Pedicle Screw Fixation

Vom Promotionsausschuss der
Technischen Universität Hamburg-Harburg
zur Erlangung des akademischen Grades

Doktor-Ingenieurin (Dr.-Ing.)

genehmigte Dissertation

von

Rebecca Anne Murray

aus

El Dorado, Kansas

2014

Erste Gutachter:	Prof. Dr. habil. Michael Morlock Ph.D.
Zweite Gutachter	Prof. Dr. Stephen Ferguson
Vorsitzender der Prüfungskommission:	Prof. Dr. Norbert Hoffmann
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Abstract

Pedicle screws are considered to be the gold standard for posterior spinal stabilization surgeries and have been used successfully for more than three decades for the treatment of diseases requiring spine stabilization, alignment or bone fusion. A loss of fixation between the bone and the screw is identified as a predominant failure mode for these medical devices. The primary aims of this thesis were: (1) to determine the pattern of this pedicle screw loosening and (2) to assess the comparative influence of certain patient, surgical and screw design parameters. Results were also used to enrich discussions on the probable loosening mechanisms and the most apt pre-clinical testing methods for pedicle screws.

To obtain these goals seven studies were performed using a variety of different testing methods. These included: clinical survey analysis, medical image analysis, laboratory mechanical testing, *ex vivo* cadaveric testing, motion analysis and the finite element (FE) method.

The loosening patterns quantified from clinical CT scans exhibited the most motion in the primary *in vivo* loading plane as well as peak displacements at the screw tip and screw entry to the vertebra. The clinically quantified patterns were characterized by: a distinct fulcrum located near the pedicle end, a ten-fold increase of loosening volume from the cranial to caudal spine, higher volumes of loosening at the marginal construct ends when compared to mid-construct, and distinct failure patterns in the different spinal regions. Furthermore, the lumbosacral spine and the marginal construct ends were identified as the regions which are the most susceptible to pedicle screw loosening. The ability to more evenly distribute the peaks in loading shown to exist at the screw entry, the screw tip or at the construct ends might be critical for mitigating pedicle screw loosening.

Patient parameters in terms of bone quality and vertebral dimensions were shown to be the most important screw fixation factors both clinically and experimentally. Since patient attributes cannot be altered, a special emphasis is placed on the initial surgical challenge to match the optimal screw designs and surgical techniques to achieve the best fixation possible. The recommended surgical positioning would be to reduce the length of the screw outside the vertebra while directing the screw along the pedicle axis. This would allow for a minimization of the lever arm, the use of a maximal screw diameter, while maximizing the vertebral depth. All of these factors were shown in the presented studies to increase screw fixation. Results suggest that severely osteoporotic patients should consider augmentation injected through the screw. The performance benefits of this method are likely due to its seven-fold increase of cement contact to the vertebral wall.

The comparable methodologies in this thesis enabled unique insights into the success and failure of pedicle screws. Across the series of experiments conducted, there is evidence to suggest that patient attributes are the most important determinants of pedicle screw fixation strength. Surgeons can utilize the current findings to optimize surgical positioning and the screw augmentation technique. Particular regions of the construct and of the screw profile which are especially susceptible to loosening should be targeted for design optimization. In addition, the results imply that pullout testing is not sufficient and should not be used to identify the pedicle screw designs which are most likely to succeed clinically.

Table of Contents

Terminology

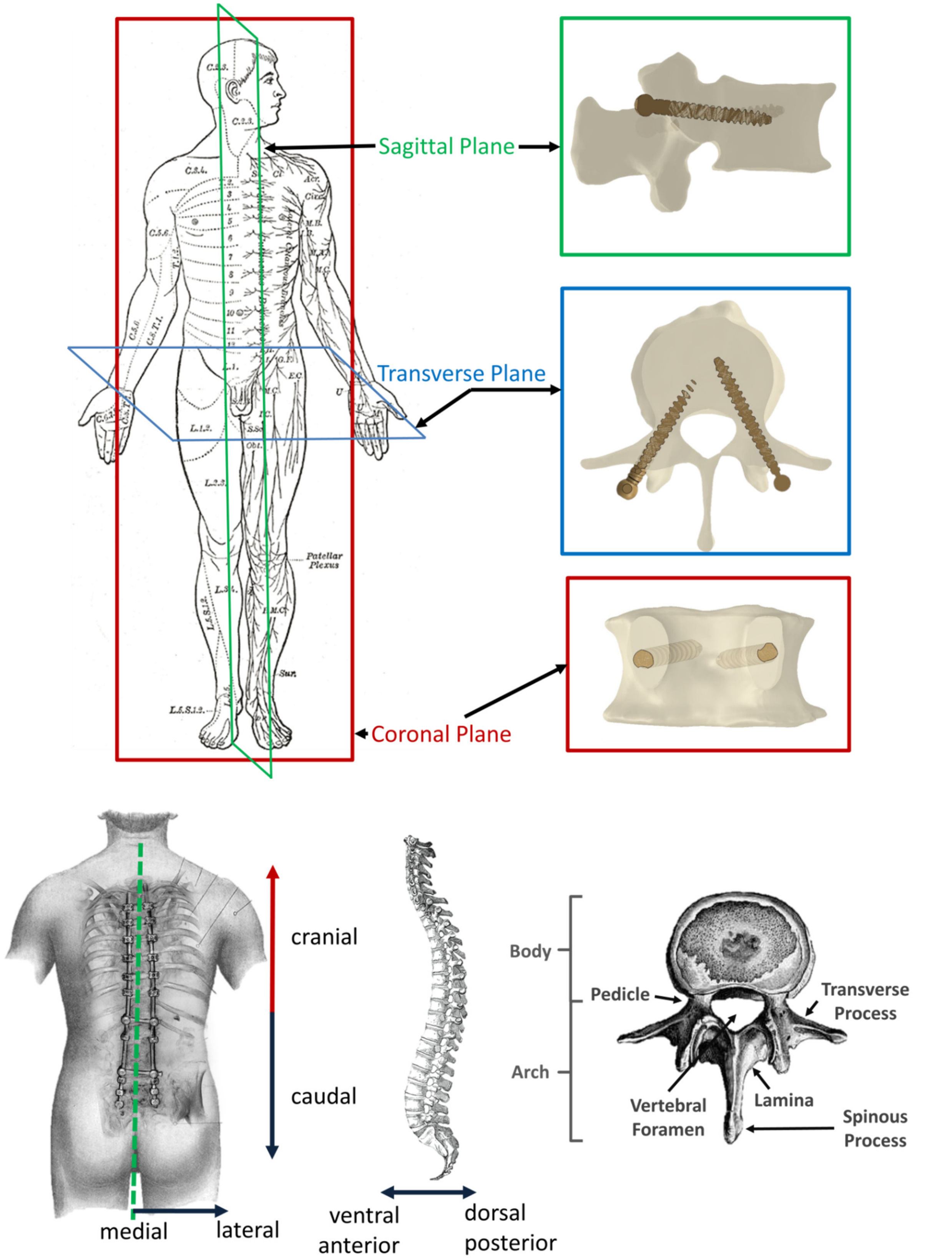


Figure i The relevant anatomical terms used to describe the locations of pedicle screws relative to patient anatomy. All terms are defined in the accompanying glossary. [Black and white drawings are adapted from Gray[89], all other images are rendered computer tomography scans of specimens]

Glossary

Anterior An anatomical location term pertaining to the front or ventral.

Bone cement Used to anchor medical implants to bone.

Bone Mineral Density (BMD) A measure of the bone density as represented by the calcium or the Hydroxyapatite content.

Bone volume to total volume (BV/TV) The ratio of the volume of bone to the total volume in a medical image. It is used as a measure of bone quality.

Cannulation A hole running the full length of the pedicle screw axis allowing for the use of guide wires as well as medical cement injection.

Caudal An anatomical localization term meaning towards the feet.

Computed Tomography (CT) A three dimensional medical imaging technique which reconstructs a series of cross-sectional scans obtained using X-rays.

Conical core A screw which has a tapering thread depth which increases towards the screw tip making the core shape of the screw conical.

Construct The stabilizing structure formed by the joining of the pedicle screws to the longitudinal rods.

Coronal plane A vertical plane which passes from cranial to caudal and divides the body into ventral and dorsal sections.

Cranial An anatomical location term meaning towards the head.

Cylindrical core A screw which has a consistent thread depth allowing for the core shape to remain cylindrical.

Dorsal An anatomical localization term pertaining to the back or posterior.

Double halo The appearance of a rim of radiopaque, dense bone outlining the area around a screw that has become loose in patient radiographs. This double halo is said to be a confirmation of screw loosening as it forms after the onset of screw loosening and is attributed to the motion of the loose screw causing repeated compaction of the cancellous bone.

Dynamic stabilization The use of a construct which is semi-rigid and allows for some motion but also restricts the range of motion in order to provide prescribed stabilization. This is a modification of the typical stabilization which attempts to remove motion.

Ecological Validity The ability of a study to approximate the real world.

Finite Element (FE) A numerical analysis technique which utilizes differential equations for finding approximate solutions to boundary value problems.

Fixation The state of being fastened securely in position.

Halo The appearance of a radiolucent gap around the pedicle screw head in the examination of patient radiographs. A radiolucent halo of 1 mm is considered the primary clinical indication that a pedicle screw has become loose.

Hydroxyapatite (HA) The chief structural element of bone which consists of a complex mineral of calcium phosphate ($Ca_5(PO_4)_3OH$). Coatings of medical implants may contain HA in order to promote fixation by promotion of bone formation.

Kyphosis The outward curvature of thoracic and sacral spine.

Lamina Two broad plates which connect to the pedicles and are fused completing the posterior rim of the vertebral arch.

Lateral An anatomical location term meaning further from the midline.

Loosening Make something fastened less tight or firm.

Lordosis The inward curvature of lumbar and the cervical spine.

Medial An anatomical location term meaning towards the midline.

Monoaxial head A screw head which is stable and cannot rotate.

Pattern of loosening The shape of the gap between the cancellous bone of the vertebra and the screw interface.

Pedicle The two short thick processes which connect the vertebral arch to the vertebral body.

Pedicle screw loosening Pedicle screw loosening is a break-down of the mechanical integrity of the bone-screw interface causing a loss of stability of the construct.

Perforation Radial holes along the screw shaft allowing for the localization of bone cement dispersion.

Pitch The spacing between the thread crests on a screw.

Polyaxial head A screw head which is free to rotate until it is attached to the rod.

Polymethyl methacrylate (PMMA) A transparent thermoplastic which is often used as the base of medical bone cements.

Posterior An anatomical location term pertaining to the back or dorsal.

Pseudarthrosis In the case of spinal fusion surgery: failure of a patient to exhibit complete boney union after surgery.

Quality Adjusted Life Year (QALY) A measure of disease burden which incorporates both the quality and the quantity of the life lived. It is used to assess the value for money of medical intervention.

Radiograph The use of X-rays to view a material with non-uniform density. In the clinical setting it is used to view the body, especially for highly dense boney structures.

Radiographic fusion The appearance of a boney bridge between two previously separated boney structures as observed radiographically.

Radiolucent Any material which permits the transmission of X-rays or other forms of radiation; appears dark on a standard radiograph.

Radiopaque Any material which blocks the transmission of X-rays or other forms of radiation; appears bright on a standard radiograph.

Sagittal plane A vertical plane which passes from cranial to caudal and divides the body into left and right sections.

Screw A fastener characterized by a helical ridge which is inserted by being rotated.

Screw head The end of the screw which is used for screw insertion and for pedicle screw fixation it is attached to the rod.

Screw tip The end of the screw which is inserted into the material.

Scoliosis A medical disorder which is characterized by an abnormal curvature of the spine.

Self-tapping A screw design feature which consists of a sharp edge that allows the ability to cut a thread in the material in which it is being inserted.

Spinous Process A boney structure which extends posteriorly and inferiorly from the junction of the lamina that serves as a point for muscle attachment to the vertebra.

Spondylolisthesis A forward dislocation of one vertebra relative to the superior vertebra.

Toggle To switch from one state to another. In pre-clinical pedicle screw testing it the application of force or displacement which changes between the cranial and caudal directions.

Transverse plane A horizontal plane which divides the body into cranial and caudal sections.

Transverse Process Two boney structures which extend laterally from the lamina.

Ventral An anatomical location term pertaining to the front or anterior.

Vertebral arch The posterior portion of the vertebra which consists of the pedicles, the laminae and seven processes.

Vertebral body The anterior portion of the vertebra which supports most of the spinal load bearing and its approximate shape of an oval cylinder.

Vertebral foramen The opening formed between the vertebral arch and the vertebral body. The spinal cord is located within this structure.

Chapter 1.
Introduction

Pedicle screws are medical implants which are implanted posteriorly into the vertebrae of the spine and longitudinally connected to a rod to form a construct which corrects spinal alignment or promotes stabilization. Pedicle screw fixation is considered to be the gold standard of spinal internal fixation due to its many benefits in a variety of debilitating spinal conditions[80]. Furthermore, it is very versatile as it can be easily adapted to individual patient anatomy and be implanted in all spinal regions (Figure 1.1). Internal spinal fixation is used to correct spinal alignment (*e.g.* scoliosis and spondylolisthesis), to promote fusion or to stabilize the spine after fracture, tumor removal, anterior strut grafting, and osteotomies[80]. After failure of conservative treatments, surgery is also increasingly being utilized as a last resort for patients with the progressively more prevalent, chronic low back pain[64,173]. The study of the fixation between the screw and the bone in which it is anchored is increasingly timely because currently there is a rise in the indications for pedicle screw use[173], the number spinal surgeries[61,64], and the number of people at high-risk for spinal fractures and poor fixation[128].

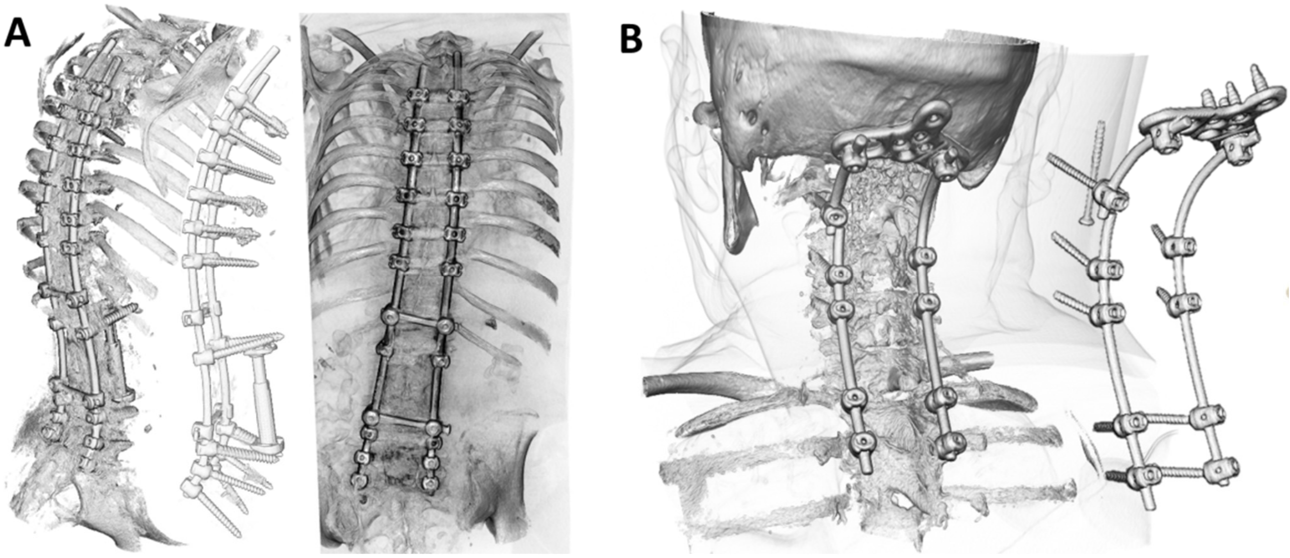


Figure 1.1 Rendered CT (computed tomography) scans of a patient with pedicle screw fixation in the thoracolumbar spine (A) and a patient with fixation in the cervical spine (B). Note the longitudinal rods connecting to the screws to form the motion and angle stabilizing construct. [Rendered CT scans of patients presented in Chapter 4]

Recently, the use of pedicle screws in non-spondylolisthesis related short fusions has been called into question[64,109]. This is due to the high costs and conflicting reports as to whether or not the instrumentation significantly improves patient outcomes[11,62,64,109]. It is important to note that even with the current criticisms of certain uses of pedicle screws, pedicle screws remain the uncontroversial choice for most of their indications. Pedicle screws have some undeniable benefits to other internal fixation techniques. They provide posterior stabilization that is, thus far, unrivaled because they utilize the strongest point of attachment, the pedicle isthmus, while traversing all three vertebral columns (Figure 1.2)[39]. This stabilization has allowed surgeons to shorten fixation constructs[5,87,214], maintain shorter periods of immobility after surgery[80], use less post-operative bracing[13,93], maintain curvature correction longer[13,93], achieve better fusion rates[83,116] and it provides opportunities for operations and procedures which were previously not possible (*e.g.* removal of large spinal tumors and certain spinal alignment corrections)[13,65,80,87,93,215]. The opportunities for new procedures stems from the pedicle screws' ability to easily adapt to individual patient anatomy, their inherent stiffness, and their ability to provide the surgeon a handle to methodically manipulate the alignment of the spine[13,29,93].

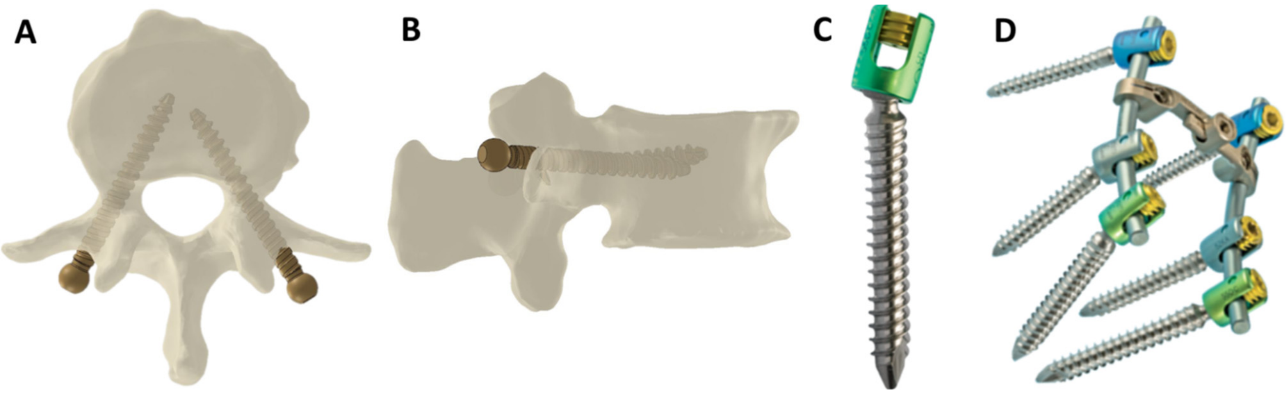


Figure 1.2 A view of a single vertebra implanted with pedicle screws (A & B). In a typical trajectory a pedicle screw passes directly through the pedicle canal and into the vertebral body with converging screw tips in the transverse plane (A) and the parallel alignment to the vertebral endplates in the sagittal plane (B). A typical poly-axial pedicle screw (C) and a modern pedicle screw construct showing screws, rods, and a cross-link device (D). [A & B rendered from specimen CT scans, C & D adapted from zimmer.com]

Though pedicle screw fixation is considered a safe and effective treatment for specific spinal disorders it is not without its complications. Introduction of more hardware introduces product specific complications. These pedicle screws complications include: malpositioning, rod or screw breakage, infection at the implant site, or loosening at the bone-screw interface[69,80,155,243]. Implant failure is generally shown to occur in the first six months post-surgery[115,155,198,217] and since 2000 the highest prevalence of failure is loosening at the bone-screw interface (Chapter 2.4).

Rates of loosening have been shown to be between 1.3 and 23.0% in the past 20 years[69,80,115,132,143,155,156,168,194,202,217,229,237,240,243]. The prevalence of loosening has increased in recent years and this is likely due to multi-factorial causes: broader indications, use in patients with poor bone quality, use of dynamic implants which place higher demand on the interface, along with better imaging techniques to make loosening more visible.

Pedicle screw loosening has been a topic of interest in the surgical community for many years and numerous studies have been performed to attempt to characterize it *in vivo*, *ex vivo*, and in the lab. The mechanisms of loosening have been often discussed but frequently with little experimental data to justify the given theories[19,39,42,58,112,115,155,156,199]. The appearance of loosening has been discussed as early as 1975[199,200]; however, quantification of the loosening area around the screw is still lacking in the literature. Lab testing to parameterize screw loosening, apart from the highly non-physiologic pullout testing, is inconsistent with regard to setup, loading configuration, operator control (force *vs*. displacement control) and the fixation parameters output.

1.1. Study Design

Two primary research questions were addressed in this thesis: (1) What is the pattern of the loosening zone around the pedicle screw? and (2) What are the primary factors which influence pedicle screw fixation? To investigate these questions, various specific aspects of pedicle screw fixation were explored within seven experimental studies. These studies used a variety of different testing methods including: clinical survey analysis, medical image analysis, laboratory mechanical testing, *ex vivo* cadaveric testing, motion analysis and the finite element (FE) method. Each study had individual primary and secondary goals, but at the same time, were linked to the two original research questions. An overall depiction of the interaction between the research questions and the studies performed is shown in Figure 1.3. The individual primary and secondary goals of each experimental study are outlined in Table 1.1.

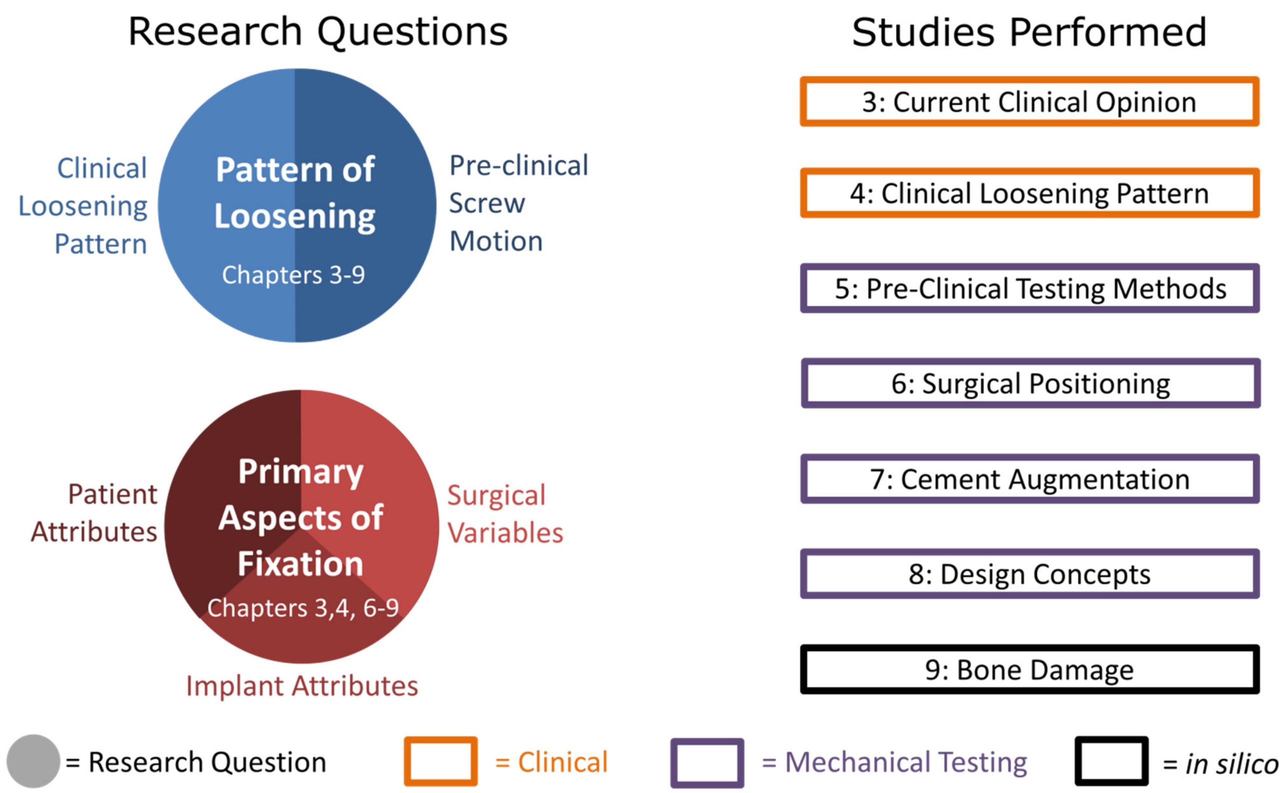


Figure 1.3 The connection between the two primary research questions (circles) to the seven conducted studies (shown in rectangular boxes). The first question (blue) can be split into two parts, how loosening appears clinically (light blue) and how the screw moves in external testing (dark blue). The second question (red) can be separated into three aspects: the patient attributes (dark red), surgical variables (light red), and the implant attributes (medium red).

Table 1.1 The experimental studies (Chapters 3-9) summarized by the experimental category, primary aim, and secondary aims.

Studies	Category	Primary Goal	Secondary Goals
Current Clinical Opinion	Clinical	Gather the current clinical opinion on the most important screw fixation aspects, failure modes and best surgical techniques	Determine the approximate loosening pattern and the time to loosening
Clinical Loosening Pattern	Clinical	Quantify the volumetric parameters of the screw loosening zone as it appears in clinical CT scans	Determine if the vertebral level or the relative location in instrumented construct influences the loosening pattern
Pre-Clinical Testing Methods	mechanical	Classify the physiologic appropriateness, sensitivity and reproducibility of three testing protocols	Define the screw motion dependent on bone quality and testing type
Surgical Positioning	*ex vivo*	Determine the influence of surgical positioning in the C1 vertebra on the fatigue loosening parameters	Determine the influence of vertebral dimensions on loosening parameters
Cement Augmentation	*ex vivo*	Determine the influence of screw diameter and cement augmentation on loosening parameters in the lumbar spine & to compare the pullout *vs* the toggling fatigue testing methods	Determine the influence of screw diameter, cement augmentation, vertebral dimensions, and bone quality on screw motion & the influence of vertebral dimensions and bone quality on loosening parameters
Design Concepts	*ex vivo*	Determine the influence of the screw thread design on loosening parameters in the thoracolumbar spine	Determine the influence of screw thread design on screw motion & the influence of vertebral dimensions on loosening parameters
Bone Damage	*in silico*	Comparatively rank the influence of bone quality, vertebral dimensions, as well as screw placement, length and diameter on damage to the surrounding trabecular bone	Investigate the use of a bone material model for studying fatigue damage at the bone-implant interface

1.1.1. Research Question 1: The Pattern of Pedicle Screw Loosening

In clinical practice, pedicle screw loosening presents as a radiolucent[194,196,199] or 'clear'[229] area surrounding the screw head in radiographs or CT scans. This is often termed clinically as a loosening 'halo'. A likely reason for this dark area is that a less dense fibrous tissue has been shown to surround loosened pedicle screws[199] and less dense materials appear darker in radiographs. Clinically, loosening is often identified by a 1 mm wide halo around the screw head; however, the reason for the 1 mm width and the shape of this halo is not described. Investigations on the *in vivo* loading of pedicle screw constructs have been performed and have revealed a primary force which acts in the cranial-caudal direction and moment acting in the screw direction[17,180,188]. When a cantilever loading is applied to an implant (*i.e.* pedicle screw) in a host material (*i.e.* bone), it has been found that the implant imparts peak stresses and strains at the entry and toward the tip of the host material[122]. These factors lead to the first hypothesis, that the clinical loosening patterns will exhibit the most motion in the primary *in vivo* loading plane as well as peak displacements at the screw tip and screw entry to the vertebra.

Most opinions in the literature state that repetitive motion or loading is the mechanism for loosening[39,42,112,129,156] rather than infection or large posterior overload of the implant[199]. In mechanical structures, failure pattern analysis is often used to gain insight into the potential failure modes and; therefore, the potential underlying mechanisms. The use of clinical images of pedicle screw loosening to more quantitatively define the observable features of the failure pattern could provide further insight into the primary mechanism of loosening.

Pre-clinical testing of pedicle screws is performed in order to assess which screws will maintain the best fixation when used in patients. Basic axial pullout has been the most widely used and accepted method to pre-clinically test screw fixation in the spine. However, this method does not mimic loading seen *in vivo*[17,181,185,188] nor is it likely to create failure patterns as they are seen in clinics. Repetitive, fatigue loading which mimics the loading seen *in vivo* would be the ideal *ex vivo* testing method to try and gather meaningful fixation parameters. Evaluating the extent to which the pre-clinical testing method can reproduce a clinical failure pattern could form part of the basis of an assessment of the clinical appropriateness of the chosen testing method. Such an assessment of the clinical relevance of the testing method can, for example, be possible via motion analysis of the screw during *ex vivo* testing[42,222,248] .Furthermore, the pattern observed can be dimensionalized allowing for further parameters which can be targeted for the optimization of screw design. When considering these factors, it is believed that the pre-clinical testing methods which more closely mimic the loading seen *in vivo* will have *ex vivo* motion patterns which more closely resemble the loosening patterns seen in clinical practice.

1.1.2. Research Question 2: Primary Factors Influencing Pedicle Screw Loosening

When investigating the influential factors in pedicle screw loosening, there was a noticeable lack of testing congruency within the literature. Differences existed according to the testing method used (*e.g.* pullout or fatigue), the testing protocol (*e.g.* test speed, controller type) and the output variables used to quantify fixation. Furthermore, due to the nature of pre-clinical and clinical testing only a few variables can be systematically controlled within a single study. These testing differences cause difficulty in the derivation of clear conclusions of the most influential factors related to screw loosening. This thesis attempts to overcome these limitations by employing methodologies which allow a consistent, direct comparison of many variables within a single study as well as by consistently measuring variables across multiple *ex vivo* studies.

The influencing factors of pedicle screw loosening were split into three categories: those pertaining to the patient attributes (*e.g.* bone quality and pedicle dimensions), the surgical variables (*e.g.* screw placement and screw augmentation with cement), and those related to the implant itself (*e.g.* screw diameter and thread characteristics). Bone quality, often operationalized as BMD (bone mineral density) or BV/TV (bone volume to total volume), has often been shown to be the most influential parameter for the fixation strength of screws as well as trabecular fracture[92,156,157,248]. Critically, the patient vertebral dimensions are the limiting factor of the two primary implant dimensions: diameter and length. This is because the diameter of the screw should not surpass the minor diameter of the pedicle in order to not compromise neurovascular structures or the structural integrity of the pedicle. In most spinal regions, the length should not cause the screw to perforate the anterior wall of the vertebra as important neurovascular structures are in close proximity (*e.g.* aorta). Minor implant design features such as the presence of a conical core and the design of the screw thread have been investigated using pure axial pullout methods and results suggest that their influence is less than that of the bone quality[1,41,92,98,112]. The relative importance of surgical positioning within the spine and its role on fixation strength is, however, still debated[49,144,174,216,242]. These previous findings have led to the hypothesis that patient attributes, especially related to bone quality and pedicle dimensions, will be the most important factors driving fixation. Other aspects of implant design (*i.e.* thread design) will have comparatively less influence on fixation than the patient attributes and the surgical placement of screws, especially in cases of osteoporotic bone quality.

1.2. Overview

The overall goal of this research is to determine the loosening pattern of pedicle screws as well as the primary influential factors of pedicle screw loosening in order to identify potential avenues to mitigate pedicle screw loosening. From the studies performed, insight was gained into the appropriateness of various pedicle screw fixation testing methods and the primary mechanisms of their failure. The main body of the thesis contains seven chapters representing individual studies which were used to address various aspects of the two research questions while simultaneously addressing more precise topics.

Chapter 2 includes the background information relevant to help understand the various aspects which are important to pedicle screw fixation and to provide a context for the thesis as a whole. Chapter 3 includes a surgeon survey which was conducted to gather the current clinical opinion on the most important aspects of screw fixation and to help direct the aspects of fixation which were investigated in the subsequent studies. Chapter 4 contains a study of clinical CT scans which exhibited clear loosening patterns. A method to quantify various areas of the loosening zone was created and the patterns which were observed are described. Chapter 5 involves a mechanical test utilizing various densities of a bone substitute material in an attempt to classify the physiological appropriateness, sensitivity and reproducibility of three fatigue testing protocols. Chapter 6 investigates how the surgical positioning within the most cranial vertebra, C1 (aka. Atlas), influences the *ex vivo* pedicle screw fixation for a cyclic, fatigue loading at the screw head. The influence of the screw diameter and the screw augmentation technique was investigated in another *ex vivo* experiment on osteoporotic specimens in Chapter 7. Within this study different testing methods were compared by investigating the differences between axial pullout and a toggling, fatigue loading. The study presented in Chapter 8 investigates the influence of various thread designs on the fatigue fixation strength of the thoracolumbar spine. The last experimental chapter, Chapter 9, involves an *in silico* study which was a comparative, parametric study of the influence that bone quality, vertebral dimensions, screw placement, screw length and screw diameter have on the damage to the surrounding trabecular bone. Chapter 10 is the general discussion of the thesis in which the findings from all experimental chapters are reviewed and synthesized according to the outlined research questions. The most important findings and take home messages are presented in its conclusions.

Chapter 2.
Background

2.1. Basic Spinal Anatomy

The spine is a complex three dimensional structure which provides three important functions for the body: protection of the spinal cord, load transmission, and the capacity for motion[161]. The spinal column typically consists of seven cervical vertebrae (C1-C7), twelve thoracic (T1-T12), five lumbar (L1-L5), the sacrum and the coccyx. The sacrum consists of five vertebrae which are fused and the coccyx (tailbone) is comprised of four small fused bones.

The major features of an individual vertebra (Figure 2.1) are similar in all regions; however, the physical dimensions increase from the cervical to the lumbar spine (Figure 2.2)[89,161]. The basic shape of the vertebrae adapt to the loading and motions experienced in their respective region. The spinous and the transverse processes allow for muscle attachment and the articular process inhibits rotation and sliding[89]. When all the vertebrae are linked the vertebral foramen combine to form the protective spinal canal. A pair of pedicles forms the narrowest, densest portion of the vertebra and connects the vertebral arch to the vertebral body (Figure 2.1). The primary role of the vertebral body is in weight bearing which is reflected by its internal structure. The vertebral body has a dense cortical shell which supplies the majority of the vertebral strength. This shell surrounds a porous cancellous core (Figure 2.4). The alignment of the trabecular struts of the cancellous core adapt to the applied forces and align with the experienced principal stress in the cranial-caudal direction[22,78].

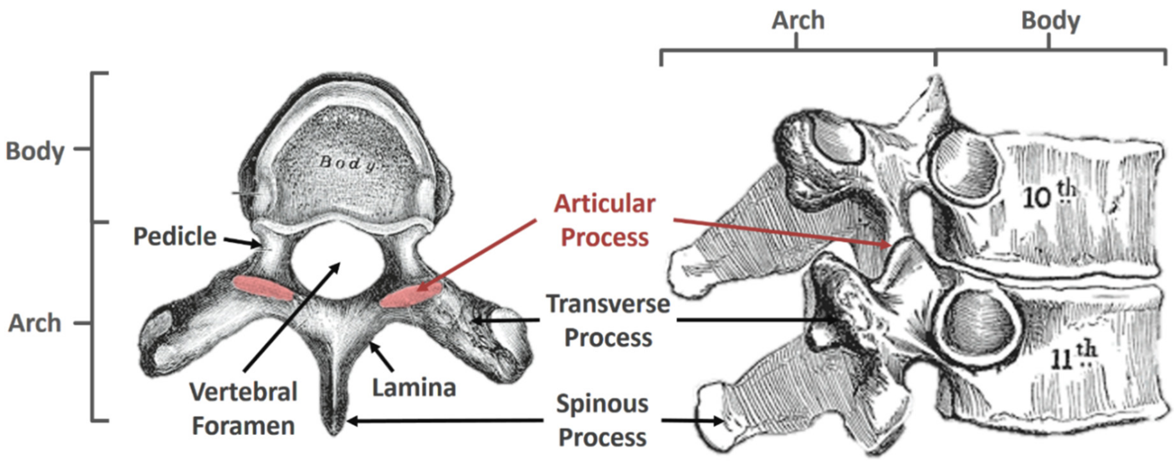


Figure 2.1 The basic anatomy of the vertebra with the major features labeled on representative thoracic vertebrae. [Adapted from Gray[89]]

When viewed in the coronal plane a normal spinal column appears straight; conversely, the overall form of the spine in the sagittal plane consists of a double-S curve (Figure 2.2, left). The S-curves are made up by two inward curvatures (termed lordosis) in the cervical and lumbar regions and two outward curvatures (termed kyphosis) in the thoracic and sacral regions. This shape allows for the spine to compensate for axial forces particularly well[161]. The cervical, thoracic, and lumbar vertebrae are connected to one another via intervertebral discs which can functionally be considered pressurized cushions that also allow the bending and rotational movements of the spine.

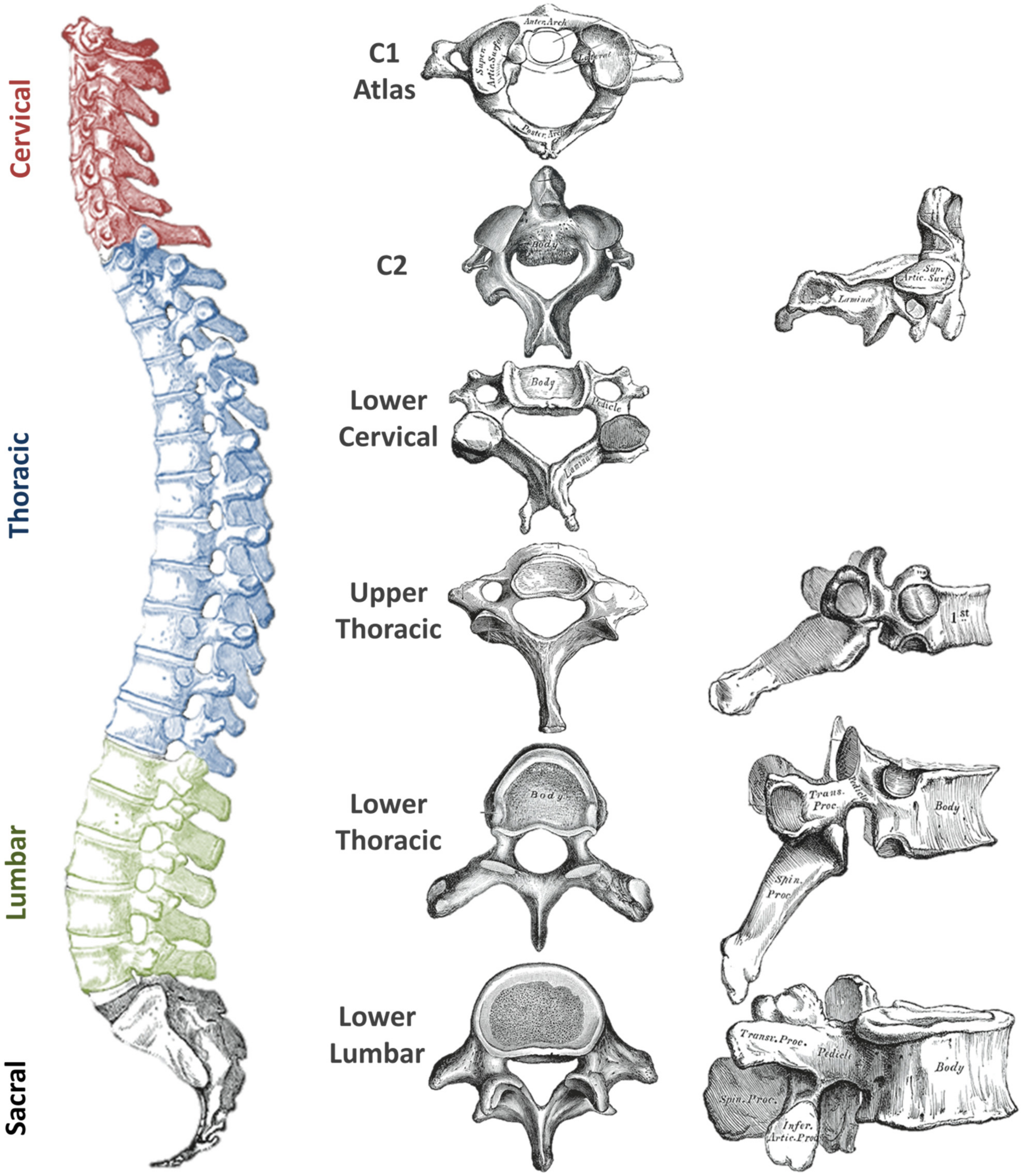


Figure 2.2 The basic anatomy of the spine. A sagittal view showing the kyphotic and lordotic curvatures and the four spinal regions: cervical, thoracic, lumbar and sacral (left). A transverse view of multiple individual vertebra showing the progression of vertebral change including a notable increase in vertebral body size from cranial to caudal (middle). Sagittal views of individual vertebrae, note the large change in the length of the spinous process when moving from cervical to lower thoracic (right). [Adapted from Gray[89]]

2.1.1. Anatomy of the Pedicle

The anatomy of the vertebral pedicle is of particular interest because it is the narrowest region where a pedicle screw passes and; therefore, it has been shown as a strong determinant of pedicle screw fixation[98]. The minor pedicle diameter (transverse pedicle width, Figure 2.3) is generally the most important consideration because it limits the diameter of the screw which can be used by the surgeon. The major diameter (sagittal pedicle width) has been shown to be a determinant of the pullout strength[248]. The pedicle is typically oval-shaped but has a complex three-dimensional structure which has been described as a teardrop[147,248]. The cortical shell of the pedicle wall is thicker medially than laterally[108,160,162]. There has been shown large variation of pedicle shape even within the same region or even the same pedicle[117]. Generally, the cortical shell thickness stays approximately constant; if there is a difference in diameter, it is the volume of the cancellous core which changes[160]. Since the pedicle has been shown to be filled more with cancellous than cortical bone[104,117,119,147,160,197], it is not surprising that pedicle screw purchase has been shown to not always engage the cortex but only the cancellous core[119,147]. However, the essential nature of cortical purchase has been stressed in order to obtain better fixation[245].

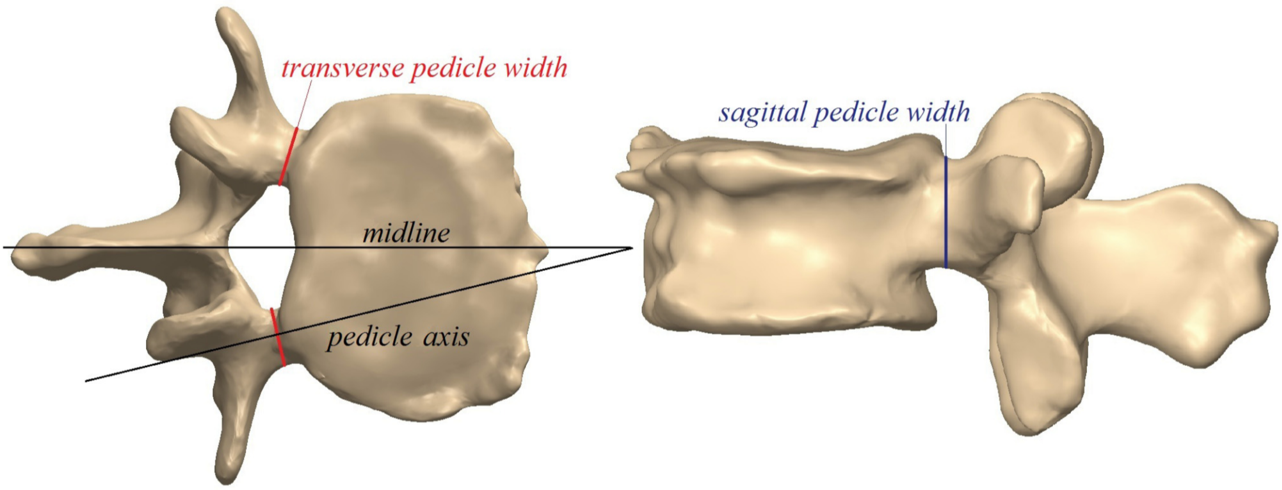


Figure 2.3 Pedicle dimensions of the narrowest vertebral area, the pedicle isthmus. The red line represents the pedicle isthmus width in the transversal plane (left) and the blue line represents the pedicle width in the sagittal plane (right). [Reproduced from Voigt[230]]

2.2. History and Benefits of Pedicle Screws

In 1907, Lambotte[127] reported the first use of a pedicle screw in combination with an external fixator. Internal fixation of the spine using screws was not described until 1944. At this time King[113] described the use of an oblique transfacet lumbrosacral fusion. Pedicle screws are known today as surgical screws which are anchored internally to vertebrae with a trajectory directly along the pedicle axis (Figure 2.3). This use of pedicle screws was first described by Roy-Camille in 1970[192]. Since this time, the use of the pedicle screws has expanded greatly and various angle-stable, rod-screw systems have been introduced; however, the basic concept has not changed.

Currently, pedicle screw fixation is the most commonly used intra-operative stabilization technique of the posterior spine[41]. Their frequent use is due to pedicle screws' comparatively high construct stiffness, enhanced stability and relative ease of implantation compared to other posterior fixation techniques[41,139,240,243]. The typical trajectory through the pedicle isthmus provides a solid base for screw insertion and allows manipulation of the spinal alignment and increases structure stability[39]. The stabilization created by pedicle screws can also promote fusion and fracture healing by decreasing motion of the affected spinal segment[196,239]. Since a pedicle screw can traverse the length of the vertebra it is the only spinal fixation technique which can stabilize all three spinal columns (Figure 2.4). Pedicle screw fixation has received wide-spread acceptance due to its proven effectiveness at achieving stability and alignment correction and is now considered the 'gold standard' of posterior spinal internal fixation[80].

