In Silico Investigations of Surgical Interventions in the Thoracolumbar and Lumbopelvic Region

PhD thesis outline

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1. INTRODUCTION

1.1. In Silico Medicine and finite element analysis

The term “in silico medicine” is frequently employed to denote the translational application of modelling and simulation in diagnosing, treating, or preventing diseases. The first biomechanical application of finite element analysis (FEA) was reported by Brekelmans et al. in 1972. Subsequently, in 2002, Fagan et al. conducted a comprehensive review of the contributions of FEA to the understanding of the spine, its components and behaviour in healthy, diseased or damaged states. Since Fagan’s study, FEA has been recognised as an effective predictive tool for assessing spinal biomechanics. The application of FEA can eliminate the difficulties, limitations and ethical concerns associated with in vitro experiments. Furthermore, FEA is more cost-effective than in vivo and in vitro experimental studies. The possibility of employing complex load cases and boundary conditions allows the investigation of biomechanical parameters that are difficult to measure by experimental methods.

1.2. Patient specific and literature-based finite element models

Musculoskeletal finite element (FE) models in the literature have varying degree of patient-specificity depending on the employed modelling strategy. Two main bone material modelling strategies are used: the "hybrid patient-specific" approach, where geometry relies on the patient's medical imaging data while the homogenous material properties are derived from literature, and the "fully patient-specific" approach. In the latter, both geometry and heterogenous bone material properties are defined based on medical images.

1.3. Proximal junctional kyphosis

Proximal junctional kyphosis (PJK) is a complication with an incidence rate ranging from 17% to 39% within 2 years of surgery. PJK is an abnormal kyphotic deformity affecting the vertebral components proximal to the upper instrumented vertebra (UIV). PJK is described by the segmental kyphosis (SK) defined by the proximal junctional Cobb angle measured between the UIV and the vertebra 2 levels cranial to the UIV (UIV+2). PJK occurs if the SK between the UIV and UIV+2 is at least 10° or if the SK increases by at least 10° after surgery. In more severe cases, PJK includes vertebral subluxation, vertebral body fracture, implant failure, damage to the posterior ligament complex, or adjacent level degeneration, thus requiring revision surgery.

Various risk factors have been linked to PJK, such as older age, higher body mass index, lower bone mineral density (BMD), presence of comorbidities, the position of the UIV, the high construct rigidity, a high degree of corrected deformity, and the number of fused vertebrae were also considered surgical risk factors. Besides these, the sudden change in rigidity between the instrumented and noninstrumented segments was also identified as a contributing factor to the onset of PJK. To address this problem, various semirigid fixation techniques (SFTs) were introduced in the literature, such as transverse process hooks

(TPH), transition rods with a smaller diameter, or the use of PEEK at the cranial end instead of metallic alloys. The purpose of such implants is to provide a more gradual transition to normal motion at the UIV level following long instrumented posterior spinal fusion, thereby reducing the probability of developing PJK. Among the previous in vitro and in silico studies of SFTs, the MRF technique has not been previously investigated in relation to PJK. Furthermore, the effect of PEEK material at the cranial end of the construct on mobility and load distribution in long posterior spinal fixations has not been previously analysed.

1.4. Sacral fractures and their impact on biomechanical properties

The sacrum serves as a biomechanical keystone by transmitting the load of the upper body to the lower extremities. Sacral fractures are usually caused by high-energy traumas such as road accidents or falls from a greater height. These traumatic, non-osteoporotic sacral fractures occur with a relatively low incidence of 2.1 per 100,000. The surgical options include iliosacral screw (ISS) and transverse iliosacral screw (TISS), posterior plating, transiliac internal fixator, unilateral or bilateral triangular fixation and S2-alar-iliac techniques. Screw loosening and hardware failure have been reported at relatively high rates, at 11.8% - 17.3%, with uncertain clinical relevance.

Several in silico biomechanical studies have been conducted to assess fixation techniques used for sacral fracture treatment. However, previous biomechanical studies employing FE analysis assumed identical bone quality at the S1 and S2 levels and employed averaged, homogeneous bone material properties. Although, the study by Radley et al. revealed that bone quality significantly varies between the S1 and S2 bodies. Nonetheless, regarding sacral fracture fixations, no previous biomechanical in silico study included patient-specific bone material properties.

1.5. Lumbopelvic reconstruction techniques after total sacrectomy

If the lumbosacral complex is affected by primary malignant sacral tumours, surgical interventions invariably emerge as the preferred treatment strategy. En bloc resection of a sacral tumour with a sufficiently wide oncological margin significantly influences the biomechanics of the lumbopelvic region, as it disrupts the continuity between the pelvis and spine. Therefore, lumbopelvic reconstruction is essential to provide sufficient biomechanical stability, enabling load-bearing and patient mobilization.

