insertion points for muscles and ligaments, spinal alignment, as well as paraspinal soft tissue distribution as described in the previous chapter. Bodies for the head–neck system, ribcage, sacrum, and pelvis are individually scaled according to Winter (2005) and equipped with relevant points for muscle insertion and integrated into the model. Neglecting facet joints and intraabdominal pressure, lumbar intervertebral joints are modeled as actuated spherical joints to ensure necessary stability. The thoracic spine, head–neck, and ribcage are modeled as one rigid body, and segment masses for soft tissue are rigidly fixed to each vertebra according to the calculated centers of mass. Segment masses relative to overall torso mass calculated from the CTs (Winter, 2005) were assigned to the bodies for head–neck and simplified arms. The masses of bony structures were calculated assuming a density of 1.5 g/cm^3 (Pearsall et al., 1996; Akhavanfar et al., 2018). Intervertebral discs, as well as ligaments, are modeled as nonlinear, viscoelastic force elements. Occurring moments in the intervertebral discs are characterized by a nonlinear load–deformation relationship (Rupp et al., 2015; White, 2022). Specific data on stiffness and neutral zones of the intervertebral discs were taken from White (2022). The model includes anterior and posterior longitudinal ligament (ALL and PLL), flavum ligament (LF), interspinal ligament (ISL), and supraspinal ligament (SSL). The characteristic force–length curve for the elastic behavior of ligaments (**Figure 4**) shows a nonlinear toe region in the region of small deformations (A),

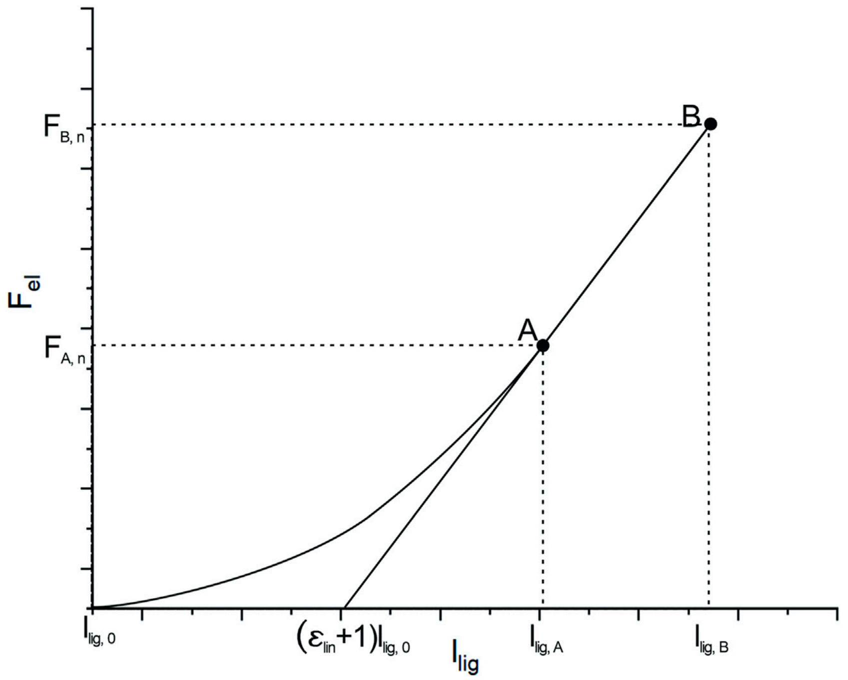

FIGURE 4 | Typical force–length curve to describe the mechanical behavior of ligaments. Transition from nonlinear to linear regions are defined by l_A and F_A and F_B and l_B marks the maximum force and elongation before failure occurs.

followed by a linear elastic region before the final failure of the ligament (B). Inspired by the study cited herein(Rupp et al., 2015), their nonlinear force–length characteristics are described in **Eq. 1**.

$$F_{el}\left(l_{lig}\right) = \begin{cases} 0, & \text{for } l_{lig} \le l_{lig,0} \\ K_{nl}\left(l_{lig} - l_{lig,0}\right)^{exp_{nll}}, & \text{for } l_{lig} \le l_{lig,A} \\ F_{A,n} + K_{lin}\left(l_{lig} - l_{lig,A}\right), & \text{for } l_{lig} > l_{lig,A} \end{cases} \quad (1)$$

with

$l_{lig,0} = (1 - \epsilon_{pre})l_{neut}$	, where l_{neut} is the individually measured length for each ligament segment in neutral position and ϵ_{pre} is the individual pre-strain
$F_{A/B,n} = \frac{F_{A/B}}{n}$	, where n is the number of parallel components for each ligament and F_A is the ligament force at point A (same for B)
$l_{lig,A/B} = (1 + \epsilon_{A/B})l_{lig,0}$	, where l_A is the length at point A and ϵ_A (same for B)
$K_{lin} = \frac{F_{B,n} - F_{A,n}}{l_{lig,B} - l_{lig,A}}$	, where K_{lin} is the elastic stiffness in the linear region
$\epsilon_{lin} = \frac{F_{A,n}}{K_{lin} l_{lig,0}}$	, where ϵ_{lin} is the strain at the intersection of the applied tangent from the linear region with the abscissa
$exp_{nll} = \frac{\epsilon_A}{\epsilon_{lin}}$	, where exp_{nll} defines the order of non-linearity of the toe region
$K_{nl} = \frac{F_{A,n}}{(\epsilon_A l_{lig,0})^{exp_{nll}}}$	, where K_{nl} is the individual factor that defines stretch/compression of the toe-region

Individual lengths for ligament segments are measured directly in the model in neutral position, which is what we considered upright standing. Values for initial ligament lengths were calculated considering values for pre-strain from the studies cited herein (Nachemson and Evans, 1968; Aspden, 1992; Robertson et al., 2013). The main difference to the mechanical law provided by Rupp et al. is that we take relative strain values for $l_{lig,A}$ and $l_{lig,B}$ instead of absolute elongations. Therefore, we guarantee uniform preloads within one ligamentous structure for the neutral position. Parameters for strains ϵ_A,ϵ_B, and Forces F_A and F_B at points A and B, are taken from the study referred herein (Chazal et al., 1985).

2.3 Muscle Force Calculation

Nine muscle groups of the lower back and abdomen are included in the model as 103 point-to-point actuators: rectus abdominis (RA), internal obliques (IO), external obliques (EO), psoas major (PM), quadratus lumborum (QL), multifidus (MF), longissimus thoracis pars lumborum (LL), iliocostalis lumborum (IL) and the interspinales lumborum (IS) (**Figure 5**). Globally acting muscles RA, IO, and EO, as well as those muscle fascicles of LL, QL, and IL attached to the ribcage, are simplified each to one actuator per side. Muscles acting locally on the lumbar spine are modeled in detail based on attachment points taken from a cadaver study

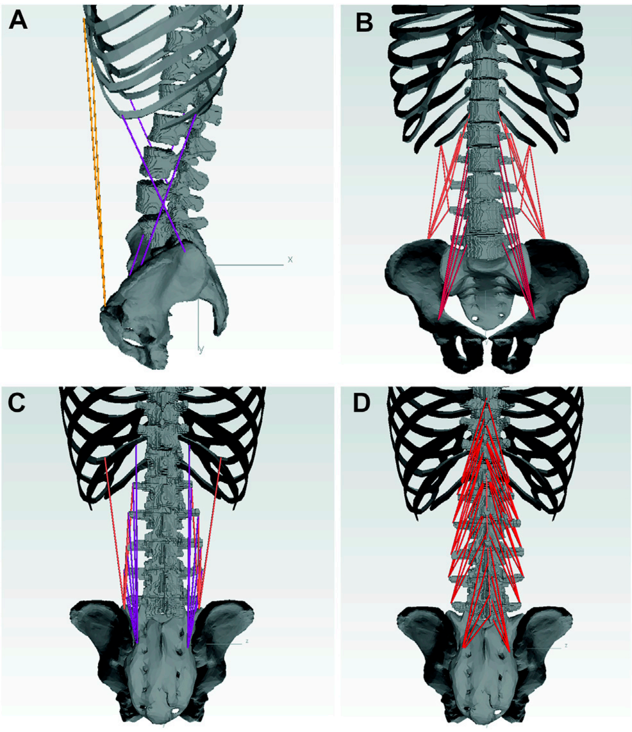

FIGURE 5 | Musclegroups included in the model with: RA, EO, IO **(A)**; QL, PM **(B)**; LL, IL **(C)**; MF, IS **(D)**.

(Bayoglu et al., 2017a). Muscle fascicles attached to the same subregion were combined and physiological cross-sectional areas (PCSA) based on Christophy et al. (2012) were assigned to respective fascicles.

The MBS model calculates necessary joint moments M to hold the imposed static positions, which are transferred to Matlab via a SIMULINK model, where muscle forces are calculated using a static optimization approach (Gagnon et al., 2001). In order to increase the chances of finding a global optimum, we used the globalsearch solver (Global Optimization Toolbox, Matlab 2020b) to solve the following optimization problem:

$$Minimize\left(CostFunktion = \sum_{i=1}^{n}\left(\frac{F_i}{PCSA_i}\right)^3\right) \quad (2)$$

subject to equality constraints

$$c_{eq} = \begin{pmatrix} M_{x,1} \\ \dots \\ M_{z,i} \end{pmatrix} = 0 \quad (3)$$

and bound constraints

$$0 \le F_i \le \sigma_{max} PCSA_i \quad (4)$$

Focusing on vertebral loading in the sagittal and frontal plane, equality constraints consider respective moments (x for frontal, z for sagittal) occurring in each lumbar intervertebral joint. Only active forces are taken into account neglecting the passive elastic behavior of muscular tissues. To guarantee compliance with the equilibrium conditions for all load cases, maximal muscle stress (MMS) was first set to 0.6 MPa, (Arjmand et al., 2009), and then to 1 MPa (Bruno et al., 2015; Beaucage-Gauvreau et al., 2019; Favier et al., 2021).

2.4 Individual Characteristics of Selected Subjects

For model validation, we built models based on two nondegenerative spine datasets (**Figure 6**). We selected datasets of two young patients (1 M, 1 F) with anthropometric data as comparable as possible to the subjects in comparative studies (Wilke et al., 2001; Takahashi et al., 2006; Rohlmann et al., 2008).

Anthropometric data, such as body height and weight, was calculated in reference to individual spine height and torso weight from CT data according to the study cited herein Winter (2005). To characterize individual spinal alignment, we measured kyphosis and lordosis angles for T1-T12, and L1-S1 in the sagittal plane, as well as Cobb angles for C7-T12, in the frontal plane and these are summarized in **Table 1**.

2.5 Model Validation

We evaluated predicted muscle forces and spinal loading for various activities. The load cases were selected based on previous studies on the measurement of intradiscal pressure and muscle activation (Wilke et al., 2001; Rohlmann et al., 2008). **Table 2** summarizes all investigated load cases.

Since the subjects from *in vivo* studies were all men (**Table 2**), we only used the model based on the dataset of the male for validation. Prior to the simulation of dedicated load cases, we used an optimization routine to determine the optimal position for upright standing. Assuming the optimal position to be energy efficient, joint angles of the lumbosacral spine (T12—Sacrum) were optimized, subject to minimization of occurring joint moments in the sagittal plane. We adopted determined joint angles as the starting posture for a neutral stance in the further course.

Applied flexion was assumed to be 40% sacral rotation and 60% lumbar flexion (Liu et al., 2018). According to the studies referred herein (Wong et al., 2006; Christophy et al., 2012), lumbar flexion was distributed 25.5% for L1/L2, 23.1% for L2/L3, 20.4% for L3/L4, 18.5% for L4/L5, and 12.5% for L5/S1.

Ligament modeling was evaluated based on their stress states during each load case with a focus on whether they were within a physiological range or whether failure could already be expected. Calculated lumbar loads were compared to respective vertebral load measurements and predicted muscle forces were evaluated in the context of measured EMG signals from experimental studies.

2.6 Potential for Systematic Analysis of Spinal Loads—Proof of Concept

To determine the potential of our pipeline regarding the systematic investigation of individual spinal loads, we compared generated results for both patients considering their individual spinal alignment. For this, compensation angles for an upright position, as well as estimated muscle forces and spinal

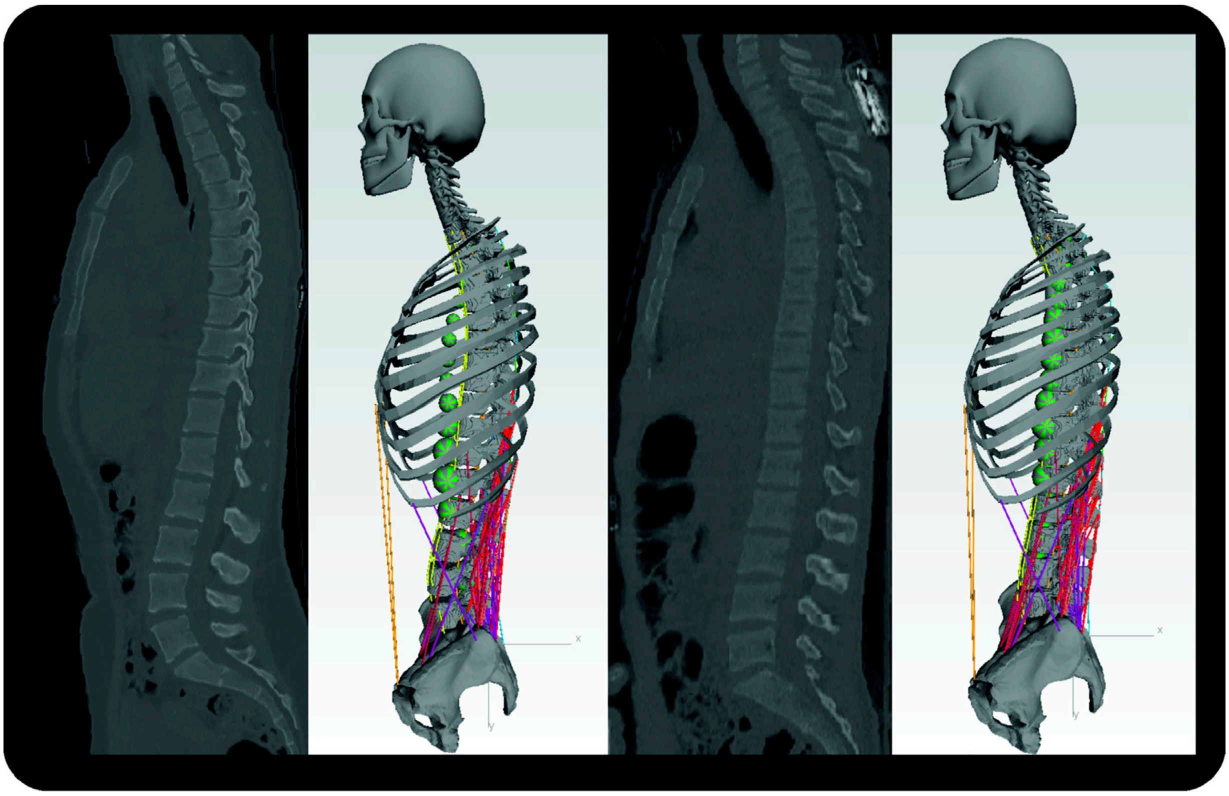

FIGURE 6 | Sagittal CT images of subject one (left) and subject two with respective MBS models. Segment masses for soft tissues are visualized by the green spheres. For the sake of clarity, the dummy bodies for the arms are not shown here.

TABLE 1 | Anthropometric data and parameters on the individual spinal alignment of selected subjects.

	Anthropometric Data	Lumbar lordosis	Thoracic kyphosis	Thoracic skoliosis
Subject 1	F	29°	31°	18°
	1.76 m	—	—	right-convex
	65 kg	—	—	—
Subject 2	M	11°	27°	—
	1.73 m	—	—	—
	86 kg	—	—	—

TABLE 2 | Load cases taken from *in vivo* studies used for validation of the model. Spinal loading was measured using intradiscal pressure (IDP) sensors (Wilke et al., 2001; Takahashi et al., 2006) or instrumented vertebral implants (Rohlmann et al., 2008).

Load cases	Subject (M)	Study type	Measured	References
Standing	1	*In vivo*	IDP L4/L5	Wilke et al. (2001)
Standing with 20 kg 20 cm from chest	—	—	—	—
Standing with 20 kg 55 cm from chest	—	—	—	—
Standing	2	*In vivo*	L1 Implant Load	Rohlmann et al. (2008)
30 deg Flexion	—	—	—	—
Elevate both arms	—	—	—	—
Standing (w/o weight and 10 kg)	3	*In vivo*	IDP L4/L5	Takahashi et al. (2006)
10 deg Flexion (w/o weight and 10 kg)	—	—	—	—
20 deg Flexion (w/o weight and 10 kg)	—	—	—	—
30 deg Flexion (w/o weight and 10 kg)	—	—	—	—

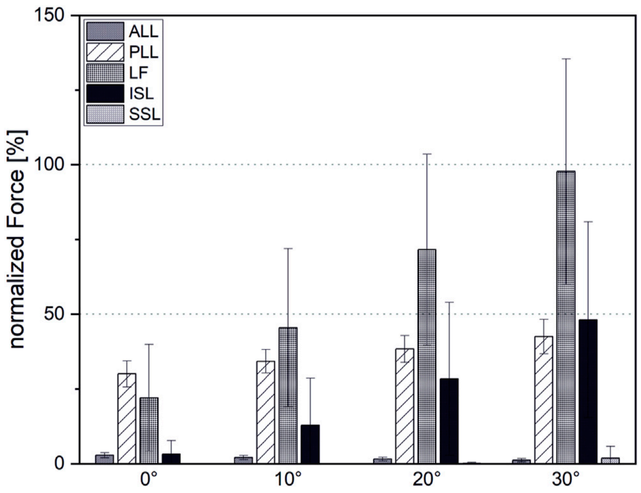

FIGURE 7 | Ligament forces normalized to maximal force at the end of the linear region before failure.