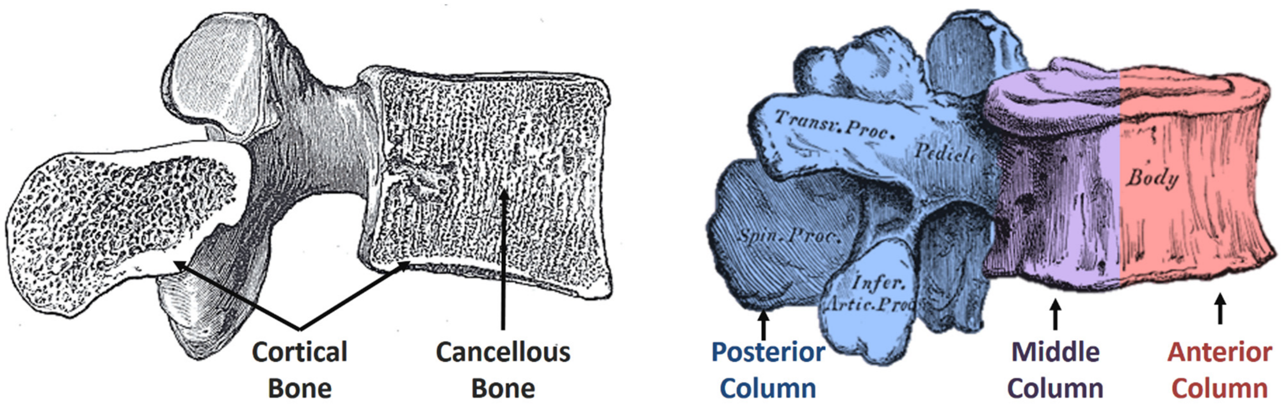


Figure 2.4 A mid-section view of a lumbar vertebra showing the cortical shell and cancellous core (left). A typical lower lumbar vertebra with the three vertebral columns highlighted (right). [Adapted from Gray[89]]

2.2.1. Prevalence, Indications and Controversy of Pedicle Screw Use

Since the early 1990's[80], pedicle screw fixation has been the method of choice to achieve stabilization or to correct severe spinal deformity in posterior surgical techniques on the spine. The high stability of pedicle screws can be attributed to their connection to longitudinal rods in various vertebral levels to form a stabilizing construct. These constructs promote stabilization of spinal segments after surgery for trauma (*i.e.* bone fracture), degenerative spondylolisthesis, degenerative disc disease, fusion surgery, lumbar fractures, deformity correction (*i.e.* scoliosis or tumor), or surgically repaired spinal pseudoarthroses.

Symptomatic damage is caused either by congenital spinal defects such as spondylolysis (dissolution of pars interarticularis), spondylolithesis (slipping of a vertebra relative to an adjacent vertebra), or ioatrenic damage after removal of a vertebral joint. Pedicle screws have enhanced the rate of fusion for spondylolisthesis patients and improved the ability to fix and maintain reduction of high grade slips[5,193,214]. Pedicle screw fixation is favored for the correction of resulting kyphotic or lordotic abnormalities which develop from symptomatic damage of the vertebral arch because it allows for the least amount of fixed vertebral levels while achieving a rigid fixation in order to lessen the risk of pseudoarthrosis[102,214].

For fractures which threaten the stability of the spine or which result in defective position or neural compression, stabilization with pedicle screws is indicated[32]. A well accepted concept for the stability of fractures is the concept of the three columns[60] (Figure 2.4). If more than one column is injured, the fracture is considered unstable and surgical intervention is indicated. Rigid fixation is achieved with a dorsal reposition and a ventral reconstruction which is resistant to compression (often accomplished with mechanical structures called vertebral body replacements and commonly referred to as cages).

Surgical treatment with pedicle screws is also indicated for tumors and infections. Pedicle screw fixation has enabled surgery on tumors which were previously inoperable. For example, pedicle screws allow for the removal of primary and metastatic tumors such as a multiple level vertebrectomy (removal of a vertebra) or a complete sacrectomy (removal of the sacrum)[65,87,215]. The goal of an operative treatment is a complete removal of the inflammatory tissue and tumor while accomplishing stabilization with dorsal fixation. Thus, the pedicle screw fixation does not treat the present disease, but simply stabilizes the spine.

Progressive scoliosis of 40-50° requires surgical intervention. The benefits of pedicle screws for scoliosis correction are the facilitated ability to manipulate spinal alignment by a lever arm and the post-operative maintenance of the corrected alignment compared to laminar hooks[13,54,93]. Further, the presence of intact anatomic landmarks such as the processes is not required. Pedicle screw instrumentation has also reduced the time to healing of a scoliosis fusion from six-to-twelve months in the 1960's to two-to-four months in the 1990's[93].

Pedicle screws are sometimes indicated for spinal fusion surgeries; however, in recent years their use with short fusions has become controversial. The rationale for spinal fusion stems from the fact that one of the most proven methods of reducing pain in diseased or deteriorated joints is to reduce the motion of that joint[163]. This is a common method that has been applied to the knee, hip, and ankle. More recently, this rationale has been applied to the spine[148] where boney fusion is sought via screws, cages, and plates in an attempt to create this pain relieving stabilization. This rationale has led to the use of short fusions for spondylosis (spinal degenerative changes), spinal stenosis without deformity (narrowing of the spinal canal), and discogenic chronic back pain. However, both the need for the short fusion procedures and the use of instrumentation with these procedures, have been questioned recently due to their high costs and conflicting reports as to whether or not they significantly improve patient outcomes[11,62,64,109]. However, some studies show that instrumentation does help to improve patient outcomes[73,83,243,244]. Yuan et al.[243] found that pedicle screw instrumentation generates significantly higher fusion rates and significantly better clinical outcomes (less pain, better function, greater neurological recovery).

Studies of the efficacy of short fusions have shown that fusion is generally more beneficial than non-fusion in terms of pain reduction and QALYs (Quality-Adjusted Life Year) but fusion is also associated with a 50% increase in cost and a higher complication rate[44,123]. There are inconsistent findings regarding the advantages of instrumented fusion (fusion with pedicle screws) over non-instrumented fusion for patient pain relief or QALYs[18,73,96,110,228,243,244]; however, radiographic fusion rates are increased at two years[83,116]. Radiographic fusion, the observation of bone connecting the adjacent vertebrae in radiographs, has not been directly linked with patient outcomes[76,96]. Although, it has been shown that after five years the reoperation rate for patients with radiographic fusion was lower than non-fused patients[96,116]. Evidence at two years post-surgery suggests posterior fixation with fusion may not be a cost-effective use of healthcare resources. Sensitivity analyses, however, show that cost-effectiveness could increase if the proportion of patients requiring subsequent surgery in the non-instrumented fusion continues to increase[179]. In summary, for spinal fusion surgery the radiographic fusion rate has been shown to increase with use of pedicle screws[83,116] and patients with radiographic fusion have been shown to have a lower reoperation rate[96,116]; therefore, the cost-effectiveness of the surgery may improve after longer followup[179].

For scoliosis, spinal fractures, osteotomies, and tumor removal the use of pedicle screws is not controversial. In contrast, questions have arisen for the rapidly increasing use of short fusions for spondylosis (spinal degenerative changes), spinal stenosis without deformity and discogenic chronic back pain[64,109]. Approximately 75% of spinal fusions performed are for these controversial indications[64]. Even as the controversy continues, the spinal implant market continues to boom and the indications and the applications of pedicle screw constructs continue to grow[11,112].

2.3. The Social and Economic Impact of Back Pain

Back pain is the most widespread illness in many industrialized nations including Germany and the USA[97]. Back pain is reported so frequently to primary care physicians that only the common cold accounts for more consultations[109]. It has been estimated that the annual prevalence ranges between 15-45% and the lifetime prevalence exceeds 80%[4,236] with a significant percentage of these cases being candidates for surgical intervention[4]. Chronic low-back pain estimations show that one-in-five Europeans are suffering from back pain and the prevalence is rising with numbers doubling since 1950[203]. The trend of an increasing prevalence is accelerating in recent years with the prevalence of chronic, impairing low back pain rising 162% in all adult age groups from 1992 to 2006[77].

Spinal surgeries are more frequently being used in the treatment of back pain which is contributing to a rapid increase in the numbers of spinal surgeries (Figure 2.5)[61,64,114,171]. Between 1998 and 2008 the annual number of the performed spinal fusions in the U.S. has increased by 137% to over 413,000 a year[171]. Furthermore, a 20-fold increase of fusions for spinal stenosis was seen from 1979-1990[224]. This continuous growth of stabilizing surgical treatments for the spine is also accompanied by an increase of indications and applications of pedicle screws[173].

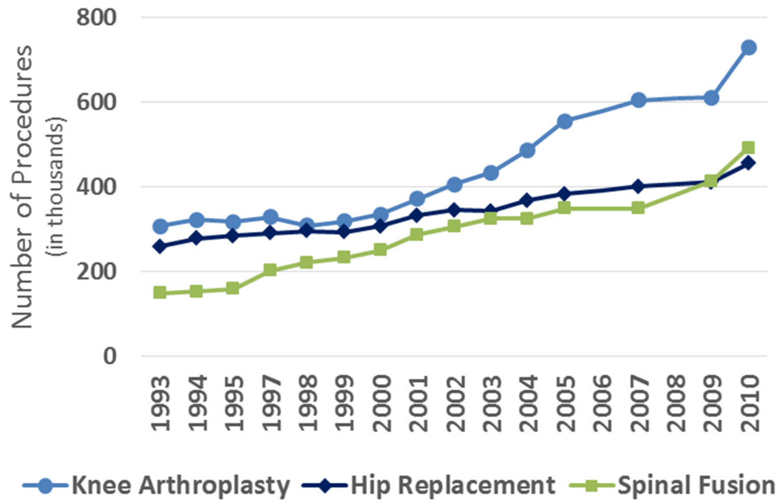


Figure 2.5 The number of spinal fusion surgeries compared to knee and hip arthroplasty from 1993 to 2010[14,146].

One of the most detrimental and costly aspects of back pain is that it often strikes otherwise healthy individuals during productive work years. It is the most common reason for activity limitation for people younger than 45 years and chronic back pain is the largest cause for early retirement in industrialized societies[4]. Due to the associated enormous direct and especially indirect costs, back pain has been shown to be more expensive than heart attacks, cancer, and AIDS combined[75]. The high costs and increasing, high prevalence leads it to be considered a modern epidemic[75]. Importantly, back pain has also been associated with a reduced quality of life and has been linked to depression and social isolation[231].

The economic cost of back pain is extremely high with US estimates in 2008 alone being US $19.6-$118.8 billion for direct costs and US $84-$624 billion for indirect costs[56]. The number and cost of selected frequent medical procedures are shown in Table 2.1. In 2007, the implantation of cardiac pacemakers were the most expensive procedure followed closely by spinal fusion at US $74,954 per procedure[14]. From 1997-2010 the rate of increase in the number of spinal fusions (143%), was higher than both knee arthroplasties (122%) and hip replacements (57%, Figure 2.5)[167].

As health care costs continue to quickly rise, more research is aimed at evaluating the cost-effectiveness of individual treatments; an accepted measure to attempt to quantify this is the quality-adjusted life years (QALY). This measure takes into account quantity and quality of life after the treatment compared to before treatment. The application of QALYs in deciding which medical care to provide is controversial in that it evokes the question: how much is a year of life worth? Past figures in the early 1990's for this were set at approximately US $50,000 and in 2001 the World Health Organization (WHO) suggested the figure should be US $108,609[234]. Generally speaking, health care providers in developed societies cover procedures which fall within this range of costs. Both primary knee and hip arthroplasty fall well within these ranges with maximum estimates given at €13,995 and €6,710 per QALY respectively[172]. However, a revision hip replacement increases the economic burden substantially to €52,274 which is similar to the cost of non-instrumented fusion (US $56,500, Table 2.2)[123]. Kuntz et al.[123] showed that the cost for an instrumented fusion per QALY rose to a staggering US $3,112,800 due to very small improvements in patient outcome scores and higher surgical costs. This figure adds figurative 'fuel to the fire' for the passionate debate about the overuse of instrumentation in spinal surgery.

Table 2.1 The number and cost of selected procedures which were performed in the USA for 2007[14].

Number & Cost for Procedures Performed in 2007 (USA)			
Procedure	**Procedures Performed**	**Procedure Mean Cost** (US $)	**Average Total Cost** (US $)
Cardiac Pacemaker	329,000	$75,902	$24,971,758,000
Spinal Fusion	350,000	$74,954	$26,233,900,000
Coronary Angioplasty	576,000	$51,812	$29,843,712,000
Hip Replacement	402,000	$48,035	$19,310,070,000
Knee Arthroplasty	605,000	$42,474	$25,696,770,000
Hemodialysis	343,000	$28,277	$9,699,011,000
Prophylactic Vaccinations	1,025,000	$5,156	$5,284,900,000

The number of surgeries has continued to increase despite the demonstrated high ambiguity of back pain localization[2,23,234], high cost, and only a moderate success rate for spinal surgery. An example of a typical moderate success rate is a 30% improvement in pain and functioning with only ~60% of patients considering themselves "better" or "much better"[79]. Taken together this combination can be considered alarming: treatment for non-specific, chronic low back pain with pedicle screw assisted fusion has only shown moderate effectiveness and is increasingly being applied to cover a range of non-specific symptoms with a high cost to society.

Table 2.2 Cost per QALY for selected procedures (in GB £ and US $)[46,106,123,130,172,179].

Cost per Quality-Adjusted Life Year (QALY)		
Procedure	**Primary**	**Revision**
Fusion (non-instrumented)	$56,500[1] or £48,588[2]	
Fusion (instrumented)	$3,112,800[1†]	
Hip Replacement	€6,710[3] or £1,372[4]	€52274
Knee Arthroplasty	€13,995[3] or £2,101[4]	
Dialysis	$129,090[5‡]	
Left-ventricular assist device	$36,255-$86,000[6]	

†=This figure reduces to $82,400 aftter adjustment for symptom relief, ‡= This was the average value, the range was $61,294-$488,360

1:Kuntz 2000, 2:Rivero-Arias 2005, 3:Räsänen 2007, 4:Jenkins 2013, 5:Lee 2009, 6:Hutchinson 2008

2.4. Clinical Problems Associated with Pedicle Screws

Although there has been improvement in recent years, there is still a very high failure rate of spinal implants; especially when compared to the successful hip and knee implants. In 1991, McAfee et al.[143] estimated that survivorship of spinal instrumentation without complications to be 80%; whereas, for hip implants it was estimated at 90%. For pedicle screws in particular, in 1994 Ohlin et al.[155] found an 85% survivorship rate in the first year and a 40% risk of loosening or implant failure at six months (determined radiographically). Both of these survivorship studies were performed fairly early stages of widespread use of pedicle screws (the early 1990's) and since then there has been a marked improvement in implant design and materials.

The moderate success of spinal treatments and surgical implants is likely largely influenced by the high ambiguity of back pain. The ambiguity of back pain stems from three factors: it is not a disease but a constellation of symptoms which are subjective sensations[23,234], the causes are extremely numerous because any structure of the spine that receives an innervation could be the source[2] and no diagnostic tool has been able to consistently identify the source of pain[3]. Since back pain is a symptom and not a diagnosis, indications for surgery are thus not clearly defined[3].

Adjacent segment degeneration is another common problem after rigid fixation of the spine; particularly, after multiple segments have been fused. There are two theories about the cause of adjacent segment degeneration; natural progression of the disease or that it is due to the increased range of motion of the end segment of the fixation construct. The occurrence of adjacent level disease and the comparatively low rates of acceptable patient outcomes have meant that there has been an increase in the use of pedicle screw systems which incorporate the philosophy of so-called 'dynamic' stabilization. Dynamic pedicle screw systems are designed to allow a certain range of movement, which is opposite of traditional systems whose aim is to rigidly fix the spine in place. The rationale of these flexible systems is to restrict the range of motion to a normal range. This restriction, may, in turn, prevent abnormal loading which is believed to be the source of pain, while still allowing some motion so as not to overload the adjacent segment[149]. The concept of allowing segmental motion does have a downside, it places more demand on the bone-screw interface of these dynamic pedicle screw systems.

Pedicle screw failures can generally be classified into three categories: (1) surgical complications (2) implant failures and (3) bone/implant interface problems. The reported incidences found in the literature for each these categories are given in Table 2.3 & Table 2.4.

Rates of surgical complications associated with pedicle screw use (pedicle fracture, neurologic-vascular-pain complications, and infection) have been shown to be statistically similar to those of patients who undergo spinal surgery with no pedicle screw fixation[243] (Table 2.3). The surgical complication specific to pedicle screws malposition, has seen an incidence reported between 0-10% with one study reporting a high rate of 25% in scoliosis patients[80] (Table 2.3). The results suggesting that malplacment is shown to decrease with an increase in surgeries completed suggests that there is a learning curve for surgeons for pedicle screw fixation[82]. Malplacement does not typically cause neurological damage or need for a revision surgery, intervention is only necessary in the most severe cases of nerve damage and/or when pain is reported[132,229].

Table 2.3 Surgical failure modes of pedicle screws and their reported incidence in the literature[69,80,132,155,168,240,243].

	Incidence of Surgery Related Pedicle Screw Failure Modes				
	Failure Mode	**Incidence**	**Cases**	**Year**	**Additional comments/References**
Surgical Complications	**Pedicle Fracture**	**0.7%***	2177	1994	No significant difference in rate (Yuan, Garfin et al. 1994)
		2.3%	617	1993	(Esses, Sachs et al. 1993)
	Neurologic/ Vascular/ Pain Complications	**6.5%***	2177	1994	3.4% of these patients underwent re-operation (Yuan, Garfin et al. 1994)
		2.8%	5756	1994	1.1% Dural tears and 1.7% neurologic deficits (Yahiro 1994)
		3.1%	160	1995	Dural tear in two, iatrogenic root injury in two, one with 'foot drop' (Lee 1995)
		3.7%	163	1994	Dural leak in three and pulmonary embolism in three (Ohlin, Karlsson et al. 1994)
		8.4%	617	1993	2.4% neuropraxia-transient, 2.3% permanent root injury, 1.9% had CSF leak, 1.1% pain, 0.5% late root injury, 0.2% vessel injury (Esses, Sachs et al. 1993)
		1%	-	1998	A review article of pedicle screw fixation (Gaines 2000)
		2%	-	1998	
		11%	-	1990	
	Infection	**2.6%***	160	1995	1.8% of these underwent re-operation (Lee 1995)
		0.6%	163	1994	(Ohlin, Karlsson et al. 1994)
		4.2%	617	1993	(Esses, Sachs et al. 1993)
		1.1%	470	1996	(Gaines 2000)
		1.2%	-	1996	
		2.3%	85	1996	
		4.2%	96	1993	
	Malposition	**3.1%**	160	1995	(Lee 1995)
		2.5%	5756	1994	(Yahiro 1994)
		2.5%	2177	1994	(Yuan, Garfin et al. 1994)
		8.8%	102	1997	8 of the 9 patients underwent re-operation for correction of misplaced screws (Pihlajamaki, Myllynen et al. 1997)
		10.4%	163	1994	(Ohlin, Karlsson et al. 1994)
		7.3%	617	1993	5.2% was unrecognized screw misplacement (the most occuring individual complication of the study) and 2.1% was prominent hardware (Esses, Sachs et al. 1993)
		0%	-	1997	The high rate (25%) was for a study involving patients with scoliosis (Gaines 2000)
		2%	-	1998	
		25%§	-	1997	

* There was no significant difference ($P < 0.05$) in any of the surgical complications of patients with pedicle screws (N=2177) compared to control group of patients who received no instrumentation only fusion (N=507).

§ High variation in rate is also attributed to a pronounced learning curve for surgeon placement of pedicle screws (Gaines 2000)

Table 2.4 Incidence of the failure modes of pedicle screws which could be influenced by implant design[69,80,115,132,143,155,156,168,194,202,217,229,237,240,243].

Incidence of Implant Related Pedicle Screw Failure Modes					
	Failure Mode	**Incidence**	**Cases**	**Year**	**Additional comments/References**
Implant Failures	Hardware Malfunctions (Broken or bent screws/rods)	**3.1%**	160	1995	screw breakage in three cases and loosening of clamp in two (Lee 1995)
		2.6%	2177	1994	(Yuan, Garfin et al. 1994)
		7.3%	5756	1994	7.1% broken screws and 0.2% broken rods (Yahiro 1994)
		10%	163	1994	Nine screw fractures (all 5 mm diameter), 3 Rod fractures, and 3 disconnection of the rod and screw (Ohlin, Karlsson et al. 1994)
		3.7%	671	1993	2.9% screw breakage and 0.8% coupling failure; screw breakage was reported at a rate of 0.6-25% for each individual surgeon (Esses, Sachs et al. 1993)
		4.2%	526	1991	(McAfee, Weiland et al. 1991)
		2.6%	-	1996	The very high rates (60% & 36%) were from studies used on patients with with highly comminuted spinal fractures and short segment instrumentation was used. (Gaines 2000)
		4.9%	-	1996	
		9%	-	1994	
		36%	-	1990	
		60%	-	1993	
Bone/Implant Interface Problems	Loosening	**1.3%**	671	1993	0.81% loosening and 0.5% cut out; loosening was reported at a rate of 0-11% for each individual surgeon (Esses, Sachs et al. 1993)
		23%	163	1994	(Ohlin, Karlsson et al. 1994)
		2.8%	2177	1994	(Yuan, Garfin et al. 1994)
		18%	102	1997	(Pihlajamaki, Myllynen et al. 1997)
		6.8%	59	2000	4% rate per screw (1 of 250 screws) (Okuyama, Abe et al. 2000)
		11%	73	2002	Used dynamic stabilization; 3.6% rate per screw (Stoll, Dubois et al. 2002)
		21% (per screw)	21	2004	A high 51% rate of loosening per screw and an 88% rate per patient (N=8) was seen for uncoated stainless steel screws (N=32) and only a 2% rate per screw was seen for HA coated screws (N=52) (Sanden, Olerud et al. 2004)
		17%	26	2006	Used dynamic stablilzation (Schnake, Schaeren et al. 2006)
		41%	190	2008	Number of patients with loosening decreased from 78 to 28 (15%) over time as bone union increased (Tokuhashi, Matsuzaki et al. 2008)
		20%	71	2010	Used dynamic stabilization; 4.6% rate per screw (Ko, Tsai et al. 2010)
		20%	126	2011	Used dynamic stabilization, 4.7% rate per screw (Wu, Huang et al. 2011)
	Pullout	**1.3%**	160	1995	Only clinical review that shows the complication of 'screw pullout' (Lee 1995)
		1.0%	102	1997	Was attributed to malposition of the screw which then lead to screw loosening and backout (Pihlajamaki, Myllynen et al. 1997)
		0.2%	617	1993	1 case of 'screw back out' was reported (Esses, Sachs et al. 1993)

The failure criteria that can be more easily influenced by implant design are implant failure (broken or bent screws/rods), loosening, and pullout (Table 2.4). Pullout has been nearly completely absent as a clinically relevant failure mechanism; only four reported cases with just one case that required revision[69,132]. Also, catastrophic implant failures (broken or bent screws/rods) are on the decrease due to better materials and new implant designs which increase support in vital load bearing locations[156]. Hardware failure is less prevalent than screw loosening (generally an incidence of less than 10%) with most reported cases taking place early in the life cycle of pedicle screws (Table 2.4). On the other hand, screw loosening is seeing an increase in reported prevalence. Since the incidence of loosening is on the rise, pullout is extremely rare and broken hardware is on the decline; screw loosening is becoming more of a focus especially in osteoporotic patients and in dynamic stabilization[115,156,194,196,229,239].

2.5. Pedicle Screw Loosening: The Primary Failure Mode

Pedicle screw loosening is a break-down of the mechanical integrity of the bone-screw interface causing a loss of stability of the construct. Overall rates of loosening ranged from 1.3% to 41%, with the reported rates increasing in recent years (Table 2.4). This increase could be attributed to multiple factors including; broader indications for pedicle screw use, the implementation of the idea of dynamic stabilization, variation in study design, variation in definition of loosening, high variability in follow-up time, and better imaging and classification criteria which cause loosening to be reported more frequently. One likely explanation for the variation in loosening incidence could be the high variance between studies in the time period between surgery and loosening evaluation. Time may influence the incidence of loosening because the primary indication for loosening, a radiographic 'halo', was shown to decrease by 67% from initial observance to final follow-up for patients who also underwent fusion[229].

2.5.1. Current Appearance of Loosening

It has been shown that the threads of loose screws are surrounded by connective tissue rather than bone[199] (Figure 2.6B). Schatzker et al.[199] showed that whenever screw motion occurred, the histological response was of connective tissue proliferation (chondrocytes and lining cells) and bone resorption (osteoblastic activity increase at the interface). However, when no motion was present, normal bone would infiltrate between the screw threads within 6 weeks and thus would increase the fixation of the screw (Figure 2.6A). Cellular reaction at the bone screw interface has been shown to be governed by the mechanical forces which are present. If compressive forces are present, then it is assumed the bone will retain its integrity[200]. These findings show that it is vital that screw motion at the interface be halted and that mechanically strong attachment of the threads to the bone is obtained.

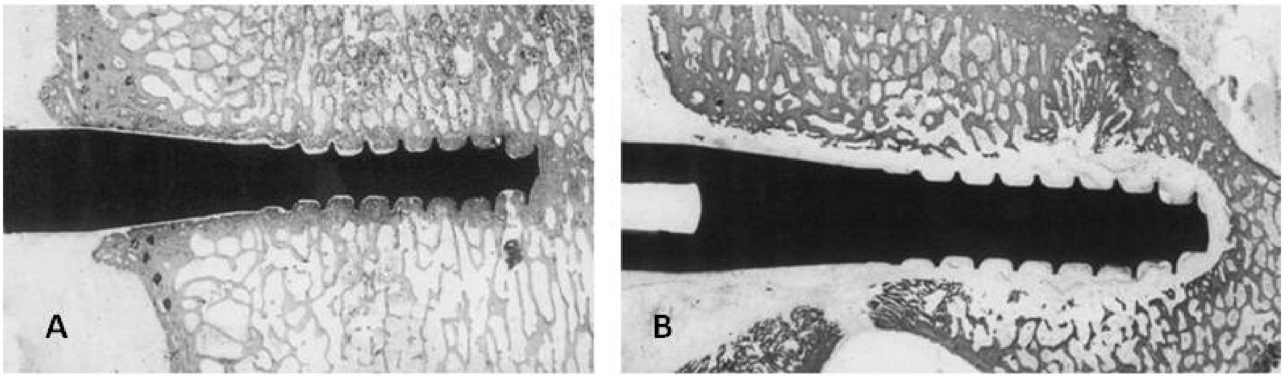


Figure 2.6 Histological evaluations of the bone screw interface. (A) Showing a screw that did not exhibit a halo- bone fills the gaps between the screw threads (B) Showing a pedicle screw which exhibited radiographic clear zone around the tip of the screw- white zone around the tip is connective tissue and not bone. [Altered from Sanden et al.[194]]

How screw loosening physically appears, however, is still debatable. The fibrous tissue surrounding the bone is less visible in radiographs and a discernible radiolucent halo can surround the screw head[199]. Therefore, clinically relevant loosening is classified as a 1 mm 'clear'[229] or 'radiolucent'[194,196,199] area around the screw head as observed on a plain radiograph (Figure 2.7). However, the reason for the distance of 1 mm, the shape (conical or cylindrical) and the other parameters such as length of the clear area around the head are not specified. Sanden et al.[194] showed that a radiolucent zone had a range of 1-4 mm surrounding the nine screws which loosened in a biomechanical sheep model. Though the presence of this 'halo' is established, it is only an indicator of screw loosening; because each loose screw does not necessarily have a 'halo'[194].

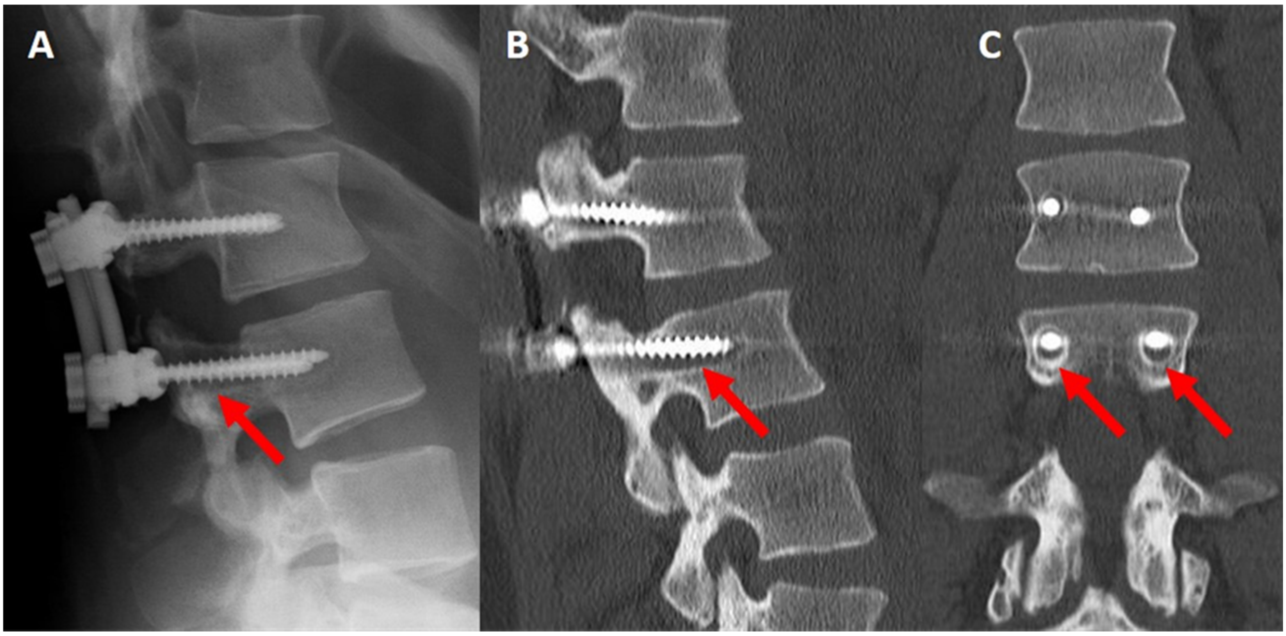


Figure 2.7 An example of pedicle screw loosening. (A) From a radiograph, (B) a CT slice in the sagittal plane and (C) a CT slice in the coronal plane. The halo can be seen in the dark area surrounding the screws (denoted by red arrows) as well as a discernible double halo shown by the white rim surrounding the dark halo. [Images acquired from Dr. V. Bullman, University Hospital Münster]

If the radiograph is unclear, than determination of loosening can be confirmed by the appearance of a 'double halo' or, alternatively, by consulting CT scans[115]. A double halo is considered the clinical confirmation of screw loosening; it appears as a radiopaque rim which outlines the area around the screw which has become loose.

The reports on visualizing screw loosening have focused on the use of plain radiographic evidence and have shown a relatively good ability to detect both of the principal signs of screw loosening: the initial halo and later the double halo[57,115,194,229]. Specificity for determining loosening was found to be 0.92[229], 1.00[194] and 0.80 for the initial halo and 0.94 for the double halo in the study of Dakhil-Jerew et al.[57]. Sensitivity was shown to be 0.93 and 0.64[194,229]. The double halo was also shown to have significantly higher specificity for diagnosing screw loosening and was then considered a good method for confirming the loose screw diagnosis in progressive follow-ups[57,115]. AP radiographs are better to visualize loosening than lateral or oblique views and often one AP radiograph is not sufficient to visualize all the screws at one time, more projections are needed to increase accuracy[57,115]. These high specificity and sensitivity values show that plain X-rays are a reliable method to observe the potential occurrence of loosening; if radiographs fail, CT scans may be consulted.

2.5.2. Clinical Relevance of Loosening

Repeated occurrence of radiolucent zones around the screw head for a period over 2 years has been associated with a greater risk of pseudarthrosis[229]. This non-union of the fusion is often a precursor to revision surgery. In a clinical study, 14 of the 15 patients which exhibited pseudarthrosis had a consistent presence of a 'halo' surrounding the screw; the remaining case had two broken screws, therefore, all 15 cases of bone non-union exhibited a breakdown of the posterior stability. For this reason, radiographic evaluation of screw loosening is recommended in order to classify bone union[229]. Although loosening was related to pesudarthrosis, patients with loose screws did not have statistically significant differences in the Oswestry Disability Index, Visual Analog Scale or Japaneese Orthopaedic Association Score[229] compared to those patients with no loose screws. The two scales used are clinically accepted standard ways to measure patient outcomes.

Loosening is clinically important as it can lead to a loss of correction, non-union, sagittal collapse of the construct, and kyphosis which can lead to an increased re-operation rate due to a need for device removal or salvage[39,156]. Loose screws can also lead to movement of the construct which may trigger painful paraspinal muscle spasms[57]. In a large cohort study, Yuan et al.[243] showed that 6.3% of patients with pedicle screws had the implants removed because of pain, irritation or prominence and another 0.6% for implant failure. For these reasons, loosening is a safety concern for the patient. Since there is such a spread in incidence (Table 2.4) and disagreement about the classification of loosening, the true incidence of screw loosening and its broader clinical implications remain somewhat unclear[115].

2.5.3. Factors and Timing of Screw Loosening in Clinics

The position of the screws in relation to their position within the screw and rod construct as well as the total length of the construct have both been shown to influence rates of loosening. Screw loosening has been shown to occur more prevalently at the cranial and caudal ends of the pedicle screw construct;

and no cases have been shown where loosening only occurred in the middle segments[115,229]. It is hypothesized that the screws on the ends of the construct undertake larger loads than the screws in the middle sections of the construct[115]. Even though the middle screws of a construct may not become loose, multi-level constructs are shown to have a significantly higher chance to include a loose screw: 19.2% of single level constructs contained a loose screw and there was a 50% or higher incidence for two or more levels (p<0.01)[229].

Pedicle screw breakage has also been reported on the cranial and caudal construct ends with fractures occurring at the junction where the screw tapper meets the screw threads[39]. Yerby et al.[241] put strain gauges in the pedicle screw and found that the bending moment increases non-linearly from the tip of the screw to the screw tapper (where it exits the pedicle). This study was used to confirm why so many early pedicle screws broke or bent at this location.

The osteoporotic spine offers an even greater challenge with several studies showing that the screws within the spine have significantly lower strength and undergo more frequent movement[16,47,92,129,139,156]. A significant increase in loosening has been shown to be related to a decrease in patient bone mineral density (BMD): screw loosening occurred in 41% of patients with normal BMD, 60% of patients with osteopenia and 78.6% of patients with osteoporosis[229]. The incidence of screw loosening was also shown to increase with an increasing age of the patient[155,237]. This is not surprising as osteoporosis is shown to have an increased incidence with an increasing age of the patient.

Tokuhashi et al.[229] showed that approximately two thirds of radiolucent zones disappeared after two years of progressive analysis of the bone-screw interface. This study was completed on patients (n=190) who also received fusion of the anterior spinal column. For every patient who exhibited the combination of (1) an initial exhibition of one or more loose screws (a halo) and (2) radiographic evidence of boney fusion: the initial halo eventually disappeared. This disappearance of the halo concords well with the study from Schatzker et al.[199], who showed that if motion at the screw interface is stopped than cancellous bone can grow into the screw threads. This illustrates that anterior stability could be a major factor in the prevalence of loose screws.

Dynamic pedicle screw systems are recently increasing in numbers and their growing prevalence may also be a contributing factor to the rise in incidence of pedicle screw loosening[115]. Since dynamic pedicle screw systems inherently allow more motion, and motion reduces bone formation around the screw head, they may be associated with larger rates of screw loosening (as reflected in the reported incidences: Table 2.4). The increase in incidence could also be due to the fact that dynamic systems often do not gain the added anterior stability from cages or fusion (which have been shown by Tokuhashi et al.[229] to enable the correction of initial screw loosening).

The literature is fairly consistent in showing that screw loosening is exhibited soon after surgery: the initial halo typically appears within the first six months[115,198,217]. Confirmation of screw loosening via observation of the double halo is done over a wider time interval: 0-16 months after the first sign of loosening[115]. Schaeren et al.[198] showed that no new loosening cases developed between 2-4 years after surgery.

2.5.4. Pedicle Screw Loosening Failure Mechanisms

Although there is a large cumulative knowledge database and many biomechanical studies on record; the questions of why and how pedicle screws fail still persists. The primary mechanisms and modes of loosening are still pondered and various opinions have been stated in the literature. Direct quotes from authors are provided in Appendix A. Micromotion, especially driven by cyclic toggle loading, seems to be the most commonly believed primary cause of pedicle screw loosening in the literature (Appendix A). Micromotion is thought to trigger bone resorption and fibrous tissue production[155,199] and cyclic loading is thought to induce bone destruction through fracture[129] compression or viscoelastic creep[42]. Only one group suggests that pullout could be a mechanism; however, they focus more on micromotion inducing bone resorption as the more prevalent mode of loosening[199]. The ability to understand the mechanisms by which current treatments fail is clinically imperative in order to select the proper screw during surgery and to optimize the development of new implant designs which mitigate specific failure modes.

2.6. Assessing Pedicle Screw Fixation

In the clinical setting, the assessment of fixation is primarily accomplished via visual inspection of radiographic images. Visual assessment is utilized because it is non-invasive and is often readily accessible in the clinical setting. In the biomechanical setting, pre-clinical testing is often performed on surgical implants in order to attempt to ensure they meet or exceed certain clinical standards. This is done in order to attempt to minimize catastrophic failure of implants. This procedure, however, does not always occur- some implants make it to market with no prior testing, and sometimes implants that look spectacular during mechanical testing fail *in vivo*. It is important that when designing and performing pre-clinical tests that selection of output parameters are clinically justifiable. Identifying areas to reduce loosening at the bone-screw interface is the primary aim of the present work. Predicting clinical loosening of implant in the biomechanical setting is usually accomplished by investigating the fixation strength of the screw. This is because it is believed that if the fixation strength can be increased, less implant loosening may occur *in vivo*.

2.6.1. Clinical Assessment of Mechanical Fixation

Quantitative mechanical definitions of screw loosening in the clinics are both sparse and variable in the literature. To the author's knowledge, Sanden et al.[194] is the only report that attempts to mechanically investigate a quantitative definition of pedicle screw loosening in the clinical setting. They showed that these radiolucent zones correlated with a significant decrease in the mechanical fixation both clinically (removal torque reduction, $p<0.001$) and in an *ex vivo* setting (pullout force reduction, $p<0.001$). From their clinical data ($n=84$ screws; 79 with data available) they extracted a mechanical definition of a loose screw in the clinic: an extraction torque less than or equal to 0.4 Nm. Since there is no standard definition of what mechanically quantifies screw loosening and a diagnosis must be made prior to an operation, the detection and classification of a loose screw in the clinical setting usually depends on the ability to visualize the gap at the bone-screw interface by plain radiographs[57,115,194,229] (the halo as described in Section 2.5.1).

2.6.2. *In vivo* Loading on Pedicle Screws

In order to assess screw loosening and the influence of various implant designs in a controlled biomechanical setting, it is important to have quantitative knowledge as to the level of forces and moments which are occurring *in vivo* on the implants. With this information, experimental designs can be created which mimic the realistic, clinically relevant situation.

Rohlmann et al.'s research group[180–188] have completed many series of *in vivo* investigations into the forces seen inside human joints by using telemeterized implants. Many of these investigations have focused on an internal spinal fixator. The studies included 10 patients; all of whom received bone grafts and the implant bridged one vertebra and two discs. The group was able to determine several trends: (1) forces were mainly compressive (0-200 N for standing, 50-250 N for walking, Table 2.5), (2) flexion bending moments typically occurred (0.5-6.0 Nm for standing, 0.5-5.0 Nm for walking), (3) loads varied depending on the anterior procedure the patient received, (4) loads generally increased immediately after the anterior operation, and (5) implant loads did not often decrease after bony fusion had occurred.

Table 2.5 Average maximum *in vivo* forces and moments seen on an internal spinal fixator for a bridging, 3-segment, screw-rod construct while walking several steps broken down by patient (extracted from Orthoload.com[17], August 11, 2013).

Patient	N	F_x (N)	F_y (N)	F_z (N)	M_x (Nm)	M_y (Nm)	M_z (Nm)	F_{total} (N)	M_{total} (Nm)
NFL	2	-32	-26	-291	-1.12	-1.50	0.27	293	1.86
JTL	2	13	23	77	-6.18	-0.82	0.01	78	6.24
BBL	2	19	15	-76	-5.03	-0.63	-0.47	80	5.08
JWL	1	2	-7	-62	-2.21	-0.34	0.15	62	2.24
AGL	4	-43	53	172	-5.56	-2.64	0.42	179	6.14
Average Max Magnitude		22	25	136	4.02	1.18	0.26	138	4.31

Patient HBL was excluded due to a large limp.

The *in vivo* data (Table 2.5) shows that the typical loading which a bridging, 3-segment, screw-rod construct would undergo during normal daily activity is around 0-250 N axial loading (normally compressive) and a 0-6 Nm bending moment (usually flexion). Axial forces on the implant were largely influenced by the spinal level (*i.e.* L3 or T12); whereas, the bending moments were affected by the stiffness of the treated segment- which was, in turn, determined by surgical procedure performed[188]. Despite this data being important biomechanically; it does, however, have some inherent limitations: various anterior techniques and spinal levels were used, and data was collected only on the rod; therefore, force information on the screw has to be determined after a shift of the reference coordinate system.

Precise motion analysis has also been performed by Olsson et al.[158] who found similar results to Rohlmann et al.[188]. Olsson et al.[158] found that implants sustained forces and motion even after boney fusion was obtained. Walking had slightly greater maximum loads than standing[181], standing forces were similar to sitting[180,185], forces while standing were larger than when lying[180], and upper body flexion and extension had little effect on implant loads[183]. The *in vivo* forces and moments determined by these groups can now be used in controlled laboratory settings to assess screw loosening and the influence of various implant designs.

2.6.3. Biomechanical Assessment of Fixation

Current pre-clinical methods to test fixation of pedicle screws generally fall under (1) pullout and (2) cyclic loading tests (often referred to as 'toggle' or fatigue tests). Both of these methods give relevant information about the mechanical stability of the screw; however, neither test represents the true clinical situation and their ability to determine a failure mechanism *in vivo* is questionable. There is considerable skepticism as to whether these methods, particularly pullout, can obtain the desired clinically relevant data. The following sections give the current relevance, benefits, drawbacks, and utilization of both toggle and pullout testing.

Pullout Testing of Pedicle Screw Fixation

Pullout testing comprises of a few basic steps. First the screw is implanted into single vertebra or bone substitute material. The vertebra is then mounted into a servo-hydraulic testing machine with the screw head being attached to a load cell. Displacement controlled loading is then placed on the screw head in a direction along the long axis of the screw until the screw is completely pulled out of the bone or, more often, after a peak force is reached (known as the pullout strength or pullout force).

This method has been used in many biomechanical studies[1,12,16,26,28,33,55,58,59,92,98,105,107,125,134,137,166,197,235]. The tests are all very similar but certain aspects are methodically changed to test for differences; these experimental variations include:

1. Type of bone (cadaveric, synthetic, animal models, or osteoporotic)
2. Loading rate (from 1 mm/min to 5 mm/sec)
3. Angle of screw insertion (in both the transverse and sagittal planes)
4. Depth of screw insertion (from just past the pedicle to bi-cortical)
5. Method of screw insertion (awl vs. tap)
6. Screw design (diameter, length, screw pitch, thread type, core type, and thread depth)
7. Augmentation (PMMA and bioactive cement types; vertebroplasty, traditional, cannulated or fenestrated augmentation methods)

Pullout testing is extremely widespread and accepted. This is highlighted and promoted by the fact that there is an ASTM standard created for it (ASTM F1691-96[7] and updated to a section within ASTM F543-13[8]). The standard has been given credit for being a useful method of comparing various designs and gaining information on the initial purchase of screws[2828,58]. However, it is criticized as having little to do with *in vivo* performance and that the outcomes of the test should not be used as a predictor of clinical performance[58]. Since pullout testing is readily found in the literature, easily comparable, and easy to implement it is straightforward to understand why many people utilize this method to gain insight into new screw designs. Conversely, little effort has gone into investigating other more physiologic testing techniques, including toggle testing.

Despite pullout continuing to be the standard test method of characterizing spine screw designs for their fixation strength, the clinical relevance of pullout testing has often been questioned. In 2003, Dawson et al.[58] definitively states that "clearly, the important failure mode is loosening;" and he adamantly rejects pullout as a clinically relevant failure mechanism of loosening by citing the lack of clinical evidence to suggest there is a systematic relationship between these phenomena (Table 2.4). Furthermore, the direction of loading which pullout testing mimics ($-F_x$) is found to be nearly negligible compared to the axial tension-compression forces (F_z) found *in vivo* (Table 2.5).

Table 2.6 Overview of the benefits and drawbacks of pullout testing of pedicle screws.

Benefits	Drawbacks
Gains information on the initial fixation of the screw	Limited obtainable data: generally only a maximum force and characterization of a force displacement curve
Easily implemented	The loading used is not present in the clinical situation
Reproducible (especially in artificial bone models)	The failure mechanism modeled is not clinically relevant
Good baseline for comparison of various designs	No information gained on the fatigue failure of the implant
Large database of literature to compare and contrast results	Destructive in nature (destroys the sample)

Fatigue Testing of Pedicle Screw Fixation

There appears to be a common agreement among authors that toggle testing is comparatively more physiological than pullout testing[19,42,58,156]. These opinions are supported by the *in vivo* studies which have shown that the pattern of compressive forces on the spinal implant during walking fluctuates in a cyclical pattern - similar to what can be mimicked by toggle testing[181]. Some authors even believe that the toggle motion is one of the possible mechanisms of screw loosening[19,42,58,156]. Since the body sustains cyclic loading in everyday life and clinical screw loosening occurs days to months after primary fixation, fatigue effects are thought to be the predominant mechanism of loosening[42].

Toggle testing uses a similar basic experimental setup to pullout testing except the loading applied to the screw head is cyclic and along the radial axis of the screw. Variations within the experimental setup include all of the variations mentioned for pullout testing except the loading rate; in toggle testing the cyclic loading rate changes from 0.5-5 hertz and the loading mode can either be displacement or force controlled.

Even though there is consensus suggesting that toggle is more physiological than pullout, the method still has limitations and room for improvement. Both toggle and pullout testing methods utilize single vertebra and not the entire construct: no rods or intervertebral discs are present to allow for load-sharing between the devices, discs, and vertebra. Both test methods also use loading protocols applied directly at from the screw head; whereas, the forces in the body are generated from the motion of the spine due to the contraction of the muscles on the spinal column. Neither toggle nor pullout methodology address the long-term changes in bone material properties or biologically active mechanisms such as bone resorption or growth around the screw (this is the case for all *ex vivo* testing).