The technical progress in lumbopelvic reconstruction techniques (LPRTs) has been continuous since the early 2000s. In 2003, Kawahara et al. introduced the sacral rod reconstruction (SRR) technique, including a horizontal sacral rod attached to L5 combined with conventional posterior stabilization components. In 2006, Shen et al. presented the four-rod reconstruction (FRR) technique, employing four longitudinal spinal rods. In 2009, Varga et al. introduced the closed-loop reconstruction (CLR) technique, consisting of a single U-shaped rod, for lumbopelvic stabilization. The CLR technique is a non-rigid fixation approach, as concluded by a comprehensive six-year retrospective clinical investigation. Furthermore, in 2011, Cheng et al. developed the improved compound reconstruction (ICR) technique, which anteriorly included the horizontal sacral rod and a bilateral fibular graft construct, while the posterior aspect was similar to the FRR technique. Bony fusion between the lumbar spine and the iliac bones is crucial for long-term clinical stability and better quality of life following a total sacrectomy. Reducing the distance between the bonny host surfaces increases the probability of successful bony fusion. Lumbopelvic distance reduction (LPDR) is often achieved by pulling down the L5 vertebra and rotating the iliac wings towards the lumbar spine. Despite these mentioned clinical benefits of LPDR, the biomechanical impact of this procedure has not been previously investigated in the existing literature.

2. OBJECTIVES

1. The objective of part I was to introduce the validation processes of different healthy anatomical regions, such as the lumbar spine, the thoracolumbar spine and the pelvis. In addition, the patient-specific bone material assignment technique is presented. The outcomes of the FE model underwent comparison with data from in vivo and in vitro and established in silico results taken from the literature, aiming to validate the healthy anatomical FE models.

2. The primary focus of part II was to investigate PJK. Previous biomechanical investigations suggest that a significant contributor to PJK is the sudden change in mobility between the instrumented and healthy spinal segments. This section of the thesis aims to evaluate the biomechanical impact of three fixation techniques, comprising one rigid and two SFTs, on the development of PJK.

3. The aim of part III was to assess and compare the biomechanical effectiveness of six ISS fixation techniques employed in the treatment of unilateral AO Type B2 (Denis Type II) sacral fractures. This evaluation was conducted utilising both literature-based and patient-specific bone material properties using the FE method.

4. Part IV's primary objective was to assess and compare the biomechanical characteristics of four LPRTs. This evaluation considered the impact of LPDR. Although many LPRTs have been previously analysed, the biomechanical effect of LPDR has not been investigated yet.

3. METHODS

3.1. Development of the healthy FE models

In all in silico investigations, FE models were developed using the quantitative computed tomography (QCT) scans of a 24-year-old male without any musculoskeletal pathology. The studies involving the human participant underwent review and approval by the National Ethics Committee of Hungary and the National Institute of Pharmacy and Nutrition. The

QCT scans with a voxel size of $0.6 \times 0.6 \times 0.6$ mm^3 were employed to capture the geometry of the FE models. For each specific FE analysis, the QCT dataset was sourced from the hospital's PACS and subsequently anonymised using Clinical Trial Processor software. This approach ensured consistency across all investigations. All the FE simulations presented in this thesis work were solved using Abaqus Standard.

3.1.1. Development of the lumbar spine FE model

The 2D images from the QCT scans were imported into Materialise Mimics software to generate a patient-specific surface geometry model through a Hounsfield Unit-based segmentation process. In the lumbar spine FE model, vertebrae were meshed with a uniform element size of 1 mm with linear tetrahedral elements. Locally defined material properties were applied to model bone heterogeneity, as the mechanical properties of the bone tissues were assigned to each element based on the QCT scans. Elements were categorised into ten equal-sized groups based on their average HU value. Elements with negative HU values were placed in an eleventh group, representing fat- and marrow-like materials with lower density. The Poisson's ratio of all bony tissues was uniformly set at 0.3.

