IN SILICO INVESTIGATION OF THE PRIMARY STABILITY OF DIFFERENT OLIF CONSTRUCTS IN NORMAL AND OSTEOPOROTIC CONDITIONS

PhD Thesis Outline

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1. INTRODUCTION

1.1. In Silico Medicine

The collaboration between clinicians and bioengineers has led to the development of tools and methodologies to improve healthcare systems, particularly in surgical interventions. Finite element analysis is a computational method used in engineering to address partial differential equations, with its application in biomechanics dating back to 1972. It is extensively used in orthopaedic engineering to study the reaction of implants to various loadings and to analyse mechanical characteristics such as structural modulus and stress distribution in complex structures. Finite element analysis is also widely employed in spinal research to understand pathologies like scoliosis, fractures, and disc degeneration, and to evaluate treatment options.

1.2. The surgical challenges posed by elderly population, and the minimally invasive Oblique Lateral Interbody Fusion technique

Lumbar interbody fusion (LIF) is a standard surgical treatment for various spinal disorders, including degenerative conditions, trauma, and tumours, with different approaches and techniques available, each with its own instruments, implants, and considerations. The global population's aging trend, driven by declining fertility rates and increasing life expectancy, alters disease epidemiology, emphasizing the need for advanced spinal fusion technologies. The minimally invasive oblique lumbar interbody fusion (OLIF) technique, introduced in 1997 and refined over the past decade, provides a secure access corridor for fusion and decompression while safeguarding nerves. Additional fixation methods like bilateral pedicle screws (BPS) or lateral plate-system (LPS) fixation, including novel systems like the Self Anchoring Standalone plate (SSA), offer options for stabilization with varying biomechanical implications, especially crucial in osteoporotic conditions common among the elderly population. Limited research exists comparing these techniques in osteoporotic conditions, underscoring the need for further investigation to optimize surgical outcomes.

1.3. Osteoporosis, and polymethylmethacrylate (PMMA) augmentation in the field of spine surgery, and OLIF

Osteoporosis entails reduced bone density and microstructure degradation, elevating fracture risk, especially in aging individuals. Biomechanical studies have revealed that screws in osteoporotic bone may induce osteolysis, increasing the risk of implant failure. To address this, PMMA augmentation can enhance implant stability, albeit with a potential for complications like leakage. While this technique is commonly used in TLIF or posterior stabilization surgeries, its application in OLIF surgeries, particularly with SSA implants, remains underexplored. Currently, there is a gap in the literature regarding the biomechanical effects of PMMA augmentation in OLIF surgeries compared to traditional BPS fixation in osteoporotic conditions.

1.4. Stanford Biodesign, a basis for innovation

Innovation involves the introduction of new and creative ideas, methods, or devices to address emerging demands and market requirements, playing a key role in economic and healthcare advancement. The Stanford Biodesign program is a leading initiative in training emerging leaders in biomedical technology, with a focus on identifying clinical needs and creating groundbreaking inventions. My research at the National Center for Spinal Disorders in Budapest focused on the increase in mechanical failures in older patients undergoing OLIF surgeries with lateral plates, highlighting the need for optimal fixation options. Employing the Stanford Biodesign process, in silico medicine was used to investigate clinical questions and generate potential solutions to address this clinical need.

2. OBJECTIVES

This thesis aimed to examine the primary stabilizing impact of various constructs employed in Oblique Lateral Lumbar Interbody Fusion (OLIF) surgery under normal and osteoporotic bone conditions, to provide a better understanding of the presented clinical question. The potential impact of polymethylmethacrylate (PMMA) reinforcement on these constructs was also assessed in the presence of osteoporosis to explore potential solutions/concepts for the identified clinical need, employing the basis of the Stanford Biodesign process. Finite Element (FE) analysis served as the fundamental framework for this study.
The key-points for the thesis were the following:

1. The construction of an intact L2-L4 bi-segmental spinal finite element model. In order to utilize this model, it was essential to undergo a validation process against a cadaveric in vivo specimen. To accurately simulate the impact of osteoporosis, the intact model had to be modified further.