Thus far in the literature, most toggle testing is completed by utilizing a displacement control[235]. However, force control rather than displacement control has been shown to be more clinically applicable[86,216]. Furthermore, toggle testing has been run using displacements with equal magnitude in the cranial and caudal directions. This equal magnitude displacement pattern is not seen *in vivo* since loading is generally shown to fluctuate only in the compressive loading range[181]. A 2008 study run by Kiner et al.[112] utilized force control as well as non-destructive loading in order to assess physiologic fatigue and damage that may occur during the initial healing after spinal fixation[28]. Kiner et al.[112] found that a primary damage effect was exhibited which could be explained by creep and stiffness loss.

Table 2.7 An overview of the benefits and drawbacks of fatigue (toggle) testing of pedicle screws.

Benefits	Drawbacks
Gains information on the initial fixation of the screw	Smaller database of literature to compare/contrast results
Gains information on fatigue damage	No standardized loading protocol to facilitate comparison
Loading used is more similar to clinical setting than pullout testing	Loading utilized thus far does not fully mimic the clinical situation
Relatively easily implemented	Often destructive in nature
Fairly reproducible (especially in artificial bone models)	No standardized loosening paramter to compare
Good baseline for comparison of various designs	
Can be non-destructive	

Few other types of biomechanical tests of pedicle screw fixation exist in the literature. Choma et al.[42] used a simple, quasi-static test where a synthetic bone block was held at an angle and the screw head was loaded in a compressive direction until failure; this method caused variable bending moments to be placed on the implant due to a coupled pullout motion. The method is similar to pullout, except the loading direction which causes the application of moments and makes it more similar to the clinical situation. Yerby et al.[241] used strain gauges inside pedicle screws at predetermined spacing in order to measure bending moments seen inside the screw. Shilling et al.[201] tested a 3 segment model for dynamic systems. They utilized a preload of 400 N and pure moments (±7.5 Nm) with a velocity of 3 °/sec for both flexion/extension and for lateral bending and axial rotation. The focus of this method was to investigate range of motion (ROM) rather than loosening, but the methodology used could be transferred to a non-destructive model of screw loosening.

2.7. Influential Factors of Pedicle Screw Fixation

There are multiple aspects of pedicle screw design that are being explored which, may ultimately be changed with the aim to decrease the frequency of loosening. These alterations include changes in screw design (*e.g.* thread design, pitch, diameter, length, screw coatings) and the surgical techniques used (*e.g.* insertion angles, surgical tools used). Other aspects such as and patient parameters (*e.g.* bone quantity and quality, anatomical dimensions) are also currently being investigated to determine their impact on loosening frequency. In order to quantify potential improvements in clinical performance, pre-clinical testing is often performed with the aforementioned pullout and toggle testing. Whether or not the methods are completely legitimate, the opinions on the probable occurrence of screw loosening and the most important factors for fixation are based upon results collected during these types of pre-clinical tests. The following sections explain how various screw design features, the surgical technique or the patient parameters have been shown to influence screw fixation in pre-clinical testing. The factors are separated by how they influence results utilizing the different pre-clinical testing methods.

2.7.1. Influence of Screw Design

Increasing pullout strength: The largest influence on pullout strength has been shown to be the outer diameter of the pedicle screw[41,58,59]. The pedicle screw should 'be of good length'[41,58,59]; reach past the pedicles and to a depth of 80% of vertebral body length or just past the neuro-central junction. An 80% depth is 32.5% stronger than 50% penetration[120]. Smaller inner diameter[41,58,59] and a shorter pitch[41,58,59] also have increased pullout strength. Mixed results have been seen with various types of screw cores: conical cores have exhibited higher insertional torque; however, the pullout force is statistically the same[125]. One study has shown conical screw cores could lead to problems with reduced pullout strength if the screws would need to be backed out even as little as 180°[135] but Abshire[1] showed no problems of reduced pullout with up to 360° backout in porcine spines. Dual core screws (inner diameter thickened around the neck) have been investigated and shown to improve fatigue strength[134]. Double threaded screws are shown to facilitate faster insertion and increase insertional torque[150].

Increasing toggle strength: Kiner et al.[112] showed that an increase in the screw's outer diameter by 2 mm had a significantly greater effect on increasing stiffness in cyclic loading than augmentation. Kiner et al.[112] found that increasing diameter is a worthwhile technique for reducing loosening in osteoporotic patients. In contrast, Hirano et al.[98] argues that other screw positioning options or augmentation should be considered due to the higher chance that large outer diameters could breach the thin pedicle walls of osteoporotic patients. A 27% increase in inner diameter[138] was shown to be associated with a 104% increase in fatigue strength. This is different from pullout where a decrease in inner diameter increases the maximum pullout force[59]; therefore, the most prevalent failure mechanism becomes important when determining the optimal inner diameter.

Other findings: Transverse connectors have been shown to increase rotational stability[136]. The neck of a monoaxial screw is the weakest portion of the screw[138,241] and the coupling is the weakest section of the polyaxial screw[74]; therefore, mechanical breakage is most likely to occur there. Chen et al. [38] showed that polyaxial screw systems exhibit greater rigidity in the lumbrosacral spine[38]. Various surface coatings and manipulations have been investigated in order to improve biological (hydroxyapatite (HA)) or mechanical fixation (increased surface roughness). Dakhil-Jerew et al.[57] concluded that the most successful way to reduce screw loosening from the studies they investigated was the use of plasma-sprayed HA screws due to osteoblast adhesion and differentiation. Hydroxyapatite coatings increase the surface area of the screw, which in turn improves load bearing ability and reduces corrosion rates which, in turn, accelerate the rate of bone formation[226]. The interface between the hydroxyapatite and the bone has been shown to be stronger than the interface between the hydroxyapatite and the implant[226].

2.7.2. Influence of Surgical Technique

Increasing pullout strength: To achieve optimal pullout strength, the dorsal cortex of the spine where the pedicle screw enters should not be violated, so tapping of the screw holes is not recommended[166]. Any surgical instruments that are used should be ≤ to the inner diameter of screw used for instrumentation[33,55]. Screws should converge in the transverse plane; a 30° convergence of pedicle screw increases pullout by 28.6%[12]. However, this finding is contradicted by Sterba et al.[216] who showed that parallel insertion in the sagittal plane produced higher strength in toggle testing.

Increasing toggle strength: Insertion of the pedicle screw which is parallel to the endplate provides the strongest stability from repeated axial loading[41,242]. Cephalad insertion should be avoided because of an increased chance for early fatigue due to increased bending moments[144,242].

General rules: Reduction of screw misplacement and dorsal cortex damage can be achieved by using a blunt technique rather than using a drill[80]. Tapping has been shown to improve screw trajectory[68]. After initial insertion of the screw, excessive manipulation of the screw is considered to be undesirable (*i.e.* back-out and reinsertion of screws) as it decreases insertional and pullout strength. A high insertional torque was strongly and directly related to BMD[55,245]; however, this correlation has not been replicated in later biomechanical studies and in the clinic[105,156,196].

2.7.3. Influence of Patient Characteristics

Increasing pullout and toggle strength: Good quality (BMD) and volume of bone has been shown to increase pullout and toggle strength[156,157,248]. In pullout testing the bone between the threads of the screw is usually fractured[41]; therefore, the quantity and quality of the trabecular bone is extremely important.

General rules: The pedicle shape is very important because 60% of pullout strength and 80% of longitudinal stiffness depends on the pedicle and not on the vertebral body[98].

Concepts for Fixation in the Revision of Pedicle Screws

Screws needed to replace failed previous screws as well as the ones used in osteoporotic patients have led to variations in typical surgical techniques as well as in screw designs. The most often used method to increase fixation in the osteoporotic spine or for revision surgeries is a larger diameter screw. Augmentation, typically with PMMA based cements, is often used in severely osteoporotic spines[88]. In recent years augmentation is becoming more popular and new methods have been developed such as injection through cannulated and fenestrated screws to increase the safety of cement augmentation in the spine by reducing leakage[41]. Multiple variations of screws which expand within the vertebral body are being explored. Double pedicle screws, extrapedicluar screws (more commonly in the thoracic spine), or additional hooks and wires are rarely implemented.

Several new, novel ideas have been proposed to mitigate screw loosening such as a cortical trajectory with smaller screws[197], a polyetheretherketone rod system to include some flexibility in the construct[169], novel augmentation techniques[107] or use of a transpedicular plate fixator[164].

2.8. Summary

Pedicle screw systems are considered to be the gold standard of posterior spinal stabilization, and their indications for use have continued to grow since the early 1990's. However, loosening of pedicle screws is quickly becoming an area of concern especially in osteoporotic spines and when dynamic stabilization is used[157,194,229]. Given that the incidence of loosening is on the rise, pullout is extremely rare, and broken hardware is on the decline; screw loosening is seemingly the predominate failure mode of pedicle screws. The most influential factors on the incidence of loosening rates reported in the literature are: the time of follow-up[229], presence of anterior column support (*i.e.* fusion or cages)[229], the use of dynamic or traditional stabilization[194], screw positioning in relation to the construct[115,229], length of construct[115,229], and bone quality[16,47,92,129,157,195,229,248].

Mechanisms of screw loosening are not fully understood and various theories have appeared in the literature. Micromotion and, more commonly, cyclic toggle loading seem to be the most common explanations of the primary cause of pedicle screw loosening (Table A**.**1). Micromotion is thought to trigger bone resorption[155,199] and cyclic loading is thought to induce bone destruction through fracture[129], compression, or viscoelastic creep[42]. The volumetric pattern of loosening has, thus far, not been fully characterized and greater understanding of the shape of the failure pattern could provide insight into the clinically relevant failure mechanisms.

Pullout and toggle tests are the most common pre-clinical pedicle screws tests. They attempt to establish which screws will be the most successful *in vivo*. Both of these methods give relevant information about the mechanical stability of the screw; however, neither test represents the true clinical situation. Pullout is a dated and unrealistic test that is still being conducted due to its ease of implementation and general acceptance in the scientific community. Despite these criticisms, noteworthy pullout studies have been performed and a large body of knowledge has been gained. Pullout testing can still be considered relatively useful as a comparative test between various designs but no information should be extrapolated to the clinical situation. Toggle testing can likely give a more realistic idea about the initial stability (from stiffness values) of an implant as well as information regarding fatigue damage during cyclic loading. This method has been utilized often enough to enable limited comparisons between research groups, but it is still comparatively underutilized. In order to translate information from toggle testing into an idea of the mechanisms behind screw loosening, comparisons with *in vivo* data[17,181] as well as clinical CTs of loosening (to compare failure patterns) should be performed.

Chapter 3.
Current Clinical Opinion

Pedicle screw fixation is the most often used intra-operative stabilization technique in the posterior spine. The high frequency of its use can be attributed to the comparatively high construct stiffness, enhanced stability and relative ease of implantation of this method compared to other posterior fixation techniques[41,139,240,243]. Loosening at the screw bone interface has been shown to be the predominant failure mechanism and its prevalence is on the rise in the recent years[57,90,202]. Multiple factors contribute to the increased loosening prevalence including: broader indications, the increased use of screws in older patients with poor bone quality, combined with improvements in imaging techniques which allows for better visualization of the bone-screw interface. Reports regarding the important aspects of fixation, the common failures seen, and the techniques used to provide best fixation have been scattered across diverse literature. The need for a consistent forum to communicate these preferences and practices is becoming increasingly urgent.

Known indications for revision in pedicle screw fixation are malposition of screws (1-12.9 % of patients)[90,240], reoccurrence of disease (21 % of patients)[57,202], infection (1.2-3.2 %)[90] and metal breakage or loosening (4-21 %)[57,90,202]. Reported loosening rates have ranged widely from 1.3-41% per patient, with rates after 2000 ranging from 7 to 20% (Chapter 2.4). Lonstein et al.[139] showed that 23% of 4790 pedicle screws studied in 879 patients needed to be removed due to either *pseudarthrosis* (non-fusion) or "pain related to instrumentation."

There is a large cumulative knowledge database with many biomechanical studies on record; however, the primary mechanisms and modes of loosening are still not fully understood. The cyclic repeated loading of the screw has consistently been discussed as the primary failure mode[19,39,42,112,129,155,156,199]. Furthermore, it is believed that the cyclic toggle loading causes bone 'crushing' or 'compressive yield or viscoelastic creep' at the bone screw interface[42,129]. Another mechanism, micromotion, causes fibrous tissue and osteoclasts to form at the screw interface resulting in the resorption of the bone[155,199]. One group which advocates micromotion as the primary mechanism of failure, also suggests that pullout could be a mechanism only for sudden failures due to a massive overload[199]. Shear forces or shear slip of the interface are also discussed as possible mechanisms of screw loosening[42,115].

Surgical techniques to mitigate screw loosening include manipulating certain implant characteristics (*i.e.* screw diameter) and specific surgical positionings and approaches. Increasing the diameter[41,58,59,112], using a dual core (inner diameter thickened around the screw neck),[41,133] increasing screw depth[41,98,120], and having a shorter pitch[41,59] have all been shown to increase biomechanical screw fixation. It has been shown that screws should converge in the transverse plane since a 30° convergence of pedicle screws increases pull-out strength by 28.6 %[12]; however, this finding is contradicted by Sterba et al.[216] who showed that parallel insertion in the sagittal plane produced higher toggle testing strength. Cephalad insertion should be avoided because of an increased chance for early fatigue due to increased bending moments[242].

Despite the plethora of experimental data, there is a distinct lack of available information about what techniques surgeons use in clinics and which techniques they believe are the most important for establishing secure fixation of the pedicle screw. Therefore, the aim of this study was to develop and distribute a survey to surgeons in order to quantify surgical opinion regarding: what clinicians currently see in clinics (failures), how they treat patients (techniques) and the important aspects of establishing good fixation (aspects).

3.1. Methods

The production of the survey was a collaborative effort with ulrich medical® and the University Hospital Münster. The survey was developed in two languages (English and German) and was available in two formats: online through a scientific survey hosting site (socialsci.com) and a printed version (see Appendix B for the full German version). Personalized emails were sent to regional managers within ulrich medical® and also to a list of surgeons (*n*=1011) of which 841 reached the corresponding inbox.

The survey structure was designed to form a balance between simplicity and statistical power (Figure 3.1). The 28 questions (with 122 total items) were presented as a Likert-type scale and asked participants to rank a series of items on a visually symmetric 8-point agree-disagree scale. Typical Likert scales consist of five choices; however, the scale utilized in this study had eight choices in order to establish a forced choice (*i.e.* no neutral response). Since there was no middle value, participants had to decide whether they typically agreed or disagreed with each statement (Figure 3.1B). Each question had multiple items to rank on a scale and items were arranged alphabetically to reduce ordering bias (Figure 3.1A).

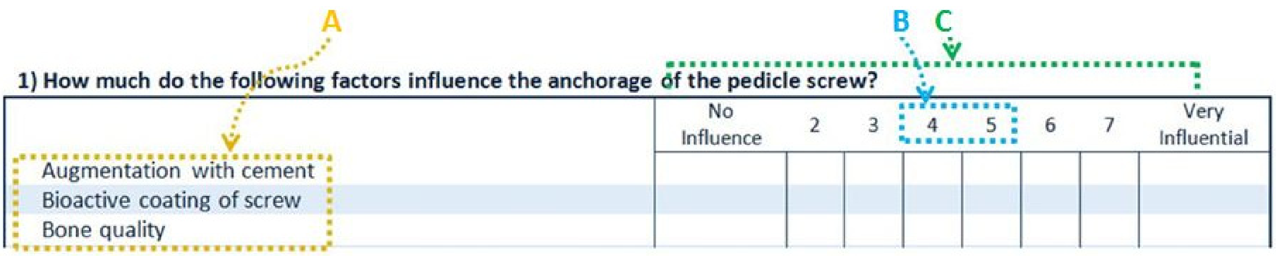


Figure 3.1 Structural characteristics of the survey that was distributed to surgeons. (A) Alphabetical ordering of items: to reduce ordering bias (B) forced choice: a scale of 8 values was used to reduce neutral responding (C) Likert-type scale of 8 factors.

It is widely debated whether the data collected using Likert-type scales is ordinal or interval; for the purposes of this study the data is treated as ordinal. A Friedman's ANOVA (non-parametric version of the repeated measures one-way ANOVA) was used to establish a mean rank order of the survey responses. *Post-hoc* analyses were run with Bonferroni corrected, Wilcoxon Signed-Rank tests in order to test differences in rank order between the items within each question. An alpha rate of 0.05 was used to determine statistical significance. Box-and-whisker plots were created for each item to display the dispersion and skewness of the surgeons' responses.

To more closely examine the relationship between surgeon experience, specialty, and place of training on specific questions, a series of chi-squared (χ^2) tests were performed. After the survey, the surgeons were asked, but not required, to complete a profile sheet. Their responses to this profile as well as to the items of each question were categorized by performing a median split of the data: responses equal to or larger than the median were classed into one group and those less than the median were classed into a second group. Surgical specialty was separated by placing neurosurgeons in one group and orthopaedics and trauma surgeons in the other. Country of surgical training was separated by surgeons who reported any training outside Europe in one group and those from Europe only in the second. The χ^2 tests were then used to determine whether the surgeon profile information influenced how the surgeons responded to the questions. Statistical results are only shown if all underlying assumptions of the statistical test were met.

3.2. Results

3.2.1. Surgeon Profile Statistics

The survey was completed by 65 of the 841 surgeons contacted, 44 of which were answered online. For the online version of the survey it took in an average time of 23.2 ± 11.4 (median: 21.5, range: 10-64) minutes with an average of 117.8 of the 122 total items ranked (range: 89-122,). Surgeon experience varied substantially with general surgical years averaging 16.8 ± 7.1 years (median: 17, range: 3-35), surgical years dedicated to spine averaging 12.3 ± 7.0 years (median: 10, range: 3-32), and the instrumentations performed per year averaging 89.1 ± 74.2 (median: 60, range: 5-275).

Neurosurgery was the most common sole specialty (41.5%) and 56.9% of surgeons reported their specialty as orthopaedics, trauma or both (Table 3.1). Most surgeons performed procedures on all regions of the spine (81.5%) with 15.4% specializing in the thoracolumbar region. Training was received in multiple countries for 30.8% of surgeons; however, the primary country of training was Germany (85.5% reported at least some training within Germany). The distribution of surgical training can be seen in Figure 3.2. In total, 21.5% of surgeons reported training from at least one country outside of Europe and 42.9% of those reported multiple non-European countries (Table 3.1 & Figure 3.2).

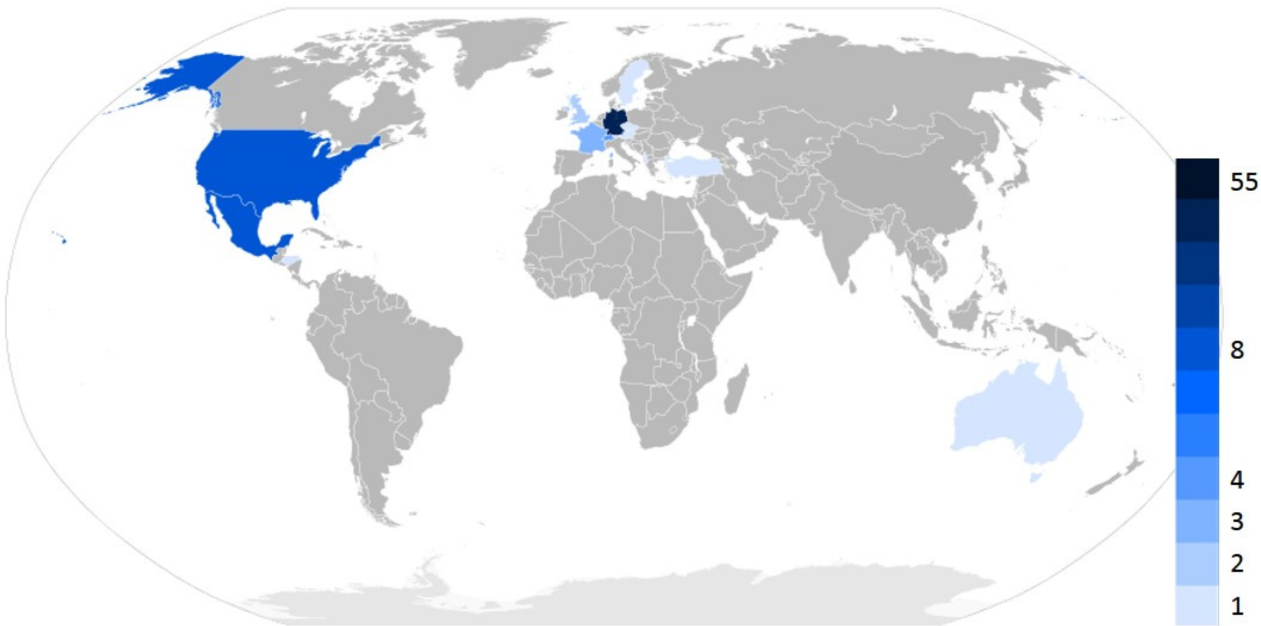


Figure 3.2 A world distribution map of the countries where surgeons in the current study received their training (modified from Wikimedia.org).

Table 3.1 Proportions of the surgeons based on their surgical specialty, country of training and their surgical region of the spine.

Surgical Specialty

	Total	%
Orthopaedics	13	20.0
Trauma	7	10.8
Neurosurgery	27	41.5
Orthopaedics & Trauma	17	26.2
Orthopaedics, Trauma & Neurosurgery	1	1.5
Did not answer or illegible: 0		

Surgical Region

	Total	%
Cervical	1	1.5
Thoracolumbar	10	15.4
Cervical & Lumbar	1	1.5
Cervical, Thoracic, & Lumbar	53	81.5
Did not answer or illegible: 0		

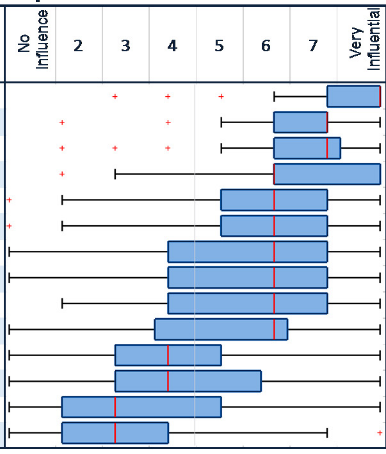
Country of Surgical Training

	Total	%
Germany	53	85.5
Mexico	8	12.9
USA	8	12.9
Switzerland	4	6.5
France	3	4.8
United Kingdom	2	3.2
Albania	1	1.6
Australia	1	1.6
Austria	1	1.6
Czech Republic	1	1.6
Honduras	1	1.6
Sweden	1	1.6
Turkey	1	1.6
Did not answer or illegible: 3		

3.2.2. Question-by-Question Analysis

The analyses of the questions are presented similarly to how they were asked during the survey; the primary question is given above the items to be ranked. Box-and-whisker plots are displayed in the response area to show the distribution of surgeon responses with the red lines representing the median. The items are now ordered from the highest-to-lowest importance as ranked by the surgeons (ordered by the mean rank obtained from the Friedman's ANOVA). The mean rank gives an estimate of the relative importance of each item within each question across surgeons. The higher the mean rank, the higher the agreement on that particular item. Corrected significant differences between ranked items were determined from the Wilcoxon Signed-Rank tests and are reported in the far right column. When a particular comparison is significant, the letter corresponding to that item is reported. For example, in question 1, item K (cross-link devices) was ranked significantly lower than items A-G. Letters in bold text signify that the comparisons are significant at the *p*<0.001 level.

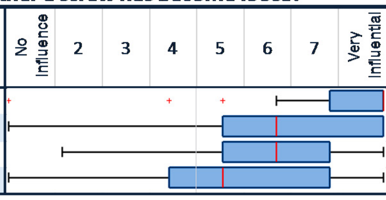
1) How much do the following factors influence the anchorage of the pedicle screw?



	Mean Rank	Significance
A) Bone quality	**12.44**	
B) Load bearing capability of the anterior column (ie. BMD)	9.85	
C) Presence of anterior support (ie. Cage, bone graft, plating)	**9.67**	
D) Screw placement (converging, towards the endplates, etc.)	9.06	A
E) High insertion torque / high press fit	**8.65**	**A**
F) Length of construct (ie. S1-L3)	8.24	**A**
G) Augmentation with cement	**7.79**	**A**
H) Intra-operative X-ray guidance (Fluoroscopy)	7.67	**A**
I) Depth of screw into vertebral body	**7.53**	**A**
J) High stiffness of construct	7.07	**A**
K) Cross-link devices	**4.96**	**A, B, C, D, E, F, G**
L) Bioactive coating of screw	4.69	**A, B, C, D, E, F,** G, H, I
M) Drill or awl usage	**4.08**	**A, B, C, D, E, F, G, H, I, J**
N) Computer navigation	3.31	**A, B, C, D, E, F, G, H, I, J**

Figure 3.3 The influence of the listed factors on pedicle screw fixation was found to differ significantly $\chi^2_F(13) = 282.8$, *p*<0.001 (Question 1). Bone quality was ranked as being significantly more influential than all other factors (D-N) except for anterior column load bearing (B) and support (C). Surgeons ranked cross-link devices (K), bioactive coatings of screws (L), drill or awl usage (M) and computer navigation (N) as having little influence as shown by the medians (red line in the box plots) all falling below the mid-line. All other factors were judged as having an influence on pedicle screw fixation (as shown by the medians falling above the mid-line).

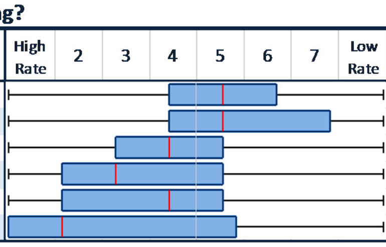
2) How important are the following points in determining whether a screw has become loose?



	Mean Rank	Significance
A) CT evidence	**3.36**	
B) X-ray evidence	2.49	A
C) Patient description of symptoms	**2.33**	**A**
D) Physical examination of the patient	1.82	**A,** B

Figure 3.4 Methods to diagnose screw loosening were found to significantly differ $\chi^2_F(3) = 59.6$, *p*<0.001 (Question 2). CT evidence was found to be significantly better than any other technique (*p*<0.002), followed by X-ray evidence.

3) How does the spinal region affect the rate of screw loosening?



	Mean Rank	Significance
A) Thoracic	**4.38**	
B) Cervical	4.19	
C) Cervical-thoracic junction	**3.49**	
D) Lumbar	3.31	A
E) Thoracic-Lumbar junction	**3.04**	**A,** B
F) Lumbar-Sacral junction	2.58	**A,** B

Figure 3.5 Influence of the spinal region on the rate of screw loosening was found to significantly differ $\chi^2_F(5) = 44.2$, *p*<0.001 (Question 3). The thoracic and the cervical regions were thought to have the lowest rates of screw loosening and to be significantly better than the lumbar, thoracic-lumbar junction, and lumbar-sacral junction (*ps*<0.03).

4) How does the length of the fixation construct affect the rate of screw loosening?

	High Rate	2	3	4	5	6	7	Low Rate	Mean Rank	Significance
A) Shorter constructs (1 segment)									**2.32**	
B) Mid-length constructs (2-4 segments)									1.99	
C) Long constructs (≥4 segments)									**1.68**	**A**

Figure 3.6 Influence of the length of the fixation construct on the rate of screw loosening was found to significantly differ $\chi_F^2(2) = 13.5$, p=0.001 (Question 4). Long constructs were more likely to be ranked as being associated with high rates of loosening compared to short constructs (p=0.002).

5) What positioning methods (see below) do you use when placing screws to provide the best fixation in the lumbar spine?

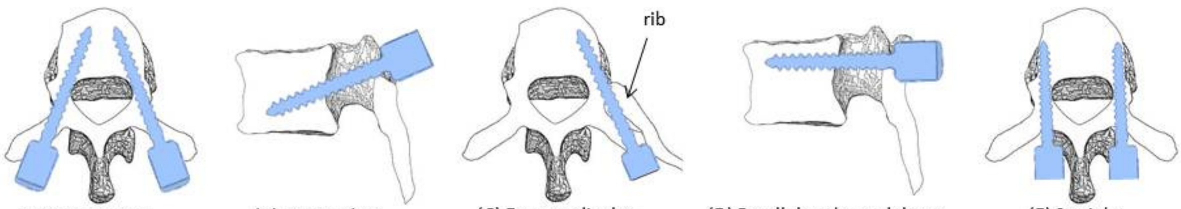
	Never Use	2	3	4	5	6	7	Always Use	Mean Rank	
i. (B) Converging in the transverse plane									**4.37**	
ii. (D) Parallel to endplates									3.88	
iii. (A) Bi-cortical alignment									**2.58**	**i, ii**
iv. (C) Descending to the caudal endplate									2.42	i, ii
v. (E) Straight									**1.75**	**i, ii, iii**

(A) Bi-cortical alignment (B) Converging (C) Descending (D) Parallel to the endplates (E) Straight

Figure 3.7 Influence of screw positioning in the lumbar spine on screw loosening was found to significantly differ $\chi_F^2(4) = 120.8$, p<0.001 (Question 5). Using converging screws in the transverse plane (median: 8) and screws parallel to the endplates (median: 7) were ranked as being the methods of choice for the lumbar spine region.

6) What positioning methods (see below) do you use when placing screws to provide the best fixation in the thoracic spine?

	Never Use	2	3	4	5	6	7	Always Use	Mean Rank	Significance
i. (A) Converging									**4.2**	
ii. (D) Parallel to the endplates									3.52	
iii. (B) Descending									**2.79**	
iv. (C) Extra pedicular (aka. Tri-cortical or in-out-in technique)									2.32	
v. (E) Straight									**2.16**	**i, ii**



(A) Converging (B) Descending (C) Extra-pedicular (D) Parallel to the endplates (E) Straight

Figure 3.8 Influence of screw positioning in the thoracic spine on screw loosening was found to significantly differ $\chi_F^2(4) = 80.0$, p<0.001 (Question 6). Converging screws in the transverse plane (median: 7) and screws parallel to the endplates (median: 6) were ranked as being the methods of choice for the thoracic spine region. Only the "straight" method was ranked as being significantly less commonly used compared to the "converging" and "parallel to the endplates" methods.

7) What positioning methods (see below) do you use when placing screws to provide the best fixation in the sacral spine?

	Mean Rank	Significance
i. (C) Converging	2.98	
ii. (D) Parallel to the endplate	2.67	
iii. (B) Bi-cortical alignment	2.51	
iv. (A) Ascending	1.85	**i, ii, iii**

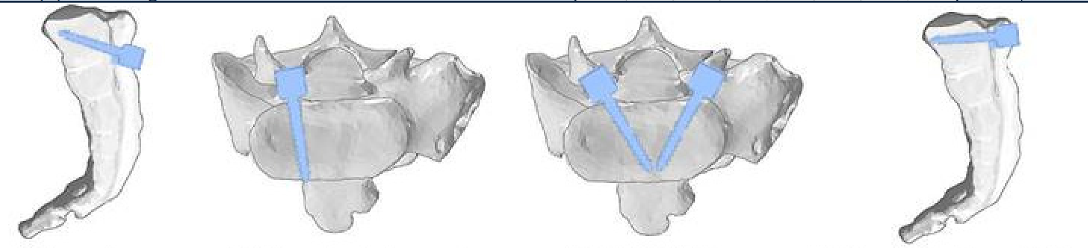
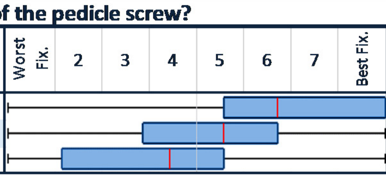


Figure 3.9 The influence of spine region on rate of screw loosening was found to significantly differ $\chi^2_F(3) = 28.8$, $p<0.001$ (Question 7). Converging screws in the transverse plane (median: 7), screws parallel to the endplates (median: 6), and bicortical screws were ranked as being more commonly used for the sacral spine region. Only the "ascending" method was ranked as being significantly less frequently used compared to all other methods.

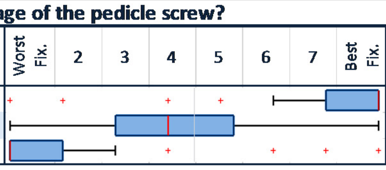
8) How do the following techniques influence the anchorage of the pedicle screw?



	Mean Rank	Significance
A) Use of awl	2.45	
B) Use of tap	1.86	A
C) Use of drill	1.69	**A**

Figure 3.10 The influence of the tool techniques used on pedicle screw fixation was found to significantly differ $\chi^2_F(2) = 22.7$, $p<0.001$ (Question 8). Use of the awl is believed to provide better fixation than use of a tap or drill.

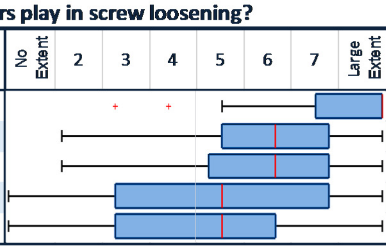
9) How do the diameters of the instruments influence the anchorage of the pedicle screw?



	Mean Rank	Significance
A) Undersize (Instrument diameter less than screw diameter)	2.66	
B) Same diameter as the screw	2.12	A
C) Oversize (Instrument diameter greater than screw diameter)	1.22	**A, B**

Figure 3.11 The influence of the tool diameters used on pedicle screw fixation was found to significantly differ $\chi^2_F(2) = 73.0$, $p<0.001$ (Question 9). Undersized instruments were ranked as providing significantly better fixation than same diameter and oversize diameter tools. Oversized instruments were ranked as being associated with a worse fixation than both other tool types.

10) In your opinion, to what extent do these mechanical factors play in screw loosening?



	Mean Rank	Significance
A) Poor initial purchase of the screw (insertional torque)	3.99	
B) Micro-motion of screw against the bone	3.21	
C) Cranial and caudal forces at the screw head	3.1	**A**
D) Rotational Forces (moments at the screw head)	2.47	**A**
E) Forces along the axis of the screw (posterior pullout)	2.23	**A, B, C**

Figure 3.12 Influence of mechanical factors on screw loosening was found to significantly differ $\chi^2_F(4) = 59.9$, $p<0.001$ (Question 10). Poor initial purchase was given the highest rank followed micro-motion and cranial/caudal forces at the screw head. Screw pullout was marked as having the least effect on screw loosening.

11) Of the removed pedicle screws, what percentage are removed or replaced for the following reasons:

	Never (0%)	1-14	15-28	29-42	43-57	58-71	72-85	86-99	Always (100%)	Mean Rank	Significance
A) Loosening										3.50	
B) Discomfort										3.12	
C) Cut out										2.80	
D) Broken screws										2.79	
E) No longer necessary										2.78	

Figure 3.13 Reasons for the removal of pedicle screws were found to significantly differ $\chi^2_F(4) = 11.9$, p=0.02 (Question 11). Pairwise comparisons did not find differences between the reasons for removal.

12) At what rate do screws become loose after surgery? Please give the estimated failure rate within the following post-surgery time periods:

	Never (0%)	1-14	15-28	29-42	43-57	58-71	72-85	86-99	Always (100%)	Mean Rank	Significance
A) 4-12 months										2.92	
B) > 12 months										2.73	
C) After discharge - 3 months										2.62	
D) During the initial hospital stay										1.73	A, B, C

Figure 3.14 Rate of screw loosening after surgery was found to significantly differ $\chi^2_F(3) = 44.5$, p<0.001 (Question 12). Loosening of screws during the hospital stay (D) was thought to be significantly less likely to happen than at any other time point (p<0.001).

13) How do screws fail? What percentage of the time do the screws fail in the following patterns (see below):

	Never (0%)	1-14	15-28	29-42	43-57	58-71	72-85	86-99	Always (100%)	Mean Rank	Significance
i. (D) Combination: Both toggle and widening										2.89	
ii. (C) Widening: Cranial-caudal wear of screw thread										2.66	
iii. (B) Toggle: Fan out of screw in cancellous bone										2.39	
iv. (A) Pullout: Posterior displacement of screws										2.06	A

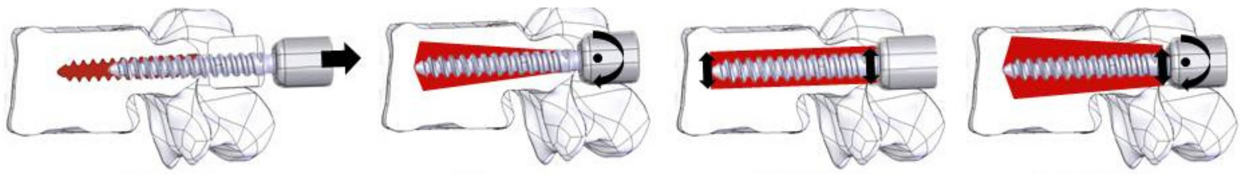


Figure 3.15 The rate of the pattern of screw loosening was found to significantly differ $\chi^2_F(3) = 20.7$, p<0.001 (Question 13). Pullout was found to be the least likely pattern of loosening.

14) In multi-segment fixation, where does screw loosening tend to occur? Please give the estimated loosening occurrence in each of the following segmental locations:

	Never (0%)	1-14	15-28	29-42	43-57	58-71	72-85	86-99	Always (100%)	Mean Rank	Significance
A) End standing cranial										2.44	
B) End standing caudal										2.28	
C) Middle screws of an instrumentation										1.28	A, B

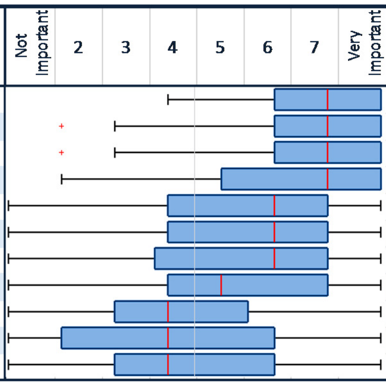
Figure 3.16 Influence of the screw location within the construct on the rate of screw loosening was found to significantly differ $\chi^2_F(2) = 61.2$, p<0.001 (Question 14). Middle screws of the construct were found to be significantly less likely to become loose than screws on either the cranial or caudal ends (p<0.001). Cranial screw were observed to be the most likely to become loose.

15) How important are the following screw features in preventing screw loosening?

	Mean Rank	Significance
A) Diameter of screw	3.7	
B) Screw length	3.42	
C) Shape of the screw core (conical or cylindrical)	2.95	
D) Pitch of the screw	2.71	A
E) Type of screw head (monoaxial or polyaxial)	2.22	A, B

Figure 3.17 Influence of screw features on screw loosening was found to significantly differ $\chi^2_F(4) = 46.3$, $p<0.001$ (Question 15). The diameter and the length of the screw were believed the most important features to prevent screw loosening. The type of screw head received a wide range of responses and was significantly worse than both diameter and length. Pitch and screw core shape were stuck in the middle.

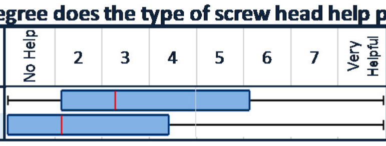
16) When considering screw design for use in OSTEOPOROTIC patients, how important are the following features in preventing screw loosening?



	Mean Rank	Significance
A) Diameter of screw	8.4	
B) Trajectory of screw into the vertebra	7.88	
C) Augmentation with cement	7.48	
D) Screw length	7.22	
E) Bi-cortical screws	6.05	A
F) Thread design (shape of the threads)	5.91	A
G) Shape of the screw core (conical or cylindrical)	5.46	A, B
H) Pitch of the screw	4.97	A, B, C, D
I) Bioactive coating of screw	4.42	A, B, C, D
J) Type of screw head (monoaxial or polyaxial)	4.13	A, B, C, D
K) Expandable screws	4.07	A, B, C, D

Figure 3.18 For osteoporotic patients the influence of screw design on screw loosening was found to significantly differ $\chi^2_F(10) = 149.9$, $p<0.001$ (Question 16). The diameter of the screw was found to be the most important followed by the placement of the screw within the vertebra, augmentation with cement, and screw length. Pitch, bioactive coatings, type of screw head and expandable screws were found significantly less important.

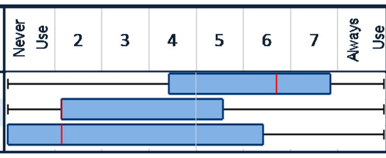
17) Consider Monoaxial and Polyaxial screw heads: To what degree does the type of screw head help prevent screw loosening?



	Mean Rank	Significance
A) Polyaxial	1.57	
B) Monoaxial	1.43	

Figure 3.19 Influence of screw head type on screw loosening was found not to significantly differ $Z = 1.76$, $p=0.08$ (Question 17). There was a wide distribution of answers given; however, the median was three or lower indicating little believed advantage between polyaxial and monoaxial screw heads.

18) How often do you use:



	Mean Rank	
A) Polyaxial screws only	2.44	
B) Monoaxial screws only	1.82	A
C) Combination of monoaxial and polyaxial screws	1.74	A

Figure 3.20 Rate of the use of different screw head types was found to significantly differ $\chi^2_F(2) = 22.2$, $p<0.001$ (Question 18). Only polyaxial screws are more often used than monoaxial screws alone or the combination of polyaxial with monoaxial ($p<0.001$).

19) Consider conical and cylindrical screw cores: To what degree does the type of screw core help prevent screw loosening?	No Help	2	3	4	5	6	7	Very Helpful	Mean Rank	Significance
A) Conical									1.52	
B) Cylindrical									1.48	

Figure 3.21 Influence between shape of core on screw loosening was found not to significantly differ Z= 0.02, p=0.98 (Question 19).

20) What are the optimum screw dimensions (relative to the size of the patient's pedicle)?	End of Pedicle	2	3	4	5	6	7	Bi-cortical	Mean Rank	Significance
A) Screw length in the lumbar spine									2.24	
B) Screw length in the thoracic spine									1.97	
C) Screw length in the cervical spine									1.8	A
	3.5mm < Pedicle Ø	-3	-2.5	-2	-1.5	-1	-0.5	Ø of Pedicle	Mean Rank	Significance
A) Screw diameter (Ø) in the cervical spine									2.11	
B) Screw diameter in the thoracic spine									2.01	
C) Screw diameter in the lumbar spine									1.88	

Figure 3.22 Desired screw length into the vertebra was found to significantly differ $\chi^2_F(2) = 12.4$, p=0.002 (Question 20A). Screws are desired to have further depth in the lumbar spine than the cervical spine (p=0.04). Desired screw diameter with respect to pedicle diameter was found not to significantly differ $\chi^2_F(2) = 2.4$, p=0.30 (Question 20B). Surgeons generally preferred screws 1 mm smaller than the pedicle diameter.

21) How do you determine the correct diameter of the screw?	Never Use	2	3	4	5	6	7	Always Use	Mean Rank	Significance
A) Pre-operative CT measurements									3.13	
B) Intra-operative tactile feedback									2.92	
C) Pre-operative radiographic measurements									2.08	A, B
D) Navigation									1.86	A, B

Figure 3.23 The rate of the use of different techniques to determine the diameter of the screw was found to significantly differ $\chi^2_F(3) = 46.3$, p<0.001 (Question 21). Pre-operative CT measurements and intra-operative measures are the more often used than pre-operative X-ray or navigation (p<0.002).

22) How do you determine the correct length of the screw?	Never Use	2	3	4	5	6	7	Always Use	Mean Rank	Significance
A) Pre-operative CT measurements									3.07	
B) Intra-operative tactile feedback									2.88	
C) Pre-operative radiographic measurements									2.03	A, B
D) Navigation									2.02	A, B

Figure 3.24 The rate of the use of different techniques to determine the length of the screw was found to significantly differ $\chi^2_F(3) = 35.7$, p<0.001 (Question 22). Pre-operative CT measurements and intra-operative measures are the more often used than pre-operative X-ray or navigation (p<0.003).

23) To what degree do these pedicle screw coatings help prevent screw loosing?	No Help	2	3	4	5	6	7	Very Helpful	Mean Rank	Significance
A) Surface roughness for bone integration									1.54	
B) Hydroxyapatite (HA)									1.46	

Figure 3.25 Influence between screw coatings on screw loosening was found not to significantly differ Z= 1.08, p=0.28 (Question 23). Screw coatings received higher marked importance (medians: 5) than screw head type (Question 17, medians: 3 & 2) and shape of screw core (Question 19, medians: 4 & 3).

24) How is the decision made whether or not to augment screws?

	Never Use	2	3	4	5	6	7	Always Use	Mean Rank	Significance
A) Pre-operatively determined risk factors (eg.									2.15	
B) Intra-operative tactile feedback									2.11	
C) Pre-operative diagnostic methods (ie. Bone quality)									1.75	

Figure 3.26 The rate of use of different techniques to decide to use augmentation or not was found to significantly differ $\chi^2_F(2) = 8.0$, p=0.02 (Question 24).

25) What would be the ideal type of cement for augmentation of screws?

	Never Use	2	3	4	5	6	7	Ideal	Mean Rank	Significance
A) Standard non-bioactive (eg. PMMA)									2.47	
B) Bioactive									2.01	A
C) Bioresorbable									1.53	**A, B**

Figure 3.27 Choice of cement type for augmentation of cement was found to significantly differ $\chi^2_F(2) = 31.1$, p<0.001 (Question 25). Standard PMMA was found to be more highly desired than bioactive or bioresorbable cements for screw augmentation (p<0.04).

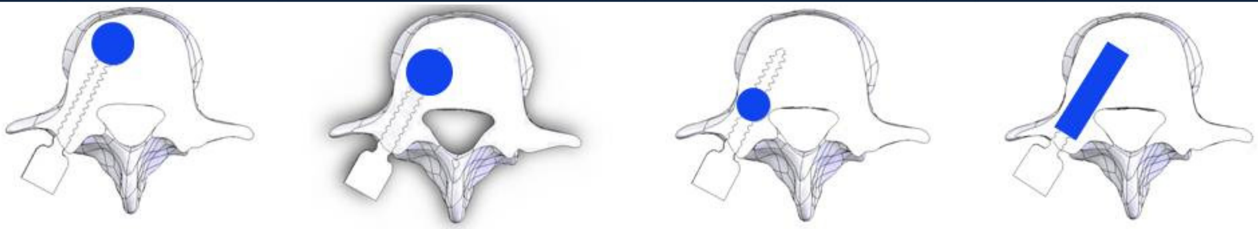
26) On average what volume of cement is used per screw for augmentation (in mL)?

0.0 - 0.5	0.5 - 1.0	1.0 - 1.5	1.5 - 2.0	2.0 - 2.5	2.5 - 3.0	> 3

Figure 3.28 Cement volume per screw generally ranges from 0.5-1.5 mL (Question 26).

27) What type of cement distribution (in which screw sector, see below) provides for the best fixation?