Soft tissues, such as the facet joints were modelled as a 0.25 mm thick cartilage layer with an initial gap of 0.5 mm between adjacent surfaces and then meshed with 6-node wedge elements. The intervertebral discs (IVD) consisted of the nucleus pulposus (NP), the annulus fibrosus (AF), including both the ground substance (GS), the fibres, and the 0.5 mm thick cartilaginous endplates (CEP). The AF GS and the NP were represented with 8-node hybrid hexahedral elements, while CEP was meshed with linear tetrahedral and pyramid elements. The fibres were modelled with tension-only truss elements in a criss-cross pattern with an alternating angle of ±30° to the axial plane of the IVD. CEPs were assigned with linear elastic material properties obtained from the literature. The NP and AF GS were modelled with a 2-parameter hyperelastic Mooney-Rivlin formulation to represent their incompressible behaviour. The mechanical behaviour of the annulus' collagenous fibres followed a nonlinear stress-strain curve from Shirazi-Adl. Facet cartilage was modelled with a hyperelastic Neo-Hooke formulation. Tension-only, nonlinear uniaxial spring elements were employed to simulate ligament behaviour.

3.1.2. Validation of the lumbar spine FE model

Three loading cases were employed to validate the lumbar spine FE model accurately. First, a pure bending moment of 7.5 Nm was applied in the three anatomical planes at the superior endplate of L1. Second, a compressive follower load of 1000 N was employed to measure the IDP without bending moments. Third, a combination of a follower load and a bending moment was used with magnitudes adopted from Dreischarf et al. During the simulations, the most caudal endplate of L5 was fixed in all degrees of freedom. The contact behaviour between the facet joint surfaces was assumed to be frictionless.

In the case of pure bending, the ROM, the intervertebral rotations (IVR), and the facet joint forces (FJF) were compared with in vitro and in silico data. In the case of pure follower load, the intradiscal pressure (IDP) in the L4–L5 NP was averaged over all elements and then compared with in vitro and in silico results. A combined compressive and bending load was applied to the FE models to measure the IVR, FJF, and IDP values at each spinal level and compared with in silico and in vivo measurements.

3.1.3. Development of the thoracolumbar spine FE model

The FE model of the thoracolumbar (T7-L5) spine was developed based on the previously presented QCT scans of a healthy 24-year-old male. The vertebrae were divided into the 1 mm thin cortical shell, the cancellous core, the 0.5 mm thin vertebral endplates, and the posterior elements. The bony components of the vertebral bodies were meshed with 1 mm linear tetrahedral elements. Linear elastic material properties were used for the cortical and cancellous bone, the vertebral endplate and the posterior elements.

The soft tissues of the thoracolumbar FE model, specifically the IVD, facet joints, CEP, NP, AF GS, AF fibres, and spinal ligaments, have been modelled identically as explained previously. The material properties of the soft tissues in the thoracic region were derived from those in the lumbar region. However, to approximate the in vitro measured IVR values in the T7-L1 region, specific adjustments were made to the material properties of the IVDs. Two scalar calibration parameters were introduced for this purpose. λ_{GS} and λ_{FIBER}.

3.1.4. Validation of the thoracolumbar spine FE model

To validate the T7-L5 intact spine model, pure bending moments were applied in the three anatomical planes to mimic flexion-extension, lateral bending, and axial rotation. Multiple FE models were created and loaded at the most cranial endplate, while the most caudal endplates were fixed in all degrees of freedom in each validation FE model. The calculated IVR values of the FE models were compared with the available in vitro data from the literature.

3.1.5. Development of the pelvis FE models

Depending on the bone modelling strategy, two different FE models were developed in the HyperWorks FE pre-processor software.

In the PSM, the sacrum and iliac bones were uniformly meshed using 1 mm linear tetrahedral elements to ensure that the elements were not larger than the slice thickness of the QCT scan. The bony elements were categorized into ten material bins based on their average HU values. Elements with negative HU values were placed in an additional group, representing fat- and marrow-like materials.

In the literature-based model (LBM), the sacrum included a trabecular core, an S1 bony endplate and a cortical layer, both 0.45 mm thick. The iliac bones were modelled with a 1 mm thick cortical shell and a trabecular core. All bony components were adaptively meshed with linear tetrahedral elements, ranging from a minimum of 1 mm to a maximum of 4 mm edge length, and assigned isotropic homogeneous linearly elastic bone material properties obtained from the literature.

The SIJ was developed as a true diarthrosis with an initial gap of 0.3 mm between the adjacent articular surfaces and were modelled with a uniform sacral and iliac cartilage thickness of 2 mm and 1 mm, respectively. The SIJ was meshed with linear tetrahedral elements, while its material properties were assigned according to a previous in silico study. The interpubic disc was modelled as an interspace structure and meshed with tetrahedral elements. Eight pelvic ligaments were included in the FE models and were modelled as tension-only uniaxial spring elements with material properties obtained from the literature.