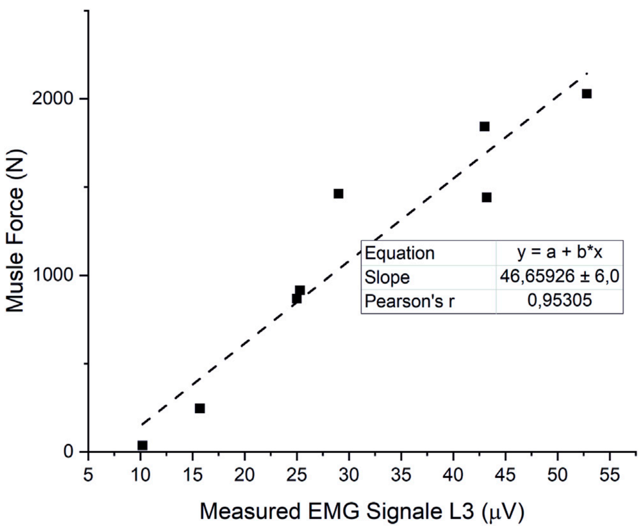

FIGURE 8 | Correlation of estimated ES forces and measured EMG signals from (Takahashi et al., 2006).

loads, were compared, put into context with the identified curvature of each subject in the frontal and sagittal plane, and analyzed for plausibility.

3 RESULTS

3.1 Ligament Forces

For initial simulations with LF pre-strain taken from the study referred herein (Nachemson and Evans, 1968), the occurring LF forces exceeded physiological maximum forces even for low-intensity flexions (< 10°). We reduced pre-strain from 10% to 5%, which still lies within the standard deviation of experimentally determined values (Nachemson and Evans,

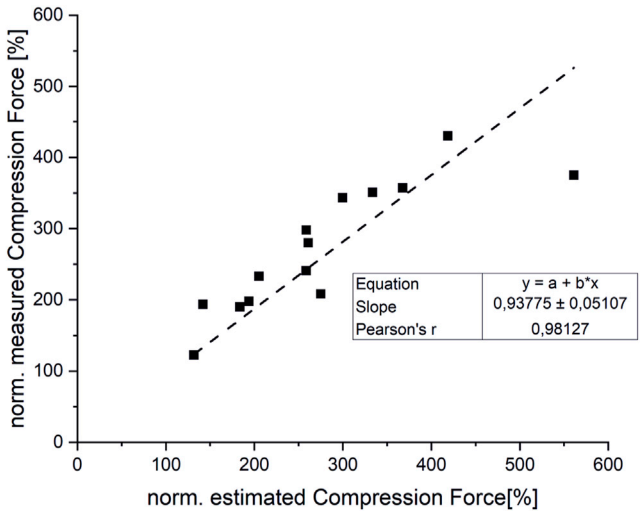

FIGURE 9 | Correlation between measured and estimated compression forces (normalized to upright standing).

1968) (**Figure 7**). Mean normalized forces were within a physiological range for all ligaments during investigated loading tasks. However, despite adjusted pre-strain, the average LF force reaches close to 100% with standard deviations of up to 37% during 30°flexion. The remaining ligament showed low (ALL, PLL, SSL) to moderate (PLL, ISL) loading, with a less than 2% and 50%, respectively.

3.2 Muscle Force Estimation

The estimated muscle forces of the erector spinae correlated closely (r = 0.95) with measured EMG-signals from Takahashi et al. (2006) (**Figure 8**). Initial simulations with a detailed muscular architecture according to Bayoglu et al. (2017a), under consideration of physiological MMS 60 N/cm^2, could not satisfy equilibrium conditions for all models, even for moderately intense activities, such as 30° flexion. Even increasing the MMS to 1 MPa was not sufficient to reliably satisfy the equilibrium conditions for all cases, though this mainly affected high-intensity cases, such as extensive flexion with additional weight. Therefore, we adapted muscle properties according to a validated musculoskeletal model from literature (Christophy et al., 2012). However, Christophy's model includes no muscle fascicles for the IS, nor those fascicles of the MF attached to the thoracic spine, which we added and in order to guarantee compliance with the equilibrium conditions, equipped with PCSAs of 1 cm^2, which is rather at the higher end of the range of measured values for MF fascicles (Bayoglu et al., 2017a).

3.3 Vertebral Loading

Overall, the estimated compression loads on intervertebral joints for various static loading tasks showed a good correlation with reported spinal load measurements (r = 0,98) (**Figure 9**). However, our model slightly underpredicted compression forces normalized to upright standing compared to measured forces from the study cited herein (Takahashi et al., 2006) by up to

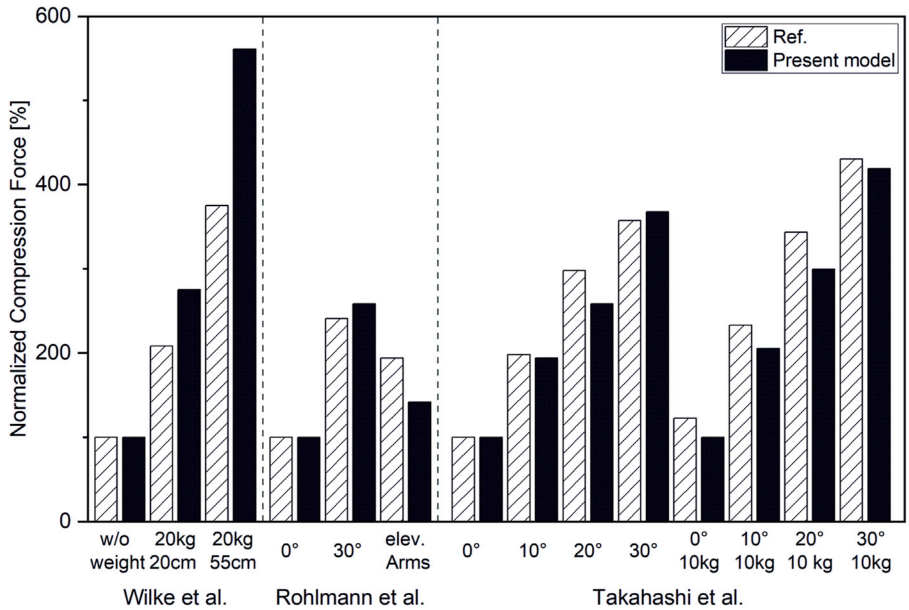

FIGURE 10 | Compression forces normalized to respective forces in upright standing position for L4/L5 (Wilke et al., 2001; Takahashi et al., 2006) and T12/L1 (Rohlmann et al., 2008).

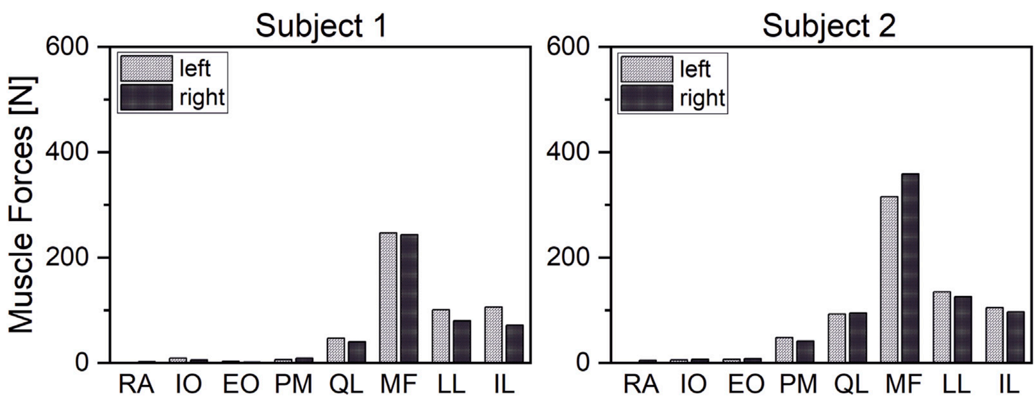

FIGURE 11 | Comparison of interindividual muscle forces at 20°flexion.

16%. Normalized compression forces for upright standing with 20 kg weight held 55 cm from the Sacrum were overestimated by 33% compared to data from the respective comparative study (Wilke et al., 2001) (**Figure 10**).

3.4 Influence of Individual Characteristics on Spinal Loads

Our results demonstrated that our patient-specific models are well suited to investigate interindividual differences. In correlation with individual spinal characteristics, distinct differences in muscle activity and vertebral loading between investigated subjects could be identified. Thus, subject two showed generally higher muscle activity than subject one (**Figure 11**). The compensation angles for the upright standing position were in the same range. In both cases, the balancing movement started to a large extent from a sacral rotation. However, subject one showed a rather extensive compensation in the lower mid-region of the lumbar spine, whereas subject two compensated within a smaller range in the upper lumbar region (**Figure 12**). Subject one showed a smaller overall compensatory flexion with -3,9° than subject two (-4,5°). The estimated shear forces showed considerable differences, especially regarding anterior–posterior loading of up to 123 N anterior and 84 N posterior for subjects one and two, respectively. Please note that this relates well to the differences in lumbar lordosis between both subjects. In terms of lateral shear forces, the differences in the thoracolumbar transition are particularly

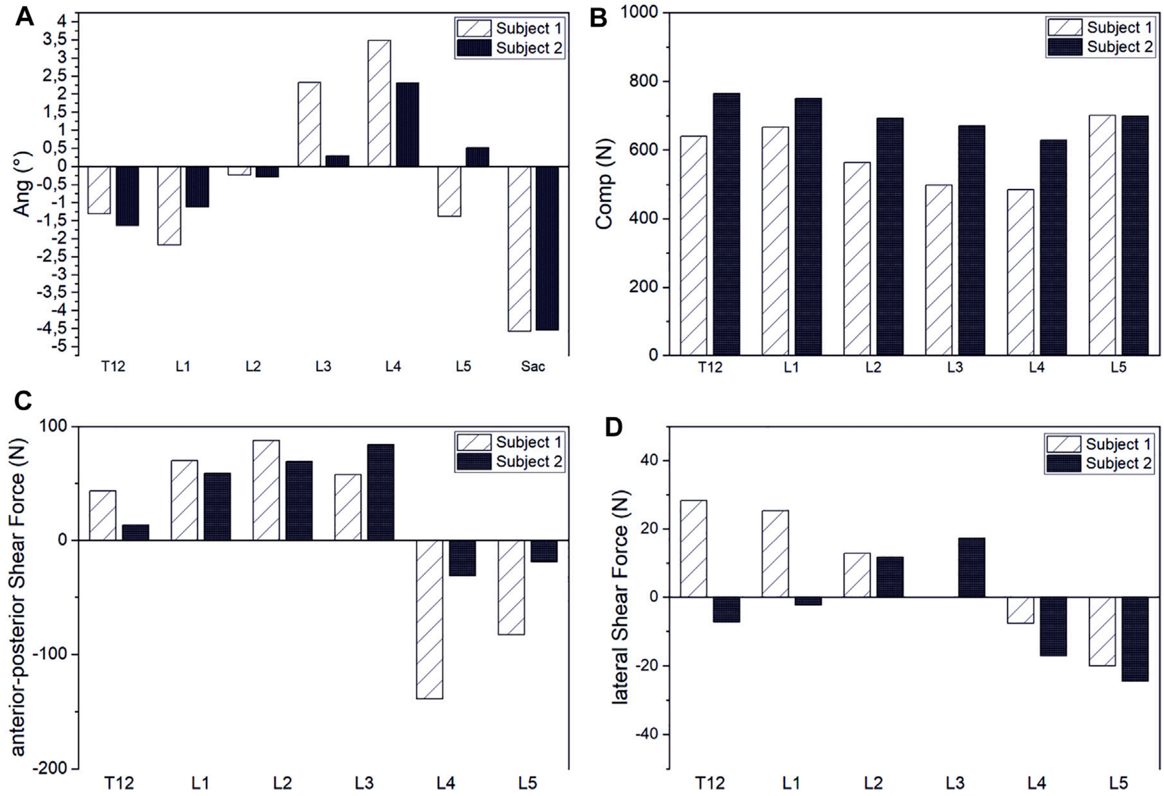

FIGURE 12 | Interindividual comparison of compensation angles for upright standing **(A)** and intervertebral joint compression **(B)**, anterior–posterior shear **(C)** and lateral shear forces **(D)**.

noticeable and considerably higher for the subject with thoracic scoliosis.

4 DISCUSSION

We created the first pipeline for the generation of patient-specific musculoskeletal models of the spine based on CT data. The models include individual vertebrae with muscle and ligament attachment points, spinal alignment, torso weight and distribution, as well as spinal ligaments and back muscles. The models are capable of simulating static activities and estimating lumbar loads and muscle forces via a static optimization approach. The automated nature of our unique process makes it suitable for large-scale interindividual comparative studies. Thus, it holds the potential to identify biomechanical risk factors for degenerative spine diseases on a quantitative basis in larger cohorts.

The SSL contributes little to spinal stability, which is consistent with observations from the literature. This can be attributed to the fact that the SSL is the only spinal ligament featuring a negative pre-strain for the upright position (Robertson et al., 2013). The large forces occurring in the LF even with reduced pre-strain might be due to the fact that our centers of rotation are located rigidly in the center of the IVD. This is only an approximation, since the physiological instantaneous center of rotation migrates considerably posterior during reclination movement (Liu et al., 2016; Aiyangar et al., 2017). Shifting the center of rotation posterior is expected to lead to a reduced strain in the ligament and therefore to lower loading (Han et al., 2013). The modeling of intervertebral joints as fixed spherical joints is one major limitation of our model, which is expected to influence not only the ligament forces but intervertebral loads as well. To address this limitation, the model has to be equipped with additional degrees of freedom. To counteract the decreased stability associated with this, facet joints and intra-abdominal pressure should be included. This will increase model complexity and require a different optimization approach to solve the redundancy problem. Possible approaches include inverse kinematics and trajectory tracking such as computed muscle control (Liu et al., 2008; Hamner et al., 2010) or forward static optimization (Shourijeh et al., 2017). Moreover, the assumption of an average fixed lombopelvic rhythm is a further simplification, which has to be adapted, especially for larger flexion angles (Tafazzol et al., 2014).

Our model was able to predict muscle forces in close correlation with myoelectric activity measurements from the literature (Takahashi et al., 2006). To ensure satisfying equilibrium conditions for all models and load cases, we overestimated MMS and partly muscle PCSAs (IS and MF attached to the thoracic spine). However, results for maximum and mean muscle activation indicate that our model would be able to meet equilibrium conditions for lower and therefore more physiological parameters as well. Nevertheless, integration of individualized muscle architecture is desirable (Bruno et al., 2017). Past studies show that apart from individual PCSAs, the proton density fat fraction has to be considered when it comes to the estimation of maximum muscle strength (Schlaeger et al., 2019). Due to software limitations, we modeled muscle fascicles as simple point-to-point actuators. Thus, we are not able to consider paraspinal redirection of the muscle fascicles. For larger flexion angles, this leads to unrealistic lines of action and therefore, incorrect moment arms. In consequence, it is likely that muscles are over- or underactivated, depending on the mechanical state of the load case.

We predicted vertebral loading in close agreement with measured *in vivo* data, although there are discrepancies. For lifting tasks, the models tended to overestimate vertebral loading with a maximum of 33%, whereas flexion rather led to underestimation with a maximum of 16%. The reasons for those deviations can be manifold. Thus, precise flexion angles are not given in all studies (Wilke et al., 2001; Rohlmann et al., 2008). We therefore based our study design on given flexion angles from the study cited herein (Bruno et al., 2015). Regarding *in vivo* data from Wilke et al., our model tended to overestimate compression forces. This difference could possibly be explained by the fact that realigning the spine to compensate for the anterior weight is likely in order to reduce necessary muscle activity. We used an optimization approach to consider those compensation effects for an unloaded upright standing position, not however, for high-intensity lifting tasks. Yet, it is precisely in these postures, like carrying an additional 20 kg in front of the chest, in which such effects are likely to occur (Kimura et al., 2001). Thus, an external load applied at the front would lead to a balancing posture that would shift the body's center of gravity backward and would reduce the occurring moment. Neglecting this "leaning backward" phenomenon will lead to an overestimation of muscle forces. Another possible explanation for the overestimation of lumbar loads during lifting tasks is the neglect of the stabilizing effect of intraabdominal pressure (IAD) (Hodges et al., 2005; Stokes et al., 2010). According to the study cited herein (Arjmand and Shirazi-Adl, 2006), consideration of IAD decreases vertebral load by a mean value of 19% for static loading tasks. Compared to experimental data from Takahashi et al. (Takahashi et al., 2006), our model slightly underpredicted vertebral loading. One possible reason for that is that the static optimization approach we use does not account for co-contraction (Ezati et al., 2019). Therefore, muscle activation of agonists does not have to react to forces from antagonists, which reduces overall muscle forces and, consequently, resulting joint forces. Apart from that, influencing factors due to respective *in vivo* study designs have to be noted. While Wilke et al. measured IDP via pressure sensors inserted directly into the intervertebral disc, Rohlmann et al. measured T12/L1 compression forces via a telemetrized instrumented implant (Rohlmann et al., 2008). To stabilize the spine, bisegmental spinal fixators were implanted additionally to the instrumented implants. Firstly, those fixators can lead to a relief of the measuring device and furthermore engage in natural spinal kinematics.

In our study, interindividual analysis of two subjects showed plausible results under consideration of individual characteristics. Thus, higher muscle activity and resulting vertebral loading were calculated for subject one, which can be attributed to the higher bodyweight and match findings from previous studies (Ghezelbash et al., 2016; Akhavanfar et al., 2018). Anterior–posterior shear forces were markedly increased for subject one, especially in the lower lumbar region. This can be explained by the pronounced lumbar lordosis and thus, strongly tilted vertebrae. Similar effects can be observed regarding lateral shear forces, which were more pronounced in scoliotic subject one as well. Focusing on occurring forces in the region of the thoracolumbal transition, these findings match the subject's mild scoliosis in the thoracic spine. However, we emphasize that due to the small patient cohort, this study's investigation of interindividual differences should be interpreted solely as a proof of concept. Further studies including larger patient cohorts are necessary to comprehensively evaluate the potential of our process for interindividual analysis.