	Worst Fix.	2	3	4	5	6	7	Best Fix.	Mean Rank	Significance
i. (D) Continuous distribution along the screw length									3.34	
ii. (B) Cement bulb towards the distal end of screw									2.84	
iii. (C) Concentrated towards the screw head									2.06	**A, B**
iv. (A) Cement bulb at the tip									1.77	**A, B**



(A) Cement bulb at the tip (B) Cement bulb toward the distal end of screw (C) Cement concentrated towards the screw head (D) Continuous distribution along the length of the screw

Figure 3.29 Influence of cement distribution patterns on fixation was found to significantly differ $\chi^2_F(3) = 64.3$, p<0.001 (Question 27). Continuous distribution along the screw length and a cement bulb towards the distal end of the screw were thought to provide better fixation than cement bulbs towards the screw head or at the very tip of the screw.

28) What type of cement distribution (see figure in Question 27) has the least risk of leakage?

	Highest Risk	2	3	4	5	6	7	Lowest Risk	Mean Rank	Significance
i. (B) Cement bulb towards the distal end of screw									3.12	
ii. (A) Cement bulb at the tip									2.88	
iii. (D) Continuous distribution along the screw length									2.03	**i, ii**
iv. (C) Concentrated towards the screw head									1.98	**i, ii**

Figure 3.30 Cement distribution pattern on the risk of cement leakage was found to significantly differ $\chi^2_F(3) = 42.3$, p<0.001 (Question 28). Cement bulbs concentrated at the distal end of the screw (B) and at the tip (A) are thought to be less likely to leak than continuous distribution (D) or a bulb towards the screw head (C).

3.2.3. Influence of Surgical Experience, Specialty, and Country of Training

The surgeon profile parameters of surgical years of experience, spinal surgical years of experience, number of instrumentations per year, surgical specialty (Neurosurgery or Orthopaedics/Trauma), and country of training were tested to see whether they had an association with how the surgeon ranked items within a question. Surgeons trained outside of Europe generally assigned more importance to the screw design features of length, pitch, and screw head type. Screw length was 16.0 and 4.0 times more likely ranked above the median by surgeons trained outside of Europe (p<0.001, Question 15 & p=0.04, Question 16). Pitch was 4.5 times more often ranked above the median for both osteoporotic fixation (p=0.05, Question 16) and for important screw features (p=0.05, Question 15) by surgeons with non-European training. Screw head design was also ranked higher as a screw feature (p=0.01, Question 15) and for osteoporotic fixation (p=0.04, Question 16). Positioning of the screw within the vertebra in terms of depth for general fixation (p=0.01, Question 1) and overall position for osteoporotic fixation (p=0.001, Question 16) was ranked of more importance by the surgeons trained outside Europe (Table 3.2).

Surgeons with more years of general surgical experience tended to rank both insertion torque (p=0.03) and the pitch of the screw (p=0.01) as having a higher impact on screw fixation than surgeons with fewer years of general experience. Augmentation with cement was given higher importance for both general (p=0.02, Question 1) and osteoporotic (p=0.04, Question 16) fixation by surgeons who perform a higher rate of instrumentations. Thread design was considered more important for osteoporotic fixation for surgeons performing more instrumentations per year (p=0.02). Surgeons who perform more than the median instrumentations per year were also 7.9 times more likely to believe the shape of the loosening pattern is widening by cranial-caudal wear of the screw (p<0.001, Question 13). Surgical years especially related to spine did not lead to bias in the answering of any items in Questions 1, 13, 15 & 16.

Neurosurgeons gave favor to the use of bi-cortical screws for osteoporotic fixation (p=0.004, Question 16) but thought the shape of the screw core was of less importance for screw design (p=0.02, Question 15) than their Orthopaedic/Trauma counterparts. Orthopaedic/Trauma specialists are 3.8 times more likely to believe the shape of screw loosening is a combination of both toggle and widening (p=0.01, Question 13).

Table 3.2 The significant association between surgical profiles (*e.g.* experience, specialty, country of training) and the way the surgeon ranked the importance of the item in the survey.

		p	λ	Odds Ratio
Experience	Surgeons with more years of general surgical experience are 3.6 times more likely to believe high insertion torque to be important for good screw fixation (Question 1).	0.03	0.29	3.6
	Surgeons with more years of general surgical experience are 4.1 times more likely to believe the pitch of the screw to be important for good screw fixation in osteoporotic bone (Question 16).	0.01	0.33	4.1
	Surgeons who perform more instrumentations per year are 3.3 times more likely to believe augmentation with cement to be important for good screw fixation (Question 1).	0.02	0.29	3.3
	Surgeons who perform more instrumentations per year are 2.9 times more likely to believe augmentation with cement to be important for good screw fixation in osteoporotic bone (Question 16).	0.04	0.26	2.9
	Surgeons who perform more instrumentations per year are 3.3 times more likely to believe the shape of the screw thread to be important for good screw fixation in osteoporotic bone (Question 16).	0.02	0.31	3.7
	Surgeons who perform more instrumentations per year are 7.9 times more likely to believe the shape of the loosening pattern is cranial-caudal wear of the screw (Question 13).	<0.001	0.47	7.9
Specialty	Surgeons who specialize in Neurosurgery are 4.8 times more likely to believe bi-cortical screws to be important for good screw fixation in osteoporotic bone (Question 16).	0.004	0.36	4.8
	Surgeons who specialize in Neurosurgery are 4.2 times less likely to believe the shape of the screw core to be important for good screw fixation in osteoporotic bone (Question 15).	0.01	-0.33	4.2
	Surgeons who specialize in Neurosurgery are 3.8 times less likely to believe the shape of screw loosening is a combination of both toggle and widening (Question 13).	0.01	-0.32	3.8
Country of Training	Surgeons trained outside of Europe are 11.5 times more likely to believe the depth of the screw within the vertebral body to be important for good screw fixation (Question 1).	0.01	-0.34	11.5
	Surgeons trained outside of Europe are significantly (p<0.001) more likely to believe the trajectory of the screw within the vertebral body to be important for good screw fixation in osteoporotic bone (Question 16).	0.001	-0.43	--
	Surgeons trained outside of Europe are 4.0 times more likely to believe the screw length to be important for good screw fixation in osteoporotic bone (Question 16).	0.04	-0.26	4
	Surgeons trained outside of Europe are 4.5 times more likely to believe the screw pitch to be important for good screw fixation in osteoporotic bone (Question 16).	<0.05	-0.25	4.5
	Surgeons trained outside of Europe are 4.0 times more likely to believe the screw head design to be important for good screw fixation in osteoporotic bone (Question16).	0.04	-0.26	4
	Surgeons trained outside of Europe are 16.0 times more likely to believe the screw length to be important for good screw fixation (Question 15).	<0.001	-0.4	16
	Surgeons trained outside of Europe are 4.5 times more likely to believe the screw pitch to be important for good screw fixation (Question 15).	<0.05	-0.25	4.5
	Surgeons trained outside of Europe are 8.0 times more likely to believe the type of screw head to be important for good screw fixation (Question 15).	0.01	-0.36	8

3.3. Discussion

3.3.1. Aspects Important for Pedicle Screw Fixation

(*n*=11, QUESTION NUMBERS: 1, 8, 9, 15, 16, 17, 19, 23, 25, 27, 28)

Responses to the primary question about what surgeons believe influence fixation the most (Question 1) show that surgeons believe that patient characteristics influence fixation to a higher degree than device design features or procedural methods (Figure 3.3). The factors regarding the structural integrity of the spine, bone quality and the anterior load bearing capability of the spine, were found to be the most influential factors of pedicle screw fixation in both the survey and in literature (Question 1, Figure 3.3)[157,248]. These items to rank cannot be influenced by the surgeon and are only factors which are present that must be taken into account when deciding on the proper procedures and equipment. The following procedural items are ones which can possibly be influenced by the surgeon and are listed in order of perceived importance: (1) proper anterior support with use of cages or bone graphs, (2) surgical positioning of the screws, (3) obtaining a high insertion torque (highly influenced by bone quality), (4) creating the shortest construct possible, (5) augmenting the screws with cement, (6) increasing the depth of the screw within the vertebral body, and (7) try to obtain a high stiffness of the construct. Items ranked as having little to do with screw fixation as shown by low median scores are: cross-link devices, bioactive coatings, drill or awl usage, and computer navigation. Even though, surgeons did not rank bioactive coatings as having much importance (Questions 1 & 16) they have been shown to significantly reduce loosening rates[20,57,194].

The importance rank order for screw design features was similar when asking surgeons about fixation in either normal or osteoporotic spines (Questions 15 & 16). Screw diameter was determined to be the most important screw design factor for both normal (Question 15) and osteoporotic bone (Question 16) which agrees directly with literature[41,58,59]. Screw length was ranked as the second most important screw design factor (Questions 15 & 16) also corresponding with the literature[41,98,120]. The screw thread profile, core type (cylindrical or conical), and the pitch of the screw received a wide variety of responses for both normal and osteoporotic fixation, but on average they were believed to be important (median: 5-6, Questions 15 & 16). Increasing surgical experience, in terms of the number of years and in number of instrumentations per year, caused a tendency for a higher ranking of importance for screw pitch and the shape of the thread (p<0.02, Table 3.2). Surgical training outside of Europe generally caused an increase of importance for screw length (p<0.04), pitch (p<0.05) and screw head type (p<0.04, Questions 15 & 16). Bioactive coatings, screw head type (monoaxial or polyaxial) and expandable screws were thought to be significantly less beneficial for osteoporotic fixation than diameter or screw length (Question 16, p<0.001). Surgeons did not distinguish significant advantages between screw head type (monoaxial vs. polyaxial, Question 17), core type (conical vs. cylindrical, Question 19) and screw coatings (hydroxyapatite vs. Plasmapore, Question 23).

Augmentation with cement received relatively high importance for screw fixation for both normal (median: 6, Question 1) and especially for osteoporotic bone (median: 7, Question 16). Surgeons who perform a higher rate of instrumentations felt augmentation obtained was of even higher importance for both general (p=0.02, Question 1) and osteoporotic fixation (p=0.04, Question 16). PMMA was judged as the most ideal type of cement for pedicle screw fixation over bio-resorbable or bioactive (Question 25). A continuous cement distribution pattern along the full length of the screw or a bulb towards the screw tip was thought to help fixation the most (Question 27); however, the distribution with the bulb towards the screw tip was judged to have less risk of leakage (Question 28). The most used volumes of cements range from 0.5-1.5 ml per screw (Question 26).

Surgeons and literature are in agreement that the use of an awl rather than a drill is best for fixation (Question 8)[33,166] and that using undersized instruments is also positive for fixation (Question 9)[33,55]. However, overall the choice of which tool to use is thought to have little influence screw fixation (Question 1, median: 3).

3.3.2. **Failures Seen in the Clinics**

(*n*=7, QUESTION NUMBERS: 3, 4, 10, 11, 12, 13, 14)

Loosening was judged to be the most often occurring failure mode, followed by discomfort, cut-out, and broken screws (p>0.05, Question 11). Loosening ranking the highest in occurrence agrees with much of the literature,[19,39] including with Dawson et al.[58] who said "Clearly, the important failure mode is loosening."

The observation that screw loosening does not tend to occur during the hospital stay (Question 12) supports the common belief reported in literature that wear or repeated loading is a primary mechanism of screw loosening[19,39,42,58,112,129,155,156,199]. This assertion gains support from answers to Question 10 where surgeons thought cranial-caudal loading and micro-motion were important mechanical factors of screw loosening (median: 6). However, surgeons still ranked poor initial purchase of the screw significantly higher than any other failure mechanism including cranial-caudal loading and micro-motion. The equivalent *in vitro* measure of initial purchase would be insertional torque and multiple pre-clinical studies do not show correlation of insertional torque with pullout strength[105,156,196]. This result can be associated with the notion that surgeons often use tactile feedback during surgery as a strong indicator of surgical outcome.

Surgeons did not give much weight to pullout as a clinically relevant failure mechanism (Question 10) nor as a failure pattern (Question 13). This matches the current belief in the biomechanics community that pullout is not clinically relevant[19,58,112]. Toggle combined with widening and widening alone were the highest ranked observed failure patterns (Question 13) and they are patterns which can intuitively be associated with fatigue. Surgeons who perform more than the median instrumentations per year were 7.9 times more likely to believe the shape of the loosening pattern is widening by cranial-caudal wear of the screw (p<0.001, Question 13). The Osteoporotic/Trauma surgeons were 3.8 times more likely to rank the shape of loosening as being combined toggle and widening higher than the median than their Neurosurgeon counterparts.

Surgeon opinion agreed with clinical results that failures tend to occur at the ends of constructs rather than the middle (Question 14, p<0.04)[229]. Longer constructs (4 or more segments) were thought to exhibit significantly higher loosening rates than short, 1 segment constructs (Question 4, p<0.05). This associates well with the clinical results of one study which found a pattern where longer constructs contained significantly more loose screws than short constructs[229]. The thoracic region of the spine was believed to have the lowest rate of screw loosening which intuitively makes sense since the ribs are present to contribute to higher stability of the spine within that region (Question 3). The areas believed to have higher rates of loosening are the junctions between the spinal sections and within the lumbar region (Question 3).

3.3.3. Surgical Techniques Currently Used in the Clinics

(*n*=10, QUESTION NUMBERS: 2, 5, 6, 7, 18, 20A & B, 21, 22, 24, 26)

The position of the screws within the vertebra is the highest-ranked, surgeon-controllable factor for good pedicle screw fixation (Question 1). Therefore, care to use and determine the best screw positionings is especially important. Widely diverse responses were received for all questions pertaining to the screw positioning methods (Questions 5-7). Every positioning option received at least one 'Always Use' and one 'Never Use' ranking. Never-the-less, the median result from the survey corresponds with literature[12]. Converging screws in the transverse plane and screws parallel to the endplates are widely considered to be the best practice for the lumbar spine region (Question 5); however, some surgeons still never use these methods and always use straight or descending screws. This can perhaps linked to the fact that individual surgeon preferences drive decision making in spinal surgery; the surgeon's preference can even outweigh patient and disease characteristics in choosing spinal surgical procedures[110].

Widely diverging surgical practices were also reported for the screw length and diameter used (Question 20A & B). Reported ranges of screw length were from the end of the pedicle to bi-cortical within the cervical region. The diameter ranged anywhere from 3.5 mm less than the pedicle diameter to using screws as wide as the pedicle for each spinal region. Large variation is also present with how the decision is made for determining the dimensions of the screw (Questions 21 & 22). The most often used methods for dimension determination are pre-operative CT scans and intra-operative measurements. The variance of preferred surgical methods and techniques show a large non-consensus in surgical practice that is evident when speaking to different groups of surgeons. Furthermore, this non-consensus has been shown on the indications for specific procedures on pain related surgeries (*e.g.* decompression *vs*. decompression and fusion)[63,110,233]. Despite the presence of high-level evidence (including randomized controlled studies) supporting specific combinations of the conditions and procedures, surgeons often still utilize their preferred technique over the method which was shown to be more beneficial[73,79]. If a consensus is not present on the procedure to use, it is not surprising that surgeons do not often agree on specific surgical placements or screw features.

Polyaxial screws are used more than monoaxial screws alone or a combination of both (Question 18). The type of screw head, received a low mean rank in Questions 15-17; however, it contained a wide variation in responses. This variation was likely due to the fact that surgeons outside of Europe tended to give head type higher scores than the median compared to surgeons only trained in Europe (p<0.04). Therefore, screw head type has a cultural bias: non-European trained surgeons are more likely to believe head type plays a more important role in screw fixation.

The ability to view the interface is of importance for diagnostic determination of screw loosening as surgeons rely on the visualization methods of CT and X-ray for primary diagnosis (Question 2). CT scans were ranked as the most prevalent imaging mode to view loosening where in literature radiographs are used[57,115,229].

3.3.4. Influence of Surgical Experience, Specialty, and Country of Training

The differences observed between the surgical experience, surgeon type, and the region of training may be partly attributed to the wide-ranging discretion that has been allowed for surgeons in their planning of spine surgery[63]. Distinct regional variation has been shown for the use of short fusions in various areas of the United States[233]. The grouping of regional variations and the fact that preferred techniques are often utilized over evidence based techniques suggest that perhaps the preferences established during surgical training may substantially influence the later choice of surgical treatment. Establishing solid evidence-based techniques from the initial training becomes increasingly important.

3.4. Conclusions

The survey methodology utilized here allowed for a consistent forum to rank 122 factors and their importance to pedicle screw fixation. The advantage of this method is that it allows for a meaningful ranking of the items listed within each question allowing for the comparison of many variables; whereas, in biomechanical or clinical testing typically only 1-3 variables can be controlled per experiment. Previously, establishing a rank of importance was not practical as it could only be achieved by attempting to synthesize results from many various literature sources which used extremely variant testing methods and outcome variables. Therefore, the results presented here are the first synthesis of the most influential factors of pedicle screw fixation where the rankings presented are meaningful for this comparatively high number of variables. However, the rankings here are inherently opinion-based and are, therefore, less controlled than previous systematic experimental methods.

The fact that bone quality and the load bearing capability of the anterior spinal column are the two highest ranked factors influencing fixation quality demonstrates that surgeons believe patient characteristics, rather than the technical details of the procedure or the devices used, are the driving aspects for good pedicle screw fixation. The primary, fixation-improving factors which can be influenced by surgeons are implanting the proper anterior column support and the proper surgical positioning of the instruments within the vertebra. The screw design characteristics of diameter and length are considered the most important for fixation.

On average the most often used surgical methods agreed with the best practices mentioned in literature. However, there was extremely high variation in the responses given for current techniques used (Questions 5-7 and 20A&B) leading one to believe the average knowledge of the surgeons is good but consistency in practice is not present. Some of this high variation could perhaps be attributed to the wide-ranging discretion allowed for planning spinal surgeries[63] and the fact that individual surgeon preferences can outweigh patient and disease characteristics when choosing spinal procedures[233]. Availability of and standard training from a cohesive, comprehensive guide to the best practices of screw fixation within the spine could help narrow this variation in practice to more closely match the best practices found in literature.

Pullout is not thought to be clinically relevant in terms of the failure pattern or the failure mechanism. The observed length of time to loosening, observed patterns of failure, and given importance to cranial-caudal wear and micro-motion as failure mechanisms leads to an inference that repeated loading on the spinal implants contributes to loosening. Both the notion that pullout is not clinically relevant and that loosening is thought to be contributed to by repeated loading strongly agree with current opinions within the biomechanical literature[19,58,112].

Chapter 4.
Clinical Loosening Pattern

Pedicle screw fixation is the most commonly used intra-operative stabilization technique in the posterior spine. Its frequent use is due to the comparatively high construct stiffness, enhanced stability and relative ease of implantation compared to other posterior fixation techniques[41,139,240,243]. This technique, however, is associated with loosening at the screw bone interface which has been shown to be a predominant failure mechanism and its prevalence is on the rise in the recent years[57,90,202]. Multiple factors contribute to the increased loosening prevalence including: broader indications[173], the use of screws in older patients with poor bone quality, combined with improvements in imaging techniques which allows for better visualization of the bone-screw interface. With the increasing prevalence of loosening and better imaging techniques, the need and the ability to distinguish the loosening pattern has also increased. Quantifying the loosening pattern could allow the areas where the screw loosens to be determined and, therefore, where it is best to reinforce the screw to mitigate screw loosening. Furthermore, clinical relevance of *ex vivo* testing could be heightened by determining *ex vivo* force patterns which recreate the failure patterns observed in clinical practice.

Once loosening occurs, fibrous tissue has been shown to surround the screw within the vertebra[199]. This radiolucent fibrous tissue appears darker in radiographs which creates a discernible radiolucent halo around the screw head. Therefore, clinically relevant loosening has been classified as a 1 mm 'clear'[242] or 'radiolucent'[194,196,199]area surrounding the screw head as observed on a plain radiograph. However, the reason for the distance of 1 mm, the shape (conical or cylindrical) and the other parameters such as the length and volume of this halo are not specified nor standardized.

If a radiograph is unclear, then the determination of loosening can be confirmed by the appearance of a 'double halo'[115]. A double halo is considered the clinical confirmation of screw loosening; it appears as a radiopaque rim which outlines the dark area around the screw which has become loose[57,115].

The strength of the fixation at the bone-screw interface is typically studied via one of two different biomechanical tests: (1) standard axial pull-out method (ASTM F 543-01 A3) or (2) toggle testing which applies a cyclic loading perpendicular to the screw axis at the screw head and causes a cranial-caudal wear pattern within the vertebra. The basic axial pull-out method does allow for the determination of an initial fixation strength and stiffness, however, it does not mimic the *in vivo* loading or failure modes within the spine[129]. Toggle testing is considered more physiologically valid than pure axial pullout[19,58,199] since it better replicates the *in vivo* forces and moments at the screw head that as shown by Rohlmann et al[185,188]. The determination of the *in vivo* volumetric wear pattern of loosened pedicle screws could offer the unique opportunity to clinically verify the utilization of a specific test method.

The volumetric pattern of loosening from CT scans has, thus far, not been fully characterized and further knowledge regarding the shape of the failure pattern could provide insight into the clinically relevant failure mechanisms. The aim of this study was to quantitatively describe the three-dimensional clinical loosening pattern of pedicle screws from CT scans in terms of volume, surface area, and optical pattern. Further goals were to establish links between the loosening pattern parameters and surgical variables (*i.e.* location in the spine, location within the construct, and the number of fused segments).

4.1. Methods

After ethics approval was received from the Hamburg ethics committee (PV 4256), CT scans from patients who exhibited pedicle screw loosening during routine clinical CT scans (n=541) were included in the study (Table 4.1). The CT scans of the patients with observable loosening (n=16) were anonymized and used for evaluation. Each of the CT scans were classified into one of the four spinal regions; if the instrumentation spanned multiple sections it was classified within the section which contained the most fused levels. The loosening rate was calculated as the percentage of the patients with loosening to the total number of patients with pedicle screws which were screened. Of the sixteen CT scans containing loosening, eight underwent further parametric analysis (Table 4.2). The remaining eight were not able segmented due to poor spatial resolution (3 mm) in the cranial-caudal direction.

Table 4.1 A breakdown of the number of CT scans with loosening, the number of CT scans with segmentable loosening and the number of CT scans with pedicle screws as screened by the radiologist. The number in parentheses represents the number of patients in which the loosening halos are derived (*e.g.* the three cervical loosening halos are from a single patient).

	CT Scans with Loosening		Segmentable Loosening		CT Scans Screened	
Spinal Level	Patients	Loosening Halos	Patients	Loosening Halos	Patients	Loosening Rate
Cervical	1	3 (1)	1	3 (1)	191	0.5%
Thoracic	3	7 (5)	1	3 (2)	91	3.3%
Lumbar	11	12 (6)	6	10 (4)	259	4.6%*
Sacral	1	13 (7)	0	7 (4)		
Total	**16**	**35**	**8**	**23**	**541**	**3.0%**

*The sacral scans with loosening is included in the lumbar loosening rate.

Table 4.2 Details of the eight patients in which the loosening patterns (n=23) were segmented and analyzed.

Patient	Age	Gender	Fused Levels	Level	Halos	Loosening Levels	Crosslink	Breakage	Resolution
2	90	Female	10 (C0-T2)	Cervical	5	C1L, C3R, C5R, T2L, T2R	no	yes	0.34x0.34x0.50
4	73	Female	14 (T5-S1)	Lumbar	4	L5L, L5R, S1L, S1R	yes	no	0.41x0.41x0.50
9	67	Female	5 (L2-S1)	Lumbar	6	L2L, L2R, L3L, L3R, S1L, S1R	yes	no	0.37x0.37x0.50
10	71	Male	3 (T11-L1)	Thoracic	1	T11R	no	no	0.50x0.50x0.50
11	53	Female	8 (T11-S1)	Lumbar	1*	S1L, S1R*	no	yes	0.50x0.50x0.50
12	75	Female	6 (L1-S1)	Lumbar	2	S1L, S1R	no	no	0.32x0.32x1.70
17	73	Female	3 (L3-L5)	Lumbar	2	L3R, L4L	no	no	0.49x0.49x0.50
19	64	Female	3 (L4-S1)	Lumbar	2	L4L, L4R	no	no	0.40x0.40x1.00

*The S1R screw was broken; therefore, the loosening halo was not fully analyzed.

The CT image data (*.DICOM) consists of stacks of two dimensional images which store information about the geometry and the spatial position of the vertebrae. The image stack has the greyscale value of its two dimensional pixels interpolated between the slices to obtain an average grayscale value for each voxel. These greyscale values are classified using the Hounsfield Scale and correspond to bodily tissues depending on their radiopacity. The osteolytic area was clearly separated from the bony structure of the vertebra by a brighter border (the 'double halo'). This loosening area was manually segmented by selecting voxels associated with the darker loosening area and then assigning them to a predefined material (Avizo, Mercury Computer Systems, CA, USA). A surface model was then created which consisted of a closed, non-self-intersecting triangular mesh representing the loosening area as a zero-thickness shell in three-dimensional space. The obtained surface model of the loosening area was saved (*.stl-file, ASCII version) for use in all subsequent analysis (MATLAB, R2012a, The MathWorks, Inc., MA, USA).

To enable comparability between loosening halos, the coordinates of the loosening halo needed to be adjusted from the global coordinate system of the CT scanner (which varied in each CT scan) to a local coordinate system of the halo (Figure 4.1). The surface model was imported to MATLAB and a local coordinate system was systematically aligned to landmarks identified from each CT scan. Five landmarks were necessary: the screw tip, three points on the surface of the screw neck, and a point in cranial direction. The origin was defined as the center point of a best-fit circle which was created from the three points on the outer surface of the screw neck. The local orientation was set so that the x-axis passed along the screw axis from the origin to the point at the screw tip. The positive z-axis was defined by a point in the cranial direction from the x-axis.

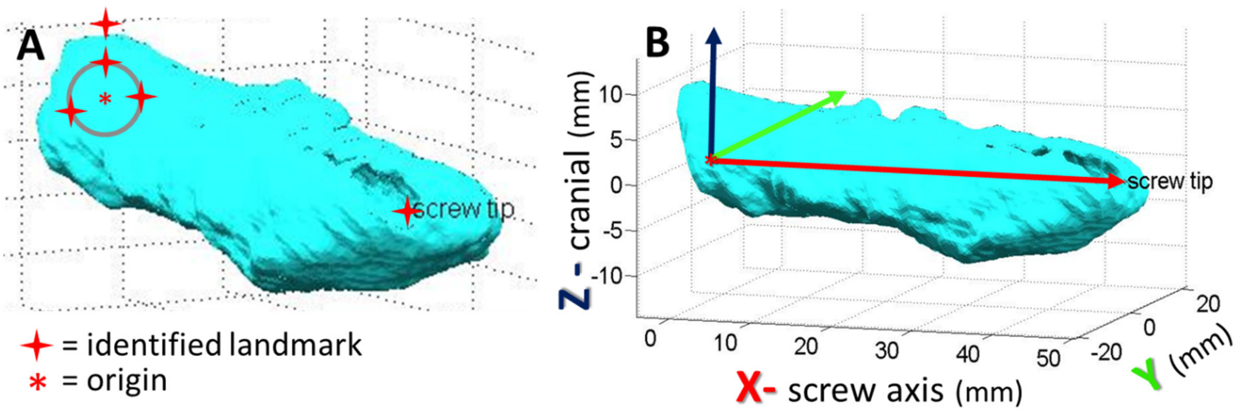


Figure 4.1 Orienting the surface mesh of the loosening pattern. (A) The globally aligned surface showing the identified landmarks and (B) the surface mesh aligned to the new coordinate system.

For further quantification of the loosening distribution along the screw axis, a volume was created from the surface and then split into sub-regions over equal intervals to measure the parameters of interest (Figure 4.2). The solid was created by filling the aligned surface with tetrahedral elements. It was then split with the frontal plane (y-z plane) into 2.5 mm thick sub-regions (this step-width could be defined by the user) along the x-axis creating sectional planes (Figure 4.2A). These planes were then meshed with a triangle mesh to enable surface area determination (Figure 4.2B). Solid slices were created by grouping the tetrahedrons based on the x-value of each element's centroid to enable volume determination (Figure 4.2C). To enable the comparison of results, a loosening halo of unit size (length of 1 mm, Figure 4.2D) was created by translation to the centroid of the coordinate system and then dividing by its length.

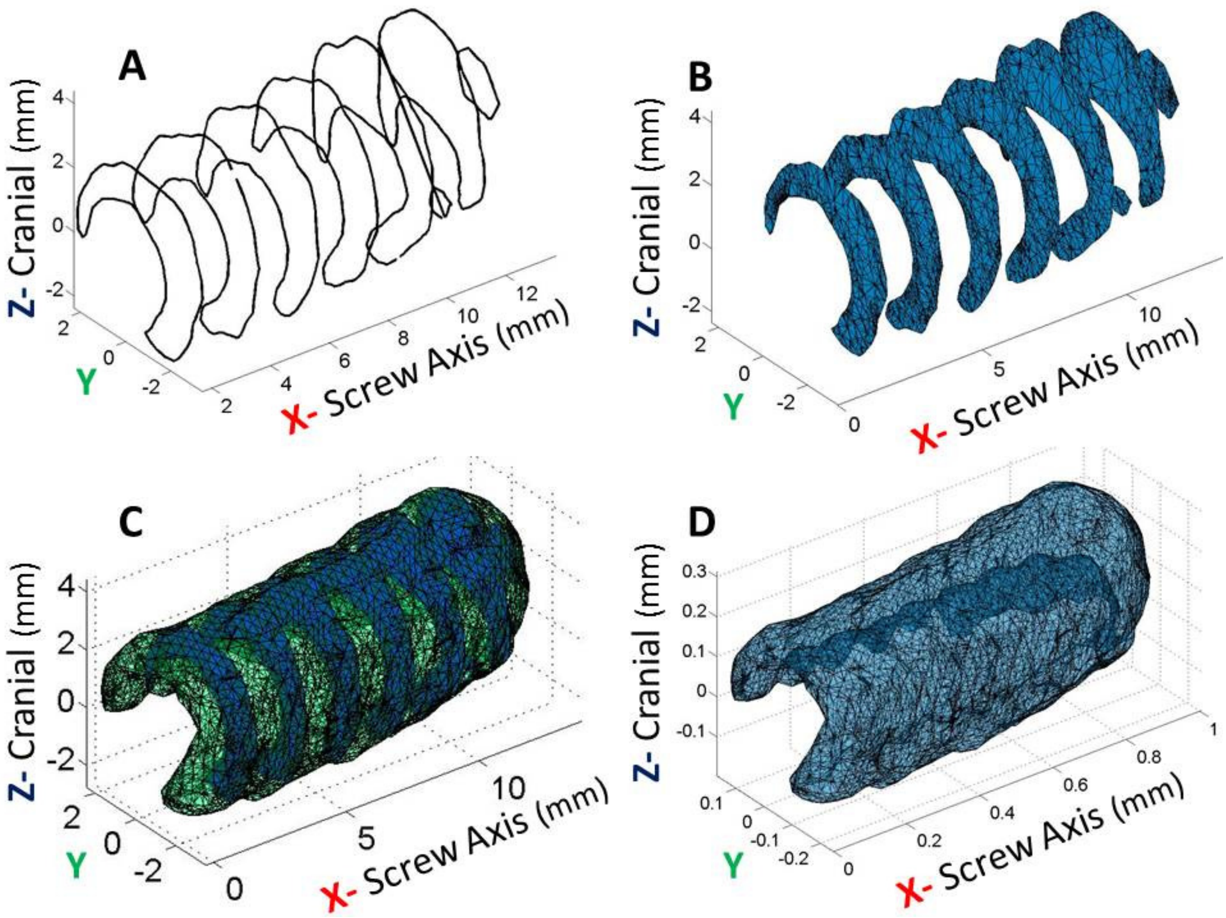


Figure 4.2 The sectioning of a representative loosening pattern. (A) A sliced halo showing the sectional planes. (B) Sectional planes filled with a triangular surface mesh. (C) A halo filled with tetrahedral elements and cut by the sectional planes. (D) A halo of unit length.

4.1.1. Measured Parameters

Parameters of interest were calculated for each halo and unit halo and were determined as follows:

- Volume: The total loosening volume was calculated as the sum of the individual volumes of each tetrahedron. The volume of each slice was determined by summation of the tetrahedral volumes within each slice.
- Area: The total surface area of the halo was the sum of the areas of the individual triangles of each surface mesh. The area of each cutting plane along the screw axis was the sum of the areas of the triangles on the sectional planes (Figure 4.2B).
- Length: The length of the loosening halo was determined by the difference between the smallest and the largest X-values (screw axis) of the tetrahedral mesh nodes.
- Center of Mass: For each tetrahedron, all three directions of the centroid coordinates were multiplied by its volume and then divided by the entire volume of the respective slice.

4.1.2. Statistical Analysis

Statistical evaluations were performed with the software package SPSS Statistics 20 (IBM Corp., Armonk, NY) with a type I error probability set to 5%. An independent-samples, Kruskal-Wallis Test (non-parametric version of the independent samples, one-way ANOVA) was used to distinguish differences in the loosening parameters (*i.e.* volume) between the regions of the spine. *Post-hoc* analyses were run with Bonferroni corrected, Wilcoxon Signed-Rank tests. A paired-samples T-test was used to test for differences between loosening volume for a screw at the end of construct vs. the loosening volume of a screw in middle of the construct for the same patient. The assumption that the sampling distribution of the differences is normally distributed was upheld for the loosening volumes. A two-way Spearman's rank correlation coefficient (r_s) was used to measure covariance.

4.2. Results

A total of 541 patients were screened for pedicle screw loosening. An overall loosening rate of 3.0% was observed with a 4.6% rate in the lumbar spine, 3.3% rate in the thoracic and 0.5% rate in the cervical regions (Table 4.1). Of the 16 patients with observed screw loosening, 14 were female. Eight patients had to be excluded from quantitative analysis due to poor image quality. In total, 23 loosening patterns were segmented and analyzed from eight patients (Table 4.2, Figure 4.3). The analyzed patients averaged 70.8 ± 9.8 years of age and had 6.5 ± 3.7 levels instrumented. The majority (74%) of the loosening halos were in the lumbar (n=10) and sacral (n=7) regions with three halos each in the cervical and thoracic regions. Crosslink devices were used in 25% of the analyzed cases and metal breakage also occurred in 2 of 8 patients.

The average loosening volume for all regions of the spine was approximately 1.5 cm^3. The loosening halo grew in size and length going from cranial-to-caudal (Table 4.3). The halos in the sacral region had non-significantly larger volumes and surface areas than any other region and longer lengths than the cervical and the thoracic regions. The volume of the sacral region was significantly greater than the cervical region (p=0.01). The lumbar region had halos with the longest length of all the regions and a greater surface area and volume than both the cervical and thoracic regions. The lumbar region had a significantly greater surface area (p=0.01) and length (p=0.01) than the cervical region. The halos in the thoracic region had a non-significant 246% greater volume, 244% greater surface area, and 142% longer length than the cervical region.

Table 4.3 Averages and standard deviations of the parameters of interest for the entire halo broken down by spinal region and overall.

Region	Number	Volume (mm^3)	Surface Area (mm^2)	Length (mm)
Cervical	3	241 ± 98	351 ± 40	15.5 ± 2.7
Thoracic	3	835 ± 780	1207 ± 650	37.5 ± 9.1
Lumbar	10	1275 ± 774	1533 ± 672	46.8 ± 3.3
Sacral	7	2530 ± 276	2300 ± 730	44.9 ± 5.6
Total	**23**	**1465 ± 1453**	**1570 ± 871**	**40.9 ± 11.4**

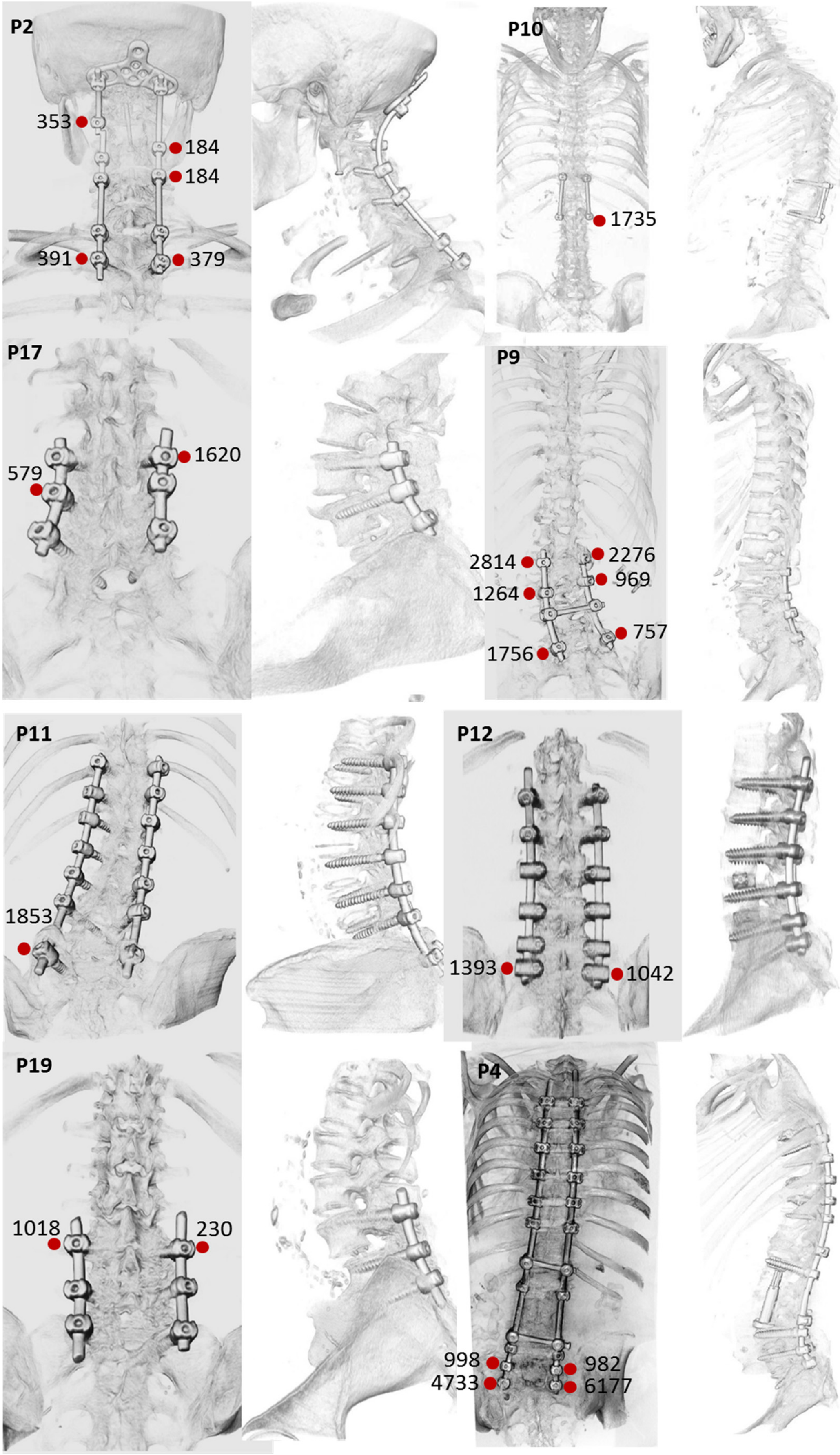


Figure 4.3 Rendered CT scans of showing the dorsal and the lateral view of the pedicle screw constructs of all analyzed patients. Red dots in the dorsal view denote screws which have become loose and the numbers given are the corresponding loosening volumes (mm^3).

All patients exhibited at least one loosened screw at an end of the pedicle screw-rod construct (Figure 4.3). In total, 70% of the analyzed loosened screws (*n*=23) were located at the construct ends with six located cranially and ten caudally. The loosening volume of the screws located at the construct ends (2340 ± 1705 mm^3) was significantly greater than the loosening volumes of a screw in the middle of the construct for the same patient (737 ± 427 mm^3, *p*=0.02). Furthermore, as the volume of the loosening at the end of the construct increased so did the loosening volume in the middle of the construct (*p*=0.02, *r*=0.82).

When considering all CT scans with loosening (*n*=16, includes the 3 mm resolution), there were nine long constructs (≥5 fused segments), six mid-short constructs (<5 fused segments) and one located solely in the pelvis. The long constructs had loosening at the caudal end of the construct in 78% of the cases; whereas, mid-short constructs only had loosening at the caudal construct end in 44% of the cases. All mid-short constructs with loosening were either located in the lower lumbar region (*n*=4) or at the thoracolumbar junction (*n*=2).

Distinct patterns of the loosening volume emerged for each spinal region (Figure 4.4). The patterns were classified using the descriptive shapes shown in Figure 4.5. All three patterns in the cervical region exhibited cranial toggle loosening due to the presentation of a small bulb towards the cranial tip of the screw. The thoracic region contained two pure widening patterns with no sharp cranial or caudal peaks as well as one small butterfly pattern. Of the ten lumbar patterns, 40% were caudal toggle (all in L4 or L5), 30% were cranial toggle + widening (L2 or L3), 20% were pure widening (L3), and one was a butterfly (L4). Of the seven sacral patterns 71% were caudal toggle + widening with the remaining two were pure widening. Peaks in one or both the cranial or caudal directions were seen in 74% (17 of 23) of the loosening patterns.

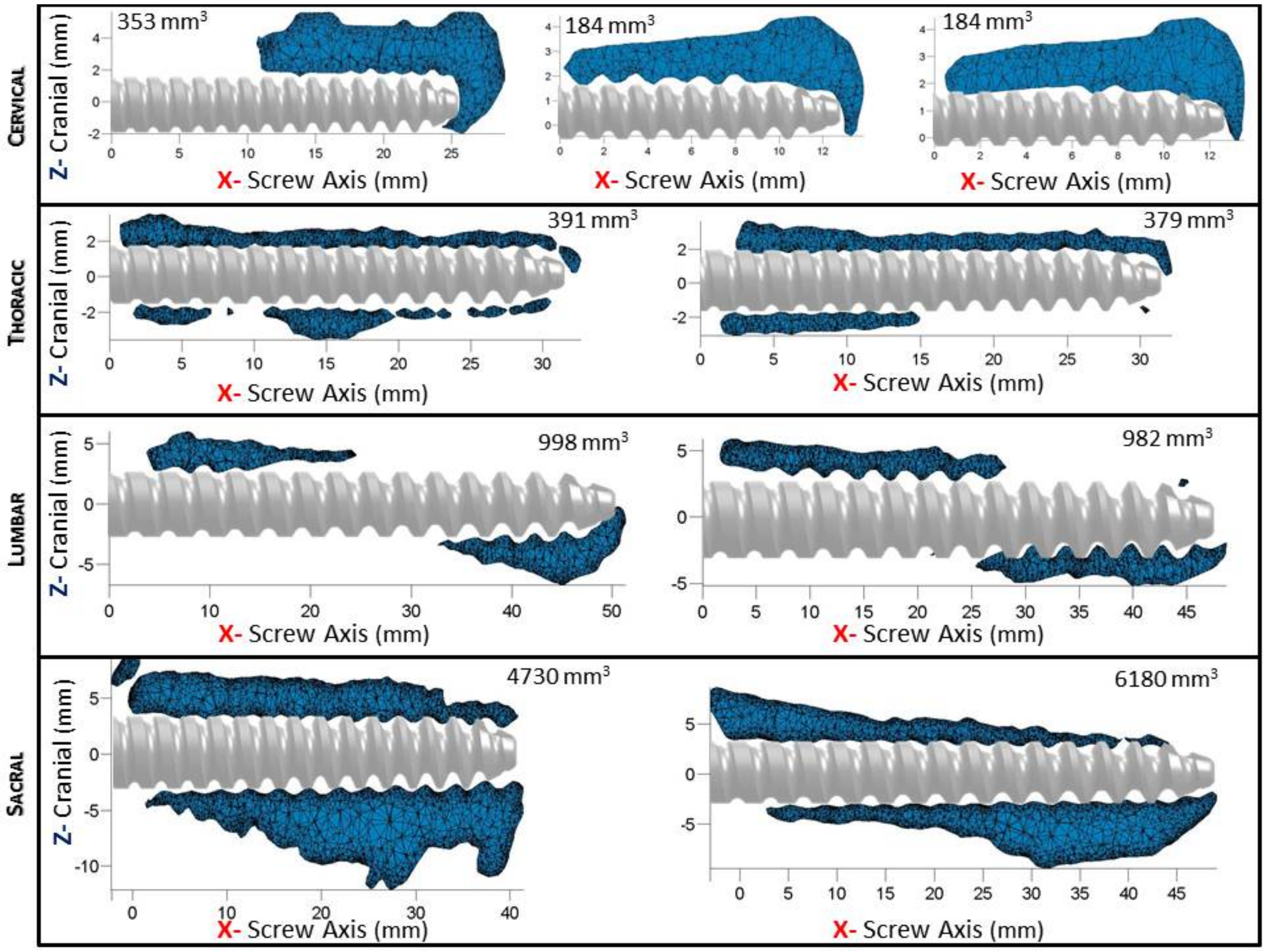


Figure 4.4 A selection of the loosening patterns in the cranial-caudal plane and volumes for each analyzed halo separated by spinal region. A representative screw has been inserted to facilitate visualization. All of the loosening patterns analyzed can be seen in Appendix C.

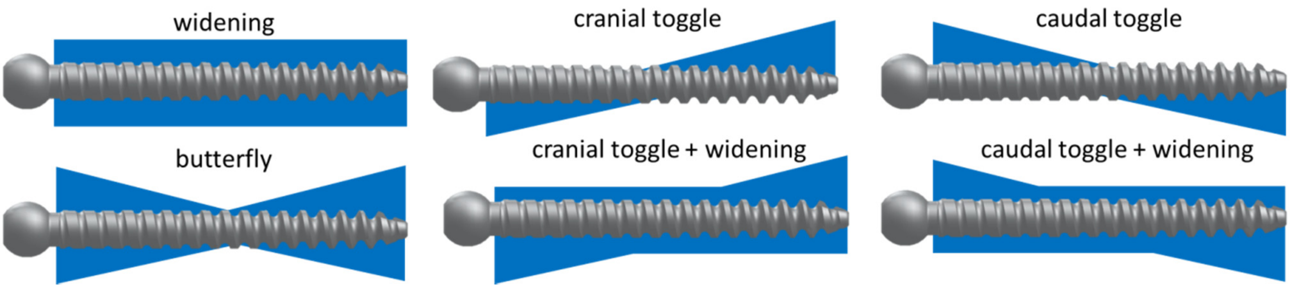


Figure 4.5 A schematic of the optical classification used to describe the failure patterns observed.