3.1.6. Validation of the pelvis FE models

To validate the LBM and PSM pelvis FE models, the displacement values of the sacrum under different loading conditions were measured and compared to the findings of a cadaveric study by Miller et al. and several in silico studies. Since the motion of the sacrum is primarily influenced by the soft tissues rather than the bone, the bony structures were modelled as rigid bodies for validation purposes. Five translational loads and four rotational loads were applied to the sacrum, while both ilia were fixed. The displacement of a reference point representing the centre of the sacrum was recorded.

3.1.7. Development of the lumbopelvic FE models

The lumbar part of the thoracolumbar FE model and the LBM pelvis FE model were combined to develop the lumbopelvic FE model. Since these models were previously validated, the intact lumbopelvic FE model was considered suitable for further biomechanical analysis. However, the surgical lumbopelvic FE models were validated to increase the reliability of the FE predictions.

3.2. FEA of different spinal fixation techniques

3.2.1. Development of spinal fixation techniques in the thoracolumbar spine

In addition to the healthy thoracolumbar spine, the FE models of one rigid and two types of SFTs were developed:

1) TRF – model with posterior fusion of the spine from T8 to L5 using bilateral pedicle screws and Ø5.5 mm titanium rods.

2) PRF – model with Ø5.5 mm PEEK rods between T8 and T9 combined with posterior stabilisation of the spine from T9 to L5 using bilateral pedicle screws and Ø5.5 mm titanium rods. Rod connector system was placed to connect the titanium and PEEK rods.

3) MRF – model with five Ø1.9 mm titanium rods between T8 and T9 combined with posterior fusion of the spine from T9 to L5 using bilateral pedicle screws and Ø5.5 mm titanium rods. Rod connector system was placed to connect the titanium and the multiple titanium rods.

3.2.2. Analysis of the semirigid spinal fixation techniques

For all FE models, the loading was applied at the superior endplate of T7, while the inferior endplate of L5 was fixed in all degrees of freedom. For a proper biomechanical evaluation of adjacent segment effects, a modified multidirectional hybrid test protocol has been applied in this PhD thesis, consisting of two subsequential loading steps.

1. Load-controlled step: The intact T7-L5 and the instrumented FE models were loaded with 5 Nm pure bending moment in the anatomical planes to simulate flexion-extension, lateral bending, and axial rotation. IVR values of the intact spine and the spinal fixation techniques were measured. Then, the IVR of the intact spine were used to normalise the results of the three instrumented FE models.

2. Displacement-controlled step: For a physiologically realistic comparison, the displacement of the TRF technique obtained from the first loading step was used as an input for the second loading step. The maximum von Mises stress values in the pedicle screws and the stress distribution at the UIV level were analysed.

3.3. FEA of different sacral fracture fixation techniques using two sets of bone material properties

3.3.1. Development of different iliosacral screw fixations in the case of sacral fractures

An AO Type B2 unilateral transforaminal sacral fracture was developed by cutting the healthy sacrum into two parts, with ligamentous tissues left intact in both the LBM and PSM. The fixations were developed by placing ISS and TISS in the fractured models. Screws with a diameter of 7.3 mm were inserted as described in the literature for fixing unilateral transforaminal sacral fractures. Thus, screws were perpendicular to the fracture plane with screw tips ending either near the counter lateral SIJ in the sacrum (ISS) or bridging both SIJ (TISS). Six types of fixations were constructed as follows: (1) ISS at S1 (ISS1), (2) ISS at S2 (ISS2), (3) ISS at S1 and S2 (ISS12), (4) TISS at S1 (TISS1), (5) TISS at S2 (TISS2), and (6) TISS at S1 and S2 (TISS12).

Ideal connection was set between the bone and the screw bodies, while a penalty contact interaction with a friction coefficient of 0.3 was defined between the interfragmentary surfaces. Balanced standing on both feet was simulated with a vertical load of 600 N applied on the cranial endplate of the sacrum while both acetabula were fixed.

3.3.2. Analysis of different iliosacral screw fixations in the case of sacral fractures

The vertical stiffness (VS) was determined by dividing the load by the vertical displacement of the sacrum. Then, these VS values were normalised to the corresponding intact sacrum for all fixation techniques in both the LBM and PSM. To evaluate the probability of implant failure, the maximum von Mises stress values in the screws were investigated. The relative interfragmentary displacement (RID) on the fracture interface was analysed to evaluate the fracture healing progress. RID distribution and the maximum RID values for both models were reported. In addition, the stress state of the fracture interface was investigated. Conventionally, fracture healing is characterised by examining the maximum stress values on the sacral fracture interface. However, due to the heterogeneity of locally defined bone material properties in the PSM, relying solely on the maximum values can be misleading. Therefore, instead of focusing on the maximum stress values, nodes from both models falling within the top 1% of stress values were analysed to ensure more accurate results.