2. Simplified 3D implant models were created by digitalizing the implants used in OLIF surgery. A virtual surgery was performed on the intact FE models with the different investigated implant constructs (BPS, SSA, LPS) creating the surgical FE models.

3. The created surgical FE models (BPS, SSA, LPS) were tested using identical boundary conditions, and loading parameters. The simulations had to be conducted under normal, and osteoporotic bony conditions. The primary stability, and the effect of osteoporosis could be interpreted from the FE simulation results.

4. The created SSA, and BPS surgical FE models needed to be altered for further investigations. Different volumes of custom made PMMA geometries were created based on the relevant literature, and integrated to the surgical osteoporotic FE models.

5. The influence of PMMA augmentation on the examined implant constructs with osteoporotic bone was assessed by comparing the primary stability of the PMMA augmented FE models to that of the original surgical osteoporotic FE models. Additionally, comparisons were made between the two different implants to determine any differences in their effects.

3. METHODS

3.1. Development and validation of an intact L2-L4 finite element model, generation of implant 3D geometries, and the creation of 3D surgical finite element models and environment

3.1.1. Generation of an L2-4 Lumbar Spine Bi-segment Finite Element Model

A CT scan of a 24-year-old patient's lumbar spine was selected from a study involving 270 patients treated for low back pain. The imaging protocol followed standards set by the MySPINE project, with images reconstructed at a voxel size of 0.6x0.6x0.6 mm^3. Segmentation procedures in Mimics software were used to define the 3D geometry of bony elements, and the accuracy was evaluated using the Dice Similarity Index (DSI). The segmented masks were then converted into triangulated surface meshes in Stereolithography (STL) format, with subsequent surface smoothing and remeshing in 3-Matic software. Various anatomical components, including intervertebral discs and facet joints, ligaments were modelled manually, and the resulting 3D surfaces were exported to Hypermesh for mesh generation. Additionally, the intervertebral disc components, such as the annulus fibrosus (AF) and nucleus pulposus (NP), were modelled according to literature specifications, accounting for their respective volumes and material properties. The material properties used in the FE model creation were taken from validated literature FE models.

3.1.2. Cage, Implant Construct and Surgical FE Model Development

A polyether ether ketone (PEEK) OLIF cage was 3D scanned and reconstructed in 3-Matic software before being simplified for use in Finite Element (FE) models. Simplified screw and plate models were also created according to the respected surgical implants. A virtual surgical procedure was done in the 3D space within the L3-4 motion segment, known for its surgical accessibility. The surgical simulation involved removing the nucleus pulposus and layers of annulus fibrosus, creating a window for cage insertion. For the BPS model, transpedicular screws and a connecting rod were employed, while lateral plate and screw fixation were used in the LPS model (no connection between the cage and the plate). In the SSA model, a smaller plate was attached directly to the cage, with screws inserted at diverging angles. Material properties were defined for each component, and the effect of osteoporosis were simulated by adjusting the bony elements' Young's modulus. Mesh quality was assessed based on aspect ratio metrics, ensuring acceptable geometric configurations for accurate simulation.

3.1.3. Material Properties, Boundary and Loading Conditions, FE model validation

Intact and surgical bi-segment FE models were exported to Abaqus/CAEv11 software, with material properties and mesh types defined accordingly. Validation of the intact L2-4 model involved applying torque in three directions to simulate physiological movements, comparing results to cadaveric data. Surgical models underwent simulations in two steps: first, a 150N Follower Load (FL) mimicking physiological loads was applied, followed by pure torque to assess stability. The FL path was based on the centre of rotation of the vertebrae, adhering to International Association for Testing and Materials (ASTM) guidelines but with reduced load to emphasize the implant constructs' stabilizing effects. These methods align with established practices in relevant literature.