The average area of loosening of a slice directly down the screw axis in the cranial-caudal plane was non-significantly larger than the area of loosening in the transverse plane. The average pattern for both surface area and volume is nearly bi-modal in nature with a valley 40-50% of the distance down the screw axis (Figure 4.6). From the average volume distribution by region (Figure 4.6B), it appears the trough occurs at 40% of the screw length for cervical, 45% for sacral, and 50% for the lumbar spine. The peak towards the tip of the screw was on average larger than the tip towards the screw entry. This pattern was more evident in the cervical and the sacral regions and can be observed when examining the individual patterns grouped in their respective spinal regions (Appendix C) as well as by viewing the average unit length volume distribution for each region (Figure 4.6B).

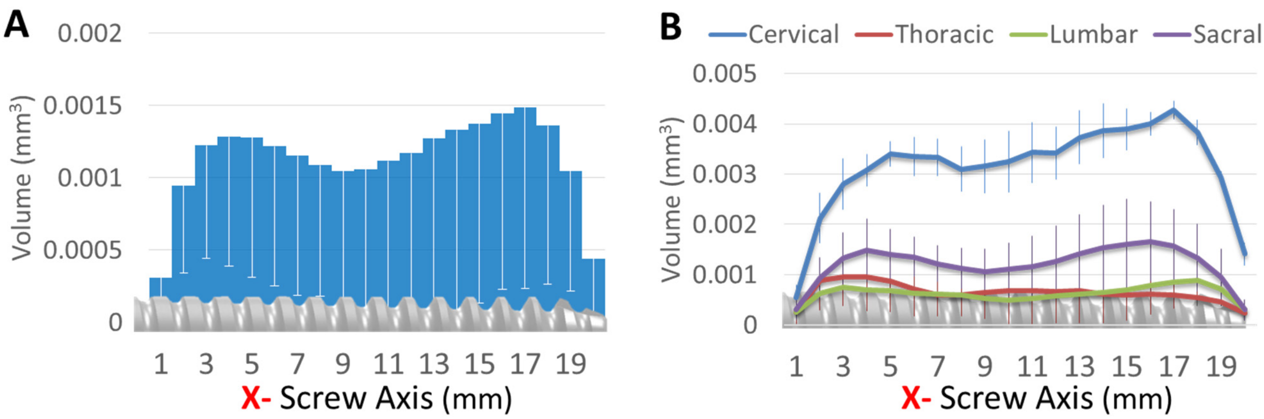


Figure 4.6 Average volume (A) and the volume distribution for each loosening pattern (B) by slice along the X-axis of the screw as calculated for the patterns of unit length (1 mm). Surface area distribution along the screw axis showed similar trends so only the volume distribution is depicted.

The total volume of loosening increased as the spinal region became more caudal (p=0.001, r_s=0.65) and positively correlated with a greater surface area (p<0.001, r_s=0.96) and a longer length (p=0.001, r_s=0.65). Total surface area increased as the spinal region moved more caudal (p<0.001, r_s=0.68) and as a greater length was measured (p=0.003, r_s=0.59). Patient age negatively correlated with the volume of loosening (p=0.04, r_s=-0.44), surface area (p=0.04, r_s=-0.43) and length (p=0.02, r_s=-0.49). However, the cervical region which contained the smallest loosening halos had a much higher age than all other regions (90 vs. 68.0 ± 7.1 years). When the cervical region was omitted, age did not correlate with volume, surface area or length (ps>0.33).

4.3. Discussion

The overall loosening rate, 3.0%, falls within the wide range of loosening rates found within literature (1.3-41%, Table 2.4)[69,80,115,132,143,155,156,168,194,202,217,229,237,240,243]; however, this rate is lower than most reported in the past 10 years. The majority of the loosening rates reported in the last 10 years typically range from 10 to 20% and are rates reported from dynamic stabilization. Dynamic stabilization typically presents with higher loosening rates than rigid instrumentation[237]. The lower rate for the present study corresponds well with the fact that rigid instrumentation is primarily used in the clinic from which the CT scans were received.

Hypothetically, it would make sense that female patients (especially post-menopausal) would exhibit a higher incidence of loosening than males. This is due to (1) the fact that on average, older females have poorer bone quality than their age-equivalent male counterparts and (2) a decreased BMD has been linked with higher loosening rates[229]. Most previous studies do not classify the loosening rates by gender, but in the four studies which do, there was no significant differences in incidence for males and females for the combined 77 patients with loosening[115,155,202,237]. This is seemingly not corroborated in the current study with the high percentage (88%) of loosening halos which belonged to female patients (14 of 16). During the initial radiographic screening only the total number of patients with pedicle screws was noted; the gender was not recorded. Therefore, conclusions about differences in the loosening incidence by gender cannot be fully assessed.

Measured loosening areas and volumes increased by a factor of 10 moving from cranial-to-caudal down the spine (Table 4.3, Figure 4.4). The reason for such great differences is probably multifactorial: in the caudal regions of the spine (1) the screw is generally longer and bigger in diameter, (2) the forces are greater and (3) there is also more trabecular bone for the screw to damage due to the increased vertebral volume. The perceived influence of screw length is supported by the fact that the length of the halo had significant positive correlations with both the volume (p=0.001, r_s=0.65) and surface area (p<0.001, r_s=0.68) of the loosening halo.

Loosing halos were also more prevalent at the ends of the constructs (74%, 17 of 23) than mid-construct (Figure 4.3). In fact every patient had at least one loosening halo located at either the cranial or caudal end of the construct. This corresponds extremely well with literature where either no mid-construct screws were loose[115,168,217,237] or one study which showed 18% of patients had a mid-construct screw loose with all of these constructs also having corresponding marginal loosening[229]. It is also interesting that here not only the rate of loosening increases for the marginal screws but also the volume of loosening was shown to significantly increase by 218% compared to the mid-construct screws within the same construct (p=0.02). Ko et al.[115] hypothesized that the screws on the construct ends experience a higher loading and; therefore, that this might be the reason for the higher prevalence of loosening of the marginal screws. This theory is similar to the often presented explanation of adjacent segment disease: the pedicle screw-rod construct introduces a stiffness gradient along the spine and the joining segment incurs the peak stresses. It would thus be suspected that an increased length of the construct would increase the stiffness gradient and result in an increased chance of the marginal screws becoming loose. Increased rates of loosening have been previously shown for longer constructs[168,229]; however, with the current data set (n=16 patients), the length of the construct was not shown to correlate with the measured loosening parameters.

The combination of (1) the mid-short length constructs were only loose either at the thoracolumbar junction or in the lower lumbar spine and (2) that the highest rates of loosening were near thoracolumbar junction and in the lumbar-sacral regions show these regions are likely to be the most problematic for loosening. Potential reasons for increased incidences in the thoracolumbar junction might relate to the fact that the thoracic spine has the protective rib cage which increases the regional stiffness, perhaps introducing peak stresses on the screws at these junctions. Due to the lower lumbar spine sustaining the highest loading, largest curvature, the most disc herniations, and most often region of reported pain, it is not surprising that loosening is also prevalent in this region.

The region and the curvature of the spine along with the presence of the rib-cage may influence the shape of the failure patterns (all failure patterns shown in Appendix C, Figure 4.5). Peaks at the head or the tip of the screw were seen in 74% of the loosening patterns with the peaks seemingly more distinctive in the areas of high spinal curvature: the cervical and the lower lumbar to upper sacral spine. The upper cervical region and the upper lumbar region both have similar curvature as well as cranial toggle failure patterns. A widening or a butterfly pattern was seen in both the thoracic region which is stabilized by the rib cage as well as in the mid-lumbar region (L3, L4) which is a transition in the spinal curvature. The lower lumbar (L4, L5) and sacral (S1) regions exhibit caudal toggling. More samples are needed to determine if the trends present in this study are generalizable.

Forces and moments imposed on the implants are different for every spine. How the construct is configured during surgery, the native spinal structure and the muscles acting on the vertebra combine to create patient specific loading patterns as observed *in vivo*[17,186,188]. The loading patterns follow general trends but do have distinctive characteristics depending on the particular patient. This is also exhibited here in the observed failure patterns by the fact that patients with multiple halos demonstrated similar patterns for all failed screws. For example, patient 9 presents with widening in all five patterns (some also with minimal cranial toggling) and patient 4 demonstrates primarily caudal toggling in all four halos. If the right combination of forces and moments are combined with the structural anatomy of the vertebrae, potential probable loading situations might be able to be reverse-engineered to fit the observed failure pattern.

The small dip in the center of the average volume distribution indicates the position of an average fulcrum approximately 40-50% down the length of the inserted screw (Figure 4.6). The location of this fulcrum is then approximately 18-25 mm for lumbar samples which roughly corresponds to the average pedicle length. The idea that the end of the pedicle acts as a fulcrum makes sense mechanically and is backed by motion analysis of *ex vivo* toggle loading. Cranial-caudal cyclic loading of the screw has shown a distinct fulcrum within, but towards the end of the pedicle[222,248]. The failure patterns in the sagittal planes of the cervical, lumbar, and sacral regions (Figure 4.4) also suggest that a distinct fulcrum exists, around which the screw pivots upon loading. This pivoting motion creates larger voids in either or both the cranial and caudal directions at the head or tip of the screw. These failure pattern peaks in the sagittal plane suggest that the primary loading is cranial-caudal. This corresponds well with the *in vivo* measured data which quantitatively show that the primary axis of loading is in fact in the cranial-caudal direction[185,188].

The peak at the tip of the average volume pattern is larger than towards the screw head (Figure 4.6), indicating there is a larger tip motion than head motion. The peaks at the tip and the head correspond well to the peaks in stress and strain which are shown to exist at implant ends[122]. Reinforcing the screw in these regions or more evenly distributing the loading may help to mitigate loosening.

The double halo is a dense radiopaque rim of compacted trabecular bone surrounding the screw and is used for the confirmation of screw loosening[57,115]. Fatigue at the bone-screw interface could be indicated by the presence of the double halo. This opaque rim surrounding the loosening halo is not seen around unloaded screws with induced infection and is also not seen in inflammation induced osteolysis of hip or knee implants. Therefore, it is hypothesized here to form from the repeated compaction of the cancellous bone by the loading of the screw. The repeated loading is thought to break the trabecular struts and displace the bone fragments until the motion is small enough to allow bone remodeling to form this continuous rim.

Taking into account both the signs of fatigue (presence of the double halo) and the indication of cranial-caudal loading (presence of a fulcrum with loosening in the cranial-caudal plane), the indicated failure mode would be cranial-caudal fatigue overload of the bone at the interface. Furthermore, the patterns observed during motion analysis of screws in cranial-caudal fatigue loading have been able to produce patterns similar to the failure patterns observed clinically in this study[222]. These factors give further credence for using a cranial-caudal, fatigue loading pattern at the screw head for *ex vivo* testing in order to mimic clinically relevant screw loosening.

All radiographic halos were segmented manually by the same observer. Manual segmentation can lead to bias but it is still considered the gold standard for medical segmentation. The analyses of the segmented halos were performed using a MATLAB script in order to obtain an unbiased, automated analysis of each segmented halo. Figure 4.7 shows a representative sample of the loosening pattern as it appears in the CT scan and as analyzed along the screw's sagittal plane. This rather qualitatively illustrates that the segmentation and analysis process could capture distinguishing characteristics of the loosening patterns.

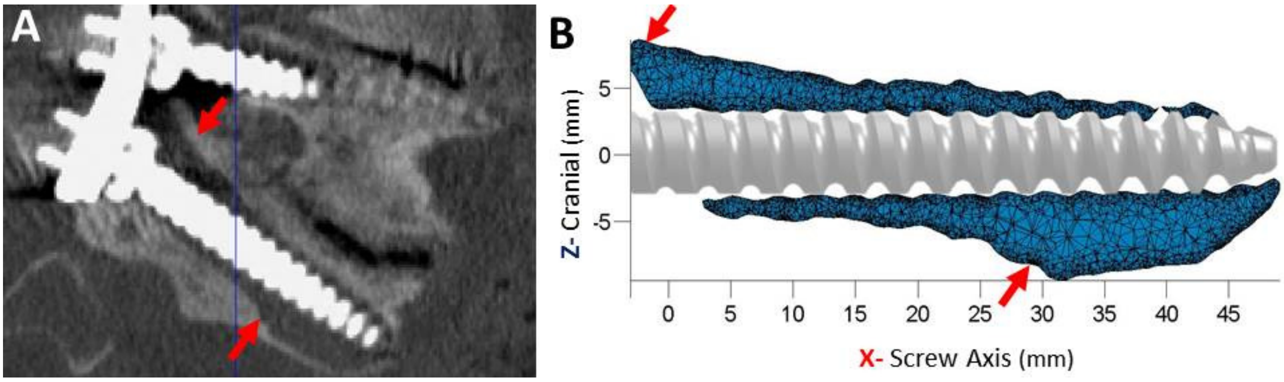


Figure 4.7 A comparative sample showing (A) an artifact-free cross section of the CT scan along the screw axis and (B) the sagittal cross section of the segmented and analyzed loosening halo. Similar maximal and minimal values in the Z (cranial) direction can be observed.

One patient (P11) had screw breakage along the screw axis (Figure 4.8). The portion of the screw which was still attached to the rod still exhibited a radiolucent halo around the axis of the screw (Figure 4.8B & C). This halo was not present for the broken screw tip. The potential disappearance of the halo concords well with the study from Schatzker et al.[199] who showed that if motion at the screw interface is stopped than cancellous bone can grow into the screw threads. Furthermore, it corroborates of theory from Tokuhashi et al.[229] who believed that the disappearance of radiographic halos was due to the halting of motion at the interface after bony fusion. In their study of 190 patients, approximately two thirds of the total radiolucent zones disappeared after two years of progressive follow-up; and 100% of the halos disappeared on the patients which exhibited radiographic bony fusion of the anterior column. The example presented here is unique as it shows that within the same patient and same level (not across patients) that the loosening halo can likely be reversed and bony ingrowth can occur if motion at the interface is terminated.

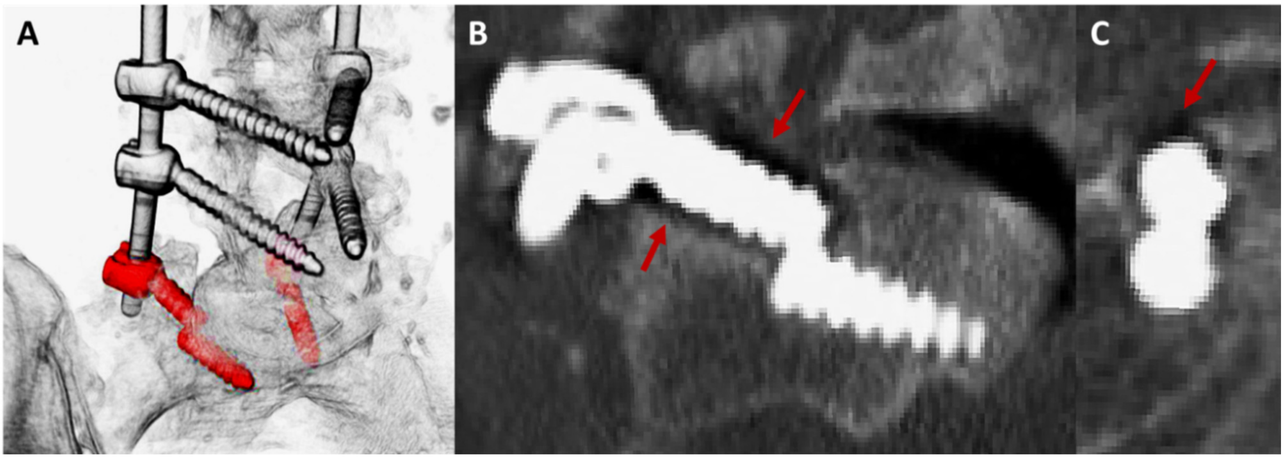


Figure 4.8 A rendered CT image (A) and views of the CT scan in the sagittal cross section of the screw (B) as well as a coronal view (C) directly down the axis of the broken S1 screw in patient 11. Red screws denote the screws which exhibited a loosening halo and arrows show the radiolucent loosening areas around the part of the screw which is still attached to the rod; notice no loosening halo is observed around the broken screw tip.

The very high volumes of loosening in the sacrum of patient 4 (Figure 4.4) could likely be influenced by the fact that the loosening was present for an extended period of time. A CT scan 17 months prior to the analyzed scan exhibited loosening around both screws in the sacrum; loosening then progressed to L5.

There is evidence of screw pullout in the cervical region of patient 2 where a loosening region 2-4 mm past the screw tip was present; however, there is also a cranial fan directly where the screw tip would have been (Figure 4.4-cervical). This pattern suggests a toggling loosening first, followed by a secondary pullout.

Much caution must be taken with these initial results due to the limited sample sizes for each region (n= 3-10). Further, the cervical region of the spine only has samples from one individual and the thoracic from two; additional samples will be needed before confirmation of any trends. Only one radiologist was used in the screening for pedicle screw loosening; therefore, no inter-observer reliability could be assessed for the confirmation of radiographic screw loosening. Additionally, important details such as bone quality, patient history, and specifics about the surgery pertaining to the implants used and reasons for spinal correction are all missing from this analysis until they are received from the clinical correspondents. The loading history of the implant is also unknown. Titanium screws are known to introduce artifacts in CT scans; however, these are much smaller than those for previously used stainless steel implants. The artifacts did not pose a noticeable issue during segmentation. Only in one specimen was there noticeable streaks which occurred at the rod and screw head connection; no disruptive artifacts appeared along the screw axis (Figure 4.7A). Finally, the presence of a radiographic loosening halo does not necessarily correspond to a decrease in the fixation strength of the screw[194]; therefore, extending these results to discussions on construct stability is cautionary. Future work will be needed to increase the sample size, quantitatively validate the method, and to extend the method to gather parameters of the screw-rod construct and the spinal anatomy.

4.4. Conclusions

Methods have been established for a semi-automated process to analyze clinical screw loosening patterns. This allows for a non-invasive, quantitative way to investigate the failure patterns and possible failure mechanisms of screw loosening. The current method can be expanded to determine parameters of the screw-rod construct and vertebral configuration to be able to further study mitigating factors of loosening.

The primary trends detected from this study correspond well with previous studies: a screw loosening rate of 3.0% and a higher incidence of loose screws at the cranial or caudal ends of the construct compared to the mid-construct screws[115,168,217,229,237]. Loosening volumes on the construct ends were significantly larger than volumes of mid-construct loosening within the same patient (p=0.02). The loosening volumes grew by a factor of 10 from the cranial to the caudal spinal regions likely due to increased screw length, vertebral volume, and spinal loading.

Distinct failure patterns were seen in the various spinal regions and could perhaps be related to spinal curvature, spinal region, and location within the construct. The graph of the average loosening volume distribution (Figure 4.6) established the presence of a fulcrum and two peaks of loosening volume were seen near the screw tip and head. Reducing or more evenly distributing the loading along the screw axis might be key to reducing these peaks and improving screw stability within the bone. Evidence of trabecular ingrowth around a broken screw tip further suggests that radiographic loosening can be reversed if interface motion is terminated.

Presented here is the first quantitative clinical evidence of the existence of a fulcrum around which the screw pivots in the cervical, lumbar, and sacral spine. Failure patterns suggest the primary amount of loosening is in the cranial-caudal plane. These findings combined with the presence of a double halo indicate that repeated toggle loading is likely the driving failure mode for pedicle screw loosening, rather than the often tested axial pullout. Now there is further evidence to support the notion that fatigue, toggle loading of screws is the more clinically relevant testing model for loosening of pedicle screws as it has previously been suggested in the literature[19,39,42,112,129,155,156,199].

Chapter 5.
Pre-Clinical Testing Methods

Posterior spinal fixation with rod and screw based instrumentation is a commonly used technique for a variety of symptoms including: vertebral fracture, spondliolysthesis, and scoliosis. Loosening at the interface has been shown to be a predominant failure mechanism and its prevalence is on the rise in the recent years[57,90,202]. This is especially important given the increasing prevalence of bone quality related diseases and difficulties associated with maintaining fixation at the bone-screw interface in our aging population. To improve the success of these procedures it is important to gain an insight into loosening mechanisms and to be able to quantitatively describe failure patterns. Three categories of complexity can be optimized in testing design: a reduction of (1) the mechanical equipment necessary (2) the medical materials needed (the number of implants needed for each test) and (3) the testing time. Reduction of testing complexity within these three categories while maintaining testing sensitivity would be the goal for determining an ideal testing method.

Many testing methods are available in literature which attempt to parameterize screw fixation; however, current methods generally are lacking with respect to at least one of the following: (1) the ability to mimic *in vivo* loading (2) the use of non-standardized methods, typically a different protocol is used for every study and (3) the measured parameters do not reflect clinically observed loosening. Repeatable methods which place physiologic loading on the bone-screw interface and allow for the operationalization of loosening are missing from the literature. This study setup is designed to compare the repeatability, sensitivity and clinical appropriateness of three purposed protocols for the parameterization of screw loosening.

The strength of the fixation at the bone-screw interface is usually studied using one of two different biomechanical tests: (1) a standard axial pull-out method (ASTM F 543-01 A3[8]) or (2) a type of toggle testing which applies a cyclic, fatigue loading to the screw head and causes a cranial-caudal wear pattern within the vertebra. The basic axial pull-out method does allow for the determination of an initial fixation strength and stiffness, however, it does not mimic *in vivo* loading or failure modes within the spine[129]. Toggle testing is considered more physiological than pure axial pullout[19,58,199] since it better replicates the *in vivo* forces and moments that have been shown to exist[185,188]. Furthermore, it can produce a pattern of failure that appears similar to those seen in the X-rays from clinics (Chapter 4)[115,229].

Recently the American Society for Testing and Materials (ASTM)[9] modified the F 1717 standard for use in fatigue testing of the bone screw interface[153,205]. The method was initially designed to test the mechanical strength of the metal constructs and thus only used extremely durable UHMWPE for the modelled, simplified vertebra. The UHMWPE vertebrae, which are traditionally used for testing, are linear elastic in the loading range and; therefore, cannot reflect the loosening damage at the bone-screw interface. Recent studies have modified the bottom vertebra to either include a human vertebra[205] or polyurethane (PU) foam models[153] in order to analyse damage (loosening) progression.

For determining the potential clinical relevance of pre-clinical, comparative testing with foam it is important to know the reasons why polyurethane foam theoretically makes a good mechanical model of trabecular bone. PU foam models have been shown to have a high uniformity and consistency in their material properties allowing for greater uniformity and reproducibility[121,208]. PU foam generally has similar macroscopic structures and stress-strain behaviour as cancellous bone (Figure 5.1). The overall macroscopic structures of both cancellous bone and PU foam are visually similar and consist of a network of interconnecting rods and plates (Figure 5.1A & B, caution no scale is given in the visual comparison). However, bone contains an open porosity whereas PU is a closed cell structure[208]. Furthermore, foam lacks hierarchical and inhomogeneous architectural features and only contains one solid porous material explicitly neglecting the liquid phase which is present in bones[50]. PU foam makes for a good testing material if reproducibility is paramount and only comparable results are required[208]. If more realistic, absolute values are necessary, then the proper internal structures and viscoelastic properties provided by biological samples is most likely required.

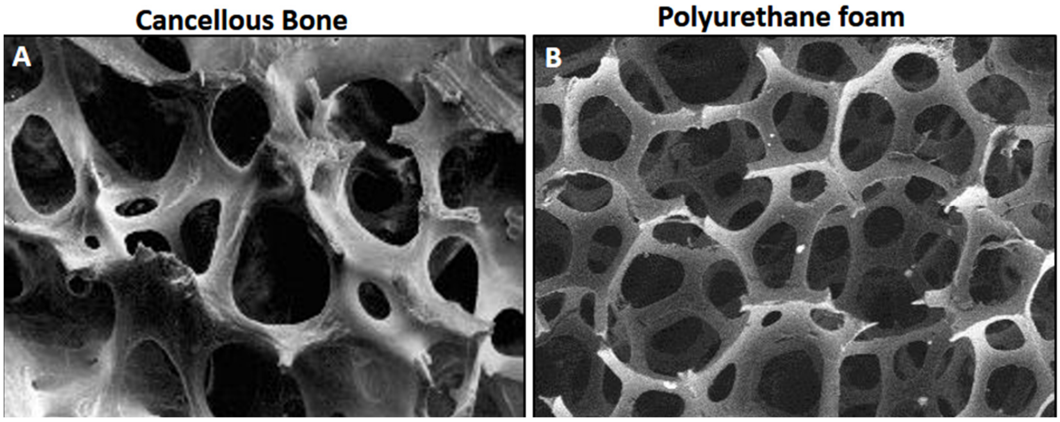


Figure 5.1 Qualitative comparison of the microstructure (A & B). [Adapted from Shim et al.[208]].

The stress-strain behaviour of PU foam and cancellous bone both consist of three distinct regions: (1) linear elastic (2) plateau (3) densification[208]. The linear elastic region represents the recoverable damage of the bending of the cell wall or trabecular struts. Further increases in strain are associated with a reduction in stiffness before the start of the plateau region in cancellous bone. The plateau region is the non-recoverable compressive collapse of the struts. The densification region is the area where the collapsed trabecular struts or cell walls contact and then compact causing a steep increase in stress per unit strain. The second and third regions of the curve are important because they illustrate how foam is a material which can sustain irreversible damage. This allows for the damage progression at the screw-bone interface to be quantified and parameterized.

Many studies have thoroughly investigated PU foam properties for use in biomechanical testing[31,220,221,227] and in 1997 the ASTM F1839[10] standard legitimized their use for pre-clinical orthopaedic device testing. Introduction of this standard brought on a rapid increase in biomechanical studies using foam: ranging from use in pelvis studies, metatarsal osteotomies to screw thread optimization[30,70,121,145,154,208]. More recently, composite bones have been created which have a layer of epoxy resin fiber glass surrounding the PU foam to mimic a cortical shell. These composite bones have been shown by Zdero et al.[246,247] to provide a satisfactory biomechanical equivalent to human bone for studying the pullout strength of the bone-screw interface. Since foam can also sustain irreversible damage it is a suitable material for studying how fatigue failure may progress at the bone-screw interface. Especially when comparative testing is required (rather than tests using absolute values), PU foam models offers a practical alternative to real bone due to heightened reproducibility and availability[208].

The goal of this study was to classify three proposed pedicle screw fixation testing methods based on their precision, sensitivity, and their biomechanical and clinical appropriateness. In addition, two variations of a simplified, composite foam vertebral model were used to mimic healthy and osteoporotic bone. The test method of axial pullout, though the most extensively tested in literature, was excluded from this investigation due to the lack of clinical evidence in terms of sparsely reported pullout failures as well as no evidence of axial loading being a primary direction of *in vivo* forces. A secondary goal, was to verify a method of parameterizing screw motion during *ex vivo* testing.

5.1. Methods

The study utilized simplified composite foam vertebrae of two different foam densities (*normal* and *osteoporotic*) with three different testing methods (*toggle*, *moment*, and *ASTM*). The different loading protocols followed a step-wise decrease in mechanical complexity. Five samples of each simulated bone quality were loaded using each testing method in order to ascertain repeatability/precision, sensitivity, and the appropriateness of the testing methods. Repeatability was quantified in terms of the relative standard deviation, sensitivity as the test's ability to distinguish between *normal* and *osteoporotic* foam, and the biomechanical and clinical relevance was a qualitative measure of each test's ability to reproduce *in vivo* loading and failure patterns.

5.1.1. Materials

The geometric dimensions of the foam samples used in this study were modeled after a simplified lumbar vertebra and taken from the ASTM 1717 standard[9] (Figure 5.2). Each foam model consisted of two distinct materials: a short fiber filled epoxy and a polyurethane foam (Sawbones Europe AB, Malmo, Sweden). The 1.64 g/cm^3 epoxy was used to coarsely mimic a 2 mm thick cortical shell (Figure 5.2). The polyurethane foam was made of one of two different densities in order to represent either *normal* (0.24 g/cm^3) or *osteoporotic* (0.08 g/cm^3) bone. A 2 mm thick vertebral pedicle canal was simulated by the addition of a 15 mm long epoxy tube filled with PU foam (Sawbones, 10 mm outer Ø, 6 mm inner Ø) and angled at 15° from the sagittal plane. The foam models were bilaterally instrumented with the same commercially available, titanium alloy pedicle screws (tangoRS™, ulrich medical®, Ulm, DE, length: 50 mm, diameter: 5.5 mm). Screws were implanted directly down the pedicle canal leaving a 12 mm spacing from the cortical wall to the apex of the screw head (Figure 5.2).

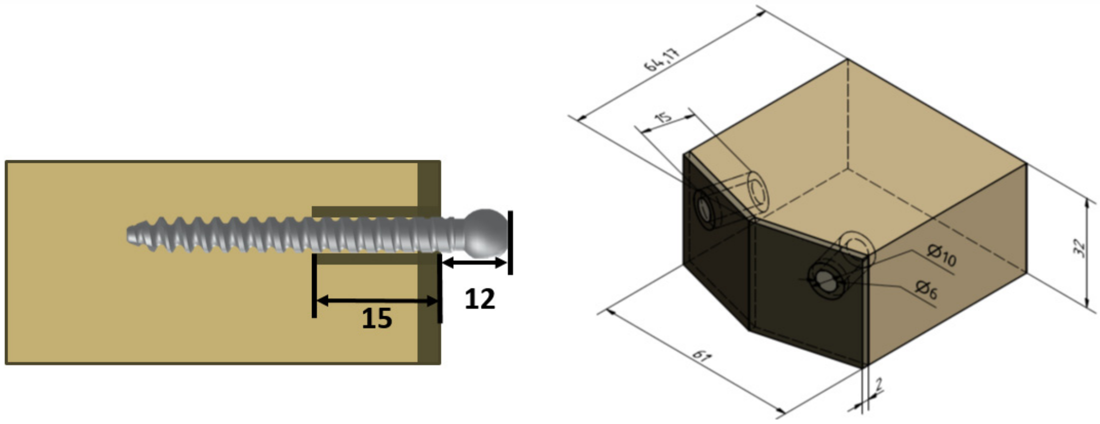


Figure 5.2 A depiction of the composite foam models. Left shows an implanted tango RS screw, the simulated pedicle canal, and the modeled cortical (dark brown) and cancellous bone (tan). Right shows the dimensions of the foam model in 3D (from Nowak[153]).

5.1.2. Test Setup

The test setups were designed to reduce complexity in a step-wise manner (Figure 5.3). The first method used a two vertebrae system including four screws and two connecting rods (*ASTM*), the second used only one vertebra while applying similar forces and moments as the ones produced in the *ASTM* setup to a moment arm attached to the screw head (*moment*). The last test method applied the loading directly onto the screw head utilizing no moment (*toggle*). Five *normal* and five *osteoporotic* foam samples were used for the *ASTM* testing. The *moment* and the *toggle* testing shared *normal* (*n*=5) and *osteoporotic* (*n*=5) samples: one method was run to completion on one screw, then the contra-lateral screw was loaded using the other test method. The testing order was assigned randomly.

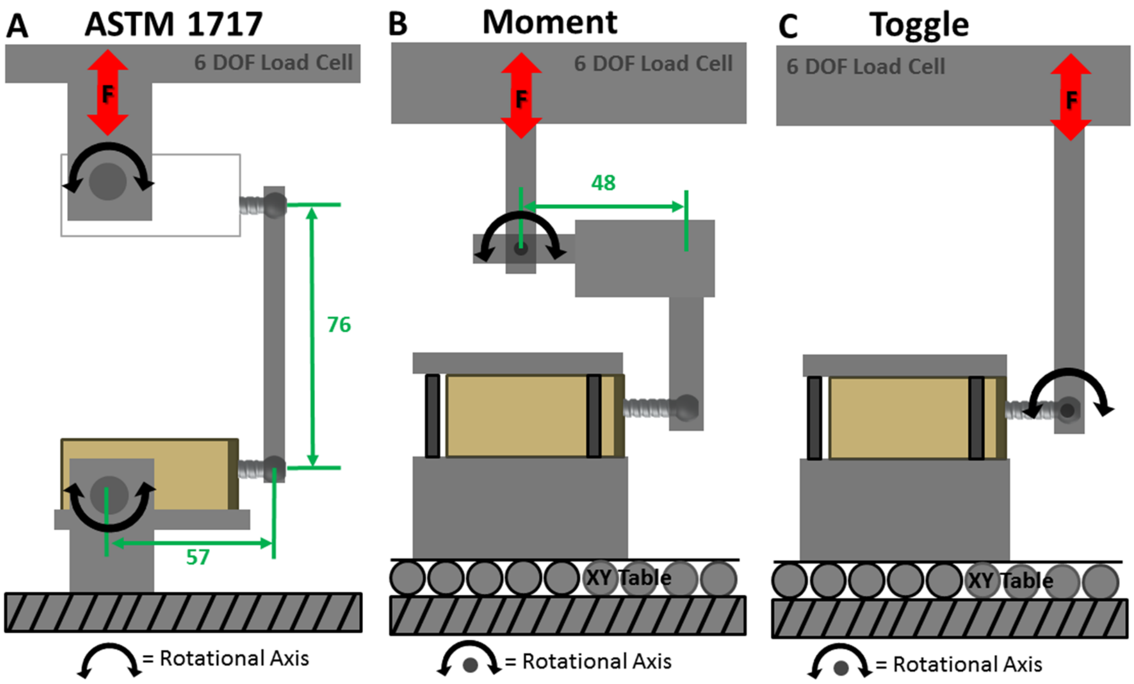


Figure 5.3 Schematics of the three test setups: (A) *ASTM*, (B) *moment*, and (C) *toggle.* Dimensions shown in green are in millimeters.

ASTM

The *ASTM* testing apparatus and all the foam models were produced in the responsibility of ulrich medical® (Ulm, DE). The dimensions and setup of the vertebrae, screws, rods, and testing apparatus were similar to specifications outlined in the ASTM 1717 standard[9]. Two parameters were purposely altered from the standard methods: the material of the bottom vertebra and the loading protocol. The composite foam model (Figure 5.2) was used as the bottom vertebra replacing the standard UHMWPE vertebra. Foam was used so that the damage inflected by the screw at the interface could be quantified later. The specimens were mounted into a servohydraulic testing machine (Zwick/Roell, Amsler HC 25, Ulm, DE, Figure 5.3A). First, a ramp loading from 0-100 N at 20 mm/min was applied. Directly after the ramp loading, a cyclic, sinusoidal loading from 100-266 N was applied for 40,000 cycles at 1.83 Hz. The loading parameters were set to approximate human gait: walking continuously for 1.5 months at a rate of 110 steps per minute. The force range used was within those measured *in vivo*[181]. Force and displacement data was collected at the peak of the first cycle and then at the minimum and maximum of every 5th cycle.

Moment

For the second method, *moment*, the foam vertebrae were clamped to a servohydraulic testing machine (858 Bionix®, MTS, Eden Prairie, MN, USA). A sinusoidal, cyclic (1.0 Hz) compressive force was applied starting from 50-75 N increasing by 0.01 N every cycle to 133 N after 5800 cycles. Force, moment, displacement and motion data collection occurred continuously at 102.4 Hz. The force was applied to a custom made lever arm (48 mm) which attached directly to the screw head (Figure 5.3B). The lever arm was rigidly connected to the screw head and was attached to the servohydraulic testing machine with an axis that was free to rotate around the transverse axis with all other degrees of freedom (DOF) fixed. This allowed motion only in the cranial-caudal plane.

Toggle

Toggle testing was performed with the same loading protocol, user, and testing machine as was used in *moment* testing. The only change was the location of the load application (Figure 5.3C). The moment arm was removed and the load was applied directly at the screw head with rotation only allowed along the transverse axis, thus, again only permitting motion in the cranial-caudal directions.

Screw Motion Data (Moment and Toggle Testing)

A motion capture system (Vicon-460, Vicon Motion Systems, LA, USA) was used to record the three-dimensional motion of the screw (frame rate: 102.4 Hz) relative to the vertebral sample for the *toggle* and the *moment* testing. The axis of the tested screw was defined by a set of 3 markers (Figure 5.4). The foam vertebra and x-y-table motion was captured with marker sets attached to the contralateral screw head and the base of the x-y-table.

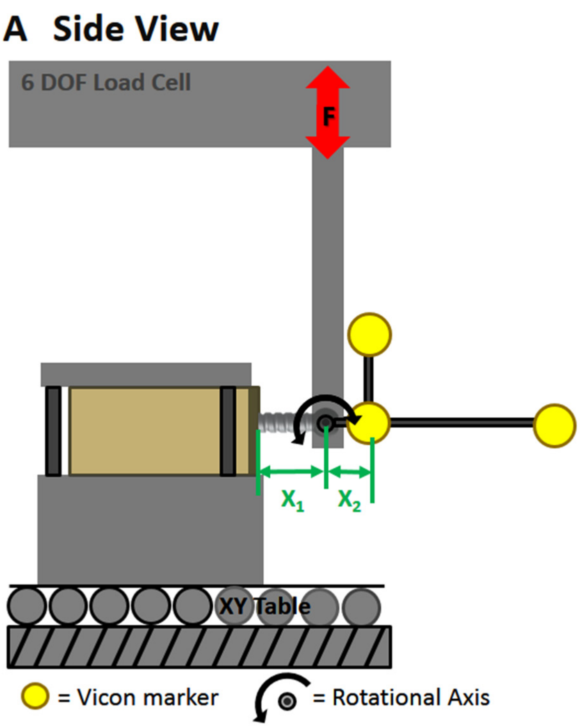


Figure 5.4 A schematic of the vicon marker setup which was used to capture the motion of the screw. The *toggle* configuration is shown; however, the same setup was used with *moment* test method.

5.1.3. Measured Parameters

Displacement, *initial stiffness*, *final stiffness* and the failure pattern were the output parameters. *Displacement* was measured as the maximum displacement for each sample. *Adjusted displacement* was defined as the maximum displacement minus the initial displacement (from the first cycle). For *ASTM,* the *initial stiffness* was measured at the end of the ramp loading cycle by taking the maximum force divided by the maximum displacement. *Initial* and *final stiffness* was calculated for the *moment* and *toggle* methods by calculating the average slope of the linear best fit of the force-displacement curve for the first and last five cycles respectively. To ensure only the linear portion of the force-displacement curve was used, the first and last 10% of data points from each loading cycle were excluded from analysis.

Quantifying Pedicle Screw Motion

Failure patterns at the bone-screw interface were observed via three methods for the *moment* and *toggle* samples: (1) an estimated loosening area using dimensions measured directly from sectioned foam models (2) using a method of image segmentation (3) via reconstruction from the motion capture data collected during testing[151]. The tested samples underwent planar grinding until the midline of each screw axis was reached. Dimensions of the foam vertebra and the failure patterns, the area of damaged foam, were then measured using standard calipers. An estimated failure area ($Area_{Fail}$) was calculated by adding the area of a rectangle using the height of the pedicle canal (*a*= 6 mm) by the depth of screw penetration (*b*) with the area of a triangle that extended from the end of the pedicle canal (*c*= 15 mm) and down to the failure pattern width at the screw tip (*d*, Figure 5.5, Equation 5.1).

$$Area_{Fail} = ab + 0.5(b - c)(d - a) \quad \text{(Equation 5.1)}$$

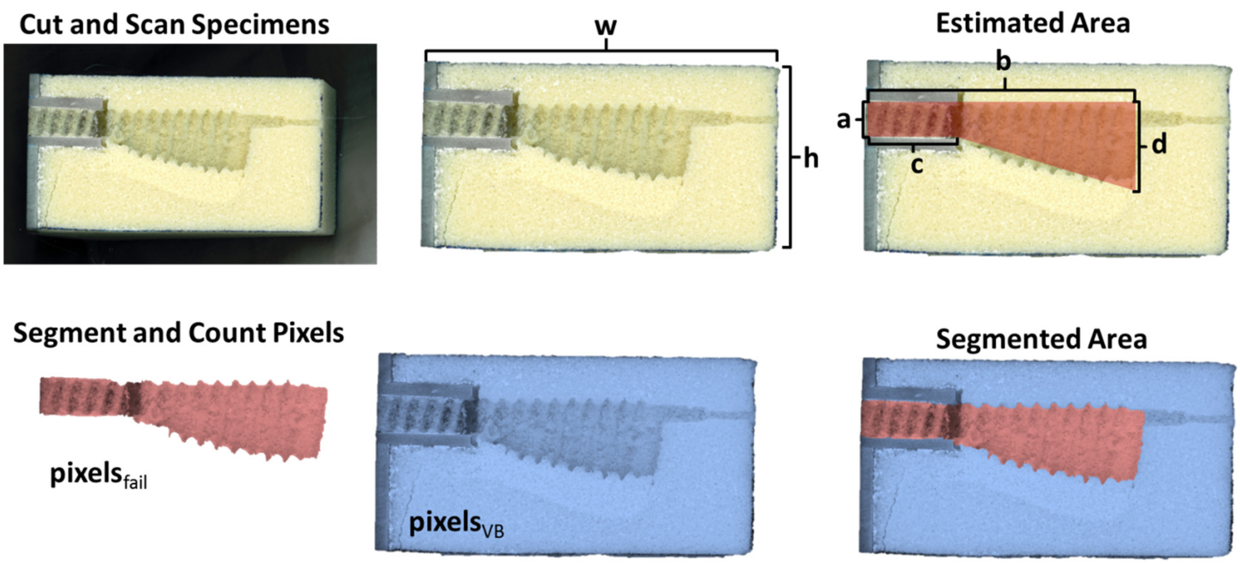


Figure 5.5 The methods used to determine the area and dimensions of the failure patterns from the cut foam samples.

A segmented failure area (*SegArea*$_{Fail}$) was then calculated utilizing image based segmentation techniques (Figure 5.5). After grinding to the midline, the samples were scanned to ensure planar images with direct lighting (1200 dpi, Model MFC-9840CDW, Brother, Nagoya, JP). The entire foam vertebral area and the failure pattern were segmented from the images using a semi-automatic tool implementing the GrabCut segmentation algorithm (Microsoft Office 2013, Redmond, WA)[190,191]. The number of pixels in the segmented failure area ($pixels_{fail}$) and for the foam vertebra ($pixels_{VB}$) were counted (GIMP 2.8, Berkley, CA, USA). The proportion of the $pixels_{fail}$ to the $pixels_{VB}$ were multiplied by the area of the foam vertebra to obtain the failure area (*w*= width, *h*= height, Equation 5.2).

$$SegArea_{Fail} = \frac{pixels_{fail}}{pixels_{VB}}\, w\, h \qquad \text{(Equation 5.2)}$$

The three-dimensional motion data was transformed from the global coordinates to a local, screw-based coordinate system with its origin at the screw head, x-axis oriented along the screw axis and the z-axis directed cranially (Figure 5.6). The displacement pattern of the screw axis was then plotted for the maximum and minimum of each cycle, assuming the screw to be a rigid body. A toggling screw motion pattern emerged with a distinct fulcrum. This fulcrum was defined as the *pivot point* which was mathematically defined as the distance from the screw head to where the failure pattern was the narrowest in the z-direction (Figure 5.7). It was calculated by determining the height of the screw axis in the z-direction for all frames in 0.1 mm increments along the screw axis (x-axis). The fan width at the screw tip (*tip motion*) and the screw head (*head motion*) were also calculated.

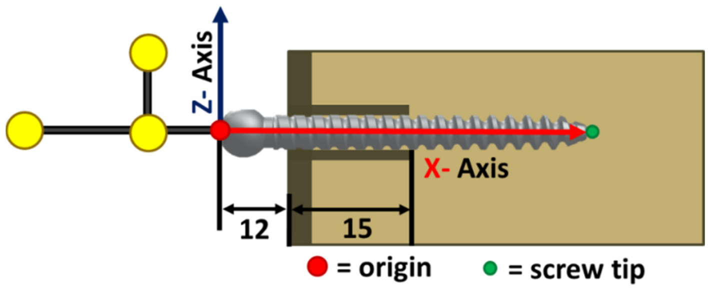


Figure 5.6 The coordinate system after translation and rotation to the screw head.

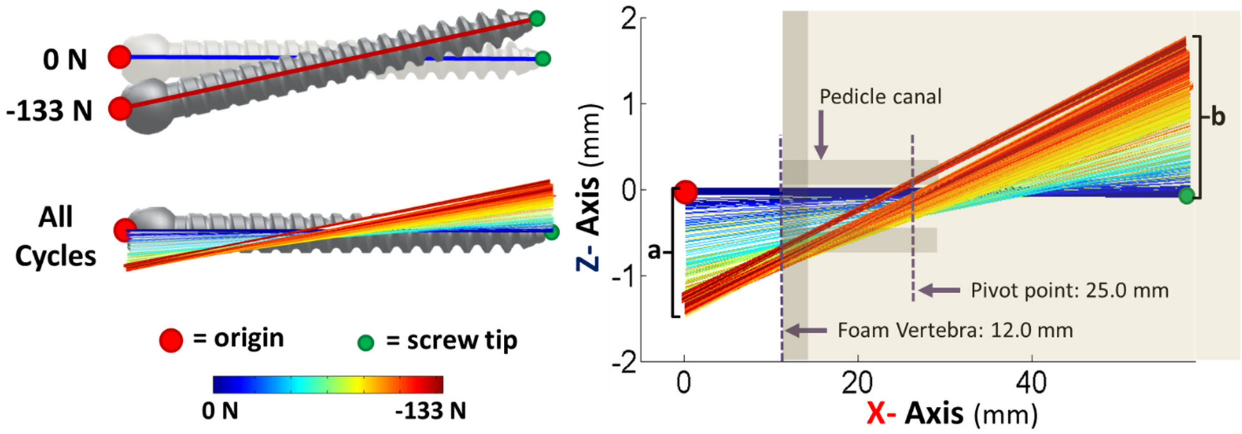


Figure 5.7 Motion analysis of the screw. A typical toggling motion pattern from a single specimen is shown along with the measured parameters of *pivot point*, *head motion* (a), and *tip motion* (b). Notice the increase in head and tip displacement with the increasing force applied (pattern becomes more red with higher forces)[151].

5.1.4. Statistical Analysis

Statistical evaluations were performed (SPSS Statistics 20, IBM Corp., Armonk, NY) with a type I error probability set to 5%. Repeatability of the testing methods was obtained by measuring the standard deviation and the relative standard deviation across the 5 specimens for each test method. The relative standard deviation was used because the results suggested that it was appropriate; it is calculated as the standard deviation divided by the average value. A t-test was used to determine whether bone quality had a significant impact on the measured parameters for each testing method. Effect size magnitude was represented by adjusted R^2 values for correlations, to account for the small sample sizes.