3.4. FEA of different lumbopelvic reconstruction techniques after total sacrectomy

3.4.1. Development of the lumbopelvic FE models after total sacrectomy

To model total sacrectomy without LPDR, the sacrum was simply removed from the intact segmentation-based geometry model without any further anatomical modification. Subsequently, the sacrectomy FE model without LPDR was created. To model total sacrectomy with LPDR, the anatomy after total sacrectomy was further modified by pulling down the lumbar spine by 1.1 cm. Furthermore, the iliac bones were moved inwards by 1.3 cm on the right side and by 1.5 cm on the left side towards the lumbar spine to achieve a distance reduction of ca. 1.7 cm on both iliac sides. Finally, the sacrectomy FE model with LPDR was created, similar to that without LPDR.

3.4.2. Development of the lumbopelvic reconstruction techniques after total sacrectomy

Using the FE models with and without LPDR, four different LPRTs were analysed: the CLR, the SRR, the FRR, and the ICR techniques. The CLR technique featured posterior stabilisation through pedicle screws between the L3 and L5 pedicles. Into the bilateral posterior inferior iliac bones, two iliac screws were inserted, the short and the long iliac screw. The pedicle and iliac screws were interconnected via a single U-shaped rod, with no additional anterior stabilisation. The posterior segment of the SRR technique included the same pedicle screws as the CLR technique, between the L3 and L5 pedicles, connected to the long iliac screws through two longitudinal rods. In the anterior part of the SRR, a horizontal sacral rod bridged the iliac bones and was attached to the inferior endplate of L5 using two screws. The FRR technique included only posterior stabilisation. Pedicle screws were inserted between the L2 and L5 pedicles using the Roy-Camille screw placement at the medial side and the Magerl screw placement at the lateral side. Four longitudinal rods were utilised in this technique, with the lateral screws connected to the short iliac screws and the medial screws to the long iliac screw. The ICR technique consisted of the posterior part of the FRR and the anterior stabilisation of the SRR technique. Additionally, two fibular flaps were positioned along the iliopectineal lines between the lumbar spine and the pelvis.

In all LPRTs, the diameters were as follows: 6 mm for the pedicle screws, 8 mm for the short iliac screws, 10 mm for the long iliac screws, 6 mm for the horizontal sacral rod, and 5.5 mm for the spinal rods. An ideal connection was modelled through shared nodes at the bone-screw and the screw-rod connections. Screws and rods were meshed with linear tetrahedron elements and were assigned with titanium material properties.

3.4.3. Validation of the lumbopelvic reconstruction techniques

Validation of the surgical models is essential to ensure the reliability of the FE results and to draw adequate conclusions. The SRR, FRR, and ICR techniques were previously examined in a cadaveric in vitro study by Cheng et al. Thus, validation was conducted for these three LPRTs using identical loading and boundary conditions. A vertical force of 500 N was applied at the superior endplate of L2, shifted anteriorly to the hip joint's centre of rotation, resulting in a moment of ca. 14 Nm. To simulate the hip function, the ileum could rotate in the sagittal plane with the two centre points of the hip joint being constrained. In addition, the pubis ramus was fixed in all degrees of freedom to represent the metal hook used in the in vitro setup. The shift-down displacement was defined as the vertical displacement of L5, and the relative sagittal rotation was calculated as the rotation of L5 in the sagittal plane relative to the ileum. To further increase the reliability of the FE models' predictions, results of a previous in silico study were also included in the validation.

3.4.4. Analysis of the lumbopelvic reconstruction techniques

Four loading cases were simulated to evaluate the LPRTs, employing combined follower load and bending moment. The follower load was applied along an optimised path through the lumbar vertebral bodies' centre of rotation, while the bending moment was applied at the superior endplate of L1. For flexion, extension, lateral bending, and axial rotation, the follower load and bending moment pairs were 1175 N with 7.5 Nm, 500 N with 7.5 Nm, 700 N with 7.8 Nm, and 720 N with 5.5 Nm, respectively. For the evaluation of LPRTs, the lower part of the ileum was fixed in all degrees of freedom.

Lumbopelvic stability was assessed based on the shift-down displacement of L5 and the relative sagittal rotation of L5, both calculated using the same methodology as in the validation process. Additionally, the stress state at the bone-implant interface and within the rods was analysed to rank the reconstruction techniques regarding screw-loosening and implant safety.