3.2. Modification of the validated L2-L4 bi-segmental finite element model, PMMA geometry creation, finite element environment creation

3.2.1. Development of L2-L4 Lumbar Spinal Bi-segmental Surgical FE Models

The 2nd part of the thesis aimed to assess the influence of PMMA augmentation on posterior and lateral plate fixation methods in osteoporotic conditions, using the novel SSA implant for comparison. Utilizing previously the validated intact and surgical FE models, including BPS and SSA constructs. The choice of L3-4 segment for surgery minimized potential surgical interferences, ensuring a consistent comparison across models. Surgical constructs, such as BPS and SSA, were meticulously designed with specified screw sizes and plate dimensions, while material properties were adjusted to simulate osteoporotic bone conditions. Tie constraints were applied to ensure realistic interactions between implant components and bone surfaces

3.2.2. Model Generation for the PMMA Augmentation

The PMMA augmentation process employs cannulated screws and provides endless variety of PMMA shapes and sizes based on vertebral trabecular structure. Uniformly shaped PMMA models were used for consistent simulation, created in Autodesk Fusion 360 CAD software using BPS and SSA screws as reference points. The PMMA models were aligned with screw tips to simulate augmentation, with volumes ranging from 1 cm^3 to 6 cm^3 per screw. In 3-Matic software, excess PMMA at intersections with cortical bone or other PMMA was removed, maintaining original volumes. The final augmented PMMA geometries were assessed by experienced spinal surgeons.

3.2.3. Boundary and Loading Conditions

16 FE models were generated, including the BPS and SSA implants with both normal and osteoporotic bone conditions, as well as gradually augmented models ranging from 1 cm^3 to 6 cm^3 of PMMA/screw. HyperWorks software was used for model assembly and modifications before exporting to Abaqus/CAEv11 for FE simulations. The simulation processes involved two steps: first, applying a 400 N follower load through the vertebral

bodies, and second, subjecting the L2 vertebral body to a 10 Nm bending moment in three anatomical planes to simulate various movements. These simulations adhered to ASTM standards, allowing for testing under higher trunk muscle loads compared to previous simulations in Part I of the thesis.

4. RESULTS

4.1. Validation of intact L2-L4 FE model

The accuracy of the L2-L4 segmentation process was evaluated by two investigators, yielding a high Dice Similarity Index (DSI) value of 94%, indicating precise segmentation. Furthermore, FE mesh quality assessment showed that the majority of elements' Aspect Ratios (ARs) fell within the acceptable range, with none exceeding the cautionary limit of 10. Range of Motion (ROM) values of the intact FE model for the L2-3 and L3-4 motion segments closely matched those reported in a previous cadaveric study by Ilharreborde et al. (2011), affirming the reliability of the created L2-4 FE model for further investigations.

4.2. Finite Element analysis results for the non-agumented surgical models

4.2.1. L3-L4 Segmental Range of Motion

The study compared the primary stabilizing properties of three investigated implants by analysing the Range of Motion (ROM) of six surgical constructs under combined loading conditions. Surgical models corresponding to BPS, LPS, and SSA fixation options with both normal and osteoporotic bone properties were examined. Following insertion of the OLIF cage, ROM at the surgical level decreased in all motion conditions compared to the intact model, with osteoporosis increasing ROM in all directions. BPS demonstrated the most stable fixation overall, particularly notable in left and right-side rotation scenarios, exhibiting lower ROM values compared to LPS and SSA systems. The highest impact caused by osteoporosis on the ROM occurred in the LPS fixation construct, where the ROM increased by 97.3% in flexion, 86.3% in extension, 30.14% in left bending, 140.26% in right bending, 50.96% in left rotation and 53.38% in right rotation. The difference in ROM between BPS and lateral plate systems was most pronounced in rotation scenarios, with BPS providing superior stability in both normal and osteoporotic conditions. For normal bone the difference in BPS vs LPS was 99%, BPS vs SSA was 119.73 %, and for the porotic bone BPS vs LPS was 158.94%, BPS vs SSA was 145.49%.