In conclusion, we established a pipeline for automated segmentation and generation of subject-specific multibody models of the lumbar spine. We validated our biomechanical model by demonstrating a close accordance with our results with previous *in vivo* studies. Our unique approach of automatically extracting vertebral geometries including attachment points for muscles and ligaments, spinal alignment, and weight and soft tissue distribution of the trunk gives us the opportunity to systematically investigate biomechanical factors influencing spinal loading. The automation allows the analysis of large patient cohorts to gain meaningful insights into the healthy and pathological biomechanics of the spine.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusion of this article will be made available by the authors, without undue reservation.

AUTHOR CONTRIBUTIONS

Simulations, result evaluation, and drafting of the manuscript were carried out by TL. The Project supervisor is JK who contributed to a large extent to the study design as well as interpretation of the results and provision of needed data. Automated generation of points of interest was carried out by MH and AB. AS was responsible for the automated segmentation pipeline. LH and KN supported the modeling process. ML and TB were responsible for CT Data supervision. VS supported the development of the study design. All authors gave valuable feedback on the manuscript itself.

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REFERENCES

Actis, J. A., Honegger, J. D., Gates, D. H., Petrella, A. J., Nolasco, L. A., and Silverman, A. K. (2018). Validation of Lumbar Spine Loading from a Musculoskeletal Model Including the Lower Limbs and Lumbar Spine. *J. biomechanics* 68, 107–114. doi:10.1016/j.jbiomech.2017.12.001

Aiyangar, A., Zheng, L., Anderst, W., and Zhang, X. (2017). Instantaneous Centers of Rotation for Lumbar Segmental Extension *In Vivo*. *J. biomechanics* 52, 113–121. doi:10.1016/j.jbiomech.2016.12.021

Akhavanfar, M. H., Kazemi, H., Eskandari, A. H., and Arjmand, N. (2018). Obesity and Spinal Loads; a Combined Mr Imaging and Subject-specific Modeling Investigation. *J. biomechanics* 70, 102–112. doi:10.1016/j.jbiomech.2017.08.009

Arjmand, N., Gagnon, D., Plamondon, A., Shirazi-Adl, A., and Larivière, C. (2009). Comparison of Trunk Muscle Forces and Spinal Loads Estimated by Two Biomechanical Models. *Clin. Biomech.* 24, 533–541. doi:10.1016/j.clinbiomech.2009.05.008

Arjmand, N., and Shirazi-Adl, A. (2006). Role of Intra-abdominal Pressure in the Unloading and Stabilization of the Human Spine during Static Lifting Tasks. *Eur. Spine J.* 15, 1265–1275. doi:10.1007/s00586-005-0012-9

Aspden, R. M. (1992). Review of the Functional Anatomy of the Spinal Ligaments and the Lumbar Erector Spinae Muscles. *Clin. Anat.* 5, 372–387. doi:10.1002/ca.980050504

Bassani, T., Casaroli, G., and Galbusera, F. (2019). Dependence of Lumbar Loads on Spinopelvic Sagittal Alignment: An Evaluation Based on Musculoskeletal Modeling. *PloS one* 14, e0207997. doi:10.1371/journal.pone.0207997

Bayoglu, R., Galibarov, P. E., Verdonschot, N., Koopman, B., and Homminga, J. (2019). Twente Spine Model: A Thorough Investigation of the Spinal Loads in a Complete and Coherent Musculoskeletal Model of the Human Spine. *Med. Eng. Phys.* 68, 35–45. doi:10.1016/j.medengphy.2019.03.015

Bayoglu, R., Geeraedts, L., Groenen, K. H. J., Verdonschot, N., Koopman, B., and Homminga, J. (2017a). Twente Spine Model: A Complete and Coherent Dataset for Musculo-Skeletal Modeling of the Lumbar Region of the Human Spine. *J. biomechanics* 53, 111–119. doi:10.1016/j.jbiomech.2017.01.009

Bayoglu, R., Geeraedts, L., Groenen, K. H. J., Verdonschot, N., Koopman, B., and Homminga, J. (2017b). Twente Spine Model: A Complete and Coherent Dataset for Musculo-Skeletal Modeling of the Thoracic and Cervical Regions of the Human Spine. *J. biomechanics* 58, 52–63. doi:10.1016/j.jbiomech.2017.04.003

Beaucage-Gauvreau, E., Robertson, W. S. P., Brandon, S. C. E., Fraser, R., Freeman, B. J. C., Graham, R. B., et al. (2019). Validation of an Opensim Full-Body Model with Detailed Lumbar Spine for Estimating Lower Lumbar Spine Loads during Symmetric and Asymmetric Lifting Tasks. *Comput. Methods Biomechanics Biomed. Eng.* 22, 451–464. doi:10.1080/10255842.2018.1564819

Blemker, S. S., Asakawa, D. S., Gold, G. E., and Delp, S. L. (2007). Image-based Musculoskeletal Modeling: Applications, Advances, and Future Opportunities. *J. Magn. Reson. Imaging* 25, 441–451. doi:10.1002/jmri.20805

Bruno, A. G., Bouxsein, M. L., and Anderson, D. E. (2015). Development and Validation of a Musculoskeletal Model of the Fully Articulated Thoracolumbar Spine and Rib Cage. *J. biomechanical Eng.* 137, 081003. doi:10.1115/1.4030408

Bruno, A. G., Mokhtarzadeh, H., Allaire, B. T., Velie, K. R., De Paolis Kaluza, M. C., Anderson, D. E., et al. (2017). Incorporation of Ct-Based Measurements of Trunk Anatomy into Subject-specific Musculoskeletal Models of the Spine Influences Vertebral Loading Predictions. *J. Orthop. Res.* 35, 2164–2173. doi:10.1002/jor.23524

Caprara, S., Carrillo, F., Snedeker, J. G., Farshad, M., and Senteler, M. (2021). Automated Pipeline to Generate Anatomically Accurate Patient-specific Biomechanical Models of Healthy and Pathological Fsus. *Front. Bioeng. Biotechnol.* 9, 33. doi:10.3389/fbioe.2021.636953

Chazal, J., Tanguy, A., Bourges, M., Gaurel, G., Escande, G., Guillot, M., et al. (1985). Biomechanical Properties of Spinal Ligaments and a Histological Study of the Supraspinal Ligament in Traction. *J. biomechanics* 18, 167–176. doi:10.1016/0021-9290(85)90202-7

Christophy, M., Faruk Senan, N. A., Lotz, J. C., and O'Reilly, O. M. (2012). A Musculoskeletal Model for the Lumbar Spine. *Biomech. Model. Mechanobiol.* 11, 19–34. doi:10.1007/s10237-011-0290-6

Cina, A., Bassani, T., Panico, M., Luca, A., Masharawi, Y., Brayda-Bruno, M., et al. (2021). 2-step Deep Learning Model for Landmarks Localization in Spine Radiographs. *Sci. Rep.* 11, 9482. doi:10.1038/s41598-021-89102-w

Cook, D., Julias, M., and Nauman, E. (2014). Biological Variability in Biomechanical Engineering Research: Significance and Meta-Analysis of Current Modeling Practices. *J. biomechanics* 47, 1241–1250. doi:10.1016/j.jbiomech.2014.01.040

Dao, T. T., Pouletaut, P., Charleux, F., Lazáry, Á., Eltes, P., Varga, P. P., et al. (2015). Multimodal Medical Imaging (Ct and Dynamic Mri) Data and Computer-Graphics Multi-Physical Model for the Estimation of Patient Specific Lumbar Spine Muscle Forces. *Data & Knowl. Eng.* 96-97, 3–18. doi:10.1016/j.datak.2015.04.001

de Zee, M., Hansen, L., Wong, C., Rasmussen, J., and Simonsen, E. B. (2007). A Generic Detailed Rigid-Body Lumbar Spine Model. *J. biomechanics* 40, 1219–1227. doi:10.1016/j.jbiomech.2006.05.030

Delp, S. L., Anderson, F. C., Arnold, A. S., Loan, P., Habib, A., John, C. T., et al. (2007). Opensim: Open-Source Software to Create and Analyze Dynamic Simulations of Movement. *IEEE Trans. Biomed. Eng.* 54, 1940–1950. doi:10.1109/TBME.2007.901024

Dreischarf, M., Rohlmann, A., Graichen, F., Bergmann, G., and Schmidt, H. (2016). *In Vivo* loads on a Vertebral Body Replacement during Different Lifting Techniques. *J. biomechanics* 49, 890–895. doi:10.1016/j.jbiomech.2015.09.034

El Ouaaid, Z., Shirazi-Adl, A., and Plamondon, A. (2016). Effects of Variation in External Pulling Force Magnitude, Elevation, and Orientation on Trunk Muscle Forces, Spinal Loads and Stability. *J. biomechanics* 49, 946–952. doi:10.1016/j.jbiomech.2015.09.036

Eskandari, A. H., Arjmand, N., Shirazi-Adl, A., and Farahmand, F. (2019). Hypersensitivity of Trunk Biomechanical Model Predictions to Errors in Image-Based Kinematics when Using Fully Displacement-Control Techniques. *J. biomechanics* 84, 161–171. doi:10.1016/j.jbiomech.2018.12.043

Ezati, M., Ghannadi, B., and McPhee, J. (2019). A Review of Simulation Methods for Human Movement Dynamics with Emphasis on Gait. *Multibody Syst. Dyn.* 47, 265–292. doi:10.1007/s11044-019-09685-1

Fasser, M.-R., Jokeit, M., Kalthoff, M., Gomez Romero, D. A., Trache, T., Snedeker, J. G., et al. (2021). Subject-specific Alignment and Mass Distribution in Musculoskeletal Models of the Lumbar Spine. *Front. Bioeng. Biotechnol.* 9, 745. doi:10.3389/fbioe.2021.721042

Favier, C. D., Finnegan, M. E., Quest, R. A., Honeyfield, L., McGregor, A. H., and Phillips, A. T. M. (2021). An Open-Source Musculoskeletal Model of the Lumbar Spine and Lower Limbs: a Validation for Movements of the Lumbar Spine. *Comput. Methods Biomechanics Biomed. Eng.* 24, 1310–1325. doi:10.1080/10255842.2021.1886284

Gagnon, D., Larivière, C., and Loisel, P. (2001). Comparative Ability of Emg, Optimization, and Hybrid Modelling Approaches to Predict Trunk Muscle Forces and Lumbar Spine Loading during Dynamic Sagittal Plane Lifting. *Clin. Biomech.* 16, 359–372. doi:10.1016/S0268-0033(01)00016-X

Ghezelbash, F., Shirazi-Adl, A., Arjmand, N., El-Ouaaid, Z., and Plamondon, A. (2016). Subject-specific Biomechanics of Trunk: Musculoskeletal Scaling, Internal Loads and Intradiscal Pressure Estimation. *Biomech. Model. Mechanobiol.* 15, 1699–1712. doi:10.1007/s10237-016-0792-3

Hajihosseinali, M., Arjmand, N., and Shirazi-Adl, A. (2015). Effect of Body Weight on Spinal Loads in Various Activities: a Personalized Biomechanical Modeling Approach. *J. biomechanics* 48, 276–282. doi:10.1016/j.jbiomech.2014.11.033

Hamner, S. R., Seth, A., and Delp, S. L. (2010). Muscle Contributions to Propulsion and Support during Running. *J. Biomechanics* 43, 2709–2716. doi:10.1016/j.jbiomech.2010.06.025

Han, K.-S., Kim, K., Park, W. M., Lim, D. S., and Kim, Y. H. (2013). Effect of Centers of Rotation on Spinal Loads and Muscle Forces in Total Disk Replacement of Lumbar Spine. *Proc. Inst. Mech. Eng. H.* 227, 543–550. doi:10.1177/0954411912474742

Han, K.-S., Zander, T., Taylor, W. R., and Rohlmann, A. (2012). An Enhanced and Validated Generic Thoraco-Lumbar Spine Model for Prediction of Muscle Forces. *Med. Eng. Phys.* 34, 709–716. doi:10.1016/j.medengphy.2011.09.014

Iyer, S., Sheha, E., Fu, M. C., Varghese, J., Cunningham, M. E., Albert, T. J., et al. (2018). Sagittal Spinal Alignment in Adult Spinal Deformity: An Overview of Current Concepts and a Critical Analysis Review. *JBJS Rev.* 6, e2. doi:10.2106/JBJS.RVW.17.00117

Jalalian, A., Tay, F. E. H., Arastehfar, S., and Liu, G. (2017). A Patient-specific Multibody Kinematic Model for Representation of the Scoliotic Spine Movement in Frontal Plane of the Human Body. *Multibody Syst. Dyn.* 39, 197–220. doi:10.1007/s11044-016-9556-1

Kaesmacher, J., Liebl, H., Baum, T., and Kirschke, J. S. (2017). Bone Mineral Density Estimations from Routine Multidetector Computed Tomography. *J. Comput. assisted Tomogr.* 41, 217–223. doi:10.1097/rct.0000000000000518

Kim, H.-K., and Zhang, Y. (2017). Estimation of Lumbar Spinal Loading and Trunk Muscle Forces during Asymmetric Lifting Tasks: Application of Whole-Body Musculoskeletal Modelling in Opensim. *Ergonomics* 60, 563–576. doi:10.1080/00140139.2016.1191679

Kimura, S., Steinbach, G. C., Watenpaugh, D. E., and Hargens, A. R. (2001). Lumbar Spine Disc Height and Curvature Responses to an Axial Load Generated by a Compression Device Compatible with Magnetic Resonance Imaging. *Spine* 26, 2596–2600. doi:10.1097/00007632-200112010-00014

Little, J. P., and Adam, C. J. (2015). Geometric Sensitivity of Patient-specific Finite Element Models of the Spine to Variability in User-Selected Anatomical Landmarks. *Comput. Methods Biomechanics Biomed. Eng.* 18, 676–688. doi:10.1080/10255842.2013.843673

Liu, M. Q., Anderson, F. C., Schwartz, M. H., and Delp, S. L. (2008). Muscle Contributions to Support and Progression over a Range of Walking Speeds. *J. Biomechanics* 41, 3243–3252. doi:10.1016/j.jbiomech.2008.07.031

Liu, T., Khalaf, K., Adeeb, S., and El-Rich, M. (2019). Effects of Lumbo-Pelvic Rhythm on Trunk Muscle Forces and Disc Loads during Forward Flexion: A Combined Musculoskeletal and Finite Element Simulation Study. *J. biomechanics* 82, 116–123. doi:10.1016/j.jbiomech.2018.10.009

Liu, T., Khalaf, K., Naserkhaki, S., and El-Rich, M. (2018). Load-sharing in the Lumbosacral Spine in Neutral Standing & Flexed Postures - A Combined Finite Element and Inverse Static Study. *J. Biomechanics* 70, 43–50. doi:10.1016/j.jbiomech.2017.10.033

Liu, Z., Tsai, T.-Y., Wang, S., Wu, M., Zhong, W., Li, J.-S., et al. (2016). Sagittal Plane Rotation Center of Lower Lumbar Spine during a Dynamic Weight-Lifting Activity. *J. biomechanics* 49, 371–375. doi:10.1016/j.jbiomech.2015.12.029

Murtezani, A., Ibraimi, Z., Sllamniku, S., Osmani, T., and Sherifi, S. (2011). Prevalence and Risk Factors for Low Back Pain in Industrial Workers. *Folia Med. Plovdiv.* 53, 68–74. doi:10.2478/v10153-011-0060-3

Nachemson, A. L., and Evans, J. H. (1968). Some Mechanical Properties of the Third Human Lumbar Interlaminar Ligament (Ligamentum Flavum). *J. biomechanics* 1, 211–220. doi:10.1016/0021-9290(68)90006-7

Naserkhaki, S., Jaremko, J. L., and El-Rich, M. (2016). Effects of Inter-individual Lumbar Spine Geometry Variation on Load-Sharing: Geometrically Personalized Finite Element Study. *J. biomechanics* 49, 2909–2917. doi:10.1016/j.jbiomech.2016.06.032

Pearsall, D. J., Reid, J. G., and Livingston, L. A. (1996). Segmental Inertial Parameters of the Human Trunk as Determined from Computed Tomography. *Ann. Biomed. Eng.* 24, 198–210. doi:10.1007/BF02667349

Périe, D., De Gauzy, J. S., and Hobatho, M. C. (2002). Biomechanical Evaluation of Cheneau-Toulouse-Munster Brace in the Treatment of Scoliosis Using Optimisation Approach and Finite Element Method. *Med. Biol. Eng. Comput.* 40, 296–301. doi:10.1007/BF02344211

Petit, Y., Aubin, C. É., and Labelle, H. (2004). Patient-specific Mechanical Properties of a Flexible Multi-Body Model of the Scoliotic Spine. *Med. Biol. Eng. Comput.* 42, 55–60. doi:10.1007/BF02351011

Robertson, D. J., von Forell, G. A., Alsup, J., and Bowden, A. E. (2013). Thoracolumbar Spinal Ligaments Exhibit Negative and Transverse Pre-strain. *J. Mech. Behav. Biomed. Mater* 23, 44–52. doi:10.1016/j.jmbbm.2013.04.004

Rohlmann, A., Graichen, F., Kayser, R., Bender, A., and Bergmann, G. (2008). Loads on a Telemeterized Vertebral Body Replacement Measured in Two Patients. *Spine (Phila Pa 1976)* 33, 1170–1179. doi:10.1097/BRS.0b013e3181722d52