4. RESULTS

4.1. Validation results of the healthy FE models

4.1.1. Validation of the patient-specific lumbar spine FE model

Against pure bending moment load, the total L1–L5 ROM in flexion-extension, lateral bending, and axial rotation, the results were: 31.58°, 28.55°, 14.12°, respectively. The nonlinear load-deflection curves illustrate the stiffening behaviour of the FE model against larger loads. The mean FJF values were calculated as 51.94 N, 8.50 N, and 83.74 N, in extension, lateral bending, and axial rotation respectively. IVR values occurred within the range of experimental measurements, except at the L2–3 and L4–5 levels in flexion, where the model slightly underestimated the in vitro measurement, although the results correlate well with the in silico data. Against pure compression load, the IDP value under the compressive follower load was 1.02 MPa.

Against combined load, the IVR results were consistent with the available literature data, although the results were outside the in vivo range in flexion at L2–3, L3–4 and L4–5. The in silico range was not reached in flexion at L1–2, in extension at L2–3 and L4–5, and in axial rotation at L1–2, L2–3 and L3–4.

4.1.2. Calibration and validation of the thoracolumbar spine FE model

Weighting factor values for the annulus GS and fibres were between 0.28 and 0.5, and between 0.4 and 0.5, respectively. The IVR results of the thoracolumbar FE model were within the range of available in vitro measurements for all load cases, except at the T9-T10 level for lateral bending. In flexion-extension and axial rotation, the predicted values showed good agreement with the in vitro mid-values, while in lateral bending, the predictions of the FE model slightly underestimated the in vitro measurements.

4.1.3. Validation of the sacrum FE model

The comparison of the FE prediction to the results of Miller et al. showed excellent agreement. For each loading case, the results fell within the standard deviation and were close to the published median values of the experimental results. However, the FE model slightly underestimated the results of the cadaveric experiment in flexion and extension. In addition, good agreement was found with the result of multiple in silico studies published in the literature.

4.2. Results of the FEA of different spinal fixation techniques

4.2.1. Hausdorff Distance

HD values were calculated to assess the quality of the alignment and registration. HD values were visualised between the segmented thoracolumbar-based L1 and the lumbar-based L1 vertebrae. Minimum and maximum HD values were equal to 0 mm and 1.37 mm (mean= 0.15 mm, rms=0.2), respectively.

4.2.2. Hybrid test protocol

Load-controlled step: At the UIV level, the IVR results normalised by the intact spine of the TRF, MRF and PRF models were 6.48%, 9.63%, and 12.90% for flexion, and 7.0%, 10.02%, and 13.14% for extension. For lateral bending, MRF and PRF gave 1.9 and 2.4 times higher IVR results than the TRF; below the UIV level, all three fixation techniques gave values lower than 2.7% of the intact's IVR. Among all the load cases, axial rotation gave the largest normalised IVR values with 8.76%, 44.77%, 60.51% for TRF, MRF, and PRF, respectively.

Displacement-controlled step: At the UIV level, TRF induced 37.26 MPa, 42.13 MPa, 44.4 MPa, and 44.59 MPa stress values in flexion, extension, lateral bending, and axial rotation, respectively. In comparison to the TRF, the application of the MRF and PRF technique reduced the maximum stress values by 17.28% and 27.72% for flexion, by 26.56% and 36.67% for extension, by 6.82% and 34.26% for lateral bending, and by 49.07% and 59.81% for axial rotation. In contrast to the other load cases, the maximum stress values below the UIV level were not reduced compared to the UIV level for axial rotation, as the results were 44.59 MPa, 45.99 MPa, 46.56 MPa, 53.26 MPa and 48.34 MPa, at T8, T9, T10, T11, and T12 respectively.

4.2.3. Stress distributions

In general, the largest area with stress higher than 10 MPa was found in the TRF model, while PRF included the least. The stress distributions in flexion and extension show a similar trend, i.e., the TRF technique results in much higher pedicle screw stress in both loading cases. In contrast, MRF gives less, while the PRF technique induces the least stress in both loading directions. For right lateral bending, the stress distribution pattern of the MRF model shows similarity with the TRF model in aspect of magnitude and expansion. In contrast, for axial rotation, the peak stress values appeared at the outer edge of the screw bodies in the instrumented models, with TRF model containing notably more area stress above 10 MPa than the MRF and PRF.

4.3. Results of the FEA of different sacral fracture fixation techniques

4.3.1. Simulation time of the literature-based and the patient specific bone models

The simulation times for the PSM and LBM were 4,270 and 1,554 seconds, respectively, indicating that the PSM required approximately 2.7 times more time on average.

4.3.2. Vertical stiffness of the sacral fracture fixation techniques

Generally, all fixation techniques increased the VS of the sacrum. The smallest VS was measured with the ISS1 technique, where LBM and PSM gave 137% and 149%, respectively, while the highest VS was achieved using the TISS12 configuration, where LBM and PSM gave 375% and 472%, respectively. No statistically significant difference was found between the LBM and PSM in terms of their VS, as determined by the Wilcoxon signed-rank pair test ($p = 0.688$).