5.2. Results

5.2.1. Displacement and Stiffness Calculations

The *ASTM* method showed the largest *displacements* for all methods for *normal* bone and the second highest *displacements* for *osteoporotic* (Table 5.1). The *ASTM* method had lowest relative variability for both *displacement* and *initial stiffness* ranging from 4.31-13.21% of all the testing methods. The average relative standard deviation of the *displacement* for *normal* samples was 4.31% and 6.10% for *osteoporotic*. However, these values increased to 10.0% and 14.8% when adjusting for the initial *displacement*. The *initial stiffness* of the *ASTM* testing method was the lowest of all three test methods for *normal* and *osteoporotic* samples with a variation of 2.38% and 13.21% respectively. The *ASTM* method was able to detect differences between bone quality when measuring *displacement* (p=0.003, R^2=0.65) but not for *initial stiffness* (p=0.46). If testing was stopped at 10,000 cycles (a 75% reduction of testing time), the *displacement* measured for *normal* samples would have been 10.25 ± 0.43 mm (4.22% relative standard deviation) and 11.57 ± 0.67 mm (5.83% relative standard deviation) for *osteoporotic* samples (Figure 5.8). A significant difference between *normal* and *osteoporotic* bone types was still present (p=0.006, R^2=0.58).

Table 5.1 Means, standard deviations, and relative standard deviations given for the primary measured parameters grouped by testing method (*ASTM, moment, toggle*) and bone quality (*normal* & *osteoporotic*). A between samples significance value is given to show whether the method was sensitive enough to detect differences in the simulated bone quality for each measured variable.

			Normal		***Osteoporotic***			
		N	Mean ± *SD*	Relative *SD* (%)	Mean ± *SD*	Relative *SD* (%)	Sig.	R^2
Disp. (mm)	*ASTM*	5†	10.3 ± 0.4	4.3	11.9 ± 0.7	6.1	0.003	0.65
	Moment	5	4.7 ± 1.4	28.9	14.1 ± 1.9*	13.4*	<0.001	0.90
	Toggle	5	0.9 ± 0.3	31.8	1.4 ± 0.4	27.9	0.04	0.27
Adjusted Disp. (mm)	*ASTM*	5	-3.3 ± 0.3	10.0	-4.5 ± 0.7	14.8	0.007	0.58
	Moment	5	-2.8 ± 0.5	18.3	-11.4 ± 1.3*	11.7*	<0.001	0.95
	Toggle	5	-0.4 ± 0.1	30.3	-0.4 ± 0.1	19.1	0.53	-
Initial Stiffness (N/mm)	*ASTM*	5	27.9 ± 0.7	2.4	27.8 ± 3.7	13.2	0.46	-
	Moment	5	82.8 ± 13.3	16.1	54.0 ± 32.1	59.3	0.05	0.21
	Toggle	5	497.1 ± 127.9	25.7	502.0 ± 70.5	14.1	0.47	-
Final Stiffness (N/mm)	*ASTM*	5	- ± -	-	- ± -	-	-	-
	Moment	5	76.8 ± 14.7	19.2	68.7 ± 44.1	64.2	0.35	-
	Toggle	5	565.8 ± 78.5	13.9	624.9 ± 126.5	20.2	0.20	-

†One *osteoporotic* specimen was discarded (an outlier > 4 *SD* from mean) and replaced with an additional specimen.
*For *moment* samples, testing was stopped before 5800 cycles if the displacement reached 15 mm. *SDs* may, therefore, not be an accurate reflection of the true variance and statistical tests should be interpreted with caution.

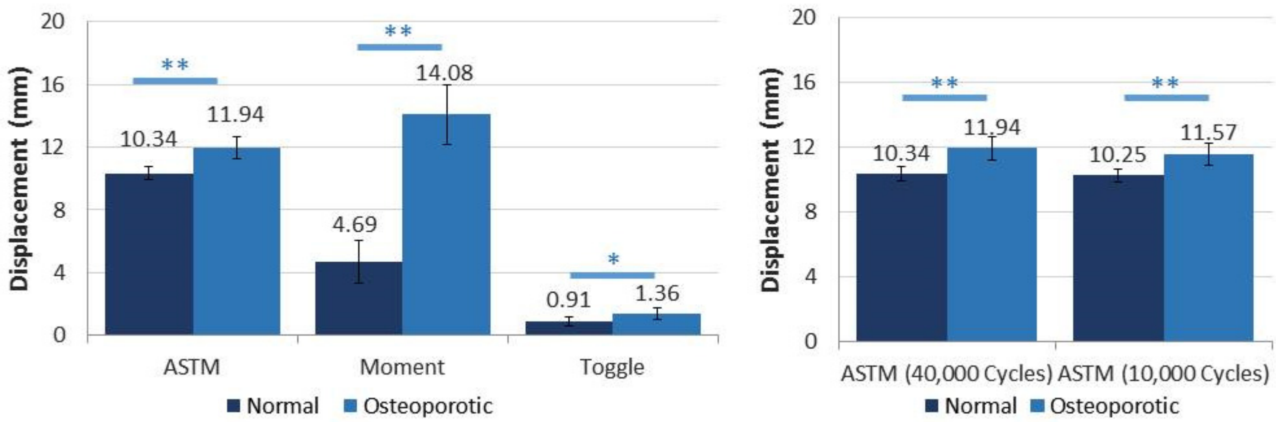


Figure 5.8 Bar charts of the *displacement* measured for each testing method (left) and for the ASTM method at a full 40,000 cycles and at 10,000 cycles (right). *Normal* samples are depicted in dark blue, *osteoporotic* in light blue. Error bars are the SD.

The *moment* test method had the second highest *displacement* (4.69 ± 1.36 mm) for *normal* samples and the highest (14.08 ± 1.89 mm) for *osteoporotic* samples (Table 5.1). For *normal* specimens it had the second lowest inter-specimen variability for *displacement* (28.88%) and had the highest variance according to *stiffness* (16.05-64.24%). When adjusting for the *initial displacement* the variability in *displacement* was reduced to 18.3% for the *normal, moment* samples. The *moment* setup was able to detect differences between bone quality when comparing *displacement* (p<0.001, R^2=0.90) and *initial stiffness* (p=0.05, R^2=0.21).

The *toggle* test method had the lowest *displacement* for both *normal* (0.91 ± 0.29 mm) and *osteoporotic* (1.36 ± 0.38 mm) samples (Table 5.1). It had the worst inter-specimen variability for *displacement* (27.90-31.77%) and generally less variance than *moment* testing when considering *stiffness* (14.05-25.73%). *Toggle* testing was the stiffest of the testing methods when comparing both *initial* and *final stiffness*. *Toggle* was able to detect differences between bone quality when measuring *displacement* (p=0.04, R^2=0.27) but not for *initial stiffness* (p=0.47). A significant positive correlation was present between the *displacement* measured with *toggle* and with *moment* testing (p=0.03, R^2=0.28).

5.2.2. Biomechanical Relevance

Biomechanical appropriateness can be qualitatively estimated by the degree to which the mechanical setup can mimic the *in vivo* loading on the head of the screw. For this reason, a summary of the average maximum values of an *in vivo* walking loading[17] on a spinal fixator for five patients and 11 data samples is given in Table 2.5. All of the tested loading modalities in the current experiment had a primary load in the same direction (Z-axis) and of similar average magnitude to the *in vivo* loading shown in (Table 2.5 & Table 5.2). When comparing the loading protocols to *in vivo* data, *toggle* testing is the least physiologic as it does not apply any moments at the screw head. The applied moments at each screw head for the *ASTM* and the *moment* testing were comparable (Table 5.2) but their maximum slightly exceeded the values seen *in vivo* during walking (Table 2.5). Therefore, the biomechanical relevance is considered comparable for the *moment* and *ASTM* test setups.

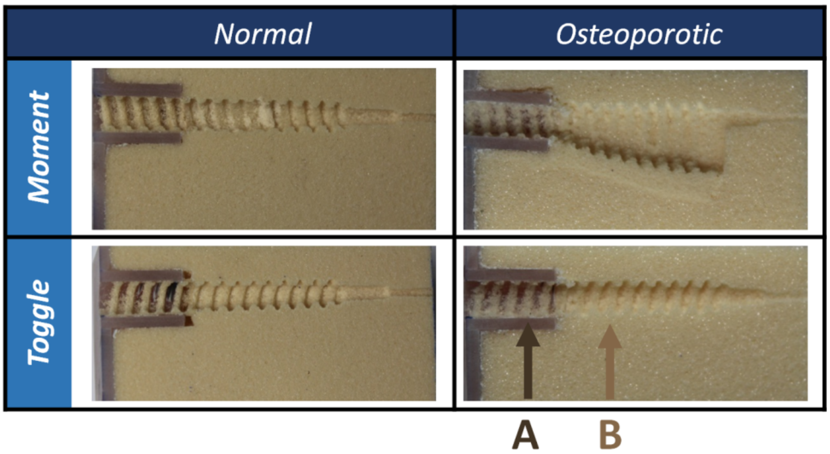
Table 5.2 Estimates of the forces (F) and moments (M) seen at the screw head for the three testing methods.

	Peak Load	F_x (N)	F_y (N)	F_z (N)	M_x (Nm)	M_y (Nm)	M_z (Nm)
ASTM	50 N	0	0	50	-2.8	-0.6	0
	133 N	0	0	133	-7.5	-1.6	0
Moment	50 N	0	0	50	-2.3	-0.6	0
	133 N	0	0	133	-6.2	-1.7	0
Toggle	50 N	0	0	50	0	0	0
	133 N	0	0	133	0	0	0

5.2.3. Failure Patterns and Areas

Since there was no observable damage to any of the *normal* samples for either testing method (*toggle* or *moment*, Table 5.3), only comparisons between the *osteoporotic* samples were used for the motion and image segmentation analysis. Furthermore, only three of the five *osteoporotic*, *moment* samples were able to be analysed because the motion capture data was unusable in two samples due to overlapping markers.

Table 5.3 Photographs of representative cross sections of the composite foam vertebrae along the screw axis. They show the failure patterns observed for the *toggle* and *moment* testing for both *normal* and *osteoporotic* bone. The cortical shell is denoted by (A) and the cancellous core by (B).



Observable differences in the failure pattern can be seen for the *moment* test between the *osteoporotic* and *normal* samples for both the images of the cut samples (Table 5.3) and with the vicon motion patterns (Figure 5.9). No macroscopic failure pattern difference can be seen for the different foam densities for the *toggle* tested specimens (Table 5.3). The vicon failure patterns show different motions of the screws for the *toggle* and *moment* testing (Figure 5.9). In the *toggle* testing the head of the screw went in the negative Z direction with the tip in the positive. The *pivot point* was located towards the end of the simulated pedicle canal at 25.0 ± 8.9 mm (the end of pedicle canal is located at 27 mm). The screw motion pattern for the *moment* samples shows the screw head moving in the positive Z direction with the tip descending into the foam vertebra (Figure 5.9). The *pivot point* for the *moment* samples was located posterior to the initial starting point of the screw head (-12.8 ± 1.3 mm). The *tip motion* was much larger for the *moment* samples (10.4 ± 0.3 mm) compared to the *toggle* samples (1.9 ± 0.5 mm); whereas, the *head motion* was similar (1.5 ± 0.2 mm vs 1.7 ± 0.5 mm). The manual measurements of the *tip motion* using standard calipers was larger than the vicon tip motion measurements (13.8 ± 0.2 mm *vs.* 10.4 ± 0.3 mm, Table 5.4).

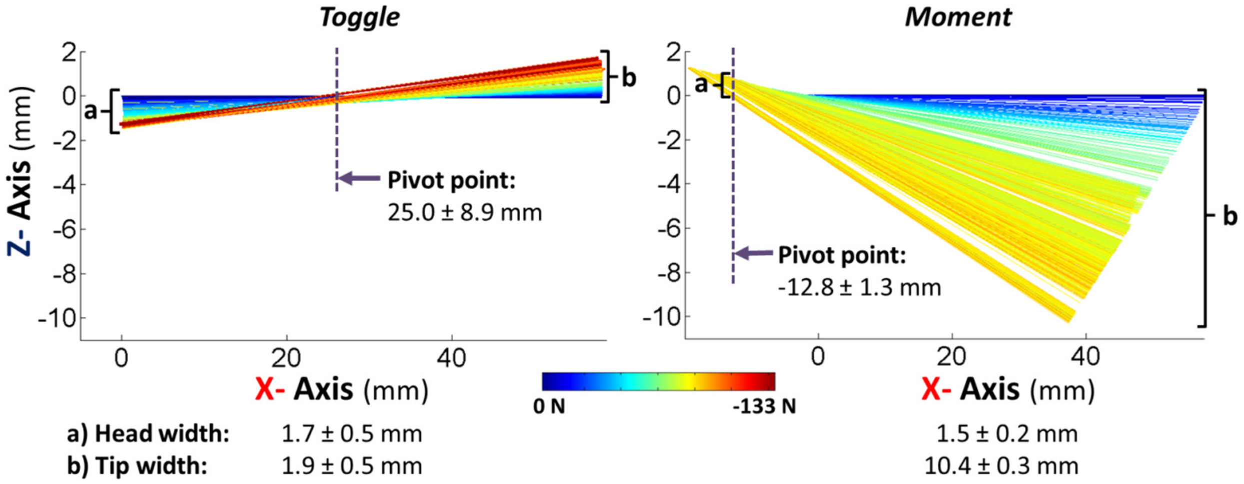


Figure 5.9 The average vicon failure patterns for the *osteoporotic toggle* (*n*=5), and the *osteoporotic moment* (*n*=3*) samples. *Two osteoporotic moment samples could not be analyzed due to unusable collected data due to overlapping markers.

Analysis of the failure pattern areas showed similar averages for the three measurement methods and all were within 2.5% of each other (between 355-364 mm^2, Table 5.4). The magnitude of the $Area_{Fail}$ and the $SegArea_{Fail}$ followed the same trends for all three samples; however, the $Area_{Vicon}$ did not. The lowest value for $Area_{Vicon}$ was the highest for both $Area_{Fail}$ and $SegArea_{Fail}$.

Table 5.4 A comparison of the areas calculated manually with calipers ($Area_{Fail}$), via image segmentation ($SegArea_{Fail}$) and with motion analysis data ($Area_{Vicon}$) for the three usable *osteoporotic moment* samples. Furthermore, tip motion measurements are given for the manual (*tip motion*$_{Manual}$) and the vicon measurements (*tip motion*$_{Vicon}$).

	$Area_{Fail}$ (mm^2)	$SegArea_{Fail}$ (mm^2)	$Area_{Vicon}$ (mm^2)	Tip $Width_{Manual}$ (mm)	Tip $Width_{Vicon}$ (mm)
Sample 3	345	343	369	13.6	10.4
Sample 6	375	372	345	14.2	10.1
Sample 9	345	365	378	13.8	10.7
Average	355 ± 12.4	360 ± 13.9	364 ± 14.1	13.8 ± 0.2	10.4 ± 0.26

5.3. Discussion

The first topics of discussion will be the abilities of the test setups to replicate results (repeatability) and the sensitivity of the setup in terms of detecting differences in the material quality (foam density). The term sensitivity, as discussed in this section, is not in the normal engineering or statistical definition. Sensitivity, for this study, is defined as the relative ability of each testing setup to detect differences between the material quality (*normal* vs. *osteoporotic*). The discussion will then shift to how well the test setups were able to reproduce *in vivo* loading patterns (biomechanical relevance) and their qualitative similarities of the foam failure patterns to the clinical failure patterns (clinical relevance). These discussions will lead to conclusions on probable advantages and disadvantages of each of the testing methods with identified areas to target for improvement.

5.3.1. Repeatability and Sensitivity

All three testing methods were able to significantly detect the change in the cancellous material by comparing the mean displacements for the *normal* vs. the *osteoporotic* bone with only 5 samples (p<0.04, Table 5.1, Figure 5.8-Left). The *moment* test appeared to be sensitive; however, the 13.41% relative standard deviations for *osteoporotic, moment* testing are right-skewed because 4 of 5 specimens were stopped when 15 mm displacement was reached rather than when the scheduled cycles were completed. This 15 mm constraint was necessary due to the test configuration and was only reached when the cortical shell cracked. Reducing the moment arm would likely help reduce the sudden breakage of the cortical shell but would likely lead to an increase in the relative standard deviation because it is unlikely that the tests would have such similar endpoints as the current design (stopping at 15 mm displacement). Importantly, *Toggle* testing was not able to produce macroscopic damage to any of the foam vertebrae at these loading levels and number of cycles. Since no damage occurred the repeatability and sensitivity cannot truly be compared. Future experiments should utilise a different loading protocol to run until damage is unquestionably reflected at the screw-“bone” interface.

Relative standard deviations are used in the comparisons presented here for multiple reasons. It is valid to use a standard deviation as a measure of precision or accuracy for the current study. This is because, for the *toggle* and *moment* testing methods, the repeatability criteria developed in 1986 by Bland and Altman[142] were met: same measurement procedure, same observer, same measuring instrument used under the same conditions, same location, and repetition over a short period of time. Relative standard deviation was used for the repeatability criteria because the testing method caused significant magnitude changes for each measured variable (Table 5.1, Figure 5.8-Left).

It was also important to adjust for the initial displacement because the *ASTM* method had the lowest inherent stiffness due to the two-vertebrae, corpectomy setup. This initial compliance of the system should theoretically be the same for all specimens since the initial dimensions were held constant for all specimens. The displacement which is interesting for this investigation is the displacement which is associated with the progression of fatigue damage to the foam vertebra- the displacement after the initial cycle. This standard initial displacement which was the same for all samples in the *ASTM* method skewed the relative standard deviation value to low. In an attempt to account for this discrepancy, the *initial displacement* (displacement recorded after the first cycle) was subtracted from the *final displacement* and the relative standard deviation was again calculated. This led to a more equal standardized comparison of the testing methods. The *ASTM* method still had the lowest relative error for *displacement* for the *normal* samples (10.0% compared to 18.3% or 30.3%) but had similar error for the *osteoporotic* samples (14.8% compared to 11.7% and 19.1%, Table 5.1). This suggests that in terms of repeatability, it appears that the *ASTM* method was the superior method before and after consideration of the *initial displacement*.

The *ASTM* testing was the most complex of the testing methods in terms of the mechanical equipment used (two rotating axes and two vertebrae), medical materials needed (four pedicle screws and two rods compared to one pedicle screw for both *toggle* and *moment*), and testing time (6.1 compared to 1.6 hours). Reduction of complexity within these three categories while maintaining testing sensitivity would be the goal for determining an ideal testing method. The *moment* and *toggle* setups were the attempts to reduce the mechanical setup complexity; however, the larger variance makes these tests less appealing with the current loading protocol for the standardized foam samples. The medical materials cannot be reduced for the *ASTM* setup due to the specifications within the standard[9]. Reduction in the testing time is the only remaining area of possible improvement. When the *ASTM* data was cut to a 75% reduction of the testing time (1.5 hours), the *end displacement* values only changed by 0.87% and 3.09% for *normal* and *osteoporotic* vertebra respectively (Figure 5.8- Right). This change did not affect the test sensitivity; the change in cancellous material was still easily detected (p=0.006, R^2=0.58). The combined sensitivity and stability of a reduced time *ASTM* testing suggest that it is a desirable testing method for testing of foam samples.

5.3.2. **Biomechanical Relevance**

When comparing loading to that seen *in vivo*, the biomechanical relevance was considered comparable for the *moment* and *ASTM* test setups. *Toggle* testing is the least physiologic as it does not apply any moments to the screw head. During testing of the *moment* setup the repetitive loading and increasing displacement caused a forward rotation along the screw axis of the mechanical lever arm. This increased the effective moment seen at the screw head beyond that of the *ASTM* testing. This could help explain why the cortical shell cracked for 4 of the 5 *osteoporotic* samples in *moment* testing.

Force control rather than displacement control was used for all testing methods. Using force control on non-redundant structures (like a vertebra) means the failure parameter (*i.e.* cycles to failure) is related to crack initiation rather than crack propagation[219]. This consequently gives a better idea of the initiation of loosening. This is important because if loosening initiation can be delayed than the screw will likely have longer *in vivo* life. A measure of crack propagation would be better if the fatigue behavior of the material the screw is in (*i.e.* bone) is being investigated. This is not generally the case for this thesis as alterations of the screw design and surgical positionings were tested.

Constant cyclic peak amplitudes, as seen in *ASTM* testing, were associated with more repeatable results and more closely mimic what is seen by the *in vivo* loading of a single patient. However, the sweeping forces in the *moment* and *toggle* testing encompass an entire range of physiologic forces and/or moments which are applied to the screw head. This sweeping pattern is not as 'patient specific' and can thus cover a range of loading patterns seen in many patients. This suggests that these testing methods may be more generalizable. Furthermore, sweeping increases in the peak amplitude and causes the loading rate at the screw head to increase as testing time progresses. This could propagate failure more suddenly and hypothetically may lead to an ability to identify loosening initiation more easily. The measured parameters (*e.g. displacement*, *stiffness*) can be followed over time to see where a rapid change is seen and hence where loosening at the interface begins. For this current study, the failure criteria for the *toggle* and *moment* setups was a specific number of cycles rather than being a known displacement where loosening must have occurred. This criteria was used in order to more closely mimic the previously performed *ASTM* setup; however, this led to not all the samples exhibiting loosening, especially for the *toggle* test setup (Table 5.3).

5.3.3. Clinical Relevance

If comparative loosening parameters are to be considered, the *osteoporotic* composite foam models used here could be a potentially useful testing material. The *osteoporotic* samples rather than *normal* foam composite vertebrae should be used as they can more readily reflect permanent loosening damage at the interface for this loading range (Table 5.3). The *normal* composite vertebrae were too hard to reflect macroscopic loosening in the cross-sectional failure patterns for all three testing methods within this loading range (Table 5.3). Furthermore, the *moment* tested *osteoporotic* composite vertebrae were able to recreate a failure pattern which shows qualitative similarities to those seen in the *in vivo* lumbar spine (Figure 5.10, similar patterns were seen for the *ASTM* setup). The *toggle* tested *osteoporotic* samples also showed a *pivot point* which existed towards the end of the simulated pedicle canal (Figure 5.11). A *pivot point* within the pedicle canal has also been demonstrated in multiple *ex vivo* tests giving the *osteoporotic* composite foam vertebra increased ecological validity for use in biomechanical testing[129,222,248].

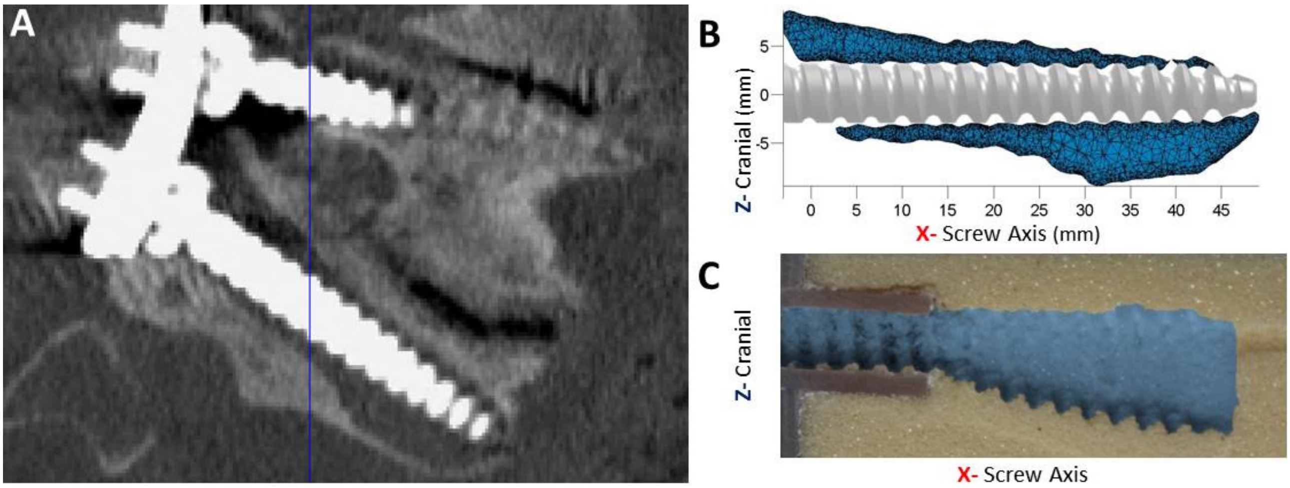


Figure 5.10 Pedicle screw loosening as seen in (A) a cross section of a clinical CT scan along the screw axis and (B) the sagittal cross section of the segmented and analyzed loosening halo and (C) *moment* testing for an *osteoporotic* composite foam vertebra (current experiment). Loosening areas highlighted in light blue.

5.3.4. Failure Pattern Analysis

The failure pattern exhibited by the motion analysis was able to produce similar features as those seen in the physical foam samples (Figure 5.11). The average failure area calculated was within 2.5% for all three measurements of failure area (Table 5.4). However, caution must be taken because this is a comparison of only three samples, the same trends in area magnitude was not seen for the vicon calculated areas as it was for the image segmented areas, and a notable pullout motion is shown in the vicon pattern which was not exhibited in the cross-sectional images. Since general motion features were able to be captured, and the magnitudes of measured parameters were similar to those calculated manually, it can be cautiously concluded that the motion based measurement can capture general motion patterns while allowing for quantitative comparisons.

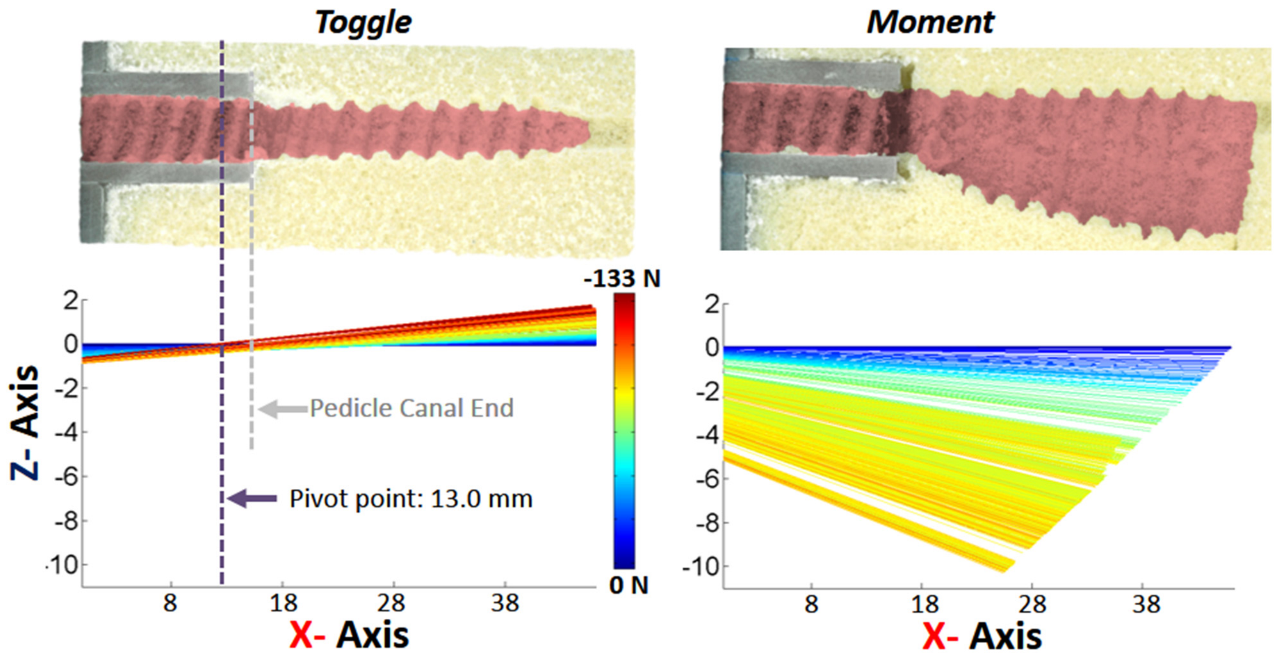


Figure 5.11 The average *toggle* and *moment* motion patterns for the *osteoporotic* samples compared to representative cross-sectional images of the cut foam samples (upper panel). The motion is shown from the entry into the screw body (lower panel).

5.3.5. Limitations

This study was very limited in its scope since only five samples for each testing method and material quality combination were tested. This small sample size reduced the statistical power and limits the strength of the conclusions. Small sample sizes may produce false positives or overestimate the magnitude of an association. This limitation is even more present in the failure pattern analysis where only three samples were useable for comparison. Although strong conclusions cannot be drawn on the basis of the statistical results; the results do give a sense of the relationship of the relative advantages of the various testing setups. Furthermore, it must be reiterated that the discussions of the biomechanical and clinical relevance are qualitative in nature, and are only able to discuss approximate similarities.

5.4. Conclusions

The *ASTM* testing method was found to be the most reproducible, to have similar biomechanical relevance while maintaining a good sensitivity and producing clinically relevant failure patterns. This makes it a seemingly robust method; however, it is also the most complex in terms of mechanical equipment, necessary medical materials and testing time. The *ASTM* testing time can be safely reduced by 75% to 1.5 hours and still produce good material sensitivity with a sample size of five. This method was also based upon an established standard testing method, making it more likely to be universally accepted. However, the testing setup does not allow for a within samples comparison necessitating larger sample sizes. This fact is especially detrimental when using biologic samples where the sample availability is often scarce as well as the fact that biologic samples often have large inter-specimen variability which would make a within sample comparison ideal.

The *toggle* and *moment* methods exhibited larger variance and, consequently, less reproducibility and sensitivity. However, no visible permanent damage was shown for either material tested with the *toggle* method; therefore, the reproducibility cannot truly be examined. The use of a set number of cycles as the failure criteria was not the optimal endpoint for these testing types. The increasing sweeping loading pattern should more appropriately be run until a specific displacement is reached where it is known loosening would have occurred. In this way, initiation of loosening can be identified by the continual monitoring of the *displacement* and *stiffness* parameters. Both the *toggle* and the *moment* methods allow for within sample comparisons where the variable of interest can be change within the same sample. This advantage is especially important for biologic samples and may outweigh the small potential *ASTM* reproducibility advantages.

The *osteoporotic* composite foam models used in this study were found to exhibit loosening in patterns which can be quantified and resemble what has been observed *in vivo.* The *osteoporotic* models can be considered a potential testing material for future comparative tests, whereas, the *normal* samples were too dense and did not undergo macroscopic loosening damage.

Vicon motion analysis can be used to capture general features of screw motion while allowing for the quantification of parameters such as the *pivot point* location, failure area, *tip motion*, and *head motion*. All three loading protocols were able to produce loosening patterns similar to those seen *in vivo*.

Chapter 6.
Surgical Positioning

The positioning of the screw through the narrowest portion of the vertebral anatomy, the pedicle, was a step forward in the fixation and stability of spinal screws when compared to previous techniques (*e.g.* laminar screws). The cervical spine and especially the uppermost vertebra, the atlas, has a unique anatomy with multiple surgical positionings currently being utilized. This combination of factors makes the atlas ideal for an investigation on the effects of surgical positioning on the screw fixation strength. The established monocortical lateral mass technique only utilizes the bone stock of the lateral mass while the emerging monocortical pedicle screw technique traverses the posterior arch and then enters the lateral mass. These techniques are compared here in a toggling, fatigue loading profile.

Instabilities of the upper cervical spine in the occipito-cervical region may result from traumatic injuries, tumors, infections, rheumatoid arthritis or congenital anomalies. Different stabilization techniques have been described in the literature and are established for clinical use to avoid persistent instability and neurological complications[25,85,94]. Unfortunately, due to the proximity of neurovascular structures these operative techniques are technically challenging and associated with a significant complication rate[131,225,238].

In 2001, Harms and Melcher published a technique involving posterior C1-C2 fusion using polyaxial screws and rod fixation[94]. Using this technique the placement of the screws in C1 is realized via the lateral mass. The entry point for the lateral mass screw is covered by a paravertebral venous plexus which if pierced can lead to extended bleeding and the C2 nerve root can be injured intraoperatively[225,238]. In order to increase the mechanical stability of lateral mass screws bicortical placement can be used[66,238]. However, this endangers the hypoglossal nerve and the internal carotid artery[52,53,99].

Monocortical C1 pedicle screws are an emerging technique in which the screws are implanted via the posterior arch rather than the lateral mass. Clinically this placement requires a careful subperiostal preparation of the posterior aspect including the exposure of the vertebral artery at the superior rim[175,225]. Therefore, the exposure of the lateral mass and accompanying structures, including the venous plexus and the C2 nerve root, is not necessary. In first clinical studies pedicle screw instrumentation was found to be effective and safe by leading to a solid arthrodesis with no signs of neurovascular complications or implant failure[140,223,225].

Biomechanically, the pedicle screw trajectory passes through the posterior arch enabling the use of longer screws with a greater bone contact area than lateral mass screws. A longer bone-screw interface has been shown to lead to improved screw stability[118]. Several biomechanical studies have investigated lateral mass screw-rod constructs[66,67,101,111,124,177]. Recently, the pullout strengths and biomechanical stabilities afforded by C1 lateral mass screws and C1 pedicle screws using bicortical and monocortical fixation techniques have been analyzed by Ma et al. 2009[238]. They showed similar pullout resistance and three-dimensional stability for bicortical C1 lateral mass screws and monocortical C1 pedicle screws; unicortical lateral mass screws provided the lowest pullout strength.

A biomechanical comparison of monocortical C1 pedicle screws with monocortical C1 lateral mass screws has not yet been described for cranial-caudal toggling, which is considered to be more physiological than axial pullout of the screw. Therefore, the aim of this *ex vivo* study was to compare the relative biomechanical fixation strengths of monocortical C1 pedicle screws versus monocortical C1 lateral mass screws in terms of cycles to failure, stiffness and removal torque by applying a cranial-caudal toggling force directly at the screw head.

6.1. Methods

The study consisted of nine human cadaveric atlas (C1) vertebrae with the only alteration being the surgical positioning of the screws. Each vertebra received one lateral mass and one pedicle screw constituting a repeated measures design. The specimens were exposed to cyclic fatigue loading at the screw head to ascertain measures of fixation strength.

6.1.1. Specimens

After approval by the University of Hamburg Ethics Committee the nine atlas vertebrae (58.0 ± 11.1 years, three female, six male) were received from the Institute of Forensic Medicine (University Medical Center Hamburg-Eppendorf). Specimens were sealed in plastic bags and stored at -20°C.

Preoperative CT scans (0.90 mm slice thickness, 0.45 mm spacing, Mx8000 IDT 16, Philips Healthcare, DA Best, NL) were performed with a phantom (QRM-BDC, QRM, Möhrendorf, DE) and were used to exclude pathological malformations or preexisting fractures as well as to determine the apparent volumetric bone mineral density (BMD). Trabecular volumetric BMD was determined by segmenting a 25 x 25 x 25 voxel cube from the center of each lateral mass (Avizo version 5.1, Mercury Computer Systems, San Diego, CA, USA). The average Hounsfield unit value was scaled linearly to the reference densities of the phantom.

6.1.2. Preparation, Fixation and Instrumentation

The night before testing the specimen was thawed to room temperature. On the day of testing all soft tissue was removed. After sample preparation a custom-made mold was created for each atlas (Figure 6.1). In order to imitate physiologic boundary conditions the mold only contacted the cranial and caudal surfaces of the facet joints. The mold was created by first placing modeling clay through the center of the atlas, over the transverse processes, and along the anterior arch (Figure 6.1A). The clay covered atlas was then aligned in a rectangular base mold (Figure 6.1B). Finally, both sides of the mold were cast at the same time by filling the mold (posterior arch facing up) with a polyurethane resin (Ureol FC53, Gößl

& Paff, Karlskron, DE) to produce level, parallel endplates for mounting. After hardening, the mold was taken apart and the clay removed (Figure 6.1C).

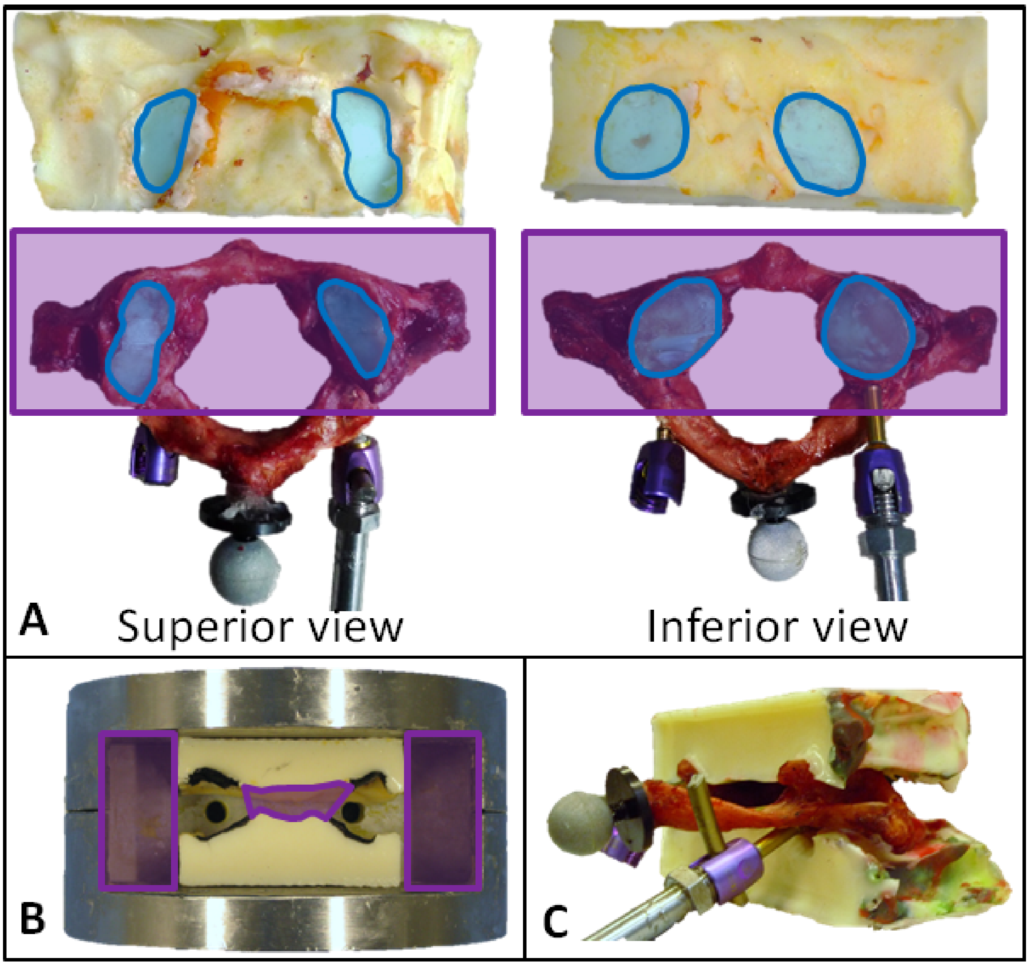


Figure 6.1 Creation of a custom-made mold for each atlas. (A) An example mold highlighting the contact area (blue) which only occurred at the cranial and caudal surfaces of the facet joints. (B) Rectangular base mold in which the molds were cast. (C) A 3D perspective of a mold with an instrumented specimen. Purple highlights in A & B show where clay would be placed.

All vertebrae were bilaterally instrumented with polyaxial screws of the same size (outer diameter: 3.5 mm, length: 26 mm, Synapse System, Synthes GmbH, Oberdorf, CH, Table 6.1). Each vertebra received one polyaxial lateral mass screw (cortical profile, 10 mm unthreaded shaft) and one polyaxial pedicle screw (cancellous profile). The side on which each screw was placed was equally allocated based on BMD, age, gender and testing order (Table 6.1).

The entry point differed for the two techniques (Figure 6.2). The lateral mass screw was inserted at the crossing of the inferior rim of the posterior arch and the middle of the lateral mass, aiming at the center with a sagittal angulation of 20°. The pedicle screw entered through the posterior arch, aiming at the center of the lateral mass, without perforating the superior rim of the lamina. Thus, the screw tips converged to the same height and depth within the bone without touching the anterior cortex (Figure 6.2). To ensure consistency, all instrumentation was performed by the same orthopedic surgeon and postoperative x-rays were taken in the axial, antero-posterior and lateral planes to confirm proper implant positioning.

Table 6.1 Testing group characteristics showing properties for both the screw design and the specimen characteristics. Since each vertebra was allocated one lateral mass and one pedicle screw the number, age, and gender balance of the groups were equal.

	Screw Design			Specimen Characteristics	
Massa Screw n=9		Outer diameter *(mm)* =	3.5	Age *(years)* =	58.0 ± 11.4
		Core diameter *(mm)* =	2.95	BMD *(gHA/mm³)* =	210.5 ± 71.6
		Thread length *(mm)* =	16	Gender =	3 Female, 6 Male
		Thread pitch =	1.25		
Pedicle Screw n=9		Outer diameter *(mm)* =	3.5	Age *(years)* =	58.0 ± 11.4
		Core diameter *(mm)* =	2.95	BMD *(gHA/mm³)* =	209.8 ± 71.5
		Thread length *(mm)* =	26	Gender =	3 Female, 6 Male
		Thread pitch =	1.75		

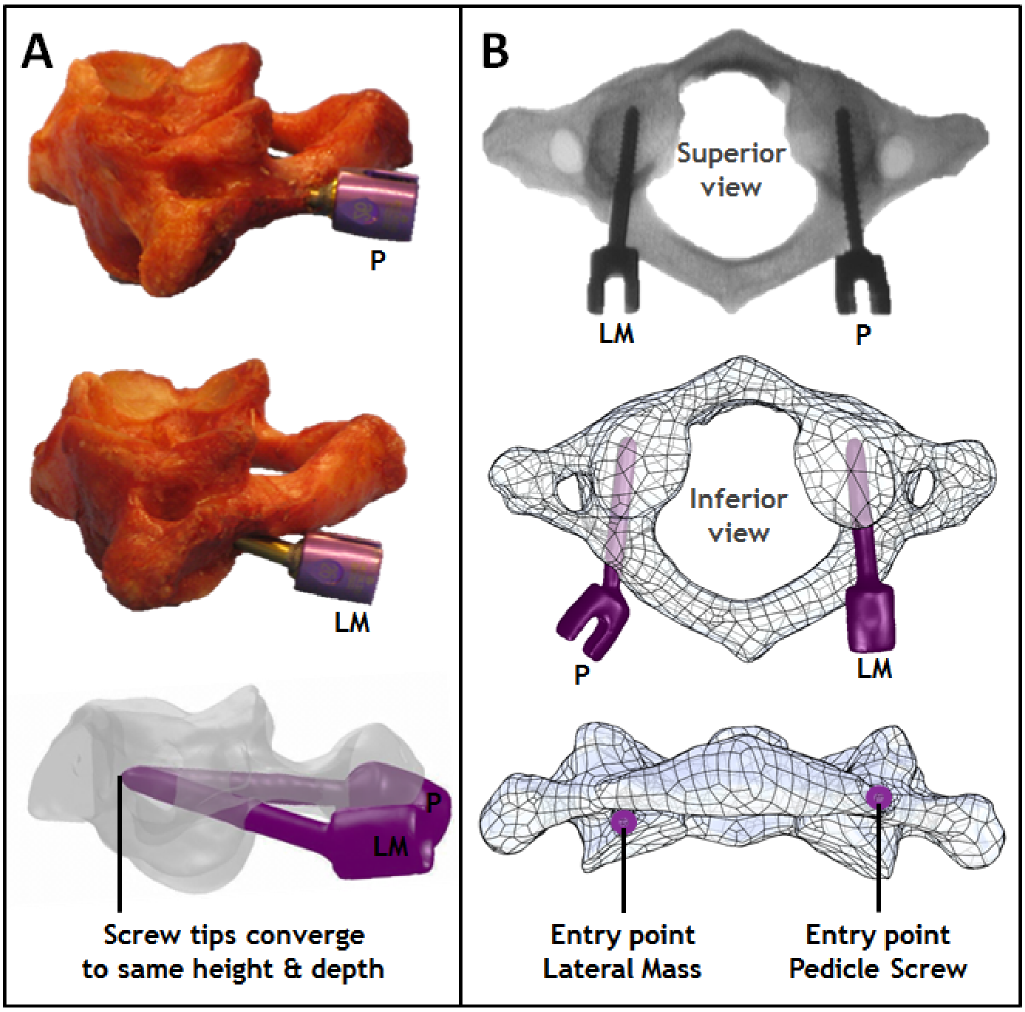


Figure 6.2 Instrumentation of C1 with one lateral mass screw (LM) and one pedicle screw (P). (A) Views showing the sagittal angulations (top & middle), depth and height match (bottom). (B) X-ray (top) and rendered CT scans showing the relative depths (middle) and entry points (bottom) of each technique.

6.1.3. Loading Modalities

After instrumentation the specimens were clamped to a servohydraulic testing machine (858 Bionix®, MTS, Eden Prairie, MN, USA, Figure 6.3). A sinusoidal, cyclic (0.5 Hz) force was applied to the screw head, which was free to rotate around the transverse axis with all other degrees of freedom (DOF) fixed. The screw head was attached to the testing machine with a customized steel locking adaptor and a 15 mm long, 3.5 mm diameter rod, to lock the polyaxial head in place. Cranio-caudal peak compressive and tensile forces started from ± 25 N and increased linearly by 0.05 N every cycle. Toggle testing was stopped when 5 mm displacement was achieved caudally. After fatigue failure of one screw, the contralateral screw was loaded with the same protocol. Testing conditions were at room temperature and specimens were sprayed with ringer solution during preparation and before testing to maintain tissue hydration. Finally, CT scans were taken with the screws *in situ* and the maximal removal torque was then measured (Torsiometer 760, Stahlwille, Wuppertal, DE).

A motion capture system (Vicon-460, Vicon Motion Systems, LA, USA) was used to record the three-dimensional motion of the screw (frame rate: 102.4 Hz) relative to the vertebra sample. The axis of the tested screw was defined by a set of 4 markers (Figure 6.3). The vertebra had a marker glued to the posterior arch and the x-y-table motion was captured with an attached marker set to the base of the x-y-table.