Rupp, T. K., Ehlers, W., Karajan, N., Günther, M., and Schmitt, S. (2015). A Forward Dynamics Simulation of Human Lumbar Spine Flexion Predicting the Load Sharing of Intervertebral Discs, Ligaments, and Muscles. *Biomech. Model. Mechanobiol.* 14, 1081–1105. doi:10.1007/s10237-015-0656-2

Sato, K., Kikuchi, S., and Yonezawa, T. (1999). *In Vivo* intradiscal Pressure Measurement in Healthy Individuals and in Patients with Ongoing Back Problems. *Spine* 24, 2468. doi:10.1097/00007632-199912010-00008

Schlaeger, S., Inhuber, S., Rohrmeier, A., Dieckmeyer, M., Freitag, F., Klupp, E., et al. (2019). Association of Paraspinal Muscle Water-Fat MRI-Based Measurements with Isometric Strength Measurements. *Eur. Radiol.* 29, 599–608. doi:10.1007/s00330-018-5631-8

Sekuboyina, A., Husseini, M. E., Bayat, A., Löffler, M., Liebl, H., Li, H., et al. (2020). Verse: A Vertebrae Labelling and Segmentation Benchmark for Multi-Detector Ct Images. *arXiv Prepr. arXiv:2001.09193.*

Senteler, M., Weisse, B., Snedeker, J. G., and Rothenfluh, D. A. (2014). Pelvic Incidence-Lumbar Lordosis Mismatch Results in Increased Segmental Joint Loads in the Unfused and Fused Lumbar Spine. *Eur. Spine J.* 23, 1384–1393. doi:10.1007/s00586-013-3132-7

Shourijeh, M. S., Mehrabi, N., and McPhee, J. (2017). Forward Static Optimization in Dynamic Simulation of Human Musculoskeletal Systems: A Proof-Of-Concept Study. *J. Comput. Nonlinear Dyn.* 12, 051005. doi:10.1115/1.4036195.051005

Stokes, I. A. F., Gardner-Morse, M. G., and Henry, S. M. (2010). Intra-abdominal Pressure and Abdominal Wall Muscular Function: Spinal Unloading Mechanism. *Clin. Biomech.* 25, 859–866. doi:10.1016/j.clinbiomech.2010.06.018

Tafazzol, A., Arjmand, N., Shirazi-Adl, A., and Parnianpour, M. (2014). Lumbopelvic Rhythm during Forward and Backward Sagittal Trunk Rotations: Combined *In Vivo* Measurement with Inertial Tracking Device and Biomechanical Modeling. *Clin. Biomech.* 29, 7–13. doi:10.1016/j.clinbiomech.2013.10.021

Takahashi, I., Kikuchi, S.-i., Sato, K., and Sato, N. (2006). Mechanical Load of the Lumbar Spine during Forward Bending Motion of the Trunk-A Biomechanical Study. *Spine* 31, 18–23. doi:10.1097/01.brs.0000192636.69129.fb

Vergari, C., Courtois, I., Ebermeyer, E., Bouloussa, H., Vialle, R., and Skalli, W. (2016). Experimental Validation of a Patient-specific Model of Orthotic Action in Adolescent Idiopathic Scoliosis. *Eur. Spine J.* 25, 3049–3055. doi:10.1007/s00586-016-4511-7

W Hodges, P., Martin Eriksson, A. E., Shirley, D., and C Gandevia, S. (2005). Intra-abdominal Pressure Increases Stiffness of the Lumbar Spine. *J. biomechanics* 38, 1873–1880. doi:10.1016/j.jbiomech.2004.08.016

White, A. A. (2022). *Clinical Biomechanics of the Spine*. Philadelphia, Pennsylvania, USA: Lippincott Williams & Wilkins.

Wilke, H.-J., Neef, P., Hinz, B., Seidel, H., and Claes, L. (2001). Intradiscal Pressure Together with Anthropometric Data - a Data Set for the Validation of Models. *Clin. Biomech.* 16, S111–S126. doi:10.1016/S0268-0033(00)00103-0

Winter, D. A. (2005). *Biomechanics and Motor Control of Human Movement*. 3 ed,. Hoboken, NJ: Wiley.

Wong, K. W., Luk, K. D., Leong, J. C., Wong, S. F., and Wong, K. K. (2006). Continuous Dynamic Spinal Motion Analysis. *Spine (Phila Pa 1976)* 31, 414. doi:10.1097/01.brs.0000199955.87517.82

Zadpoor, A. A., and Weinans, H. (2015). Patient-specific Bone Modeling and Analysis: The Role of Integration and Automation in Clinical Adoption. *J. biomechanics* 48, 750–760. doi:10.1016/j.jbiomech.2014.12.018

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Musculoskeletal spine modeling in large patient cohorts: how morphological individualization affects lumbar load estimation

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Introduction: Achieving an adequate level of detail is a crucial part of any modeling process. Thus, oversimplification of complex systems can lead to overestimation, underestimation, and general bias of effects, while elaborate models run the risk of losing validity due to the uncontrolled interaction of multiple influencing factors and error propagation.

Methods: We used a validated pipeline for the automated generation of multibody models of the trunk to create 279 models based on CT data from 93 patients to investigate how different degrees of individualization affect the observed effects of different morphological characteristics on lumbar loads. Specifically, individual parameters related to spinal morphology (thoracic kyphosis (TK), lumbar lordosis (LL), and torso height (TH)), as well as torso weight (TW) and distribution, were fully or partly considered in the respective models according to their degree of individualization, and the effect strengths of these parameters on spinal loading were compared between semi- and highly individualized models. T-distributed stochastic neighbor embedding (T-SNE) analysis was performed for overarching pattern recognition and multiple regression analyses to evaluate changes in occurring effects and significance.

Results: We were able to identify significant effects ($p < 0.05$) of various morphological parameters on lumbar loads in models with different degrees of individualization. Torso weight and lumbar lordosis showed the strongest effects on compression ($\beta \approx 0.9$) and anterior–posterior shear forces ($\beta \approx 0.7$), respectively. We could further show that the effect strength of individual parameters tended to decrease if more individual characteristics were included in the models.

Discussion: The induced variability due to model individualization could only partly be explained by simple morphological parameters. Our study shows that model simplification can lead to an emphasis on individual effects, which needs to be critically assessed with regard to *in vivo* complexity. At the same time, we demonstrated that individualized models representing a population-based cohort are still able to identify relevant influences on spinal loading while considering a variety of influencing factors and their interactions.

KEYWORDS

spinal biomechanics, multi body dynamics, subject-specific modeling, individualization, automated model generation, spinal loading

1 Introduction

Chronic back pain is a multi-factorial problem (Murtezani et al., 2011; Rabey et al., 2019). Apart from psychological and social causes (Tagliaferri et al., 2020), spinal degeneration is often associated with back pain, but it also comes with a variety of possible sources itself (Kalichman et al., 2009). Thus, age- or disease-related changes in passive structures can lead to pain and disability, as well as individual anthropometric conditions, such as body weight or spinal alignment and deformities (Kalichman et al., 2017). *In vivo* investigations on spinal loading are rare and usually consider single individuals and spinal levels (Wilke et al., 2001; Takahashi et al., 2006; Rohlmann et al., 2008), providing the necessary basis for model validation but being unsuitable for comparative studies on the potential influences of inter-individual characteristics on spinal loads.

For systematic analyses of spine biomechanics, numerical modeling and simulation have been widely established in the past few years (de Zee et al., 2007; Christophy et al., 2012; Bruno et al., 2015; Ignasiak et al., 2016). Although finite element simulation is primarily suitable for the examination of deformation states and internal stresses in single flexible bodies (Périé et al., 2002; Little and Adam, 2015; Ghezelbash et al., 2016a; El Ouaaid et al., 2016; Naserkhaki et al., 2016; Vergari et al., 2016; Akhavanfar et al., 2018; Eskandari et al., 2019), multi-body modeling allows the consideration of the biomechanics of the spine from a more comprehensive perspective and can take multiple aspects of mechanical loading into account (Lerchl et al., 2023). However, the vast majority of published studies use generic models to focus on the effects of factors such as sagittal alignment (Bruno et al., 2012; Bruno et al., 2017; Galbusera et al., 2014; Bassani et al., 2019; Müller et al., 2021) or body weight (Akhavanfar et al., 2018). Although those studies are inevitable to examine isolated effects of the parameters of interest, they fail to capture the complexity of clinical practice. Each patient comes with a unique combination of influencing factors that interact with each other and lead to individual loading scenarios. To address this complexity, a recent trend toward individualized models has emerged in the relevant literature (Burkhart et al., 2020; Overbergh et al., 2020; Fasser et al., 2021; Lerchl et al., 2022; Banks et al., 2023). Individualized modeling is usually time-consuming, and therefore, respective models are often only available in small sample sizes. However, in order to obtain meaningful and statistically significant results, the analysis of large and diverse patient cohorts is essential. Due to diagnostic and clinical practice as well as large population-based cohort studies (e.g., the German National Cohort and the UK Biobank), such datasets are available for scientific interest, and during the past decade, developments in data analytics—especially in the field of artificial intelligence—have been providing promising tools to make these datasets accessible for further analysis (Sekuboyina et al., 2020).

For all the potential that individualized models hold, they also pose special challenges. The balancing act between sufficient model complexity and necessary simplifications is an integral part of any modeling process, enabling us to draw distinct conclusions from the obtained results. Taking into account multiple individual characteristics inevitably increases model complexity, carries the risk of generating noise, increases result variance, and therefore makes it difficult to draw clear conclusions. On the other hand, oversimplified models can also lead to biased results, such as the overestimation of individual effects due to the neglect of other parameters and their interrelations. The question of the right level of detail is, therefore, crucial in biomechanical modeling. To the best of our knowledge, there are no musculoskeletal modeling studies published that examine the effects of multiple parameters on spinal loading based on a large patient cohort and critically analyze how different degrees of individualization influence simulation results using a population-based cohort.

We used a pipeline for the automated generation of individualized multi-body models of the trunk (Lerchl et al., 2022) to investigate the influence of different degrees of model individualization on the observed effects of morphological factors on spinal loading. We analyzed how the effects of individual parameters on spinal loading change with the increasing degree of individualization of the underlying models. Highly individualized models included a patient-specific spine as well as torso weight (TW) and its distribution, which was combined with a generic pelvis, sacrum, ribcage, head–neck, and simplified arms. We carried out analyses based on a large patient cohort representing a diverse population in terms of spinal morphology and alignment as well as torso weight and its distribution (n = 93, M = 55, F = 38, and age = 70 ± 7.6) (Table 1). Parameters of interest were thoracic kyphosis (TK), lumbar lordosis (LL), torso height (TH)TW, and left of mass of the torso in anterior–posterior and superior–inferior directions (CoM AP and CoM SI). According to the degree of individualization, we combined individualized and uniform representations of those parameters for different model configurations.

2 Methods

2.1 Musculoskeletal modeling and simulation

We used our pipeline for the automated generation of individualized musculoskeletal models of the trunk, including upper extremities and head–neck, to segment vertebral

TABLE 1 Summary of average dataset characteristics, namely, the sample size (n), age, TK, LL, TH, TH, CoM AP, and CoM SI in reference to the sacrum.

	n	Age	Av. TK [°]	Av. LL [°]	Av. TH [m]	Av. TW [kg]	Av. CoM AP [m]	Av. CoM SI [m]
Full	93	70.0 ± 7.6	42.2 ± 11.5	37.4 ± 12.0	0.43 ± 0.03	25.1 ± 5.9	0.03 ± 0.01	0.21 ± 0.01
Males	55	70.9 ± 7.1	42.0 ± 11.6	36.3 ± 11.7	0.45 ± 0.02	27.0 ± 5.1	0.03 ± 0.01	0.21 ± 0.01
Females	38	68.6 ± 8.1	42.6 ± 11.5	38.9 ± 12.3	0.41 ± 0.02	22.4 ± 5.9	0.02 ± 0.01	0.20 ± 0.01

geometries, as well as torso weight and distribution, from computed tomography (CT) scans of 93 patients. Therefore, we labeled and segmented vertebrae using an automated deep learning-based process (Sekuboyina et al., 2020) and subsequently derived individual body weight and distribution, spinal alignment, and points of interest for muscle and ligament attachments (Lerchl et al., 2022). A medical professional clinically assessed TK and LL based on the imaging data of each patient.

TH was measured from the upper endplate of T1 to the lower endplate of L5. TW and CoM were calculated from the soft tissue segmentation derived from the imaging data. Torso weight was subdivided into segments for each vertebral level. For each segment, the algorithm calculated its left of mass and total weight, corresponding to its individual tissue distribution. We assume an average density of 0.25 g/cm^3 for the lungs, 0.96 g/cm^3 for fat, and 1.06 g/cm^3 for the remaining soft tissues (Pearsall et al., 1996; Akhavanfar et al., 2018). Subsequently, we calculated the CoM across all levels, considering its anterior (AP) and superior (SI) directions in reference to L5 in our analysis. An overview of the sample characteristics is summarized in Table 1.

For each patient, we generated three models using multi-body simulation software SIMPACK 2023x (Dassault Systèmes, France): one model with individualized spine and torso (Indiv), one with uniform spine and individualized torso (uniSpine), and one with uniform torso (uniTorso) and individualized spine. The uniform spine was derived from patient data, representing the average healthy spine of a 67-year-old male (TK = 29°, LL = 44°, and TH = 0.45 m). The uniform torso weight was customized to a TW of 23.3 kg, with fixed distribution and moment arms for each level along the thoracolumbar spine. More precisely, highly individualized models (Indiv) describe models with patient-specific spine anatomy and torso weight and distribution. Semi-individualized models, respectively, only include individualized spinal anatomy (uniTorso) and individualized torso weight and distribution (uniSpine) (Figure 1).

All models further included generic bodies for the head–neck, ribcage, sacrum, pelvis, and simplified arms (Figure 2). Intervertebral discs and paraspinal ligaments are modeled as non-linear elastic elements. Intervertebral joints L1–L5 are modeled as spherical joints, and the thoracic spine and ribcage are simplified as one rigid body. We incorporated detailed generic muscle architecture for the lumbar spine, including the rectus abdominis (RA), internal oblique (IO), external oblique (EO), psoas major (PM), quadratus lumborum (QL), multifidus (MF), longissimus thoracis pars lumborum (LTL), iliocostalis lumborum (IL), and interspinales lumborum (IS), based on data from the literature (Christophy et al., 2012; Bayoglu et al., 2017).

We simulated four static loading tasks for each model, leading to a total of 1,116 simulations. The investigated load cases were three variations: upright standing in a neutral position, lifting 10 kg in front of the chest with a distance of 25 cm from T3 (10 kg, 25 cm), and lifting 10 kg with stretched arms with a distance of 55 cm (10 kg, 55 cm) and 30° flexion. Respective joint angles were assumed to be 40% sacral rotation and 60% lumbar flexion (Liu et al., 2019a), while lumbar flexion was distributed as 25.5% for L1/L2, 23.1% for L2/L3, 20.4% for L3/L4, 18.5% for L4/L5, and 12.5% for L5/S1 (Wong et al., 2006; Christophy et al., 2012). Muscle force estimation was carried out using combined inverse dynamics and static optimization, minimizing the sum of cubed muscle stress (Crowninshield and Brand, 1981). We defined inequality constraints to account for occurring moments in the intervertebral joints during each load case and bound constraints to set maximal muscle stress to 1 MPa (Bruno et al., 2015; Beaucage-Gauvreau et al., 2019; Favier et al., 2021). To account for changes in posture due to the supine position during CTs, a previous optimization was carried out to find the optimal neutral standing position by optimizing lumbosacral sagittal angles (Lerchl et al., 2022). Model validation was carried out based on *in vivo* studies (Wilke et al., 2001; Takahashi et al., 2006; Rohlmann et al., 2008) using two individualized models, showing a good overall correlation with measured spinal loads (r = 0.98) and muscle activity (r = 0.95). Model generation and validation are described in detail by Lerchl et al. (2022). Lumbar loads were evaluated based on compression and anterior–posterior shear forces, which were defined locally in reference to the respective functional spine unit (FSU). Thus, the compression force was assumed to be normal to the upper-end plate of the lower vertebra of the FSU, while the anterior–posterior shear force is defined in the midplane of the vertebra orthogonal to the compression force, pointing posteriorly.