4.2.2. Cage Caudal Displacement Values

Osteoporosis increased the cage displacement in caudal direction for all of the fixation constructs. The highest increase in displacement was found in right bending for the LPS (from 0.115 mm to 0.24 mm, 109%), and for the SSA (from 0.113 mm to 0.237 mm, 110%). With the exception for flexion and left bending, the BPS fixation had lower displacement values both for normal and osteoporotic condition compared to LPS and SSA. Overall, the cage displacement values were similar for the SSA and LPS.

4.2.3. L4 Upper Endplate Stress

To evaluate the interaction between the inserted cage and the bony endplate below it, the endplate's surface stress distribution (von Mises stress peaks) was investigated. Compared to normal bone, the stress peaks increased in the osteoporotic models for extension, right bending and right rotation. In flexion and left bending the stress peaks for the BPS model were much higher compared to the other models (LPS, SSA) regardless of the bone material properties (Von Mises peaks for BPS were 10.92 MPa and 13.31 MPa for flexion and left bending in normal bone and 14.43 MPa and 16.06 MPa in osteoporotic condition). To investigate this phenomenon the von Mises stress distribution on the L4 upper cortical endplates were visualised using contour plots. This showed that the exceling von Mises stress peaks in flexion and left bending for the BPS models are stress concentrations at the place of the fenestration of the anulus fibrosus and the OLIF cage border.

4.2.4 Screw-tip displacement

Screw displacement within the L4 vertebra was measured by measuring the distance between screw tip locations before and after simulation steps across all three constructs. Osteoporosis consistently increased screw displacement in L4 compared to normal bone models, with the highest increase observed in LPS fixation for left (100%) and right (100%) rotation. BPS fixation exhibited lower screw displacement increases across all motion scenarios compared to LPS and SSA implants, indicating potentially superior stability in the presence of osteoporosis. Screw displacement increase in BPS model for flexion: 61.38%, extension: 40.38%, left bending: 31%, right bending: 39%, left rotation: 36.32 %, right rotation: 33.48%, For the LPS model 67,2% in flexion, 65,21% in extension, 39,2 % in left bending, 81,35% in right bending, 100% in left rotation, 100% in right rotation. For the SSA model 65,82% in flexion, 66,66% in extension, 49,48 % in left bending, 82,81% in right bending, 52,17% in left rotation, 56,71% in right rotation.

4.3. Finite Element analysis results for the augmented surgical models

4.4.1. L3-L4 Segmental Range of Motion

Segmental ROM values at the L3-L4 level under combined loading conditions were measured. In normal bony conditions, the BPS system generally displayed smaller ROM values compared to the SSA, except for left bending. Osteoporosis led to increased segmental ROM across all bending moments for both implants, further accentuating the existing difference between them. Gradual PMMA augmentation reduced ROM in both BPS and SSA constructs with osteoporotic bone, with notable decreases observed at 3 cm^3 and 6 cm^3 of injected PMMA volume per screw. At 3 cm^3 of injected PMMA per screw (half of the investigated maximum amount), the segmental ROM values for BPS decreased by 27.3% in flexion, 10.5% in extension, 13.0% in right bending, 6.3% in left bending, 11.4% in right rotation, and 7.5% in left rotation compared to the non-augmented osteoporotic ROM values. For SSA. the values decreased by 41.3% in flexion, 49.1% in extension, 61.9% in right bending, 30.3% in left bending, 41.9% in right rotation, and 36.7% in left rotation. Compared to the non-augmented ROM values in osteoporosis, at 6 cm^3 injected PMMA volume per screw, the difference between the two implants reduced by 25.9% in flexion, 98.3% in extension, 36.5% in right bending, 62.9% in right rotation, and 76.5% in left rotation.