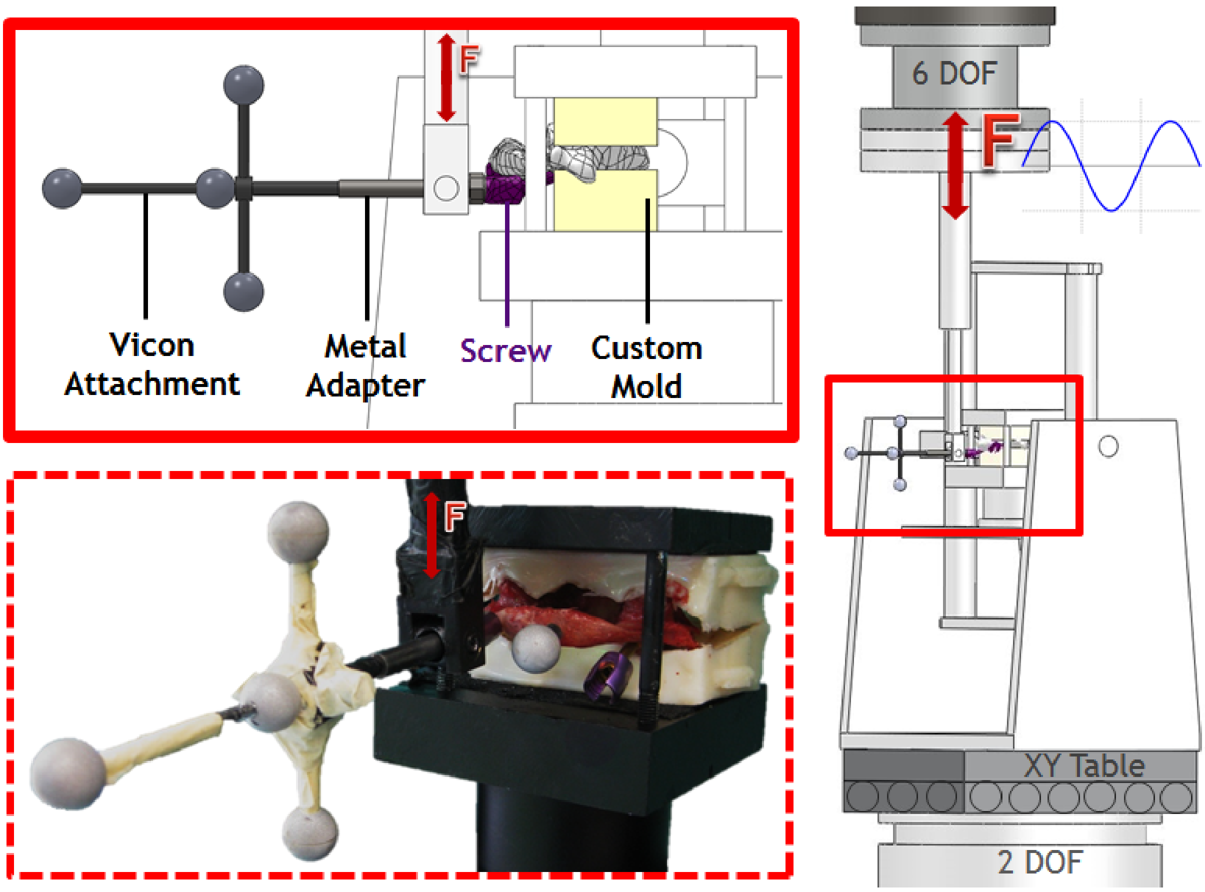


Figure 6.3 Schematic of mechanical test setup with red box denoting an expanded view of the clamped specimen attached via the custom-made metal adapter. The red dashed box is a photograph of the clamped specimen.

6.1.4. Data Analysis

Cycles to failure, *displacement*, *removal torque*, and *initial* and *end stiffness* were output variables. Stiffness was defined by the slope of the caudal force-displacement loading curve. The slope was calculated from a linear best-fit for each cycle with the first and last 10% of the cycle's data not included to ensure only the linear portion was considered. *Initial stiffness* was defined from the average of the first five caudal loading cycles and *end stiffness* from the last five. The screw length into the vertebra and the sagittal angle were measured directly from the post-testing CT scans (Avizo version 5.1). Screw motion was quantified from the motion capture data as described previously in section 5.1.3 in terms of *pivot point*, *head motion*, and *tip motion*.

Statistical evaluations were performed (SPSS Statistics 20, IBM Corp., Armonk, NY, USA) with a type I error probability set to 5%. A paired-samples *t*-test was used to test differences between groups (lateral mass *vs*. pedicle screws) and the effect size between the groups was determined with a point-biserial correlation. The assumption that the sampling distribution of the differences is normally distributed was upheld for the variables: *cycles to failure*, *force at failure*, *initial stiffness*, *end stiffness* and *screw depth*. A Pearson correlation coefficient was used to measure covariance. Effect size magnitude is represented by adjusted R^2 values to account for small sample sizes and was determined by linear regression.

6.2. Results

6.2.1. Fixation Strength

The pedicle screw technique consistently and significantly out-performed the lateral mass technique in all measures of bone-screw fixation strength analyzed (Table 6.2). This included *cycles to failure* (p=0.004, R^2=0.48), *force at failure* (p=0.002, R^2=0.45), *initial stiffness* (p=0.05, R^2=0.14), *end stiffness* (p<0.001, R^2=0.63) and *removal torque* (p=0.04, R^2=0.18). Distinct differences were seen in the progression of both the average *displacement* and average *stiffness* between groups (Figure 6.4 & 6.5). The screw loosening rate was higher for the lateral mass screws (100%) than for pedicle screws (33%).

Table 6.2 Output parameters with the averages and standard deviations given by group.

	Massa Screw	Pedicle Screw	Significance
Cycles to Failure (#)	684 ± 240	1078 ± 166	** p=0.004 R^2=0.48
Force at Failure *(N)*	-62.4 ± 12.3	-83.0 ± 10.4	** p=0.002 R^2=0.45
Initial Stiffness *(N/mm)*	23.9 ± 3.9	27.6 ± 4.1	** p=0.05 R^2=0.14
End Stiffness *(N/mm)*	10.9 ± 2.7	18.0 ± 2.7	** p<0.001 R^2=0.63
Removal Torque *(N*m)*	0.13 ± 0.09	0.70 ± 0.78	* p=0.04‡ R^2=0.18
Screw depth *(mm)*	15.4 ± 0.6	21.9 ± 1.0	** p<0.001 R^2=0.94
Sagittal Angle *(°)*	23.6 ± 5.5	10.2 ± 3.1	** p<0.001‡ R^2=0.70
Loose *(torque)*†	100%	33%	

† Clinical loosening is defined as a removal torque of less than 0.40 N-m[194]. ‡Differences were not normally distributed.

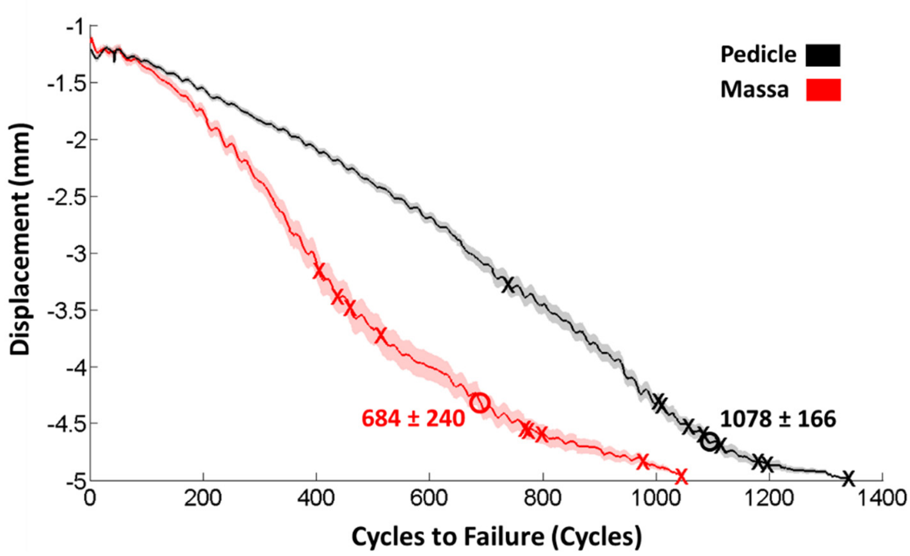


Figure 6.4 Graph of the average displacement vs. cycle number, showing pedicle screws having a much higher resistance to structural deformation. After about 100 cycles a diverging of the displacement curves exists. An 'X' represents the cycle number for a specimen failure, circles are the averages and the shaded areas represent the standard error.

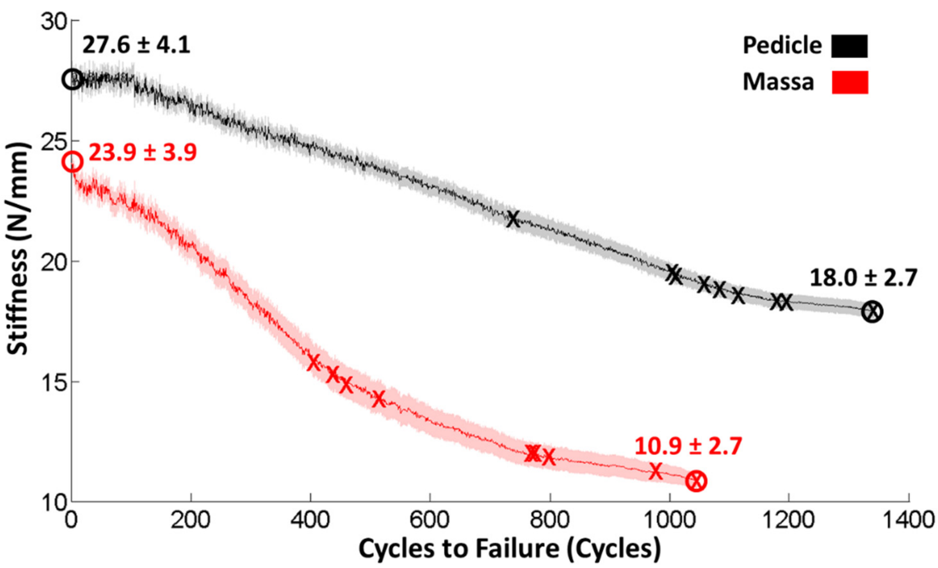


Figure 6.5 Graph of the average stiffness *vs*. cycle number, showing pedicle screws having a significantly higher *initial* and *end stiffness*. Stiffness loss (distance between curves) was similar throughout testing. An 'X' along the curve represents a cycle number where a specimen failed and the shaded areas represent the standard error.

6.2.2. Surgical Technique Effects

The *screw depth* and the *sagittal angle* were different between surgical techniques (p<0.001) and correlated negatively with each other (p<0.001). With increasing *screw depth* (Figure 6.6), there were increases in *cycles to failure* (p<0.001, R^2=0.57), *force at failure* (p=0.001, R^2=0.50), *initial stiffness* (p=0.05, R^2=0.23), *end stiffness* (p<0.001, R^2=0.74), and *removal torque* (p=0.04, R^2=0.19). With increasing *sagittal angle* (Figure 6.6) the *cycles to failure* (p=0.001, R^2=0.47), *force at failure* (p=0.01,

R^2=0.25), and *end stiffness* (p=0.001, R^2=0.45) all decreased. As desired, the *transverse angle* did not vary with surgical technique (p=0.19).

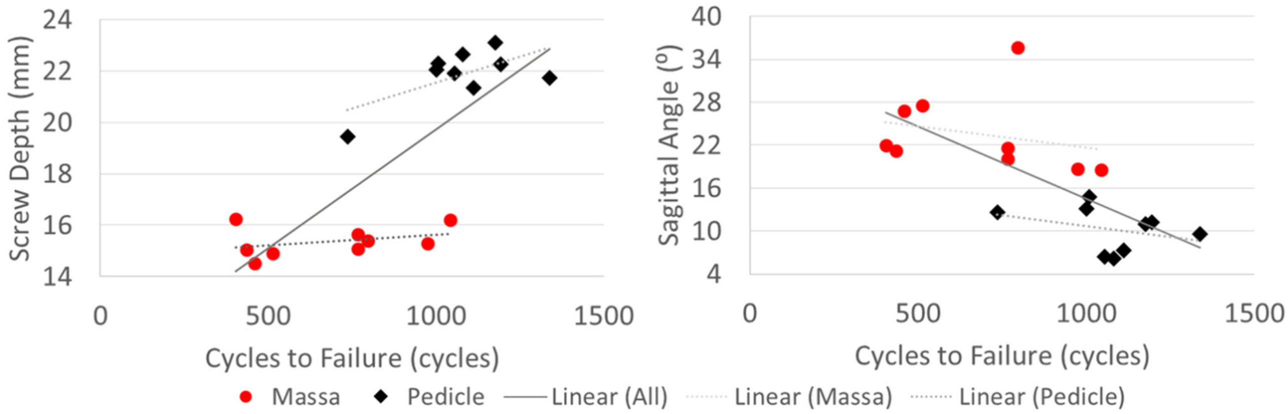


Figure 6.6 The *screw depth* (left) and *sagittal angle* (right) vs. the *cycles to failure* broken up by group.

6.2.3. Specimen Geometry and Bone Quality

The specimens were of normal bone quality (BMD=210 ± 71.6 mgHA/cm^3). BMD did not correlate significantly with any measured parameters, including *cycles to failure*, *force to failure*, *removal torque*, age, gender, or *stiffness* values (p>0.14). Specimen width correlated positively with age (p=0.008, R^2=0.32) and was higher for male specimens (p=0.02). Specimen height correlated positively with *initial stiffness* (p=0.03, R^2=0.30) but not with *end stiffness* (p=0.13).

6.2.4. Screw Motion

A butterfly shaped pattern with a distinct *pivot point* was seen for each specimen (Figure 6.7). The *pivot point* was shown to differ between groups (p=0.002) and was inside the vertebra for 7 of 9 *pedicle* screws and only one *massa* screw. A decreasing *pivot point* correlated to an increased *cycles to failure* (p=0.006, R^2=0.34), *force to failure* (p=0.007, R^2=0.34), *removal torque* (p=0.02, R^2=0.26), *initial stiffness* (p=0.03, R^2=0.21), *end stiffness* (p<0.001, R^2=0.65), *screw depth* (p<0.001, R^2=0.54). *Pivot point* correlated positively with the *sagittal angle* (p=0.008, R^2=0.33). *Head motion* did not differ between groups (p=0.65) nor did it with any fixation parameters (p>0.12). The *tip motion* was lager for *pedicle* screws (p<0.001) and correlated positively with *cycles to failure* (p<0.001, R^2=0.75), *force to failure* (p<0.001, R^2=0.80), *initial stiffness* (p=0.04, R^2=0.20), *end stiffness* (p<0.001, R^2=0.56), and *screw depth* (p<0.001, R^2=0.64). *Tip motion* correlated negatively with the *sagittal angle* (p=0.001, R^2=0.51).

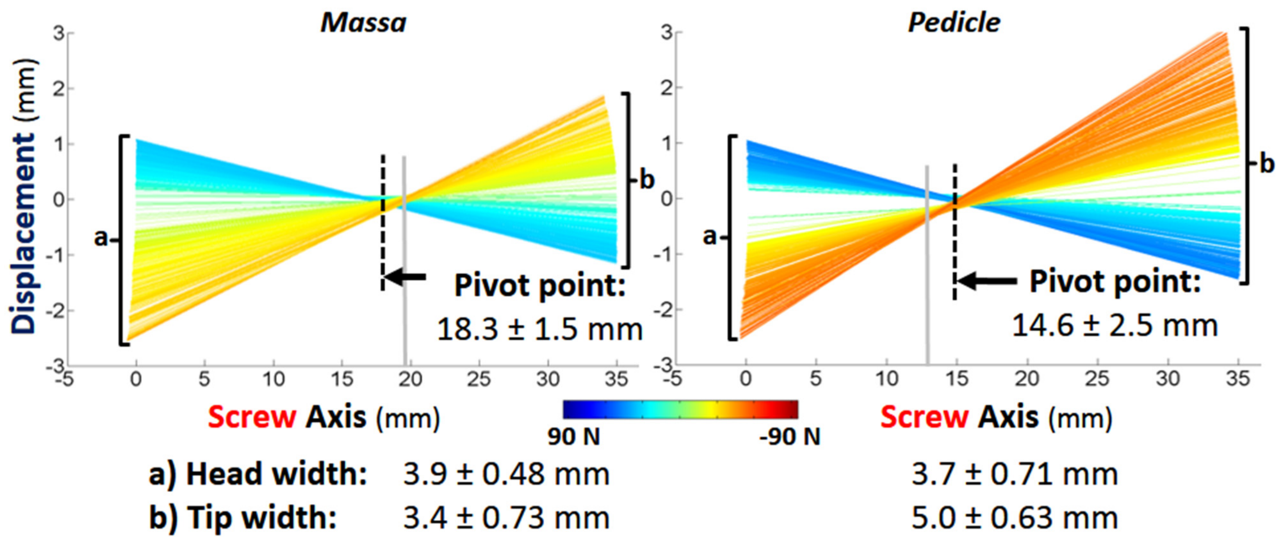


Figure 6.7 Average screw motion patterns for the *massa* and *pedicle* screws. The grey lines represent the average position where the screw entered the vertebral body; notice the average *pivot point* is outside the vertebra for the *massa* screw and is inside the vertebra for the *pedicle* screw group.

6.3. Discussion

6.3.1. Biomechanical Relevance

The placement of monocortical C1 pedicle screws is an emerging technique which enables the use of longer screws with a greater bone contact area in comparison with monocortical C1 lateral mass screws[81]. In this present study, the biomechanical advantage of C1 pedicle screws was shown for C1 lateral mass screws with regard to *cycles to failure*, *stiffness*, *removal torque* and *loosening criteria* (p< 0.05, Table 6.2). In fact, the longest lasting lateral mass screw (1048 cycles) did not reach the average *cycles to failure* of the pedicle screw group (1078 ± 168 cycles, Figure 6.4). Under repeated loading, pedicle screw placement provides a higher resistance to structural deformation, shown by the diverging average displacement curves after 100 cycles (Figure 6.4). The pedicle screw technique also started with, and maintained, a higher *stiffness* during testing (Figure 6.5), showing that pedicle screw placement provides primary stabilization as well as longer term fixation benefits. These findings correspond well with the results of a recent study where unicortical C1 lateral mass screws showed weaker pullout strength in comparison with C1 pedicle screws[238].

In accordance with previous findings an increased screw depth in bone has been shown to improve fixation strength in vertebrae[118]. The 6.5 mm (42%) greater *screw depth* for the pedicle projection compared to lateral mass projection is in line with a previous anatomic study which demonstrated the mean intraosseous depth to be 10 mm higher[81].

There was an inverse correlation of *sagittal angle* and *screw depth* (p< 0.001). This is expected because a higher *sagittal angle* was necessary for the tip of the lateral mass screw to achieve the same implantation height as the pedicle screw in the sagittal plane due to a more inferior entry point. Less *screw depth* was achieved since the bone stock of the posterior arch was not utilized. This interaction leads to difficulty in distinguishing the relative influence of the different factors. However, since *screw* *depth* explained more of the variance in *cycles to failure* (57%), *initial stiffness* (23%), and *end stiffness* (74%) than the *sagittal angle* (47%, 12%, 45% respectively) it is suggested that *screw depth* may be more important for fixation.

The current toggling fatigue setup was utilized because it allows for the progressive measurement of loosening parameters over time and within the physiologic loading range. Furthermore, it produces an *in vivo* like failure pattern in which the loosening zone expands at the screw tip. Whereas, pullout testing produces purely primary stability data (no effect of time) for a non-physiologic force as well as a failure pattern which is not reported clinically. The loading was applied directly to the screw head to eliminate factors related to the screw-rod connections. A repeated, continually increasing force was used to achieve a sweep of forces within the physiological range, as well as an accelerated failure to reduce the effects of specimen degradation.

6.3.2. Clinical Relevance

In recent biomechanical studies different posterior stabilization techniques have been investigated for the atlantoaxial complex[66,67,101,111,124,177]. Superior stability was demonstrated for transarticular screws, which pass through the C1–C2 articulation, in comparison with established posterior wiring techniques[67,177]. Unfortunately, in up to 23% of the cases, safe placement of these transarticular screws is not possible due to anatomic limitations of the vertebral artery[45,175,223].

C1 lateral mass screw-rod constructs were established as an alternative to transarticular screws because they have shown similar stability and fewer anatomical constraints[67,101,111,124]. C1 screws combined with separate instrumentation of C2 allow for the active manipulation and reduction in non-mobile atlantoaxial (sub-) luxation which is not possible with transarticular screws[218]. The monocortical pedicle screw technique has potential unevaluated clinical benefits over the lateral mass technique including a minimization of blood loss and a decreased neurovascular complication rate[52,53,99,225,238].

Anatomical studies have demonstrated the potential of inserting a 3.5 mm C1 pedicle screw safely through the posterior arch[45,81,140,223]. Nevertheless, the thinnest height of the screw tract underneath the groove of the vertebral artery (to which close intraoperative attention must be paid), was measured to be less than 4 mm in 8% to 31.7% of specimens analyzed. Therefore, preoperative CT scans are necessary to determine anatomic dimensions, plan acceptable screw projection, and to evaluate the feasibility of C1 pedicle screw placement. Further, care must be taken for children or patients presenting with rheumatoid arthritis due to additional anatomical variants.

The limitations of this *ex vivo* study include the natural variation of the specimens, small sample sizes, and the variation of the pitches for the screw threads. Natural variation was reduced as far as possible by utilizing a repeated measures design; with one lateral mass screw and one pedicle screw per specimen.

6.4. Conclusions

When only altering the screw path within the atlas, a higher toggle force as well as higher stiffness throughout and after testing was withstood by monocortical pedicle screws when compared to the lateral mass screws. From a biomechanical point of view, the clinical use of pedicle screws in C1 is a promising alternative to lateral mass screws. The fixation advantages of using monocortical C1 pedicle screws probably arises from a greater insertion depth into the bone, as well as a smaller canal width which may increase compression on the screw threads. From a clinical point of view, this procedure offers a potential to minimize blood loss and to decrease neurovascular complications which suggests both an economic and a clinical improvement. Nevertheless, careful attention must be paid to ensure proper spacing of the screw tract from the vertebral artery and further clinical studies are necessary to evaluate this procedure in appropriate detail.

Chapter 7.
Cement Augmentation

Pedicle screw fixation is the technique most commonly used to stabilize the posterior spine[41]. Pedicle screws offer a relative ease of implementation, high construct stability, better fusion record than without fixation, and better hardware survival than the traditional hook/rod systems[41,139,240,243]. Though there are many benefits to the pedicle screw and rod systems they also have their pitfalls. Loosening at the bone screw interface is proving to be a challenge, especially with surgical indications being extended to the older, osteoporotic population and to the increasing use of dynamic stabilization[115,237].

To determine the possible clinical benefits of new screw designs or surgical techniques two modes of pre-clinical testing have been developed to quantify fixation strength: axial pullout and fatigue in toggling. There is a vast historical database of pullout test results and a standardized testing method is established (ASTM F543)[8]. Pullout is considered a relatively easy and consistent test to perform. However, there is increasing debate over its clinical relevance, especially since pullout has rarely been reported clinically as a failure mechanism (reported rates of 0-1.3%, Table 2.4). Fatigue failure of the bone under cyclic toggling loading is believed to be more clinically relevant[42,58,112]. Furthermore, *ex vivo* cranial-caudal, toggling loading protocols can be applied which can mimic the *in vivo* loads experienced during gait[17].

Bone quality has been shown to be the best predictor for pedicle screw fixation and stabilizing a screw in osteoporotic bone is considered clinically challenging[92,212]. Augmentation of pedicle screws is somewhat controversial; however, it is gaining clinical acceptance and approximately 2/3 of German surgeons expressed its use in osteoporotic patients in a survey[88]. It is further supported by a growing amount of recent biomechanical studies for use with poor bone quality due to cement augmentation demonstrating an approximate two-fold increase in pullout strength[43,212]. Two modes of pedicle screw augmentation are currently available: (1) injecting cement into the vertebra prior to screw insertion (the established method) and (2) cement injection through the inserted screw. Fixation benefits of these augmentation techniques have recently been tested in pullout showing that injection through the screw provides higher pullout strength than traditional screw augmentation[43]. However, to the author's knowledge these techniques are not tested in the more physiological toggling fatigue.

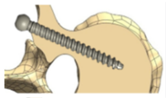
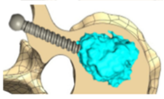
Other methods to establish improved fixation of screws in osteoporotic bone include using large screws with diameters encroaching on the cortical bone within the pedicle. A study by Kiner et al.[112] demonstrated that increasing the screw diameter was more beneficial than the traditional augmentation in toggling fatigue, however, the screw injected augmentation was not investigated.

There were two primary goals of the study. The first, was to determine whether the results from pullout testing can be directly translated to the more physiological fatigue testing. The second, was to compare the stability of a native control to three current fixation techniques within the osteoporotic spine: (1) traditional prefilled augmentation, (2) screw injected augmentation and (3) unaugmented screws with an increased diameter.

7.1. Methods

Screws were inserted into both pedicles of osteoporotic vertebral specimens, according to one of four fixation treatment groups: (1) *native* (control group) (2) *big diameter* (3) *prefilled* and (4) *screw injected* (Table 7.1). *Fatigue* testing was completed on one screw then the contralateral screw was loaded in *pullout* to enable pairwise comparisons of the *testing method*.

Table 7.1 Group and specimen characteristics classified by experimental group (averages ± standard errors); bone quality (*e.g.* BMD) and vertebral level were used to allocate the specimens equally between groups.

	Group	N	Age (years)	BMD (gHA/cm^3)	Screw Ø (mm)	Screw Length (mm)
	***Native***	10	74.3 ± 1.7	93.7 ± 13.4	5.5	50
	Big Diameter	10	77.4 ± 2.5	94.6 ± 11.1	6.5	50
	***Prefilled***	9*	76.4 ± 2.2	89.9 ± 14.1	5.5	50
	Screw Injected	10	78.5 ± 2.3	93.7 ± 10.0	5.5	50
	Overall	39	76.7 ± 1.1	93.1 ± 5.9	-	-

*L3 of one specimen unusable due to prior fracture of the lamina and pedicles

7.1.1. Specimens, Implants and Preparation

Vertebrae were dissected from ten osteoporotic human lumbar spines (L1-L5), with informed consent of the donors. All donors were over 69 years of age (76.7 ± 1.1 years). Directly after harvesting, specimens were sealed in plastic bags and stored at -22°C until testing.

Specimens were CT scanned (1.3 mm slice thickness, 0.6 mm spacing, Mx8000 IDT 16, Philips Healthcare, DA Best, The Netherlands) with a phantom (QRM-BDC, QRM, Möhrendorf, DE) in order to obtain their geometry and apparent volumetric BMD. Trabecular volumetric BMD was determined by segmenting a 26x26x26 voxel cube from the center of the vertebral body (Amira® 5.4, Mercury Computer Systems, San Diego, CA, USA). The average Hounsfield unit value was scaled to the reference densities of the phantom.

The specimens were distributed between the four testing groups by separating them equally based on both BMD and vertebral level (L1-L5). Commercially available titanium alloy, self-tapping, conical core screws (tangoRS™ system ulrich medical®, Ulm, DE) were used for testing. The screws were 50 mm long, with an outer diameter of 5.5 mm for all groups except the *big diameter* group (Ø=6.5 mm).

Specimens were defrosted the night before testing. On the day of testing, the lumbar sections were separated into individual vertebral bodies and all soft tissue was removed. A surgeon used fluoroscope guidance to inject the cement and implant the screws. The preferred sagittal alignment of the screws was parallel to the endplates and with a transverse alignment along the pedicle axis with converging screw tips. The specimens were then embedded in the potting fixtures, ensuring parallel alignment of the endplates to the planes of the potting fixtures. To help preserve tissue constitution, the specimens were sprayed with Ringer solution throughout preparation and wrapped in moist tissue prior to testing.

In the *prefilled* group, cement (Cemex resin, TECRES medical®, Verona, Italy, 3:1 powder and liquid mixing proportions) was first injected into the vertebral body through a prepared hole and the screw was then inserted (Figure 7.1). In the *screw injected* group, the screw was first inserted and cement was then injected from a syringe through the head of the screw, down the central cannulation and out into the vertebral body through radial perforations near the tip of the screw (Figure 7.1). The cement was mixed according to the manufactures instructions and injected into the vertebral body until either a filling from endplate to endplate could be observed fluoroscopically, leakage was detected, or no more cement could be injected through the screw.

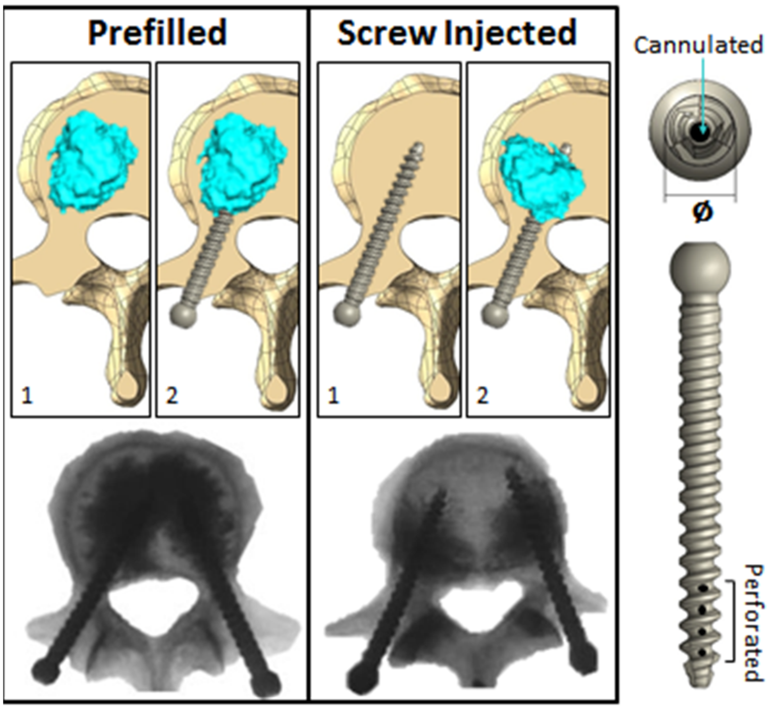


Figure 7.1 A diagram showing the different methods of augmentation and the screw used for testing. Left: Illustration of the *prefilled* group where (1) the vertebral body was filled with cement and then (2) the screw was inserted. Middle: The *screw injected* group (1) the screw was first inserted and (2) cement was then injected through the screw. Different patterns emerged: the *prefilled* group generally had a larger volume of cement and a more anterior bias. Right: The tangoRS^{TM} screw used for testing; note the radial holes (perforations) and the hole along the entire screw axis (cannulation) to enable cement injection.

7.1.2. Mechanical Setup

After preparation and implantation specimens were mounted in a servo-hydraulic testing machine (858 Bionix®, MTS, Eden Prairie, MN, USA, Figure 7.2). A sinusoidal, cyclic (1.0 Hz) compressive force was applied to the screw head, which was free to rotate around the transverse axis with all other degrees of freedom (DOF) fixed. The peak compressive force was increased step-wise by 25 N every 250 cycles starting from 25-75 N (Locati test design). This loading was chosen to reflect a range of loads measured *in vivo*[17,181]. Data was sampled at a rate of 101.6 Hz and testing was stopped when the displacement of the screw head reached 5.4 mm, which translated to an approximate 20° rotation.

After *fatigue* testing the specimen was rotated in its fixture and tested in pure axial *pullout*. The screw head was hooked at the base by a fork and a ramp displacement was applied (5 mm/min) until specimen failure. Force, moment and displacement data was sampled at 101.6 Hz.

An optical motion capture system was used (Vicon-460, Vicon Motion Systems, LA, USA) to record the three dimensional motion of the screw during *fatigue* testing (data collection rate: 100 Hz). Markers were mounted on the screw head and on the base of the x-y-table.

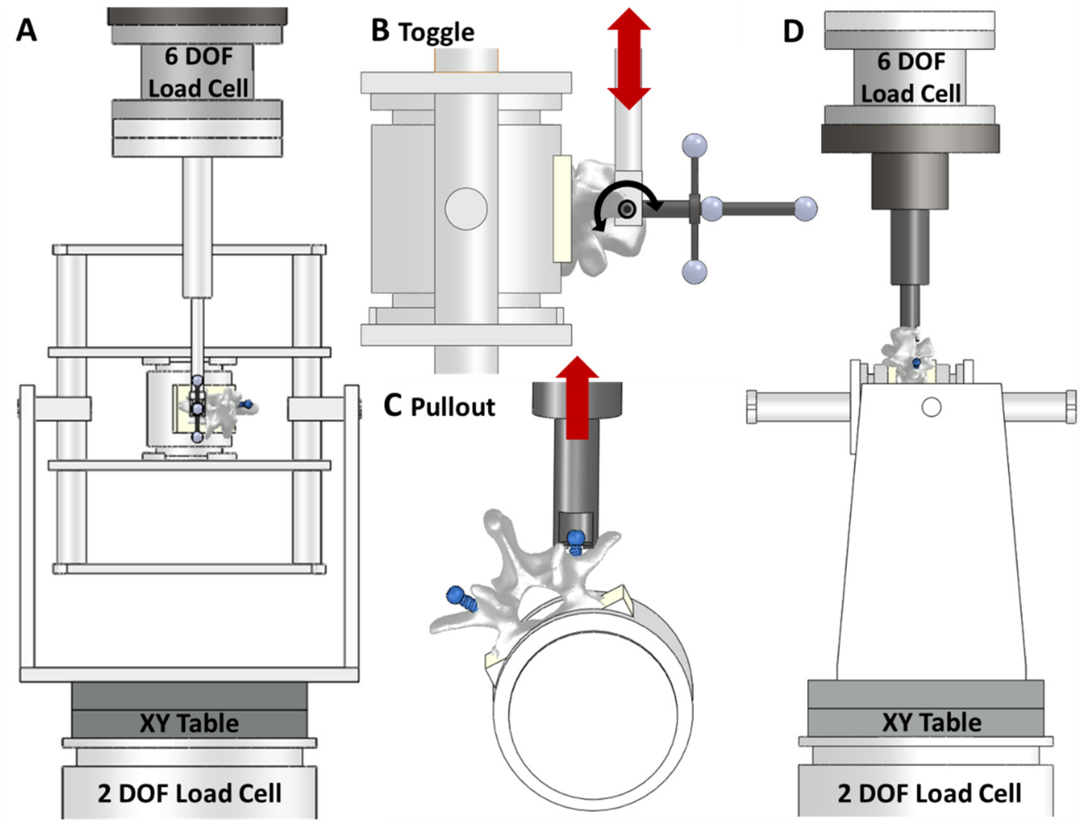


Figure 7.2 A schematic showing the *fatigue* (A & B) and the *pullout* (C & D) test setups.

7.1.3. Measured Parameters

The *pullout force* was defined as the peak force measured during axial ramp loading of the *pullout* testing which was followed by a drop in force of greater than 5% of the total applied force. The *fatigue force* was defined as the maximum force recorded at the screw head before the test was stopped at the predefined 5.4 mm caudal displacement. *Stiffness* was defined as the slope of the best-fit line to the force-displacement data of each cycle. Ten percent of the data from the maximum and minimum peak force were discarded to ensure only the linear portion of the curve was fit. The average *stiffness* for all cycles was calculated for both the first fatigue loading level (25-75 N compressive) and for the level at which the specimen failed. Screw motion parameters of *pivot point*, *head motion*, and *tip motion* were calculated as previously described in section 5.1.3.

Surgical Positioning and the Cement Distribution Pattern

Post-testing CT scans were taken (0.90 mm slice thickness, 0.45 mm spacing, Mx8000 IDT 16, Philips Healthcare, DA Best, NL) in order to determine screw positioning parameters (Figure 7.3), cement dispersion patterns, and vertebral characteristics. Screw positioning parameters consisted of *sagittal angle*, *transverse angle*, *pedicle depth*, *overhang*, *lever arm,* and *relative depth*. The cement dispersion parameters were *radial subvolume* and the *radial dispersion* along the screw axis. Vertebral parameters were the *pedicle area*, *pedicle width*, and *max incircle diameter* as well as the *ventral thickness*, *lateral thickness*, *pedicle thickness, cortical contact,* and *cortical volume*. Extensive methodological details and results for the screw positioning parameters, cement dispersion patterns, and the vertebral characteristics are covered by Schulz[204], Voigt[230] and Borrmann[24].

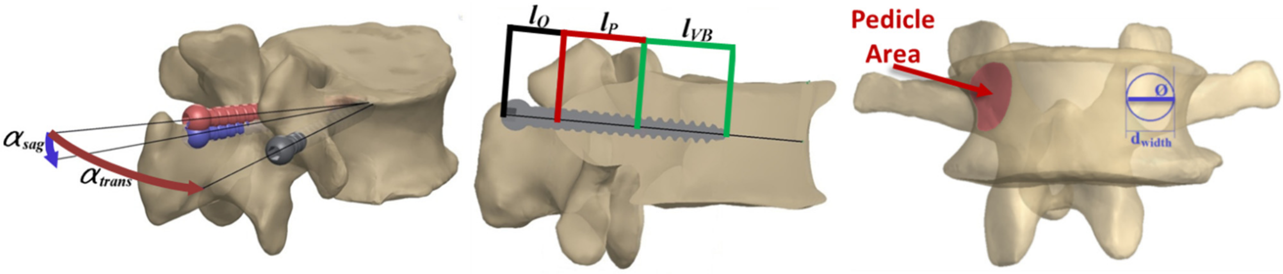


Figure 7.3 The measured angles (left) and depths (middle) for the pedicle screw in relationship to the vertebra. The measured pedicle dimensions are shown on the right with the *pedicle area* (red area), *max incircle diameter* (Ø) and the *pedicle width* (d_{width}). [Altered from Voigt[230]].

The individual vertebral bodies and pedicle screws were segmented and exported as a 3-Dimensional surface file (*.stl, Amira® 5.4, Mercury Computer Systems, San Diego, CA, USA). The surface file was transformed into a solid material for the creation of a local coordinate system in the center of the vertebral body and the determination of the positioning parameters (SolidWorks® 2011, Dassault Systèmes S.A., Vélizy, FR). The geometry of the pedicle screw was provided as a solid from ulrich medical®. The pedicle screw geometry was rigidly aligned to the segmentation of the pedicle screw geometry from the CT scans in Amira®. The determined transformation matrix from the rigid alignment was then applied within SolidWorks® to obtain an oriented vertebra with both pedicle screws positioned as they were in testing for each specimen. The *sagittal angle* was the measured angle between the pedicle screw axis and the transverse plane (Figure 7.3 left). The *transverse angle* was the measured angle between the pedicle screw axis and the sagittal plane. The *pedicle depth* (l_p) is the length from the screw entry to the end of the pedicle where it enters the vertebral body space. The *overhang* (l_o) is the distance from the head of the screw to the screw entry (Figure 7.3 middle). The *relative depth* is equal to the percentage of the distance from the pedicle end to the screw tip (l_{VB}) over the potential length from the end of the pedicle to the ventral vertebral wall. The *lever arm* was defined as the *overhang* plus the *pedicle depth* (l_o+ l_p). The *pedicle area* is the area of the pedicle cut at the narrowest region of the pedicle isthmus (Figure 7.3 right). The *pedicle width* is the width at the pedicle isthmus. The *max incircle diameter* is the maximum diameter of a circle which can safely fit within the area of the isthmus of the pedicle canal (Figure 7.3 right).

To quantitatively analyze the cement distribution patterns for the *prefilled* and the *screw injected* groups the vertebral shell and the cement with the screw were segmented manually (Avizo® 7.1, Mercury Computer Systems, VSG Group San Diego, CA, USA) and automatically (V6.5-1, Scanco Medical AG, CH). The script '*Calculate Auto Contour Trabecular Bone'* was used to automatically segment the vertebral cortical shell (P7 settings: 10-12-9-4-1-0) and the cement and screw (P7 settings: 10-6-6-2-3-1). From the segmented cortical shell a total volume was calculated (*cortical volume*) and an average thickness was determined from a rectangular region of the central ventral vertebral body wall (*ventral thickness*), the lateral vertebral body wall (*lateral thickness*), and along the superior portion of the pedicle (*pedicle thickness*, Figure 7.4).

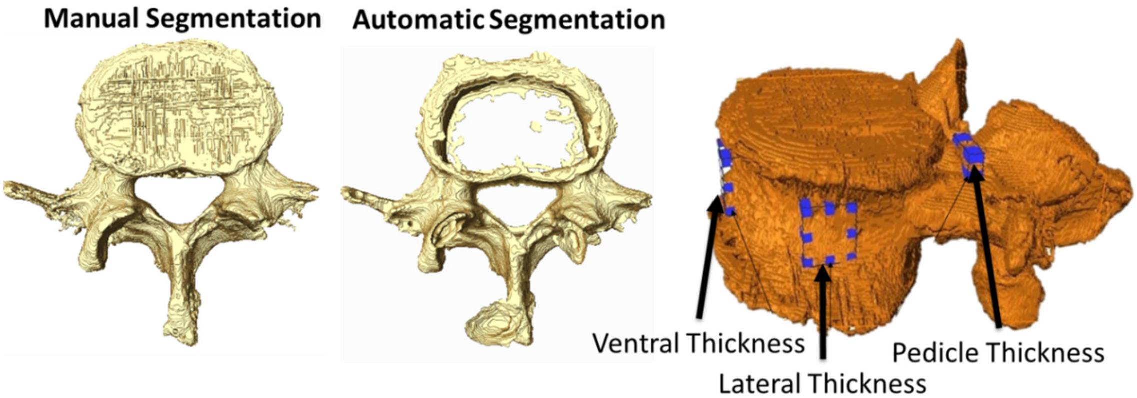


Figure 7.4 Images the cortical shell as segmented manually (left) and automatically (middle). The rectangular regions where the average cortical shell thickness was determined is shown (right). [Altered from Borrmann[24]]

The cement distribution pattern was quantified from the segmentations of the cement and screw (Figure 7.5). The segmentation was aligned directly down the screw axis with the cranial-caudal and medial-lateral axes aligned visually to the planes of the segmented vertebra. The segmentation was cut at the narrowest point of the pedicle isthmus. Five subvolumes along the screw axis were created (Figure 7.5). Each were cut at a length equal to 20% of the distance from the pedicle isthmus to the screw tip. A sixth and even seventh region was created if the cement was distributed past the screw tip. The volume of each of these regions was calculated (*radial subvolume*) along with a representative radius to estimate the amount of *radial dispersion* achieved by the cement. The *radial dispersion* (r) of each subvolume was calculated using the simplifying assumption that each region was cylindrical using Equation 7.1 (with: V=*radial subvolume*, h=length of the subvolume along the screw axis).

$$r = \sqrt{\frac{V}{\pi h}} \qquad \text{(Equation 7.1)}$$

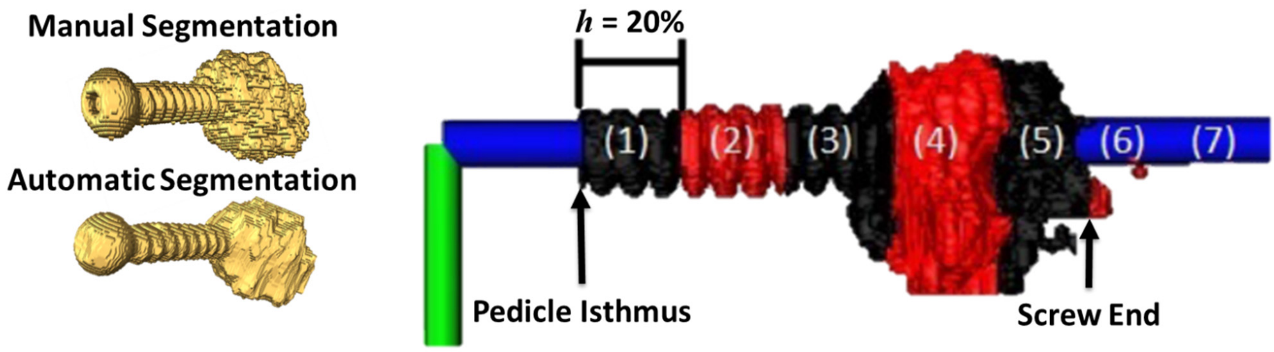


Figure 7.5 Perspective images are shown for the manual and automatic segmentations of the screw and cement (left column). A schematic of the subvolumes used to quantify cement dispersion (right). [Altered from Borrmann[24]]

The amount of contact the cement shared with the cortical shell, *cortical contact*, was also determined (Figure 7.6). The number of voxels which were manually segmented for both the cortical shell as well as for the cement were determined by combining the segmentations (using the 'relabel' tool in Avizo®), and then the *cortical contact* volume was calculated by multiplying by the volume of each voxel.

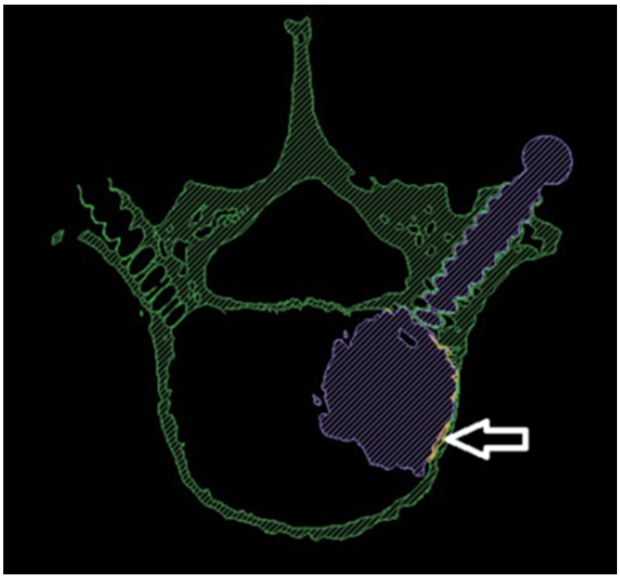


Figure 7.6 A representative slice showing the cortical shell (green) and the cement and screw (purple) segmentations. The area of overlap, the *cortical contact* (orange), is highlighted by the white arrow. [Reproduced from Borrmann[24]]

7.1.4. Statistical Analysis

Statistical analysis was performed using SPSS Statistics 20 (IBM Corp., Armonk, NY, USA) with a type I error probability set to 5%. Effect size magnitude is represented by Pearson Correlation (r) values and by partial eta squared (η_p^2) values for ANOVAs. For determining the relationship of *treatment group* to the primary fixation parameters of *fatigue* and *pullout* forces, a one-way analysis of covariance (ANCOVA) was used to adjust for the covariate BMD. For the ANCOVA analysis, the dependent variable was either the *fatigue* or the *pullout* force, and the independent variable, *treatment group*, included four levels: *native*, *big diameter*, *prefilled*, and *screw injected*. The conditions of independence, homogeneity of variance, homogeneity of the regression slopes and linear dependence of the covariate were met. Normality was confirmed according to the Kolmogorov-Smirnov test in all groups except for the *prefilled pullout* force group (p=0.04); under visual inspection of the histograms and normal Q-Q plots all groups appeared normal. A 2X4 mixed factorial ANOVA was used to detect if an interaction effect of the *testing method* (*pullout* vs. *fatigue*) on the force measured between the *treatment groups* existed. The *testing method* was the within-samples, repeated measures variable and the *force* measured was the dependent, between-samples variable. In general, the reported p-values are from an independent-samples, t-test except for the main comparison of *treatment group* to the *fatigue* and *pullout* forces in which the ANCOVA values are reported.