2.2 Statistical analysis

First, we qualitatively examined our simulation results for potential overarching patterns across all lumbar levels. Therefore, we MinMax scaled absolute compression and shear forces under consideration of respective signs and applied t-distributed stochastic neighbor embedding (T-SNE) (Van der Maaten and Hinton, 2008), a statistical method that maps high-dimensional data to a virtual two- or three-dimensional space while preserving local similarities. Therefore, higher-dimensional data are converted into a visualizable space while concisely containing the underlying information. In other words, similar data points are clustered closely, while those that differ strongly are displayed with a matching distance. It is used for non-linear dimension reduction, pattern recognition, and visualization of high-dimensional data. In our case, this enabled us to visually analyze possible trends overarching all lumbar levels. We used the Python package scikit-learn for statistical analysis and

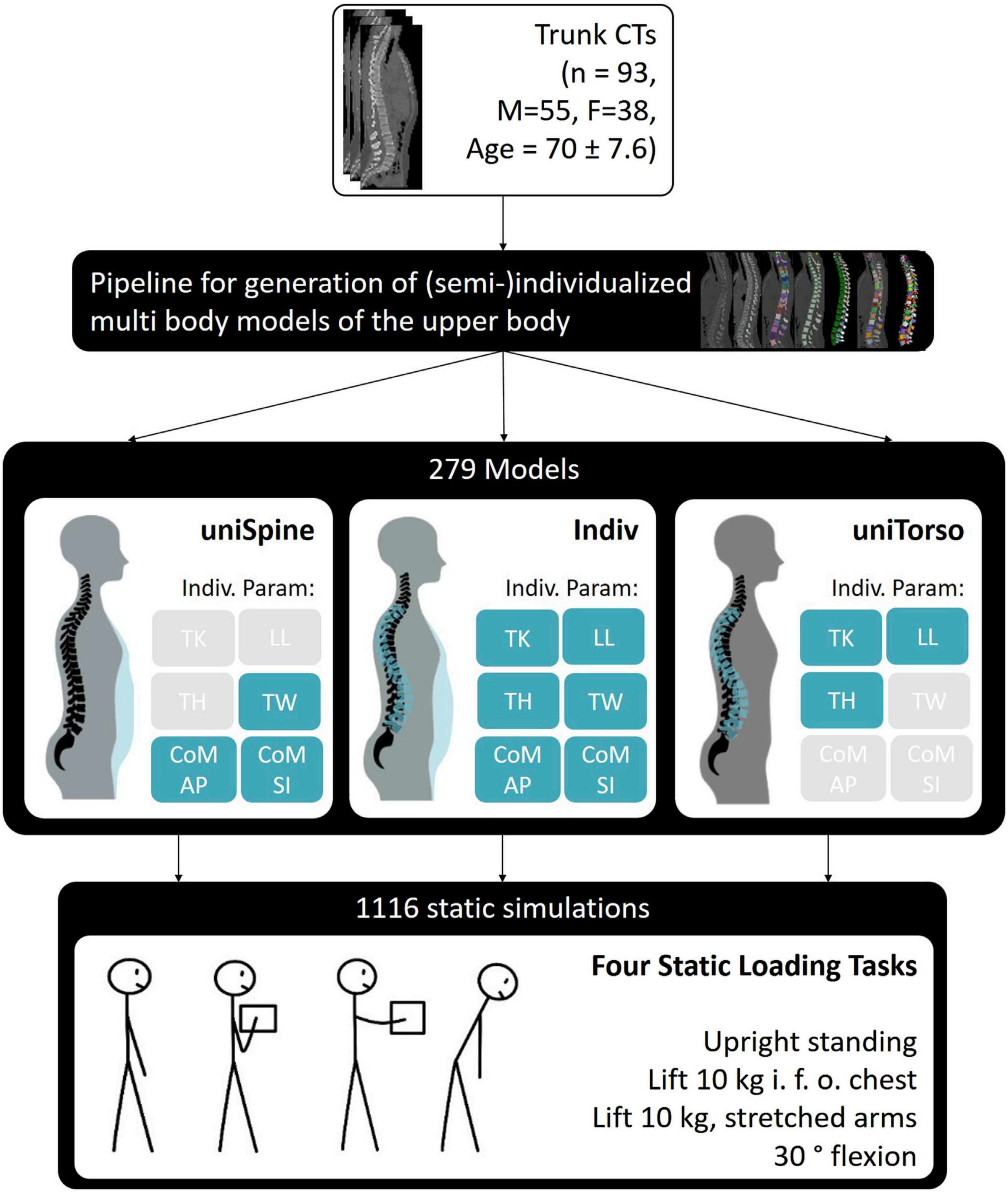

FIGURE 1
Model generation based on 93 patients with different degrees of individualization. For each of the overall 279 models, 4 static loading tasks were simulated.

applied T-SNE first to the complete dataset for compression and anterior–posterior shear forces individually, as well as for combined loading, including both components simultaneously. Using color mapping, we subsequently analyzed potential influences of considered individual factors (TK, LL, TH, TW, CoM AP, and CoM SI) across all lumbar levels in individualized models.

For quantitative load case- and level-specific analysis of possible influences on lumbar loading, we used multiple regression based on the least squares method. Independent variables were TK, LL, TH,

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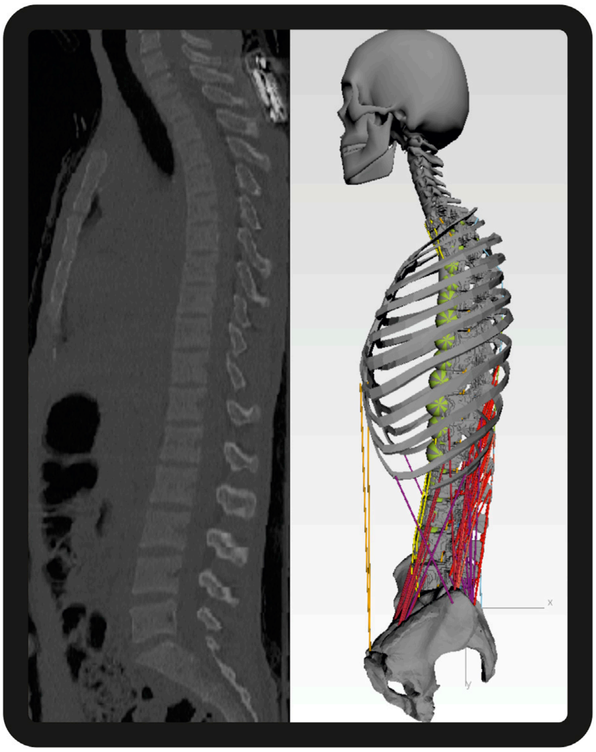

FIGURE 2
Sagittal CT images of one subject with the respective MBS model. Segment masses for soft tissues are visualized by the green spheres. For the sake of clarity, the dummy bodies for the arms consisting of two scaled cylinders centrally attached to T3 are not shown here [adapted from Lerchl et al. (2022)].

TW, CoM AP, and CoM SI, while compression and anterior–posterior shear forces were defined as dependent variables. To ensure comparability despite different underlying scales, we lefted and standardized the data. We compared the regression coefficients β of the respective parameters of interest as a measure of the observed effect strength. The significance of the results was evaluated based on the determined p-value. Significance levels were set to 0.05 (*), 0.01 (**), and 0.001 (***). According to the individualized parameters in the respective models, we applied multiple regression with three independent variables related to spinal alignment (TK, LL, and TH) for uniTorso models and three independent variables related to torso weight and distribution (TW, CoM AP, and CoM SI) for uniSpine models. For highly individualized models (Indiv models), we performed multiple regression with all six independent variables. We investigated changes in the observed effect strength (β) and significance (p-value) of each parameter for different degrees of model individualization. To investigate how the inclusion of additional individual parameters affects the generated results, we compared the results from highly individualized models (Indiv) with those from only partly individualized models, namely, those with a uniform spine and individualized torso weight and distribution (uniSpine) or uniform torso and individualized spine (uniTorso). Furthermore, the coefficient of determination (R^2) was used to evaluate whether the included parameters were able to explain the observed variability.

3 Results

3.1 T-SNE analysis

We used T-SNE analysis to map results from all lumbar levels to a two-dimensional space and therefore identify possible effects on overall lumbar loading. We qualitatively investigated data scattering for different model configurations and potential patterns due to applied loading and morphological factors. Concisely clustered data indicate similar loading overall lumbar levels, while high scattering data represent vastly differing loading. T-SNE analysis for different model configurations showed clear load case-specific clustering for combined loading and compression for each model configuration as well as in the full dataset, including all models (Figure 3). Although semi-individualized models form closely grouped clusters for each load case, transitions between clusters in highly individualized models are rather smooth, indicating that the load cases are less determining for resulting loads if models include more individual parameters. Anterior–posterior shear forces, primarily resulting from 30° flexion, tended to form a single cluster, while the resulting groups for unloaded and loaded upright standing merged into one another with a pronounced overlap for neutral and loaded standing with 10 kg in front of the chest. However, this effect was not present in models with a uniform spine, which showed concise clustering for respective load cases. Furthermore, the patterns in the results from those models indicated that the results are highly dependent on one intrinsic factor.

Regarding the considered morphological parameters, a strong gradient for LL in anterior–posterior shear forces overarching all load cases could be detected (Figure 4N). Less pronounced but still notable were the effects due to the anterior CoM location (Figure 4Q) and superior CoM location (Figure 4R). Detailed overarching effects of other parameters on lumbar loads could not be identified conclusively over all load cases (Figure 4) and needed to be investigated in detailed level- and load-case-specific analyses.

3.2 Multiple regression

We carried out multiple regression analyses for each load case and lumbar level to investigate the potential effects of various morphological parameters on lumbar loading. For the sake of clarity, we will focus on exemplary results at the L4/L5 level under upright standing load conditions, while briefly addressing other load cases. The results will be discussed specifically for compression forces and anterior–posterior shear forces while specifically emphasizing the changes due to model configuration. Note that a negative β in compression indicates unloading, while in anterior–posterior shear forces, it indicates anterior shifting of the load. Descriptive statistics on the absolute L4/L5 loading from the simulations are provided in Table 2.

3.2.1 Effects of torso weight and distribution

During lifting tasks, TW showed highly significant strong effects ($p < 0.001$) on L4/L5 compression during for all model configurations (Figure 5). Effect strength tends to decrease with an increased degree of model individualization, especially in more

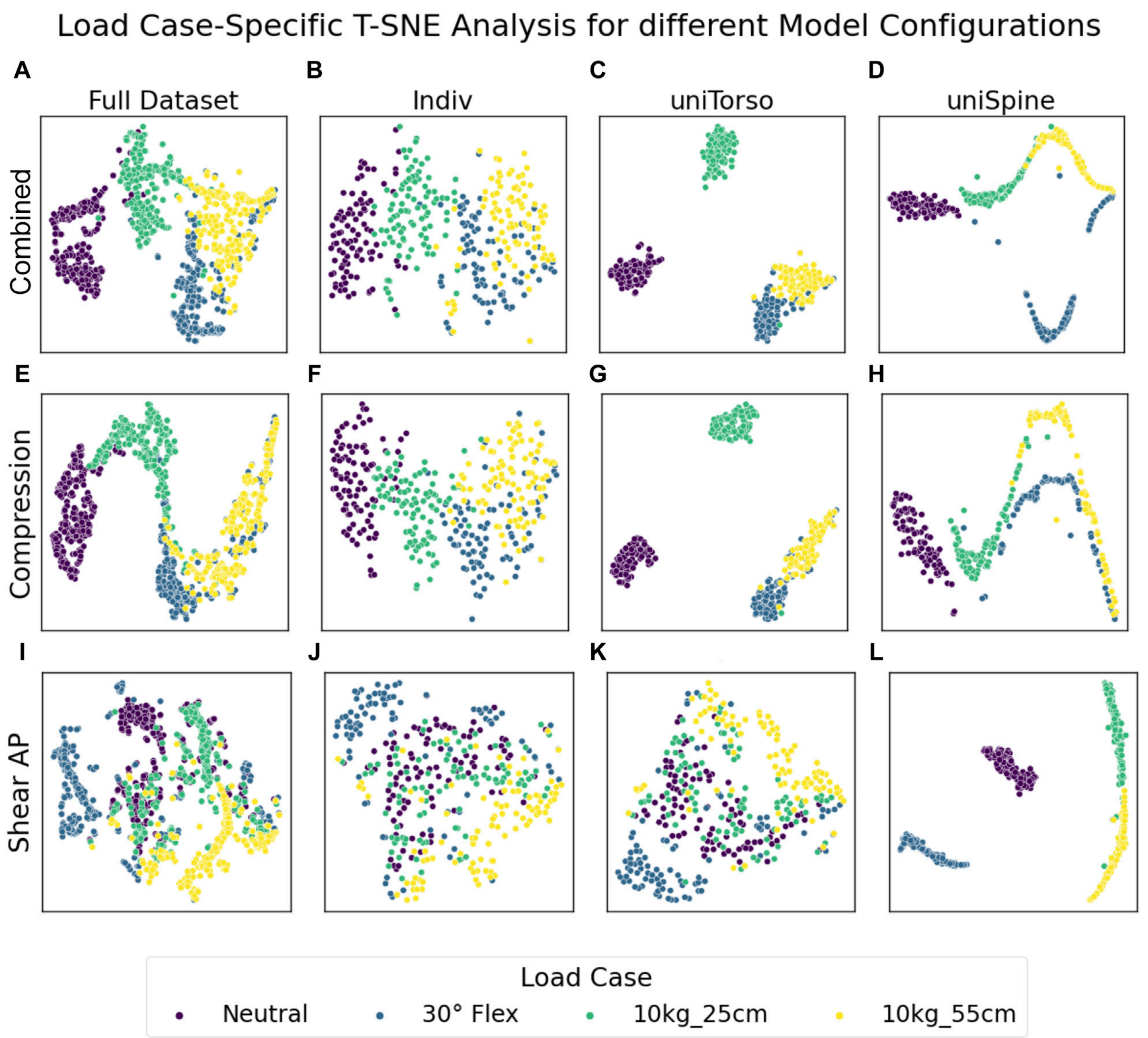

FIGURE 3
Load case-specific T-SNE analysis for the full dataset **(A, E, I)** and each model configuration isolated **(B–D, F–H, J–L)**. Semi-individualized models (uniSpine and uniTorso) showed concise clustering, especially in combined loading and compression **(C, D, G, H)**, while the inclusion of more individual parameters (Indiv) showed that results due to specific load cases were more similar to each other while still preserving clear clusters **(B, F)**. Note that only individualization of the spine **(K)** resulted in comparable scattering in anterior–posterior shear forces as individualization of both the torso and spine **(J)**. *X* and *y* axes represent a virtual space, which serves for projection and is not directly interpretable in terms of the measure and scale of the underlying data.

demanding load cases such as flexion and lifting tasks. In comparison, the left of mass location barely influenced compression forces.

TW led to more pronounced anterior shear forces for neutral and moderately loaded upright standing (10 kg, 25 cm) for both model configurations, while only significant correlations could be detected between TW and posterior shear forces while lifting 10 kg with stretched arms. Significant effects of the calculated left of mass in the sagittal could only be detected for the anterior position in uniSpine models, increasing posterior shear forces. No such effects were observed for Indiv models.

3.2.2 Effects of sagittal alignment and torso height

For compression forces, strong unloading effects could be correlated to TK in both model configurations during loaded upright standing (Figure 6). However, effect strength decreased notably in Indiv models compared to uniTorso models. LL and TH showed significant weak effects for those models, while most of these effects were no longer detectable in Indiv models.

For anterior–posterior shear forces, LL showed the strongest effects for both model configurations. In this study, the respective effects hardly differ depending on the degree of individualization. Looking at the influence of TK on shear forces, significant

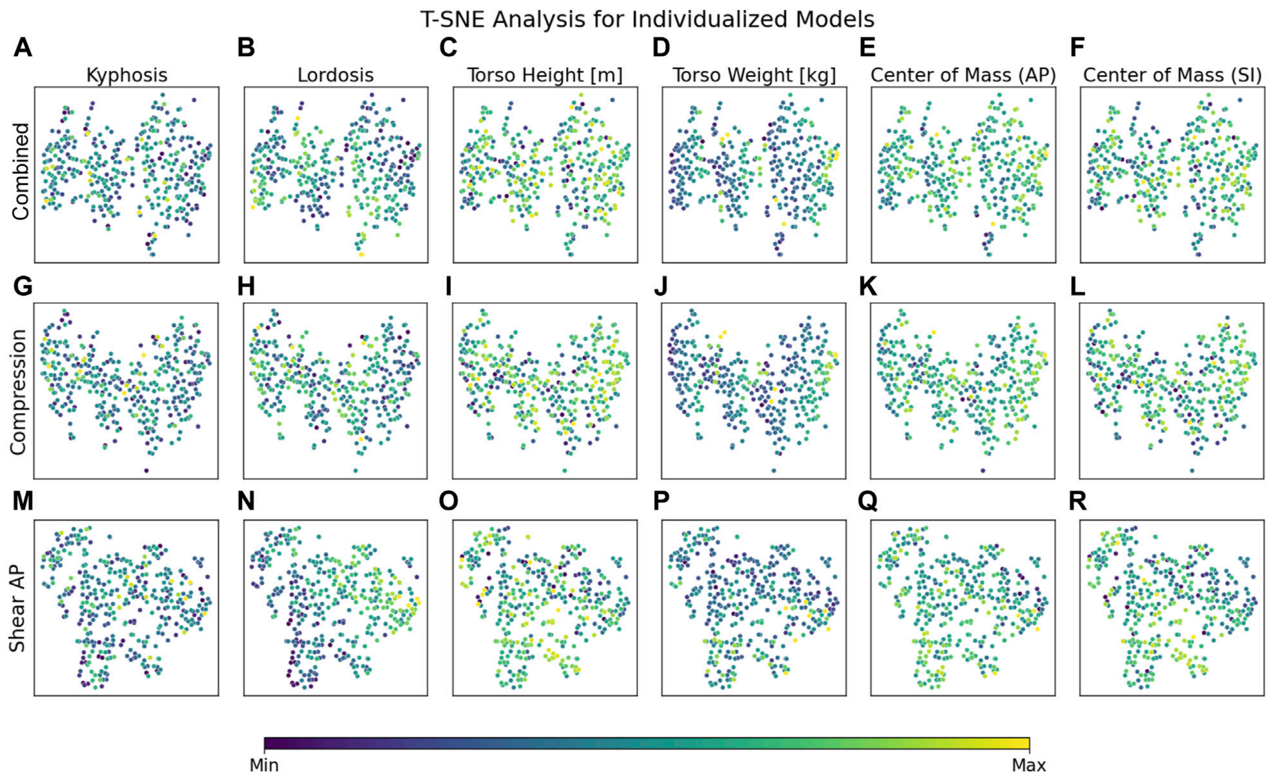

FIGURE 4
T-SNE plots for combined **(A–F)**, compression **(G–L)** and anterior-posterior shear **(M–R)** loading in highly individualized models. T-SNE plots based on individualized models show clear clustering for 30° flexion and for LL across all load cases based on anterior–posterior shear forces **(N)**. The effects of other parameters need to be investigated in detailed level- and load-case-specific analyses. *X* and *y* axes represent a virtual space that serves for projection and is not directly interpretable in terms of the measure and scale of the underlying data.

correlations were detected in terms of a posterior shift of force for increased TK. These effects were even less pronounced in uniTorso models than in Indiv models. Similar trends could be observed for other load cases, whereas no more significant effects of TK could be observed in uniTorso models.