4.3.3. Maximum von Mises stress values measured in the iliosacral screws

The LBM's maximum von Mises stress value predictions in the implants were 73.3, 59.9, 40.4, 65.3, 44.2, and 35.2 MPa for ISS1, ISS2, ISS12, TISS1, TISS2 and TISS12, respectively. PSM, however, increased the maximum stress values by 19.3, 16.3, 27.8, 2.3, 24.4 and 7.8%, respectively. Statistically significant difference was found between the LBM and PSM in terms of their maximum implant stress, as determined by the Wilcoxon signed-rank pair test ($p = 0.031$).

4.3.4. Relative interfragmentary displacement

The distribution of the RID values was analysed with the contact opening output from the Abaqus software. the maximum RID values were between 0.10 and 0.47 mm for all fixation techniques in both models. In LBM, the maximum RID values were 0.47, 0.27, 0.25, 0.37, 0.15 and 0.14 mm for ISS1, ISS2, ISS12, TISS1, TISS2 and TISS12, respectively. No statistically significant difference was found between the LBM and PSM in terms of the maximum RID values, as determined by the Wilcoxon signed-rank pair test ($p = 0.438$).

4.3.5. Von Mises stress values in the bone at the fracture surface

The stress distribution between the LBM and PSM revealed strong statistically significant differences across all fixation techniques ($p < 0.001$ for all pairs), as determined by the two-sample Kolmogorov-Smirnov test. In the PSM, the median stress values were 6.5, 7.2, 4.4, 6.1, 6.0 and 3.8 MPa for ISS1, ISS2, ISS12, TISS1, TISS2 and TISS12, respectively. However, LBM increased the median stress values by 280.1, 138.8, 212.9, 261, 132.4 and 234.7% compared to PSM. In the case of the maximum stress values, for ISS1, ISS2, ISS12, TISS1, TISS2 and TISS12, the LBM gave higher values by 255.1, 20.3, 156.4, 286.9, 41.1 and 171.1% compared to PSM.

4.4. Results of the FEA of different lumbopelvic reconstruction techniques

4.4.1. Validation of the lumbopelvic reconstruction techniques

The results were within the standard deviation range of the in vitro experiment for all three reconstruction techniques. In the case of SRR and ICR, good agreement with the mean results of the in vitro experiment was observed, while for the FRR, the displacement and rotation of L5 were underestimated. However, excellent agreement was found with the in silico results for all LPRTs and both parameters.

4.4.2. Shift-down displacement of L5

The LPRTs ranked from smallest to highest displacement values as ICR<SRR<FRR<CLR for all loading cases, regardless of LPDR. For the ICR technique, the displacement values were 1.0 mm, 0.1 mm, 0.4 mm, and 0.4 mm for flexion, extension, lateral bending, and axial rotation, while for the CLR technique, 13.2 mm, 2.7 mm, 6.7 mm, and 6.9 mm, respectively. LPDR consistently reduced the displacement values. On average, the displacement was reduced by 25% in CLR, 61% in SRR, 15% in FRR, and 46% in ICR, based on all loading cases.

4.4.3. Relative sagittal rotation of L5

The LPRTs ranked from smallest to highest relative sagittal rotation values as ICR<SRR<FRR<CLR for all loading cases, regardless of LPDR. Without LPDR, the relative rotation values for the ICR technique were 1.0°, 0.2°, 0.5°, and 0.5° for flexion, extension, lateral bending, and axial rotation, while for the CLR technique, 10.8°, 2.3°, 5.5°, and 5.6°, respectively. LPDR consistently reduced the relative sagittal rotation of L5. On

average, the rotation was reduced by 21% in CLR, 73% in SRR, 11% in FRR, and 53% in ICR, based on all loading cases.

4.4.4. Stress state at the bone-implant interface

Without LPDR, the highest mean stress values were measured in the SRR technique with 217.5 MPa, 40.1 MPa, 105.9 MPa, and 108.8 MPa for flexion, extension, lateral bending, and axial rotation, respectively. With LPDR, the FRR technique gave the highest mean stress values for flexion, lateral bending, and axial rotation with 174.0 MPa, 82.1 MPa, and 89.1 MPa. However, in extension, the SRR technique induced the highest mean stress result with 36.1 MPa. With or without LPDR, the smallest mean stress predictions were given by the ICR technique for flexion, lateral bending, and axial rotation. Nonetheless, in extension, both with and without LPDR, the CLR technique yielded the smallest mean stress predictions with 32.3 MPa and 26.9 MPa, respectively. In general, LPDR decreased the mean stress values. On average, the mean stress values decreased by 13% in CLR, 26% in SRR, 19% in FRR, and 27% in ICR, based on all loading cases.