4.4.2. Cage Caudal Displacement Values

The maximal caudal displacement values of the inserted OLIF cage at the end of each simulation were measured. Under normal bone conditions, the BPS system generally exhibited smaller displacement values compared to the SSA system, except for left bending and flexion. Osteoporosis increased displacement values in both constructs, exacerbating the existing disparity between BPS and SSA. PMMA augmentation in osteoporotic bone gradually reduced displacement values in both implants, with notable decreases observed at 3 cm^3 and 6 cm^3 of injected PMMA volume per screw. At 3 cm^3 of injected PMMA volume per screw (half of the investigated maximum amount), the cage's caudal displacement values for BPS decreased by 61.5% in flexion, 13.2% in extension, 31.9% in right bending, 18.9% in left bending, 28.7% in right rotation, and 54.2% in left rotation compared to the non-augmented osteoporotic caudal displacement values. For SSA, the values were decreased by 35.2% in flexion, 43.9% in extension, 58.3% in right bending, 3.0% in left bending, 66.5% in right rotation, and 66.1% in left rotation. Compared to the non-augmented values in osteoporosis, at 6 cm^3 injected PMMA per screw, the difference in the cage's caudal displacement values between the two implants reduced considerably: 49.0% reduction in flexion, 76.0% in extension, 96.8% in right bending, 48.6% in left bending, 89.9% in right rotation, 96.7% in left rotation.

4.4.3. L4 Upper Endplate Stress

The maximal Principal Stress values at the end of each bending cycle were investigated as well. PMMA injection reduced maximal stress values on the endplate beneath the cage, with both BPS and SSA. The largest stress peak was observed in the SSA system during right bending (17.8 MPa), significantly increased by osteoporosis (25.2 MPa). This value in osteoporosis at 3 cm^3 PMMA augmentation is decreased by 54.4%, at 6 cm^3 by 71%. At 3 cm^3 of injected PMMA volume per screw (half of the investigated maximum amount), the maximal L4 endplate Principal Stress values for BPS decreased by 59.9% in flexion, 15.0% in extension, 37.4% in right bending, 32.2% in left bending, 48.8% in right rotation, and 10.3% in left rotation compared to the non-augmented osteoporotic values. For SSA, the values decreased by 45.1% in flexion, 44.8% in extension, 54.4% in right bending, 24.9% in left bending, 45.8% in right rotation, and 46.8% in left rotation. Compared to the non-augmented values in osteoporosis, at 6 cm^3 injected PMMA per screw, the difference in the endplate stress values between the two implants reduced considerably: 95.2%

reduction in flexion, 81.2% in extension, 86.7% in right bending, 57.4% in left bending, 83.1% in left rotation.

5. CONCLUSIONS

The aging population in developed countries presents an ongoing challenge for spine surgeons due to decreased bone quality, and comorbidities. Minimally invasive surgery can be a solution for this frail population, but it has drawbacks. Based on the results of Part I of this thesis bilateral pedicle screw (BPS) and rod fixation provided superior biomechanical stability for OLIF cages, compared to self-anchored standalone (SSA) or lateral plate-screw fixated (LPS) cages both in normal and osteoporotic conditions. The osteoporosis amplified the difference between the stability of the bilateral pedicle screw fixation and the two other investigated fixation methods. Clinically, in the case of decreased bone quality (primary or secondary osteoporosis), the surgeon has to take into consideration the limits of the SSA and LPS, despite the advantage that there is no need for a second step in the surgery by turning the patient to prone position to perform the percutaneous pedicle screw fixation.

Part II of this thesis aimed to investigate the effect of PMMA augmentation on the BPS, and SSA constructs. Based on the results, PMMA augmentation can improve stability in both constructs, narrowing the gap between them. It is important to note that increasing the volume of injected PMMA raises the risk of leakage. The research suggests that injecting between 3 cm^3 and 4 cm^3 of PMMA per screw can achieve comparable stability to the BPS system in the SSA construct. Currently, there is no consensus-based guideline on when to use PMMA augmentation in OLIF surgery or the appropriate amount to inject, and further biomechanical studies are required to understand the effects and risks of PMMA augmentation. According to the results of the study and the clinical need, the concept of an SSA augmentation device is desirable but currently not available on the market. These findings suggest opportunities for continued research, potential advancements/innovations, and the development of new products for the marketplace

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