3.2.3 Fit of the applied regression models

Based on the coefficient of determination R^2 we evaluated, we determined to what extent the applied multiple regression analyses were able to explain the observed variability (Table 3). For uniSpine models, multiple regression with only three independent variables (TW, CoM AP, and CoM SI) was able to explain the variability almost completely for all load cases ($R^2 > 0.93$). In comparison, for uniTorso models, the applied regression models showed a rather poor fit ($R^2 < 0.47$). For models, R^2 during 30° flexion was notably lower than in other load cases.

4 Discussion

We investigated how model individualization affects results from musculoskeletal modeling studies on lumbar load estimation. One objective was to determine whether significant effects and clear trends can still be identified despite the increased variance in the results that come with increased model individualization. Furthermore, we aimed to investigate how the effect strengths of single parameters change compared to their respective results in semi-individualized models. Our study indicates that model individualization in combination with large patient cohorts holds the potential to obtain statistically significant results on relevant influencing factors on spinal loading while considering multiple aspects and their interactions. When comparing to semi-individualized models, we could detect changes in effect strength and significance for single influencing parameters, which might lead to misconceptions on the relevance of those parameters for spinal loading when only considering strongly simplified models.

4.1 Results from multivariate analysis

Load case-specific T-SNE analysis showed that for all degrees of individualization, similar trends could be detected (Figure 3). However, it is noticeable that the clusters from simulations with semi-individualized models (uniTorso and uniSpine) were considerably more compact than those from highly individualized models (Indiv). This already shows how different degrees of individualization in the model can influence the results. Considering only semi-individualized models could lead to the assumption that different load cases will result in clearly differing lumbar loading. However, including more individual parameters diffuses the cluster and thus weakens this apparent correlation while still preserving the initial trend.

TABLE 2 Statistics on simulation results, exemplary for level L4/L5.

Load case	Model configuration	Count	Mean	Std	Min	25th Perc.	50th Perc.	75th Perc.	Max
Compression [N]									
Neutral	Indiv	93	604.8	115.7	405.0	518.0	578.3	671.6	933.3
	uniTorso	92	584.0	63.8	479.1	539.0	572.6	622.1	799.2
	uniSpine	93	589.5	104.4	367.9	522.6	571.8	643.0	893.4
30° Flexion	Indiv	88	1,650.9	379.2	1,073.8	1,424.6	1,548.3	1764.3	3,625.2
	uniTorso	89	1,543.4	265.3	1,325.0	1,437.3	1,487.7	1549.3	3,494.7
	uniSpine	93	1,644.0	379.0	921.7	1,405.8	1,586.7	1789.6	2,867.2
10 kg, 25 cm	Indiv	93	964.0	152.5	692.3	850.8	928.6	1059.5	1,393.8
	uniTorso	93	961.1	79.6	816.2	914.8	949.9	989.8	1,291.7
	uniSpine	93	1,004.4	159.1	707.0	893.8	981.4	1090.9	1,516.0
10 kg, 55 cm	Indiv	93	1,677.1	268.7	1,241.2	1,507.7	1,639.8	1796.1	2,755.5
	uniTorso	93	1,655.4	166.9	1,381.4	1,550.3	1,622.7	1696.8	2,326.9
	uniSpine	93	1,738.6	341.4	1,211.0	1,501.6	1,649.7	1879.6	2,895.7
Shear AP [N]									
Neutral	Indiv	93	−99.6	84.9	−312.2	−146.6	−95.9	−42.5	119.4
	uniTorso	92	−92.0	79.1	−334.5	−137.9	−90.3	−35.9	89.6
	uniSpine	93	−125.6	16.1	−169.9	−135.3	−124.2	−116.2	−79.4
30° Flexion	Indiv	88	−108.0	167.8	−734.5	−169.0	−98.0	−3.6	264.1
	uniTorso	89	−101.1	155.3	−777.4	−156.5	−95.7	−5.3	247.0
	uniSpine	93	−99.5	51.3	−522.1	−108.1	−100.9	−89.6	62.8
10 kg, 25 cm	Indiv	93	−120.6	107.3	−476.1	−166.2	−105.6	−46.9	159.2
	uniTorso	93	−115.9	106.2	−522.0	−167.6	−106.2	−50.3	136.1
	uniSpine	93	−136.7	25.6	−262.8	−146.3	−131.3	−119.5	−89.5
10kg, 55 cm	Indiv	93	−219.8	179.0	−916.4	−294.9	−202.1	−95.2	275.2
	uniTorso	93	−213.6	183.7	−978.9	−294.6	−203.1	−93.0	240.4
	uniSpine	93	−212.4	48.0	−517.9	−232.0	−220.8	−198.6	−47.6

Count is the number of successful optimizations. Note that 93 is the maximum number of optimizations carried our per load case and model configuration.

For detailed analysis, we performed multiple regression analyses on simulation results for each load case and level separately. In this context, we focused on the potential effects of torso weight and distribution, as well as sagittal alignment and torso height. In agreement with the literature, TW had the strongest effect for both model configurations (Han et al., 2013; Hajihosseinali et al., 2015; Ghezelbash et al., 2016b). Compression forces were highly affected by TW for both the uniSpine and Indiv models, with decreasing effect strength when individualization was increased. Thus, although both model configurations indicate a relevant influence of TW, one might overestimate the effect of torso weight on lumbar loading when only considering generic models.

Regarding the effects of LL on anterior–posterior shear forces, the tilting of the lumbar vertebrae might most likely be one explanation for this observation. However, this strictly geometric explanation does not address the effect of TK on lumbar loading. Although the observed effects of LL (decreasing compression and increasing anterior shear) are in accordance with the literature (Müller et al., 2021), the observed effects of TK did not support findings from published studies, stating that spinal compression forces increased with increasing TK, with the most pronounced effects in the thoracolumbar and lumbar regions (Bruno et al., 2012). In our study, no significant correlation between TK and compression could be found for the T12/L1 level for both the Indiv and uniTorso models, while significant unloading effects were detected for L4/L5. Apart from the effect of posture, which was additionally stated by Bruno et al. (2012), one reason for this discrepancy could be that increased TK might also be correlated with other morphological factors, such as LL, and therefore leads to changes in muscle activity, which could not be assessed using generic models, where changes in TK are specifically induced without including other possible influences that might come along. To

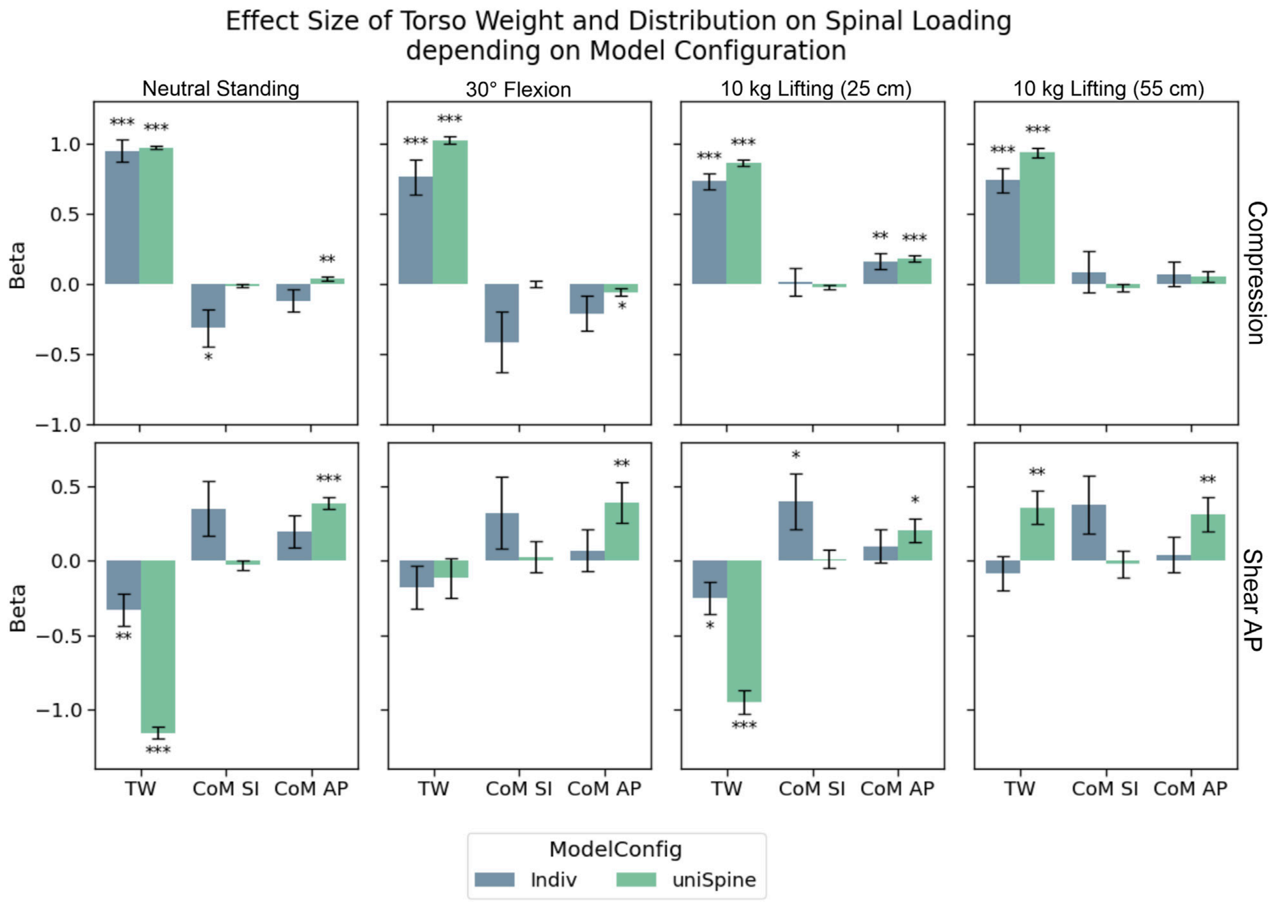

FIGURE 5
Effects of torso weight and distribution on compression and anterior–posterior shear in L4/L5. Significance levels were set to 0.05 (*), 0.01 (**), and 0.001 (***), and error bars depict the standard error of the estimate. Regarding anterior–posterior shear forces, including more individualized parameters in the models (Indiv) leads to a decrease in effect strength and even loss of significance, while effects are highly significant in semi-individualized models (uniSpine). Similar but less pronounced effects could be detected for compression.

check for such a correlation, we performed linear regression analysis, resulting in a moderately significant correlation between LL and TK ($\beta = 0.4$) but a low R^2 (0.16), indicating that only a small part of the variability of thoracic TK can be correlated to LL. In addition, an influence of spinal alignment on the lever arms of the back muscles is conceivable, leading to potentially altered muscle activation and, therefore, changes in resulting lumbar loading. This, however, goes beyond the scope of this study and should be investigated separately.

Significant, slightly unloading effects of TH could mainly be observed for compression forces in upright standing in models with a uniform torso. This effect vastly disappeared in individualized models, making TH the least relevant parameter for lumbar loading in the present study. Assuming that taller subjects tend to have larger vertebrae and, therefore, larger lever arms of respective muscles, leading to decreased necessary muscle forces, could be one possible explanation for this slightly unloading effect (Han et al., 2013; Ghezelbash et al., 2016b). However, this correlation was not specifically investigated in this study and should be addressed in future work.

Overall, a decrease in effect strength and significant correlations with increasing model individualization could be detected, which supports the thesis that vast model simplification can lead to an overestimation of the influence of single parameters. Most striking is the observation that rather strong significant correlations were detected for the effect of TW in anterior–posterior shear forces, which either vanished completely or decreased strikingly with increased model individualization. Anterior–posterior shear forces, therefore, indicate that there are other strong influences that were not considered in this study. This observation underscores the relevance of considering multiple aspects to draw meaningful conclusions from numerical simulation studies.

Comparing the generated forces from highly and semi-individualized models (Figure 7) showed that uniSpine models, in particular, led to high deviation when compared to Indiv models. This effect is more evident for anterior–posterior shear forces, which remain in the same range despite different body weights. This can be observed in different load cases. This emphasizes the relevance of including individualized spines in musculoskeletal modeling when it comes to analyzing large, diverse patient cohorts. Observed outliers could be assigned to individuals with morphological characteristics that differed strongly from the average. Thus, extreme compression forces were mainly observed in one subject with a calculated torso weight of more than 40 kg, which is an increase of almost 20 kg

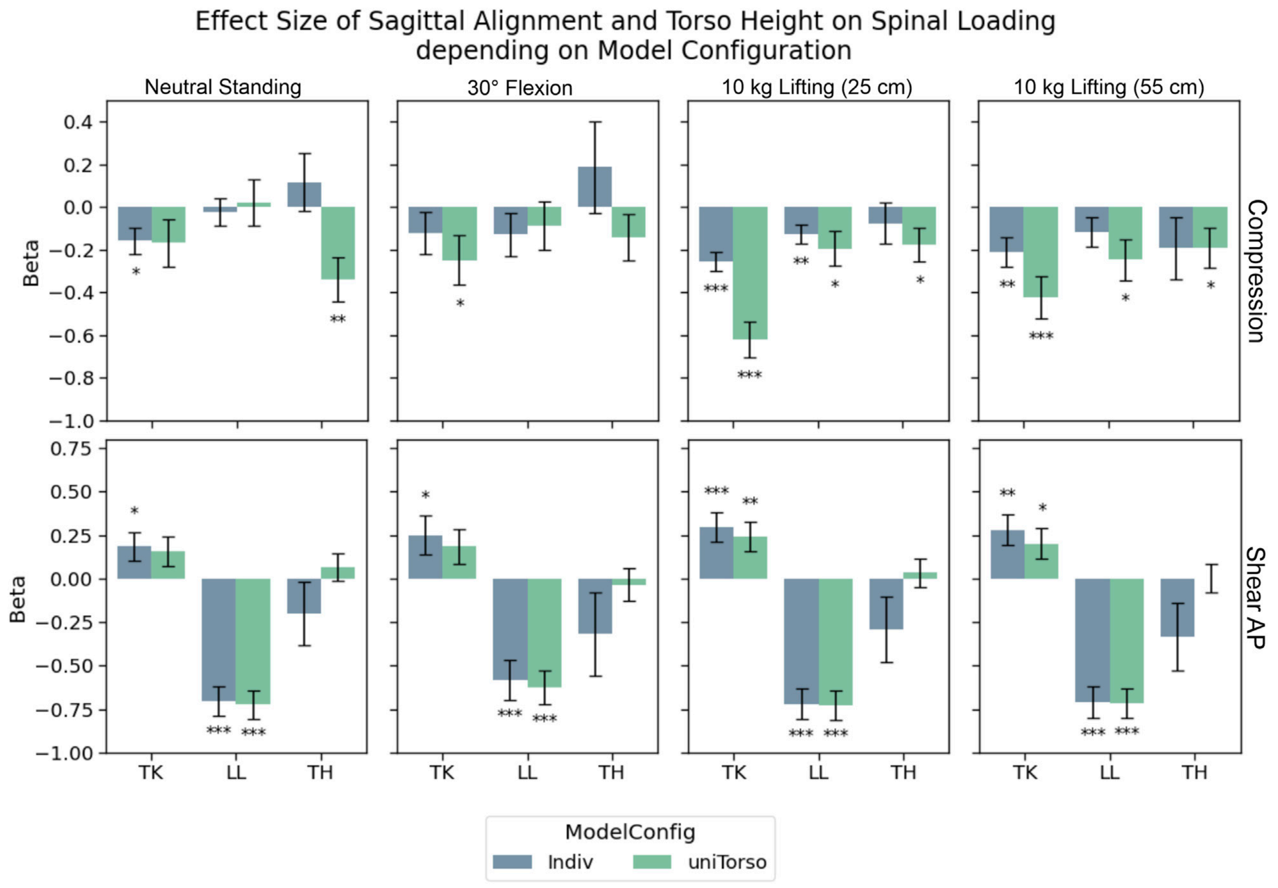

FIGURE 6
Effects of TK, LL, and TH on compression and anterior–posterior shear forces in L4/L5. Significance levels were set to 0.05 (*), 0.01 (**), and 0.001 (***), and error bars depict the standard error of the estimate. Effect strength for TK and LL decreased for compression forces, when models were highly individualized (Indiv) compared to semi-individualized (uniTorso).

TABLE 3 Summary of R^2 values from regression analysis in L4/L5 during neutral standing (neutral), 30° flexion, lifting of 10 kg in front of the chest (10 kg, 25 cm), and with stretched arms (10 kg, 55 cm).