4.4.5. Stress state within the rods of lumbopelvic reconstruction techniques

The LPRTs ranked from smallest to highest mean stress values as ICR<SRR<FRR<CLR for all loading cases, regardless of LPDR. Without LPDR, in flexion, extension, lateral bending, and axial rotation, the ICR technique gave the smallest mean stress results with 346.5 MPa, 108.0 MPa, 186.2 MPa, and 199.7 MPa, while the CLR technique yielded the highest mean stress values with 955.9 MPa, 271.7 MPa, 585.6 MPa, and 585.0 MPa, respectively. Based on all loading cases, LPDR lowered the mean stress values within the rods by 25% and 12% in the SRR and ICR techniques, respectively. However, based on the average of all loading cases, in the FRR and CLR techniques LPDR slightly increased the mean stress values by 5% and 2%, respectively.

5. CONCLUSIONS

In the development of the lumbar spine, the aim was to present the development and validation process of the healthy human lumbar spine FE model using a patient-specific bone material assigning technique. The results of the FE model were compared with in vivo, in vitro, and well-accepted in silico data from the literature. Validation was performed considering ROM, IVR, IDP, and FJF variables against pure and combined loads. Based on the parameters and loads investigated, the developed FE model can be used to model the biomechanical properties, such as ROM, IVR, FJF, and IDP of the lumbar spine, as it is in good agreement with the previously published results in most investigated variables. However, substantial differences in computational time between the literature-based and patient-specific bone material assignment techniques were observed.

In part II, the previously developed and validated literature-based thoracolumbar spine was used to investigate PJK. In this part, FEA has been used to evaluate the effect of two SFTs compared to one conventional rigid fixation technique. In agreement with the literature, based on the findings in this FEA, less rigid fixations at the cranial part of the stabilisation construct allow a more gradual transition in motion between the instrumented and intact spine segments. Decreasing the load on the pedicle screws at the upper instrumented level could help prevent the development of PJK.

Part III analysed six fixation techniques for treating unilateral sacral fractures using FEA employing both patient-specific and literature-based bone material properties. Only ISSs or TISSs were used for sacral fracture fixation, thus preserving lumbar mobility. Based on the results, all analysed configurations provide clinically sufficient stability. From a biomechanical perspective, TISS12 outperformed all other fixations, delivering the greatest vertical stability and the least interfragmentary displacement and implant stress. These findings suggest that sacral fracture fixations should prioritise the S1 level over the S2 as both ISS2 and TISS2 increased the stress on the fracture interface and the bone-implant surface compared to ISS1 and TISS1, respectively. Both the PSM and LBM pelvis models consistently ranked the fixation techniques based on their ability to provide vertical stability and based on RID values. However, the observed differences in stress distribution emphasise the need for meticulous care when selecting the suitable bone modelling strategy depending on the aim of the study. It is important to note that the PSM, while offering more realistic stress distribution results, requires additional computational resources compared to the LBM.

In Part IV, the lumbar part of the literature-based thoracolumbar spine FE model and the pelvis FE model were combined to evaluate and compare the biomechanical characteristics of four different LPRTs while considering the effect of LPDR. Regardless of the reconstruction techniques employed, LPDR improves lumbopelvic stability following total sacrectomy by reducing the shift-down displacement and relative sagittal rotation of L5. Furthermore, LPDR decreases the stress at the bone-implant interface, lowering the risk of screw loosening. This technique also reduces the stress within the rods, particularly in techniques combining both anterior and posterior stabilisation. The ICR technique demonstrated the highest lumbopelvic stiffness, while the CLR technique showed the lowest. However, based on the findings, all techniques are suitable for lumbopelvic reconstruction. The ultimate selection of the appropriate technique should be a decision made by the surgical team based on their expertise and various patient-specific aspects.

In conclusion, through the development and validation of FE models, insights were gained regarding the biomechanical properties of the lumbar spine, thoracolumbar spine, and pelvis, as well as various fixation techniques and reconstruction methods. These findings provide practical contributions to evidence-based clinical decision-making and potentially enhance patient outcomes in spinal care. Nonetheless, further biomechanical investigations and long-term clinical trials are recommended to validate the presented findings and ensure their applicability in real-world clinical practice.

6. BIBLIOGRAPHY OF THE CANDIDATE'S PUBLICATIONS

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