Model configuration	Independent variables	Load case	R^2 (F_{Compr})	R^2 ($F_{ShearAP}$)
Indiv	TK, LL, TH, TW, CoM AP, CoM SI	Neutral standing	0.75	0.54
		30° flexion	0.44	0.29
		10 kg, 25 cm	0.87	0.52
		10 kg, 55 cm	0.70	0.48
uniTorso	TK, LL, TH	Neutral standing	0.11	0.48
		30° flexion	0.09	0.32
		10 kg, 25 cm	0.47	0.47
		10 kg, 55 cm	0.29	0.45
uniSpine	TW, CoM AP, CoM SI	Neutral standing	0.99	0.92
		30° flexion	0.96	0.11
		10 kg, 25 cm	0.97	0.69
		10 kg, 55 cm	0.93	0.38

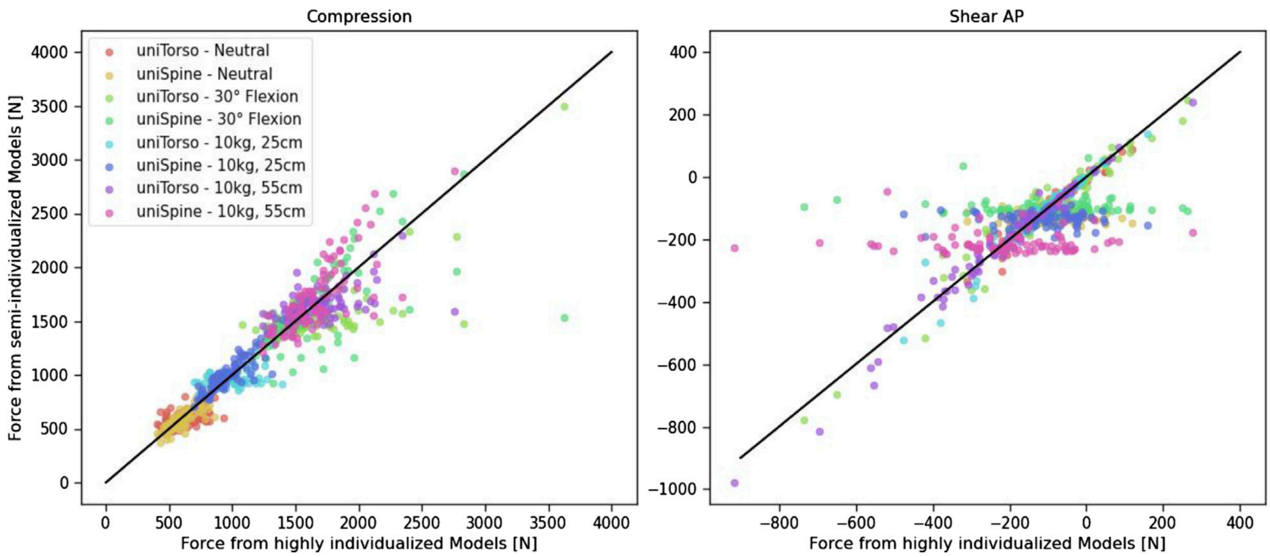

FIGURE 7
Comparison of generated forces from highly and semi-individualized models. The straight black line represents the perfect fit and is only added for orientation.

compared to the average of the cohort. In anterior–posterior shear forces, such extreme values were mainly detected in subjects with conspicuous features in terms of spinal alignment, such as scoliosis or hypolordosis.

4.2 Limitations and future perspectives

There are several limitations to this study. The used dataset with an overall sample size of 93 individuals and an average age of 70 years (Table 1) represents only a small sample of an elderly population and thus does not allow deriving conclusions for a general population. We did not directly include the influence of sex, age, or medical history in this study since respective information on their related effects on biomechanical properties was not available. However, associated parameters might be influential to spinal biomechanics in terms of individual mechanical properties of connective tissue, muscle morphology, or potential fat infiltration. Due to the lack of relevant information in our dataset, we included data from the literature (Panjabi et al., 1976; Christophy et al., 2012; Bayoglu et al., 2017). Therefore, referring to "model individualization" throughout this work, it should be emphasized that even highly individualized models here are only partly individualized, neglecting the variability in those parameters. Individual characteristics of the abdominal muscles, such as physiological cross-sectional areas or potential fat infiltration, can be associated with reduced capacity for muscle force production (Avesani et al., 2023) and, therefore, could lead to changes in spinal loading. In the literature, studies can be found that correlate these parameters to spinal degeneration and low back pain (Shi et al., 2022; Liao et al., 2024). Thus, they should be considered in individualized musculoskeletal modeling of the torso in the future. Although respective muscle-related parameters can be derived *in vivo* from imaging data (Niklasson et al., 2022), the mechanical properties of passive structures can currently only be determined with the help of *in vitro* studies (Panjabi et al., 1976; Pintar et al., 1992; Ashton-Miller and Schultz, 1997; Heuer et al., 2007; White, 2022), which require the isolation of the structure of interest to mount them in respective testing machines and therefore cannot represent the mechanical properties of the modeled subject. In order to obtain consistent datasets for biomechanical models, alternative, noninvasive methods must be developed to determine these parameters in large subject cohorts, e.g., using a combination of experimental studies, multimodal imaging, and artificial neural networks (ANNs), as suggested in earlier publications (Lerchl et al., 2023; Nispel et al., 2023). Furthermore, we neglected the effects of intraabdominal pressure (IAP) on spinal biomechanics. However, individual IAP measurements are usually carried out via the urinary bladder and require standardized conditions, which is why respective information is not accessible in large patient cohorts (Malbrain et al., 2006). However, the biomechanical relevance of the IAP has been subject to several studies in the past, stating its unloading and stabilizing effects on the spine (Arjmand and Shirazi-Adl, 2006; Mokhtarzadeh et al., 2012; Liu et al., 2019b; Guo et al., 2021). Thus, the IAP should be included in future studies, although not necessarily in a patient-specific manner.

Apart from general model-related limitations, which are discussed in detail by Lerchl et al. (2022), we want to emphasize one major limitation related to muscle modeling. Muscles are modeled as simple point-to-point actuators acting on a straight line between the origin and insertion of the respective fascicle. Considering especially multi-articulate muscles, this can induce bias, e.g., due to individual alignment or vertebral geometries. For example, in models with a pronounced LL, this can lead to lever arms that are considerably larger compared to models that redirect muscle fascicles along the spine. In the future, this should be addressed by including via-points along the spine to ensure realistic lines of action and, consequently, lever arms.

Complex models require the conscientious application and reflection of appropriate analyses. Evaluation of the coefficients of determination (R^2) showed that most of the variability in uniSpine models could be explained by TW and CoM, while R^2 decreased strikingly for uniTorso models. This can most likely be explained by the fact that the included individual representation of the trunk weight as simple point masses in a calculated left of mass does not induce further variability in the models apart from the parameters considered in the regression (TW, CoM AP, and CoM SI). However, individualization of the spine during this study included more parameters than only TK, LL, and TH, such as individual vertebral geometries. For one thing, this leads to a variation in the deformation of the included passive structures, namely, the intervertebral disc and the paraspinal ligaments, during joint deflection. The elastic properties produce a mechanical response in the form of forces and moments in the respective structures. In combination with individual vertebral geometries, this will result in individual additional loading for each subject and, therefore, individual loading of the intervertebral joints. On the other hand, individual vertebral geometries may affect lever arms for muscles and therefore muscle activation, ultimately resulting in lumbar loading, which could also be the reason for slightly unloading effects with increased TH. This might be one reason for the poor fits detected during 30° flexion for model configurations with individualized spines. It is noticeable that models that neglect the influence of TW (uniTorso) generally show the poorest fit of the regression model. The overall decrease in the R^2 value could be an indicator that TW is the most important determinant of spinal loading. If this is neglected, other parameters, such as vertebral geometries, become more evident and thus reduce the proportion of variability explained by the applied regression model. In the future, it will be essential to examine the underlying datasets in depth with regard to those parameters and potential interrelations between them prior to simulation in order to enable a profound and responsible interpretation of the intended correlation analyses.

Finally, an ultimate evaluation of the different approaches regarding their accurate representation of the *in vivo* biomechanics of a diverse population cannot be made directly. We validated our highly individualized model of a single male based on spinal loading and muscle activation of few subjects from *in vivo* data in a previously published study (Lerchl et al., 2022), but respective data are usually available only for small sample sizes due to the invasive character of *in vivo* measurements. Therefore, a population-based validation of the models in their different configurations is not feasible. However, there are several indications in the literature that model individualization in biomechanics leads to more accurate and realistic results (Akhundov et al., 2022; Davico et al., 2022; Meszaros-Beller et al., 2023). Thus, Davico et al. (2022) explored the influence of individualization in neuromusculoskeletal knee models of children. Based on experimentally derived data, models with different degrees of neuromusculoskeletal individualization were developed, and the obtained muscle and joint reaction forces were evaluated regarding physiological plausibility. In that context, the authors concluded that personalization of musculoskeletal anatomy and muscle activation patterns had the largest overall effect (Davico et al., 2022). Furthermore, the diversity of potential causes for spinal degeneration also supports the assumption that the strong reduction of individual influencing factors does not do justice to the complexity of spinal biomechanics (Kalichman et al., 2017; Kalichman et al., 2009). Thus, we are convinced that consideration of biological variability in musculoskeletal modeling is necessary and will increase a profound understanding of the complex interaction of various parameters influencing spinal loads and eventually leading to spinal degeneration due to overloading. One possible way to deal with such limited validation possibilities is to investigate potential correlations between spinal loading and clinical parameters, such as possible degenerative changes, based on large-scale, longitudinal studies (e.g., the German National Cohort). This can help us understand whether and how morphological and biomechanical characteristics can actually lead to mechanical overloading and, eventually, spinal degeneration.

5 Conclusion

In this study, we systematically investigated the effects of different degrees of individualization in multi-body models of the spine on generated lumbar loads and their potential correlations with morphological parameters. We used our validated pipeline for the automated generation of multi-body models of the trunk to create 279 models based on CT data from 93 patients. The influence on observed correlations was analyzed with respect to significance, effect strength, and explainability of observed variability in the results from static simulations based on multiple regression analysis. We were able to identify significant effects on lumbar loads for all load cases in models with different degrees of individualization. However, our results show that the degree of individualization influences the observed effect strength of individual parameters. For instance, in semi-individualized models, TW was the main influencing factor in both compression and shear loading. Including additional individualized parameters, however, showed that LL is more determinant for anterior–posterior shear forces and thus relatively reduces the importance of TW in this aspect. Based on the results of this study, we conclude that model individualization in combination with large patient cohorts holds the potential to obtain statistically significant results on relevant influencing factors on spinal loading while considering multiple aspects and their interactions. They can help identify potential risk factors or mechanical overloading based on data that represent the complexity of spinal biomechanics in a more realistic way than generic models can. However, a special focus should be put on the systematic and vastly holistic consideration of included parameters in applied analyses to be able to draw meaningful conclusions from studies including individualized models.

Data availability statement

The raw data supporting the conclusion of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving humans were approved by the ethics committee at the Technical University of Munich (date of approval: 26.02.2019, ID 27/19 S-SR). The studies were conducted in accordance with the local legislation and institutional requirements. The ethics committee/institutional review board waived the requirement of written informed consent for participation from the participants or the participants' legal guardians/next of kin because of the anonymous, retrospective analysis of the project.

Author contributions

TL: conceptualization, methodology, writing–original draft, and writing–review and editing. KN: methodology and writing–review and editing. JB: methodology and writing–review and editing. AS: methodology and writing–review and editing. ME: methodology and writing–review and editing. CF: methodology and writing–review and editing. VS: writing–review and editing. JK: conceptualization, funding acquisition, methodology, project administration, supervision, and writing–review and editing.

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Conflict of interest

JK and AS are co-founders of Bonescreen GmbH.

The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Publisher's note

References

Akhavanfar, M. H., Kazemi, H., Eskandari, A. H., and Arjmand, N. (2018). Obesity and spinal loads; a combined mr imaging and subject-specific modeling investigation. *J. biomechanics* 70, 102–112. doi:10.1016/j.jbiomech.2017.08.009

Akhundov, R., Saxby, D. J., Diamond, L. E., Edwards, S., Clausen, P., Dooley, K., et al. (2022). Is subject-specific musculoskeletal modelling worth the extra effort or is generic modelling worth the shortcut? *PloS one* 17, e0262936. doi:10.1371/journal.pone.0262936

Arjmand, N., and Shirazi-Adl, A. (2006). Role of intra-abdominal pressure in the unloading and stabilization of the human spine during static lifting tasks. *Eur. Spine J.* 15, 1265–1275. doi:10.1007/s00586-005-0012-9

Ashton-Miller, J. A., and Schultz, A. B. (1997). Biomechanics of the human spine. *Basic Orthop. biomech.* 2, 353–385.

Avesani, C. M., de Abreu, A. M., Ribeiro, H. S., Brismar, T. B., Stenvinkel, P., Sabatino, A., et al. (2023). Muscle fat infiltration in chronic kidney disease: a marker related to muscle quality, muscle strength and sarcopenia. *J. Nephrol.* 36, 895–910. doi:10.1007/s40620-022-01553-0

Banks, J. J., Alemi, M. M., Allaire, B. T., Lynch, A. C., Bouxsein, M. L., and Anderson, D. E. (2023). Using static postures to estimate spinal loading during dynamic lifts with participant-specific thoracolumbar musculoskeletal models. *Appl. Ergon.* 106, 103869. doi:10.1016/j.apergo.2022.103869

Bassani, T., Casaroli, G., and Galbusera, F. (2019). Dependence of lumbar loads on spinopelvic sagittal alignment: an evaluation based on musculoskeletal modeling. *PloS one* 14, e0207997. doi:10.1371/journal.pone.0207997

Bayoglu, R., Geeraedts, L., Groenen, K. H. J., Verdonschot, N., Koopman, B., and Homminga, J. (2017). Twente spine model: a complete and coherent dataset for musculo-skeletal modeling of the lumbar region of the human spine. *J. biomechanics* 53, 111–119. doi:10.1016/j.jbiomech.2017.01.009

Beaucage-Gauvreau, E., Robertson, W. S. P., Brandon, S. C. E., Fraser, R., Freeman, B. J. C., Graham, R. B., et al. (2019). Validation of an opensim full-body model with detailed lumbar spine for estimating lower lumbar spine loads during symmetric and asymmetric lifting tasks. *Comput. Methods Biomechanics Biomed. Eng.* 22, 451–464. doi:10.1080/10255842.2018.1564819

Bruno, A. G., Anderson, D. E., D'Agostino, J., and Bouxsein, M. L. (2012). The effect of thoracic kyphosis and sagittal plane alignment on vertebral compressive loading. *J. Bone Mineral Res.* 27, 2144–2151. doi:10.1002/jbmr.1658

Bruno, A. G., Bouxsein, M. L., and Anderson, D. E. (2015). Development and validation of a musculoskeletal model of the fully articulated thoracolumbar spine and rib cage. *J. biomechanical Eng.* 137, 081003. doi:10.1115/1.4030408

Bruno, A. G., Burkhart, K., Allaire, B., Anderson, D. E., and Bouxsein, M. L. (2017). Spinal loading patterns from biomechanical modeling explain the high incidence of vertebral fractures in the thoracolumbar region. *J. Bone Mineral Res.* 32, 1282–1290. doi:10.1002/jbmr.3113

Burkhart, K., Grindle, D., Bouxsein, M. L., and Anderson, D. E. (2020). Between-session reliability of subject-specific musculoskeletal models of the spine derived from optoelectronic motion capture data. *J. biomechanics* 112, 110044. doi:10.1016/j.jbiomech.2020.110044

Christophy, M., Faruk Senan, N. A., Lotz, J. C., and O'Reilly, O. M. (2012). A musculoskeletal model for the lumbar spine. *Biomechanics Model. Mechanobiol.* 11, 19–34. doi:10.1007/s10237-011-0290-6

Crowninshield, R. D., and Brand, R. A. (1981). A physiologically based criterion of muscle force prediction in locomotion. *J. biomechanics* 14, 793–801. doi:10.1016/0021-9290(81)90035-X

Davico, G., Lloyd, D. G., Carty, C. P., Killen, B. A., Devaprakash, D., and Pizzolato, C. (2022). Multi-level personalization of neuromusculoskeletal models to estimate physiologically plausible knee joint contact forces in children. *Biomechanics Model. Mechanobiol.* 21, 1873–1886. doi:10.1007/s10237-022-01626-w

de Zee, M., Hansen, L., Wong, C., Rasmussen, J., and Simonsen, E. B. (2007). A generic detailed rigid-body lumbar spine model. *J. biomechanics* 40, 1219–1227. doi:10.1016/j.jbiomech.2006.05.030

El Ouaaid, Z., Shirazi-Adl, A., and Plamondon, A. (2016). Effects of variation in external pulling force magnitude, elevation, and orientation on trunk muscle forces, spinal loads and stability. *J. biomechanics* 49, 946–952. doi:10.1016/j.jbiomech.2015.09.036

Eskandari, A. H., Arjmand, N., Shirazi-Adl, A., and Farahmand, F. (2019). Hypersensitivity of trunk biomechanical model predictions to errors in image-based kinematics when using fully displacement-control techniques. *J. biomechanics* 84, 161–171. doi:10.1016/j.jbiomech.2018.12.043

Fasser, M.-R., Jokeit, M., Kalthoff, M., Gomez Romero, D. A., Trache, T., Snedeker, J. G., et al. (2021). Subject-specific alignment and mass distribution in musculoskeletal models of the lumbar spine. *Front. Bioeng. Biotechnol.* 9, 721042. doi:10.3389/fbioe.2021.721042

Favier, C. D., Finnegan, M. E., Quest, R. A., Honeyfield, L., McGregor, A. H., and Phillips, A. T. M. (2021). An open-source musculoskeletal model of the lumbar spine and lower limbs: a validation for movements of the lumbar spine. *Comput. Methods Biomechanics Biomed. Eng.* 24, 1310–1325. doi:10.1080/10255842.2021.1886284

Galbusera, F., Brayda-Bruno, M., Costa, F., and Wilke, H.-J. (2014). Numerical evaluation of the correlation between the normal variation in the sagittal alignment of the lumbar spine and the spinal loads. *J. Orthop. Res.* 32, 537–544. doi:10.1002/jor.22569

Ghezelbash, F., Shirazi-Adl, A., Arjmand, N., El-Ouaaid, Z., and Plamondon, A. (2016a). Subject-specific biomechanics of trunk: musculoskeletal scaling, internal loads and intradiscal pressure estimation. *Biomechanics Model. Mechanobiol.* 15, 1699–1712. doi:10.1007/s10237-016-0792-3

Ghezelbash, F., Shirazi-Adl, A., Arjmand, N., El-Ouaaid, Z., Plamondon, A., and Meakin, J. R. (2016b). Effects of sex, age, body height and body weight on spinal loads: sensitivity analyses in a subject-specific trunk musculoskeletal model. *J. biomechanics* 49, 3492–3501. doi:10.1016/j.jbiomech.2016.09.026

Guo, J., Guo, W., and Ren, G. (2021). Embodiment of intra-abdominal pressure in a flexible multibody model of the trunk and the spinal unloading effects during static lifting tasks. *Biomechanics Model. Mechanobiol.* 20, 1599–1626. doi:10.1007/s10237-021-01465-1

Hajihosseinali, M., Arjmand, N., and Shirazi-Adl, A. (2015). Effect of body weight on spinal loads in various activities: a personalized biomechanical modeling approach. *J. biomechanics* 48, 276–282. doi:10.1016/j.jbiomech.2014.11.033

Han, K.-S., Rohlmann, A., Zander, T., and Taylor, W. R. (2013). Lumbar spinal loads vary with body height and weight. *Med. Eng. Phys.* 35, 969–977. doi:10.1016/j.medengphy.2012.09.009

Heuer, F., Schmidt, H., Klezl, Z., Claes, L., and Wilke, H.-J. (2007). Stepwise reduction of functional spinal structures increase range of motion and change lordosis angle. *J. biomechanics* 40, 271–280. doi:10.1016/j.jbiomech.2006.01.007

Ignasiak, D., Dendorfer, S., and Ferguson, S. J. (2016). Thoracolumbar spine model with articulated ribcage for the prediction of dynamic spinal loading. *J. biomechanics* 49, 959–966. doi:10.1016/j.jbiomech.2015.10.010

Kalichman, L., Carmeli, E., and Been, E. (2017). The association between imaging parameters of the paraspinal muscles, spinal degeneration, and low back pain. *BioMed Res. Int.* 2017, 1–14. doi:10.1155/2017/2562957

Kalichman, L., Guermazi, A., Li, L., and Hunter, D. J. (2009). Association between age, sex, bmi and ct-evaluated spinal degeneration features. *J. back Musculoskelet. rehabilitation* 22, 189–195. doi:10.3233/bmr-2009-0232

Lerchl, T., El Husseini, M., Bayat, A., Sekuboyina, A., Hermann, L., Nispel, K., et al. (2022). Validation of a patient-specific musculoskeletal model for lumbar load estimation generated by an automated pipeline from whole body ct. *Front. Bioeng. Biotechnol.* 10, 862804. doi:10.3389/fbioe.2022.862804

Lerchl, T., Nispel, K., Baum, T., Bodden, J., Senner, V., and Kirschke, J. S. (2023). Multibody models of the thoracolumbar spine: a review on applications, limitations, and challenges. *Bioengineering* 10, 202. doi:10.3390/bioengineering10020202

Liao, Y., Liu, X., Xu, T., Li, C., Xiao, Q., and Zhang, X. (2024). Association between paraspinal muscle fat infiltration and regional kyphosis angle in thoracolumbar fracture patients: a retrospective study. *Sci. Rep.* 14, 2364. doi:10.1038/s41598-024-53017-z

Little, J. P., and Adam, C. J. (2015). Geometric sensitivity of patient-specific finite element models of the spine to variability in user-selected anatomical landmarks. *Comput. Methods Biomechanics Biomed. Eng.* 18, 676–688. doi:10.1080/10255842.2013.843673

Liu, T., Khalaf, K., Adeeb, S., and El-Rich, M. (2019a). Effects of lumbo-pelvic rhythm on trunk muscle forces and disc loads during forward flexion: a combined musculoskeletal and finite element simulation study. *J. biomechanics* 82, 116–123. doi:10.1016/j.jbiomech.2018.10.009

Liu, T., Khalaf, K., Adeeb, S., and El-Rich, M. (2019b). Numerical investigation of intra-abdominal pressure effects on spinal loads and load-sharing in forward flexion. *Front. Bioeng. Biotechnol.* 7, 428. doi:10.3389/fbioe.2019.00428

Malbrain, M. L., Cheatham, M. L., Kirkpatrick, A., Sugrue, M., Parr, M., De Waele, J., et al. (2006). Results from the international conference of experts on intra-abdominal hypertension and abdominal compartment syndrome. i. definitions. *Intensive care Med.* 32, 1722–1732. doi:10.1007/s00134-006-0349-5

Meszaros-Beller, L., Hammer, M., Riede, J. M., Pivonka, P., Little, J. P., and Schmitt, S. (2023). Effects of geometric individualisation of a human spine model on load sharing: neuro-musculoskeletal simulation reveals significant differences in ligament and muscle contribution. *Biomechanics Model. Mechanobiol.* 22, 669–694. doi:10.1007/s10237-022-01673-3

Mokhtarzadeh, H., Farahmand, F., Shirazi-Adl, A., Arjmand, N., Malekipour, F., and Parnianpour, M. (2012). The effects of intra-abdominal pressure on the stability and unloading of the spine. *J. Mech. Med. Biol.* 12, 1250014. doi:10.1142/s0219519412004508

Müller, A., Rockenfeller, R., Damm, N., Kosterhon, M., Kantelhardt, S. R., Aiyangar, A. K., et al. (2021). Load distribution in the lumbar spine during modeled compression depends on lordosis. *Front. Bioeng. Biotechnol.* 9, 661258. Cited by: 1; All Open Access, Gold Open Access, Green Open Access. doi:10.3389/fbioe.2021.661258

Murtezani, A., Ibraimi, Z., Sllamniku, S., Osmani, T., and Sherifi, S. (2011). Prevalence and risk factors for low back pain in industrial workers. *Folia medica.* 53, 68–74. doi:10.2478/v10153-011-0060-3

Naserkhaki, S., Jaremko, J. L., and El-Rich, M. (2016). Effects of inter-individual lumbar spine geometry variation on load-sharing: geometrically personalized finite element study. *J. biomechanics* 49, 2909–2917. doi:10.1016/j.jbiomech.2016.06.032

Niklasson, E., Borga, M., Dahlqvist Leinhard, O., Widholm, P., Andersson, D. P., Wiik, A., et al. (2022). Assessment of anterior thigh muscle size and fat infiltration using single-slice ct imaging versus automated mri analysis in adults. *Br. J. Radiology* 95, 20211094. doi:10.1259/bjr.20211094

Nispel, K., Lerchl, T., Senner, V., and Kirschke, J. S. (2023). Recent advances in coupled mbs and fem models of the spine—a review. *Bioengineering* 10, 315. doi:10.3390/bioengineering10030315

Overbergh, T., Severijns, P., Beaucage-Gauvreau, E., Jonkers, I., Moke, L., and Scheys, L. (2020). Development and validation of a modeling workflow for the generation of image-based, subject-specific thoracolumbar models of spinal deformity. *J. Biomechanics* 110, 109946. doi:10.1016/j.jbiomech.2020.109946

Panjabi, M. M., Brand, R., and White, A. (1976). Mechanical properties of the human thoracic spine as shown by three-dimensional load-displacement curves. *JBJS* 58, 642–652. doi:10.2106/00004623-197658050-00011

Pearsall, D. J., Reid, J. G., and Livingston, L. A. (1996). Segmental inertial parameters of the human trunk as determined from computed tomography. *Ann. Biomed. Eng.* 24, 198–210. doi:10.1007/BF02667349

Périé, D., Sales De Gauzy, J., and Hobatho, M. C. (2002). Biomechanical evaluation of cheneau-toulouse-munster brace in the treatment of scoliosis using optimisation approach and finite element method. *Med. Biol. Eng. Comput.* 40, 296–301. doi:10.1007/BF02344211

Pintar, F. A., Yoganandan, N., Myers, T., Elhagediab, A., and Sances Jr, A. (1992). Biomechanical properties of human lumbar spine ligaments. *J. biomechanics* 25, 1351–1356. doi:10.1016/0021-9290(92)90290-h

Rabey, M., Smith, A., Kent, P., Beales, D., Slater, H., and O'Sullivan, P. (2019). Chronic low back pain is highly individualised: patterns of classification across three unidimensional subgrouping analyses. *Scand. J. pain* 19, 743–753. doi:10.1515/sjpain-2019-0073

Rohlmann, A., Graichen, F., Kayser, R., Bender, A., and Bergmann, G. (2008). Loads on a telemeterized vertebral body replacement measured in two patients. *Spine* 33, 1170–1179. doi:10.1097/brs.0b013e3181722d52

Sekuboyina, A., Husseini, M. E., Bayat, A., Löffler, M., Liebl, H., Li, H., et al. (2020). *Verse: a vertebrae labelling and segmentation benchmark for multi-detector ct images. arXiv preprint arXiv:2001.09193.*

Shi, L., Yan, B., Jiao, Y., Chen, Z., Zheng, Y., Lin, Y., et al. (2022). Correlation between the fatty infiltration of paraspinal muscles and disc degeneration and the underlying mechanism. *BMC Musculoskelet. Disord.* 23, 509. doi:10.1186/s12891-022-05466-8

Tagliaferri, S. D., Miller, C. T., Owen, P. J., Mitchell, U. H., Brisby, H., Fitzgibbon, B., et al. (2020). Domains of chronic low back pain and assessing treatment effectiveness: a clinical perspective. *Pain Pract.* 20, 211–225. doi:10.1111/papr.12846

Takahashi, I., Kikuchi, S.-i., Sato, K., and Sato, N. (2006). Mechanical load of the lumbar spine during forward bending motion of the trunk-a biomechanical study. *Spine* 31, 18–23. doi:10.1097/01.brs.0000192636.69129.fb

Van der Maaten, L., and Hinton, G. (2008). Visualizing data using t-sne. *J. Mach. Learn. Res.* 9.

Vergari, C., Courtois, I., Ebermeyer, E., Bouloussa, H., Vialle, R., and Skalli, W. (2016). Experimental validation of a patient-specific model of orthotic action in adolescent idiopathic scoliosis. *Eur. Spine J.* 25, 3049–3055. doi:10.1007/s00586-016-4511-7

White, A. A. (2022). *Clinical biomechanics of the spine*. Lippincott Williams & Wilkins.

Wilke, H.-J., Neef, P., Hinz, B., Seidel, H., and Claes, L. (2001). Intradiscal pressure together with anthropometric data – a data set for the validation of models. *Clin. Biomech.* 16, S111–S126. doi:10.1016/S0268-0033(00)00103-0

Wong, K. W. N., Luk, K. D. K., Leong, J. C. Y., Wong, S. F., and Wong, K. K. Y. (2006). Continuous dynamic spinal motion analysis. *Spine* 31, 414–419. doi:10.1097/01.brs.0000199955.87517.82

Conference Abstracts

A MULTIVARIANT ANALYSIS ON THE EFFECTS OF MORPHOLOGICAL PARAMETERS ON LUMBAR LOADING IN A LARGE PATIENT COHORT

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Introduction

Multibody models of the torso allow the systematic investigation of spinal biomechanics from a comprehensive perspective and can take multiple aspects of mechanical loading into account. However, the vast majority of published studies uses generic models to focus on the effect of single factors such as sagittal alignment [1] or body weight [2]. Those studies however, fail to capture the complexity of clinical practice. Therefore, a trend towards individualized models has emerged in the relevant literature [3,4]. To obtain meaningful and statistically relevant results, the analysis of large and diverse patient cohorts is essential. Population-based cohort studies (e.g. German National Cohort) provide such datasets and during the past decade, developments in data analytics - especially in the field of artificial intelligence [5] - have provided promising tools to make them scientifically accessible.

Methods

We used a validated pipeline for automated generation of individualized multibody models of the torso [3, 5] to examine the effects of six parameters on lumbar loading in a cohort of 93 patients: thoracic kyphosis (TK), lumbar lordosis (LL), torso height (TH), torso weight (TW), anterior-posterior, and superior-inferior position of center of mass (CoM AP, CoM SI). Models included individual vertebral geometries, spinal alignment as well as torso weight and its distribution, combined with a generic ribcage, head-neck, pelvis, intervertebral disks and spinal ligaments. We simulated four static loading tasks: neutral standing, 30° flexion, and upright standing with a weight of 10 kg lifted close to the chest and with stretched arms using inverse dynamics and static optimization. Subsequently, we performed t-distributed statistic neighbor embedding (T-SNE) to identify possible patterns across all load cases and lumbar levels and multiple regression to analyze normalized effect sizes (β) and significance (p) of possible correlations between the investigated parameters and sagittal lumbar loading for each level and load case separately.

Results

T-SNE analysis showed cross-level and –load case effects of lumbar lordosis on anterior-posterior shear forces. Multiple regression for each load case and lumbar level showed highly significant ($p < 0.001$) strong correlations of the body weight and compression forces ($\beta > 0.6$) over all levels and load cases (Figure 1).

Regarding anterior-posterior shear forces, strongest significant effects could be detected for alignment-specific parameters (TK, LL) with a more pronounced effect in the lower lumbar spine ($\beta \approx 0.5$, $p < 0.001$). In 30° flexion, only few significant correlations could be detected, mainly for TW on compression. R^2 values ranged for loaded and unloaded standing from ~0.6 to ~0.9, but decreased to ~0.4 for 30° flexion.

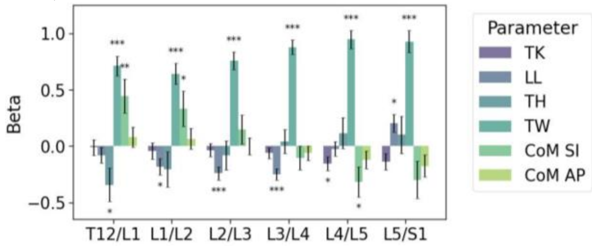

Figure 1: Effect sizes β of investigated parameters on compression forces in neutral standing. Significance levels were set to 0.05 (*), 0.01 (**) and 0.001 (***).

Discussion

We were able to identify significant correlations for different parameters on lumbar loading using individualized models derived from a large diverse patient cohort. However, the obtained R^2 values indicate, that the given variability can only partially be explained by the investigated parameters. Especially during flexion, a considerable proportion of the influencing factors remain unaddressed by the analysis carried out. For example, effects of passive structures, which, in combination with individual vertebral geometries, lead to additional loading, were not taken into account in our analysis. We therefore conclude, that individualized models hold the potential to investigate diverse spinal biomechanics. However, a comprehensive analysis of the underlying patient data is necessary to do justice to the complexity at hand.

References

1. Müller et al, Front. Bioeng. Biotechnol. 9:661258, 2021.
2. Akhanvanfar et al, J Biomech, 70:102-1012, 2018.
3. Lerchl T et al, Front Bioeng Biotechnol. 10:862804, 2022.
4. Fasser et al., Front. Bioeng. Biotechnol. 9:721042, 2021.
5. Sekuboyina et al, J MedIA 73:103266, 2021

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The Role of Spinal Muscles for Lumbar Loads during Static Loading Tasks in Large Patient Cohorts: A Musculoskeletal Modeling Study

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INTRODUCTION

Numerical models of the musculoskeletal system are an integral part of biomechanical and clinical research. Multibody modeling allows the consideration of biomechanical systems from a holistic perspective, and thus, takes into account multiple influencing factors of mechanical loads. Being the source of major health issues worldwide, the human spine is subject to a variety of studies using these models to investigate and understand healthy and pathological biomechanics of the upper body. Models usually consider muscle mophology from cadaver studies or imaging data from a single individual. However, muscle morphology is highly individual, depending on various factors, such as age, fitness, genome, or pathological changes of the musculoskeletal system of the respective subject. To this date, only few studies exist, that systematically investigate the effects of altering muscle morphology on spinal loading[1].

METHODS

We used our validated pipeline for automated generation of individualized models of the torso with detailed lumbar spine[2] to assess the influence of altering muscle physiological cross sectional area (PCSA) on spinal loading in 93 patients. For abdominal muscle force estimation, we used a combination of inverse dynamics and static optimization (*global search*, *fmincon*, *Matlab*). The cost function was defined as the sum of cubed muscle stress and maximum muscle stress was set to 1MPa. We simulated static upright standing, 30° flexion, and symmetric lifting of 10kg close to the chest and with stretched arms. The PCSA of single fascicles of erector spinae (ES) and multifidus muscle (MF) were each set to 0%, 30%, and 50%. Resulting spinal loads were compared to results from simulations with full muscle architecture considering the patient's individual upper body weight and spinal alignment.

RESULTS AND DISCUSSION

Depending on individual lumbar alignment, effects were most evident in upper (T12/L1) and lower levels of the lumbar spine (L5/S1) in loading tasks with a 10 kg weight lifted with stretched arms. Normalized anterior-posterior shear loads increased to 128 % on average, with a maximum of 208 % at T12/L1 for ES PCSA reduced to 30%. Simultaneously, compression forces were increased up to 120% (Figure 1).

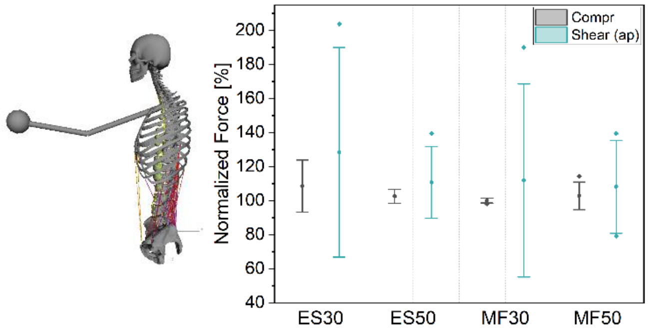

Figure 1 Normalized anterior-posterior shear and compression forces in T12/L1 during lifting of 10 kg with stretched arms under consideration of individual anthropometry and spinal alignment.

Static equilibrium conditions could not be met for the vast majority of models with disabled ES or MF. With increasing body weight or lumbar malalignment, models with reduced MF were less likely to meet static equilibrium conditions for challenging loading tasks.

CONCLUSIONS

Our results indicate that the loss of functional muscle cross sectional area, e.g. due to muscle atrophy or intramuscular fat, leads to increased spinal loading with a pronounced effect on anterior-posterior shear forces. Furthermore, our study emphasizes the relevance of paraspinal musculature for spinal stability and associated malalignment[3] to prevent potentially pathological overload.

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REFERENCES

[1] Wang K et al, *Bioengineering (Basel)*. **10**(1):67, 2023.

[2] Lerchl T et al, *Front Bioeng Biotechnol*. **10**:862804, 2022.

[3] Muellner M et al, *Spine J*. **22**(12):2006-2016, 2022