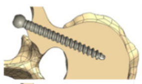
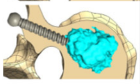
7.2. Results

The study design of equal allocation of BMD (p>0.99), gender (p>0.57), and vertebral level (p>0.83) was confirmed. The testing side (left or right) was also evenly distributed between the *testing methods* (p=0.67).

7.2.1. Primary Fixation Measures and the Effect of the Testing Method

The *pullout force* was significantly higher for both of the augmentation groups compared to the *native* group (*ps*<0.04, Table 7.2, Figure 7.7A). The *screw injected* was also significantly stronger in *pullout* than the *big diameter* group (p=0.001). The main effect was significant, with the *treatment group* influencing the *pullout force* (F(3,31)=10.072, p<0.001, η_p^2=0.49).

Table 7.2 The measured forces, stiffness, and motion parameters for both the pullout and the toggle testing broken down by the experimental groups (averages ± standard errors).

		Pullout Testing		Toggle Testing						
	Group	N	Force (N)	N	Force (N)	Stiffness First Level (N/mm)	Stiffness Last Level (N/mm)	Pivot Point (mm)	Head Motion (mm)	Tip Motion (mm)
	*Native*	10	782 ± 75.1	10	283 ± 39.7	324 ± 56.5	192 ± 20.8	30.7 ± 1.1	5.05 ± 0.33	4.07 ± 0.36
	Big Diameter	10	973 ± 144	10	298 ± 35.3	298 ± 40.2	213 ± 21.2	33.3 ± 1.8	4.66 ± 0.33	3.40 ± 0.31
	*Prefilled*	8*	1292 ± 105	9	262 ± 25.7	227 ± 31.1	136 ± 10.8	33.9 ± 1.2	4.74 ± 0.14	3.22 ± 0.29
	Screw Injected	7†	1485 ± 191	9‡	358 ± 47.4	274 ± 35.2	164 ± 17.9	34.0 ± 1.4	4.94 ± 0.10	3.30 ± 0.34
	Overall	**35**	**1094 ± 76.8**	**38**	**300 ± 19.0**	**291 ± 21.0**	**169 ± 9.4**	**32.9 ± 0.7**	**4.85 ± 0.13**	**3.51 ± 0.17**

*Mechanical malfunction during testing (S1L2). †During preparation no cement passed through two screws (S2L4 & S15L2) and a mechanical malfunction during testing (S9L5). ‡During preparation no cement passed through one screw (S13L3).

The *screw injected* group had the highest *fatigue force* (360 ± 27.4 N) which was significantly higher than that for both the *native* (281 ± 26.0 N, p=0.05) and the *prefilled* groups (268 ± 27.5 N, p=0.02) but not from the *big diameter* group (294 ± 26.0 N, p=0.09, Table 7.2, Figure 7.7B). The main effect of t*reatment group* on the *fatigue force* was not significant for the BMD adjusted model (F(3,33)=2.237, p=0.10, η_p^2=0.17).

There was a significant interaction of *testing method* and *treatment group* (Figure 7.7 C, F(3,31)=7.017, p=0.001[1], η_p^2=0.40). Some differences seen between the *treatment groups* in the conventional *pullout* testing did not hold true for testing in *fatigue* (*e.g. native vs. prefilled* was significant for *pullout* (p=0.002) but not for *toggle* (p=0.73).

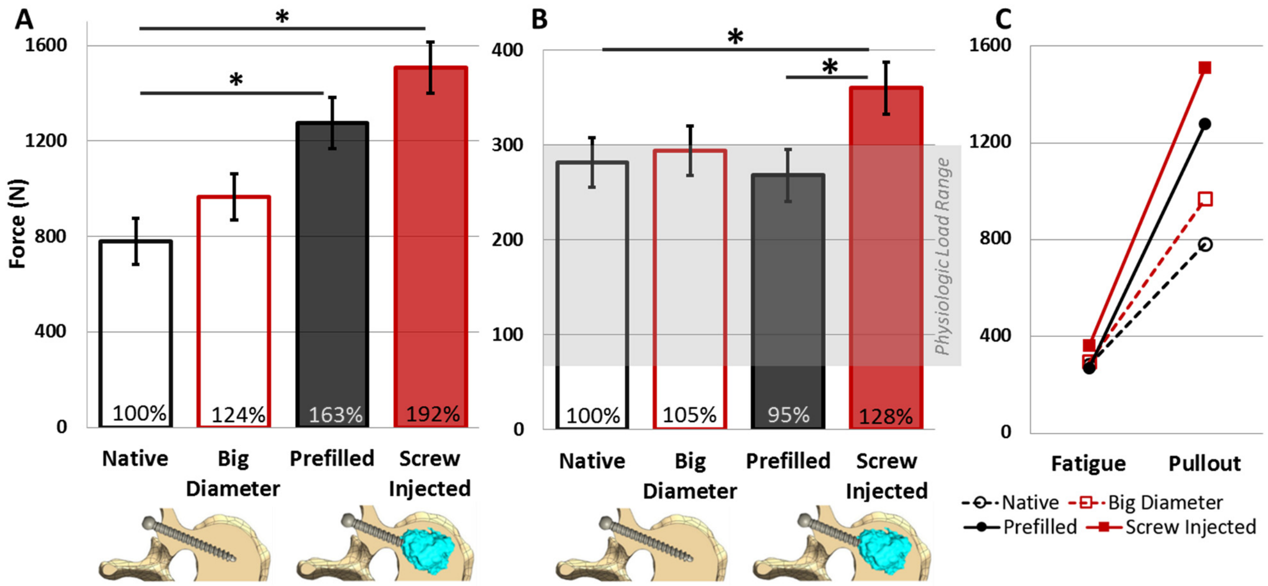


Figure 7.7 Graphs showing the *pullout force* adjusted for BMD (A) and *fatigue force* adjusted for BMD (B, error bars represent standard error). The grey box in B represents the range of forces measured *in vivo* during walking[181]. Hollow bars are unaugmented samples, whereas, filled bars are specimens with cement augmentation. The crossing slopes of the lines in the third graph (C) illustrate the significant interaction of *testing method* ($p<0.001$, $\eta_p^2=0.48$) between the *treatment groups*.

7.2.2. Influence of the Surgical Technique

A one millimeter increase in the outer diameter of the screw lead to a 24% increase in *pullout force* and a 5% increase in *fatigue force*. Furthermore, it led to the highest *stiffness* in the final loading level with a significant 39% increase from the prefilled group (*p*=0.01). The big diameter group also had the least reduction (-29%) of *stiffness* from the first to last levels of loading during testing, followed by *prefilled* (-40%), *screw injected* (-40%), and *native* (-41%, Table 7.2).

Both screw augmentation techniques significantly increased the pullout force from the native group (*ps*<0.04). Screw injected augmentation significantly increased pullout force by 92% (p<0.001) from the native group and by 36% from the big diameter group (*p*=0.001, Table 7.2). The prefilled group had a significant 63% increase in pullout force from the native group (*p*=0.04). Fatigue results were mixed with the screw injected group increasing the fatigue force by 28% from the native group; whereas, the prefilled group reduced the fatigue force by 5%. Augmentation led to a lower first and last level stiffness than the native group (Table 7.2). The stiffness of the first level was reduced by 15% and 30% for the screw injected and the prefilled respectively.

The augmentation technique did not alter the rate of cement leakage with both augmentation groups having leakage in 6 of 9 vertebrae (Table 7.3). The injection of the cement through the screw (screw injected) led to a reduction in cement volume in comparison to the prefilled group (*p*=0.001, *r*=0.52, Table 7.3). Furthermore, in 17% of the screws (3 of 18) cement did not pass through the screw tip. There was no difference between cement volume for the testing method (*p*=0.40). When both augmentation groups were analyzed together the cement volume did not correlate to fatigue or pullout force (*p*>0.21). However, for individual group analysis, the screw injected group exhibited an increase in both fatigue and pullout force with an increase in cement volume (*p*=0.01, *p*=0.03 respectively). The prefilled group exhibited no volume effects (*p*>0.53). The cement volume did not correlate with any stiffness value (*p*s>0.09) or with pivot point location (*p*s>0.14) overall or by augmentation technique.

Table 7.3 The values measured for the cement volume and distribution as well as the vertebral characteristics of cortical shell volume and cortical thicknesses (averages ± standard errors).

Group	N	Cement Volume (cm^3)	Cement Leakage Yes	Cement Leakage No	N	Cortical Contact (mm^3)	Max. Radial Dispersion (mm)	Max Radial Subvolume (cm^3)	Cortical Shell Vol. (cm^3)	Pedicle Thickness (mm)	Ventral Thickness (mm)	Dorsal Thickness (mm)
Prefilled	9*	3.1 ± 0.4	6	3	5†	9.7 ± 2.6	6.5 ± 0.4	2.04 ± 0.20	17.1 ± 2.2	2.5 ± 0.4	1.0 ± 0.1	1.1 ± 0.1
Screw Injected	9‡	1.8 ± 0.4	6	3	5†	70.2 ± 24.5	6.1 ± 0.4	1.99 ± 0.17	19.3 ± 1.4	2.4 ± 0.5	1.0 ± 0.1	1.2 ± 0.1
Overall	**18**	**2.5 ± 0.3**	**12**	**6**	**10**	**40.0 ± 15.4**	**6.3 ± 0.3**	**2.01 ± 0.12**	**18.2 ± 1.3**	**2.5 ± 0.3**	**1.0 ± 0.1**	**1.2 ± 0.1**

*L3 of one specimen was unusable due to prior fracture of the lamina and pedicles. ‡During preparation no cement passed through one screw (S13L3). †Five representative samples from each group were chosen for this analysis.

Cement distribution patterns changed with the augmentation technique (Figure 7.1). The maximum *radial dispersion* and *radial subvolume* did not differ between groups (*p*s>0.51, Table 7.3); however, the distribution of where the peaks occurred in relationship to the pedicle were different (Figure 7.8). The *prefilled* group generally had a larger, more anterior distribution extending along the screw axis. Peaks in the *radial dispersion* and *radial subvolumes* occurred from 60-120% of the screw depth into the vertebral body (Figure 7.8 left). The peaks from 80-120% of the screw depth (the 5th and the 6th subvolume) were significantly higher for the *prefilled* group when compared to the *screw injected* group (*p*s<0.03). The *screw injected* group had a more posterior distribution with peaks in the *radial dispersion* and *radial subvolumes* occurring from 40-80% of the screw depth into the vertebral body (Figure 7.8 right). The *screw injected* group had a higher peaks in the 3rd subvolume of both the *radial dispersion* (*p*=0.09) and *subvolume* (*p*=0.04) than the *prefilled* group (Figure 7.8). The peaks in the 3rd subvolume (40-60% of screw depth) of both *radial dispersion* and *subvolume* for the automated technique were significantly positively correlated to the *fatigue force* (*p*s<0.005, *r*s>0.77).

The volume of the cement in contact with the cortical shell (*cortical contact*) was significantly larger for the *screw injected* group (70.2 ± 24.5 mm^3) than the *prefilled* group (9.7 ± 2.6 mm^3, *p*=0.03). The volume of *cortical contact* positively correlated with the specimen *fatigue force* (*p*=0.004, *r*=0.81), first level *stiffness* (*p*=0.008, *r*=0.77), and last level *stiffness* (*p*=0.03, *r*=0.67) when the one influential outlier (Cook's distance=3.6, standardized DFFit=-4.2: where values greater than 1 are considered influential outliers[72]) was removed.

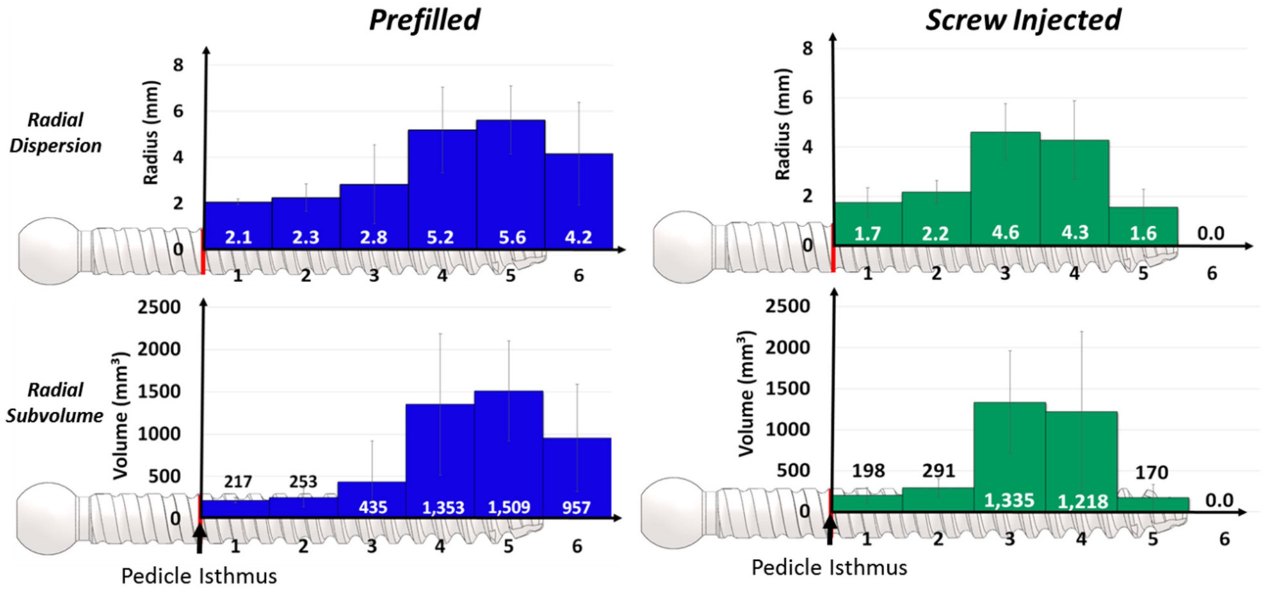


Figure 7.8 The cement dispersion patterns in terms of *radial dispersion* and *radial subvolumes* along the screw axis for both the *prefilled* (blue) and the *screw injected* (green) groups. There were no significant differences between the manually segmented cement dispersion patterns and the automatically segmented patterns; therefore, only the values for the manual segmentation are shown.

7.2.3. Surgical Positioning Parameters

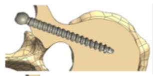
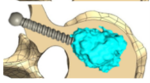
As desired, none of the measured surgical positioning parameters were significantly different between the *treatment groups* (*p*s>0.32, Table 7.4). The surgeon was able to achieve a sufficient screw depth by obtaining a depth of 77-79% of the possible length within the vertebral body (relative depth, Table 7.4). No surgical positioning parameters correlated with pullout force when considering all samples (*p*s>0.38) or for only including the native group (*p*s>0.26). The pedicle depth (range: 34.7-48.5 mm) correlated with the fatigue force (p=0.02, r=-0.39), and the stiffness of the first (p=0.001, r=-0.51) and last loading level (p=0.007, r=-0.44) but not with pullout force (p=0.29, Table 7.4). The overhang (range: 9.7-17.7 mm) did not correlate with any fixation parameter (*p*s>0.43). The lever arm[1] (range: 27.5-37.7 mm) had similar results as the pedicle depth but often with more variance explained. The lever arm correlated with the fatigue force (p=0.002, r=-0.48), stiffness of the first (p<0.001, r=-0.60) and last loading level (p=0.01, r=-0.40) but not with pullout force (p=0.65). The relative depth did not correlate with any fixation parameter (*p*s>0.28).

The sagittal angles covered a range from -7.6° to 17.0° and the transverse angles from 10.2° to 40.4°. The sagittal angle did not significantly correlate with any fixation parameter; however, there were trends with the fatigue force (p=0.06, r=0.31) and the stiffness of the first level (p=0.08, r=0.30). The angle of the screw in the transverse plane, transverse angle, did not correlate with any fixation parameter (*p*s>0.35).

[1] Since the *overhang*, *pedicle depth,* and the vertebral body depth all sum to equal the screw length, the *lever arm* (*overhang* + *pedicle depth*) and the vertebral body depth are intrinsically related. Only the *lever arm* correlations are reported.

When only considering native group the pedicle depth (*ps*>0.21) overhang (*ps*>0.28), lever arm (*ps*>0.39), relative depth (*ps*>0.57), and sagittal angle (*ps*>0.19) did not correlate with any fixation parameter. The transverse angle correalted with a decreased stiffness of the last level (*p*=0.03, *r*=-0.73).

Table 7.4 The measured screw positioning parameters broken down by *treatment group* (averages ± standard errors).

	Group	N	*Pedicle Depth* (mm)	*Overhang* (mm)	*Lever Arm* (mm)	*Relative Depth* (mm)	*Sagittal Angle* (°)	*Transverse Angle* (°)
	*Native*	9†	18.1 ± 0.6	13.4 ± 0.7	31.5 ± 0.8	77% ± 2%	4.5 ± 1.0	29.5 ± 1.7
	Big Diameter	10	19.0 ± 0.8	13.6 ± 0.6	32.6 ± 0.6	78% ± 2%	2.3 ± 1.8	26.8 ± 1.7
	*Prefilled*	9*	20.1 ± 0.8	12.7 ± 0.6	32.8 ± 0.8	78% ± 2%	-0.6 ± 2.0	24.6 ± 2.3
	Screw Injected	9‡	19.2 ± 1.2	12.3 ± 0.5	31.5 ± 1.2	79% ± 3%	1.7 ± 2.5	27.2 ± 3.2
	Overall	**37**	**19.1 ± 0.4**	**13.0 ± 0.3**	**32.1 ± 0.4**	**78% ± 1%**	**2.0 ± 1.0**	**27.0 ± 1.1**

†One specimen missing because there was no post-testing CT scan. *L3 of one specimen unusable due to prior fracture of the lamina and pedicles. ‡During preparation no cement passed through one screw (S13L3).

7.2.4. Influence of the Patient and the Vertebral Characteristics

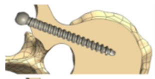
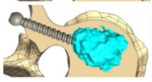
The specimen bone quality in terms of BMD was the only parameter which significantly correlated with all four fixation parameters: *pullout force* (*p*=0.003, *r*=0.48), *fatigue force* (*p*<0.001, *r*=0.69), *stiffness* of the first (*p*<0.001, *r*=0.67) and last level (*p*=0.003, *r*=0.65). Volume of the cortical shell was approximately 30% of the entire vertebral body. It correlated with an increase in the *stiffness* of the first level (*p*<0.001, *r*=0.60). The cortical shell thickness was consistently around 1.0-1.2 mm for the ventral and the lateral walls of the vertebral body. The thickness of the pedicle canal was double that of the vertebral body walls at 2.5 ± 0.3 mm (Table 7.3). Cortical shell thickness as determined by manual segmentation did not influence any of the fixation parameters.

The anatomical dimensions of the pedicle significantly influenced the screw fixation strength of the *native* group. The *pedicle area* negatively correlated with the *fatigue force* (*p*=0.03, *r*=-0.721) and *stiffness* of the last loading level (*p*=0.04, *r*=-0.68) when only considering the *native* group. The *max incircle diameter* correlated with the *stiffness* of the first level (*p*<0.05, *r*=-0.67). *Pedicle width* (*ps*>0.09) did not influence the fixation parameters. When all specimens were included, the *pedicle width* (*ps*>0.21), *pedicle area* (*ps*>0.16), and *max incircle diameter* (*ps*>0.44) did not influence fixation.

All the measured specimen anatomical characteristics were not significantly different between *treatment group* (*ps*>0.38, Table 7.5). The *vertebral volume* and the *vertebral body volume* did not correlate with any fixation parameter (*ps*>0.16). The volume of both the vertebra and the vertebral body increased from L1 to L4 (Table 7.6). The only surgical positioning parameter which was influenced by vertebral anatomy was the *transverse angle* (Table 7.7). The *transverse angle* increased from L1-L5, this goes along with the alignment of the screw along the pedicle axis.

Pedicle dimensions were shown to change with the vertebral level; increasing from cranial to caudal (Table 7.6). The maximum diameter which could safely pass through the pedicle without piercing the cortical shell (*max incircle diameter*) was similar (≤0.5 mm) to the minor pedicle diameter (*pedicle width*) for L1-L3; however, as the teardrop shape of the pedicle increased with a more caudal vertebral level the average discrepancy increased to 3.5 mm for L4 and a substantial 7.9 mm for L5 (Table 7.6).

Table 7.5 The measured specimen anatomical characteristics parameters broken down by *treatment group* (averages ± standard errors).

	Group	N	*Vertebral Volume* (cm^3)	*Vertebral Body Vol.* (cm^3)	*Pedicle Width* (mm)	*Max Incircle Ø* (mm)	*Pedicle Area* (mm^2)
	***Native***	9†	64.2 ± 5.1	42.3 ± 3.4	13.0 ± 1.0	11.5 ± 0.5	170 ± 17.1
	Big Diameter	10	62.8 ± 5.2	40.1 ± 3.4	12.8 ± 2.1	9.9 ± 0.9	149 ± 24.4
	***Prefilled***	9*	66.4 ± 5.4	44.0 ± 3.6	14.4 ± 2.1	11.4 ± 1.1	181 ± 30.0
	Screw Injected	9‡	61.7 ± 3.5	40.8 ± 2.1	12.5 ± 1.5	9.8 ± 0.9	135 ± 14.0
	Overall	**37**	**63.7 ± 2.4**	**41.8 ± 1.6**	**13.1 ± 0.8**	**10.6 ± 0.4**	**159 ± 11.1**

†One specimen missing because there was no post-testing CT scan. *L3 of one specimen unusable due to prior fracture of the lamina and pedicles. ‡During preparation no cement passed through one screw (S13L3).

Table 7.6 The measured specimen anatomical characteristics broken down by vertebral level (averages ± standard errors).

Level	N	*BMD* (gHA/cm3)	*Vertebral Volume* (cm^3)	*Vertebral Body Volume* (cm^3)	*Pedicle Width* (mm)	*Max Incircle Ø* (mm)	*Pedicle Area* (mm^2)
L1	7	104 ± 13.0	57.4 ± 5.2	39.1 ± 3.4	9.8 ± 0.9	9.4 ± 1.0	130 ± 20.0
L2	8	80 ± 12.6	60.0 ± 5.4	39.8 ± 3.7	9.5 ± 0.9	9.3 ± 0.8	123 ± 17.7
L3	6	80 ± 15.6	65.3 ± 6.0	41.7 ± 3.8	10.9 ± 1.2	10.4 ± 1.2	143 ± 23.1
L4	9	98 ± 13.0	68.4 ± 4.5	44.5 ± 3.0	14.5 ± 1.3	11.0 ± 0.7	163 ± 18.8
L5	7	103 ± 14.0	67.0 ± 6.0	43.2 ± 4.2	20.9 ± 1.3	13.0 ± 0.8	235 ± 27.1
Overall	**37**	**93 ± 6.0**	**63.7 ± 2.4**	**41.8 ± 1.6**	**13.1 ± 0.8**	**10.6 ± 0.4**	**159 ± 11.1**

Table 7.7 The measured surgical positioning parameters broken down by vertebral level (averages ± standard errors).

Level	N	*Pedicle Length* (mm)	*Vertebral Depth* (mm)	*Relative Depth* (mm)	*Overhang* (mm)	*Sagittal Angle* (°)	*Transverse Angle* (°)
L1	7	20.0 ± 0.8	25.8 ± 1.0	76% ± 3%	12.4 ± 0.6	0.6 ± 2.2	22.0 ± 3.3
L2	8	18.5 ± 1.0	26.0 ± 1.0	77% ± 2%	13.6 ± 0.5	1.0 ± 2.0	23.9 ± 1.5
L3	6	18.9 ± 1.2	25.0 ± 1.1	74% ± 3%	14.3 ± 0.8	3.4 ± 2.7	29.3 ± 2.1
L4	9	18.4 ± 0.8	27.3 ± 0.7	81% ± 2%	12.4 ± 0.6	1.4 ± 1.6	28.5 ± 1.9
L5	7	19.8 ± 1.2	25.6 ± 1.1	80% ± 3%	12.8 ± 0.7	3.9 ± 2.7	31.7 ± 2.4
Overall	**37**	**19.1 ± 0.4**	**26.1 ± 0.4**	**78% ± 1%**	**13.0 ± 0.3**	**2.0 ± 1.0**	**27.0 ± 1.1**

7.2.5. Screw Motion during Compressive Fatigue Testing

A similar failure pattern emerged for all *treatment groups* in which the screw head displaced caudally and the screw tip cranially. A distinct fulcrum (*pivot point*) was located near the end of the pedicle for all *treatment groups* (Figure 7.9). The average *pivot point* was shown to be closest to the screw head and within the pedicle for the *native* group (30.7 ± 1.1 mm). The average *pivot point* moved further into the vertebra and was just outside the pedicle end for the *big diameter* (33.3 ± 1.8 mm), *prefilled* (33.9 ± 1.2 mm), and *screw injected groups* (34.0 ± 1.4 mm, Table 7.2). The *pivot point* moved further towards the screw tip with a lower specimen BMD (p=0.004, r=-0.46), decreasing *fatigue force* (p=0.04, *r*=-0.34), decreasing *stiffness* of the first level (*p*=0.01, *r*=-0.43), and decreasing *tip motion* (*p*<0.001, *r*=-0.83).

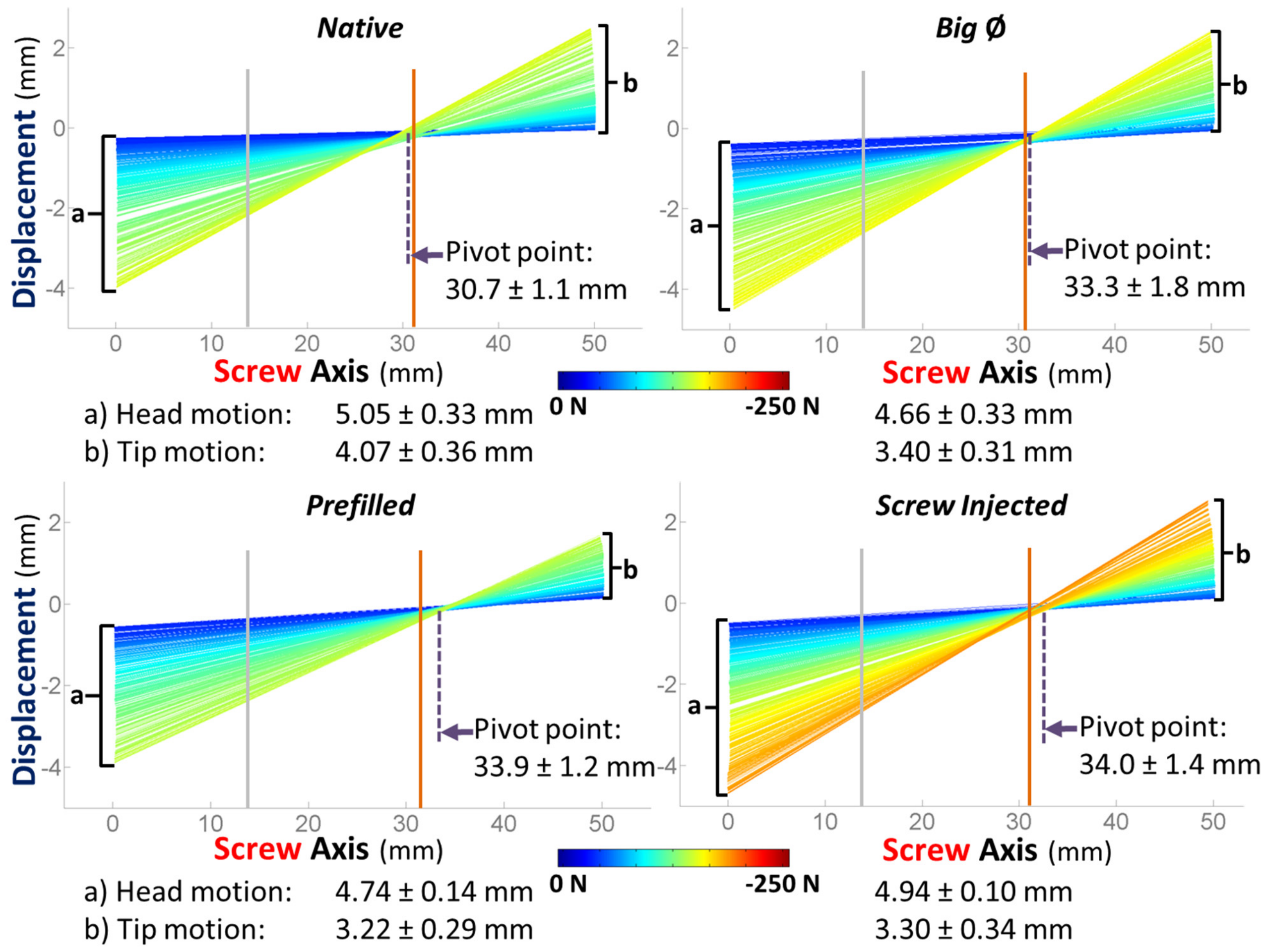


Figure 7.9 The average motion patterns for the four *treatment groups* showing caudal displacement of the screw head, a cranial displacement of the screw tip and a distinct *pivot point* near the end of the pedicle. The grey line represents the entry of the screw into the vertebra (*overhang*) and the orange line represents the average *pedicle depth*.

7.3. Discussion

The stepwise increase in the *pullout* force which was exhibited for the treatment groups was not exhibited for *fatigue* force (Figure 7.7). A significant interaction occurred between the *testing method* (p=0.001, η_p^2=0.4) and *treatment group* (Figure 7.7C). This was likely driven by the fact that the significant increase in *pullout* strength seen for the *prefilled* group compared to the *native* group was not seen during *fatigue* testing. On the contrary, the *prefilled* group actually had the lowest average *fatigue force* of all treatment groups (Table 7.2). The presence of this interaction suggests that performing *pullout* testing alone could lead to the never experimentally desired false positive (Type I error). A false positive could potentially be clinically detrimental. Fixation strength determined by these pre-clinical testing techniques (*pullout* and *fatigue*) are used to gain insight into which screw designs or surgical techniques should perform best in clinical practice. False positives may lead to the adoption of techniques which do not help, or in the worst case scenario, can perhaps negatively influence clinical results. Although *pullout* testing was more sensitive, the differences detected did not hold true for the more physiological *fatigue* testing, thus casting further doubt that the differences determined by *pullout* are clinically relevant. This is even further highlighted by how poorly *pullout* is received as a clinically relevant failure mode[58].

The *screw injected* group exhibited a marked rise of *fatigue force* (~80N) from the other three treatment groups. The magnitude of this *fatigue force* increase may be of clinical note because it places the *screw injected* group out of the physiologic loading range experienced during *in vivo* walking (75-300 N)[17,181].

In agreement with comprehensive biomechanical literature[16,26,28,43,212,235,248], both augmentation techniques were shown to increase the *pullout force* of pedicle screws in osteoporotic bone ($p<0.002$). The choice of augmentation technique was also shown to influence the fixation strength of the screw: the *screw injected* technique showed both a higher *pullout* (15%) and a higher *fatigue* (37%) strength than the *prefilled* technique. This matched the study by Cholma et al.[43] who showed an increase in *pullout force* for cement injected through the screw over a prefilled technique.

Since the cement used for the two augmentation techniques was the same it lead to the question: where does the benefit of the *screw injected* technique originate? It seems as though the pattern of cement dispersion played a key role. The breadth of the cement pattern, *radial dispersion,* and the amount of cement in contact with the cortical shell, *cortical contact,* have both previously been shown to influence the fixation strength of pedicle screws[206,213]. Since the maximum magnitude of the *radial dispersion* and *radial subvolumes* of the cement did not differ and the location of the peaks did, it leads one to believe that the location of the *radial dispersion* peaks is the driving factor for fixation. The *screw injected* technique had a significantly wider distribution of the cement closer to the pedicle which is shown by the distribution patterns along the screw axis (subvolume 3, Figure 7.8). Furthermore, the *screw injected* group was able to obtain a significant 7 fold increase in cement contact with the cortical shell (Table 7.3). Since both (1) an increase in the volume or the *radial dispersion* in the 3rd subvolume, and (2) an increase in the *cortical contact* both correlated with an increase in *fatigue force* it leads one to believe that a cement distribution pattern closer to the pedicle end which can obtain high *cortical contact* is best for screw fixation.

The screw injected technique is perceived to have less chance of leakage due to the controlled release through the tip of the screw after screw placement. This was not corroborated in this study as both techniques resulted in 6 of 9 vertebra with cement leakage. The high rate of loosening is likely due to the surgeon applying cement until no more could be injected or leakage was detected. The *screw injected* technique resulted in 17% of screws without cement at the tip as well as a significant reduction in cement volume compared to the *prefilled* technique (p=0.001, r=0.52). Careful attention should be paid to the viscosity of the cement and the timing of injection to ensure proper dispersion.

An intriguing effect was a loss of *stiffness* of the specimens after augmenting the vertebra with a cement whose stiffness is three times that of the osteoporotic trabecular bone. This effect was seen previously by Kiner et al.[112] in a toggling fatigue study with specimen augmented prior to screw insertion. In order to explain the decrease in stiffness the location of the *pivot point* is important. With both augmentation and an increase in diameter the *pivot point* moved further into the vertebral body (Table 7.2). This increase in *pivot point* depth resulted in an increase in the *lever arm* which in turn allowed the screw head to deform more easily, characterized but the loss of fatigue *stiffness*.

A parameter to quantify the damage to trabecular bone is the loss in stiffness of a sample[112]. From this measure the *big diameter* group would be the least damaging treatment method. This corresponds well with the results of Kiner et al.[112] which showed an increase in diameter by 2 mm decreases the damage of the specimens over that of no treatment or cement augmentation. The combination of a reduced *stiffness* loss and an increase in both *pullout* and *fatigue* strength would suggest using larger diameter screws to be a valuable method for osteoporotic fixation.

Although increasing the screw diameter appears to be beneficial to fixation, the screw size is limited by the anatomical constraints of the pedicle canal. The minor pedicle diameter has been shown to be the limiting factor for the diameter used in surgery. This was confirmed in this study for the levels of L1-L3; however, the tear drop shape of the pedicle in L4 and L5 created a pathway which could not receive a screw the width of the minor diameter. This is shown by the fact that the *max incircle diameter* was smaller than the *pedicle width* by 3.5 and 7.9 mm in L4 and L5 respectively (Table 7.6). Nevertheless, the screw diameters used in this study (5.5 and 6.5 mm) and often in orthopaedic lumbar surgery are likely well within the anatomic limits for the lower lumbar region, as the average *max incircle diameter* was >11.0 mm (Table 7.6).

7.3.1. Influence of the Surgical Positioning Parameters

Neither the angles nor the depths of the screw correlated with the *pullout force* (*p*s>0.26). The depth of the screw and the amount of screw protruding from the vertebra seemingly influence the *fatigue* fixation more than the angles of insertions. For the lumbar spine, the fatigue fixation parameters increased with decreasing both the *lever arm* and the *pedicle depth* as well as with a greater depth in the vertebral body. The length of the screw within the pedicle (*pedicle depth*) is highly dependent on the anatomy of the patient and; therefore, the focus for surgical placement should be on minimizing the distance of the screw protruding out of the vertebra as well as maximizing the length within the vertebral body. A lumbar surgical placement directly down the pedicle axis could be ideal since it would minimize the length within the pedicle and a similar, maximal vertebral depth can be achieved. The angles and depths were not systematically varied, therefore, the correlations presented are results from a random effects analysis.

7.3.2. Influence of the Vertebral Characteristics

Bone quality in terms of both BMD and cortical shell volume influenced the *fatigue* fixation parameters of the pedicle screw. Increasing BMD was related to a shallower *pivot point* (increases *fatigue force*, p=0.04, r=0.34), an increase in *stiffness* (increases *fatigue force*, p<0.001, r=0.72), and increase in *tip motion* (increases *fatigue force*, p=0.02, r=0.37). This combination explains the highly positive correlation of BMD to *fatigue force* (p<0.001, r=0.69). Furthermore, BMD correlated with all four fixation parameters and had larger power than any of the cortical shell measurements. Therefore, it is believed that BMD has greater influence than the other measured cortical shell or vertebral volume parameters on the fixation parameters. However, one distinct limitation for this comparison is that the cortical shell parameters only had ten samples which were measured and all were augmented with cement. The pedicle dimensions of *pedicle area* and *max incircle diameter* were shown to correlate with *fatigue* fixation when only the *native* group was considered but not when including the augmentation groups. Perhaps the addition of augmentation reduces the influence of the pedicle dimensions on the fixation parameters.

7.3.3. Screw Motion during Compressive Fatigue Testing

The *fatigue* loading profile used induced a cranial toggle failure pattern () which has been shown to exist in the clinical loosening patterns of the upper lumbar and the cervical regions of the spine (Chapter 4, Appendix C). The motion was characterized by a distinct fulcrum (*pivot point*) which was located near the end of the pedicle. The presence and the location of the *pivot point* corresponds well with previous studies[129,222]. Decreasing the *pivot point* moved the center of rotation closer to the pedicle canal from the vertebral body. If the *pivot point* moved into the narrow canal surrounded by cortical bone this would accomplish two things: to shorten the *lever arm* and allow for more support from the stronger cortical bone. Both of these could help explain why a decrease in *pivot point* increased *stiffness* (p=0.007, r=-0.43) and increased *fatigue force* (p=0.04, r=-0.34). Perhaps altering the screw design to ensure a *pivot point* at the strongest point of attachment- the center of the pedicle isthmus- could be a way to increase screw fixation.

One limitation of this study is the relatively small sample size which is often the case in biomechanical cadaveric testing due to limitation of sample availability. This is clearly highlighted in the analysis of *fatigue force* in which for the overall model the *treatment group* did not have a significant effect on the *fatigue force* (p=0.10) even though there was a large effect size (η_p^2= 0.17)[48]. Not finding significance is likely due to not having sufficient numbers in the groups (n=9-10, observed power =0.52). This limitation of sample size was not present in *fatigue* testing due to a nearly tripled effect size (η_p^2=0.49) which led to an observed power of 1.0. This power of the experiment can be increased in future experiments by using the varying treatment groups on the same specimen but opposite pedicles to allow for a within groups analysis rather than between groups. This study used the *testing method* as the within groups variable because determining if there was an interaction between *pullout* and *fatigue* was the primary goal.

7.4. Conclusions

Although *pullout* testing is the standard screw fixation test for the spine[8], *pullout* has not been shown as relevant failure mechanism. This is due to the lack of clinically reported cases and biomechanically it is not believed to be the mechanical mechanism of screw loosening[58,112]. The significant interaction of the *treatment group* and the *testing method* (p=0.001, η_p^2=0.4) casts doubt that significant findings from *pullout* testing can correspond to increases in the more physiologic *fatigue* testing let alone the clinical situation.

This study reproduced the classic effect that screw augmentation with any technique significantly increases the axial *pullout* strength of pedicle screws (*p*<0.002). The pattern of the cement dispersion in the *screw injected* technique likely led to an increase in fixation due to a more posterior cement distribution and a significant seven-fold increased the *cortical contact* (*p*=0.03).

Screw injected augmentation had the highest *fatigue* and *pullout* strength of all groups. The magnitude of the *fatigue* strength increase is perhaps clinically significant because it raises the average above the maximum *in vivo* forces for walking or sitting (Figure 7.7)[17,181,185].

Increasing screw diameter by one millimeter increased *pullout* by 24% and *fatigue* strength by 5% from the *native* group while inducing the least loss in *stiffness* during *fatigue* testing. Reducing the length of the screw outside the vertebra and within the pedicle while increasing the screw depth in the vertebra were all shown to increase the fatigue fixation strength. These findings highlight the importance of using the anatomical dimensions to the fullest: a diameter near the minor pedicle diameter and a depth close to ventral vertebral wall while minimizing *overhang* and using a trajectory directly down the pedicle axis would be ideal.

Chapter 8.
Design Concepts

Pedicle screw fixation has been shown to be safe and effective in promoting fusion and in restoring vertebral alignment and sagittal balance. However, after instrumentation loosening at the screw-bone interface can occur, especially in osteoporotic patients. This loosening has been shown to be a predominant failure mode and can often lead to non-fusion or the necessity for revision surgery. Alterations of the screw thread design have generally not been studied in terms of a physiologic fatigue force but only with a simple posterior pullout[1,6,36,59,121,125,210] test which cannot give time dependent fatigue behavior. The specific goals of this project were to quantify fatigue strength at the bone screw interface for changes in screw pitch, core shape, adding posterior support or for lateral placement of a screw.

There are multiple avenues that are being explored to decrease the frequency of pedicle screw loosening with the regard to changes in screw design such as thread design, diameter, length, and screw coatings. Due to vertebral geometry restrictions the length and the diameter are limited. Therefore, investigations into the screw thread design, external support or screw positioning are of interest.

The volume of bone between the screw threads has been shown to be the primary factor which influences the resistance against pullout[121,209,210]. The projected bone screw contact area (often termed the FOA, the flank overlap area) has thus been identified as an important parameter for pullout strength. In general, decreasing the pitch increases the contact area and is shown to increase pullout strength. However, both Asnis et al.[6] and Krenn et al.[121] showed that if the pitch becomes too narrow the trabecular bone does not fill the thread space and the strength is reduced. Conversely, Skinner et al.[210] determined that a greater pitch leads to a better screw performance while pullout testing due to more bone being in each thread valley due the greater distance between each crest. This finding was non-significant when the same outer diameter was used.

A human vertebral study of insertional torque and pullout force showed that a conical core was able to significantly increase insertional torque but not pullout strength[125]. Abshire et al.[1] used a porcine model to investigate one conical and one cylindrical screw design and found better pullout strength which was attributed to progressive compression of the surrounding bone. After either a 180° or 360° backout no fixation strength was lost. However, another study showed a 180° backout can reduce the fixation[135].

The primary objective of this *ex vivo* study was to compare five various screw designs and one variety of surgical positioning based on screw fatigue stability of the human lumbar spine in terms of *cycles to failure*, *removal torque*, *initial stiffness*, *final stiffness* and failure patterns. It was hypothesized that a greater outer surface area or an external support touching the posterior cortical shell may more evenly distribute the concentrated loading along the screw profile. It was thought that this could in turn reduce the risk of screw fatigue loosening.

8.1. Methods

In order to isolate effects of screw design on fatigue fixation strength the effect of specimen variability was reduced as much as possible by utilizing a repeated measures design. Each vertebra received one *prototype* and one *reference* screw. There were five prototype groups (*pitch1*, *pitch2*, *krypton*, *offset*, and *positioning*) tested against the *reference* screw using a steadily increasing cranial-caudal, sinusoidal loading.

8.1.1. Study Materials

Fourteen male thoracolumbar spinal specimens (T12-L3) were received after ethics approval (Hamburg Ethics Committee, PV 3940). The specimens were sealed in double plastic bags and stored at -20°C.

Preoperative CT scans (0.90 mm slice thickness, 0.45 mm spacing, Mx8000 IDT 16, Philips Healthcare, DA Best, NL) were performed with a phantom (QRM-BDC, QRM, Möhrendorf, DE) and were used to exclude anatomical malformations or fractures and to determine the apparent volumetric bone mineral density (BMD). Trabecular volumetric BMD was determined by segmenting a 75 x 75 x 25 voxel cube from the vertebral center (Avizo version 7.1, Mercury Computer Systems, San Diego, CA, USA). The average Hounsfield unit value was then scaled linearly to the reference densities of the phantom.

The thirty-nine human lumbar vertebrae were distributed between the testing groups by separating them equally based on BMD, vertebral level (T12-L3), and age (Table 8.1). Prior to use, the specimens were subjected to an extra freeze thaw cycle and on the night before testing they were thawed at 8°C. Each specimen was separated into single vertebrae and all soft tissue was removed. Ringer solution was used to reduce tissue degradation by spraying during preparation and by covering the specimen in a soaked tissue-layer throughout testing.

Table 8.1 A break-down of specimen characteristics given by group. Values given are mean ± standard deviation. The numbers given for the side reflect how many *prototype* screws were tested on that side; values for the *reference* group would be opposite.

	Pitch1	Pitch2	Krypton	Offset	Positioning	Total	p
N	8	8	8	8	7	39	-
BMD (mgHA/cm^3)	107.4 ± 12.50	103.7 ± 19.33	107.8 ± 9.69	106.7 ± 15.94	107.0 ± 21.60	106.5 ± 15.41	> 0.99
Age (years)	47.1 ± 4.70	48.4 ± 2.33	47.9 ± 4.36	48.6 ± 4.17	48.9 ± 6.28	48.2 ± 4.29	> 0.95
Level	2 T12, 2 L1, 2 L2, 2 L3	1 T12, 2 L1, 3 L2, 2 L3	2 T12, 2 L1, 2 L2, 2 L3	2 T12, 2 L1, 2 L2, 2 L3	1 T12, 3 L1, 2 L2, 1 L3	2 T12, 2 L1, 2 L2, 2 L3	> 0.99
Side	2 Left 6 Right	4 Left 4 Right	7 Left 1 Right	3 Left 5 Right	4 Left 3 Right	20 Left 19 Right	> 0.13
Vertebra Length (mm)	34.2 ± 2.3	37.3 ± 2.3	35.9 ± 1.9	35.3 ± 3.7	35.9 ± 3.2	35.7 ± 2.8	> 0.26
Vertebra Width (mm)	49.0 ± 4.4	50.1 ± 4.3	48.5 ± 4.0	48.9 ± 5.3	47.7 ± 3.9	48.9 ± 4.2	> 0.88
Vertebra Height (mm)	28.6 ± 3.0	30.1 ± 1.5	29.3 ± 1.5	28.9 ± 3.5	29.3 ± 1.1	29.2 ± 2.3	> 0.79
Endplate Area (cm^2)	13.2 ± 1.6	14.7 ± 1.7	13.7 ± 1.5	13.6 ± 2.7	13.5 ± 2.0	13.7 ± 1.9	> 0.62
Vertebral Volume (cm^3)	37.8 ± 6.2	44.2 ± 6.0	40.1 ± 5.5	39.6 ± 10.3	39.6 ± 6.7	40.3 ± 7.1	> 0.50

8.1.2. Instrumentation and Screw Design

All instrumentations were performed by the same orthopaedic surgeon using a preferred sagittal alignment parallel to the endplates and with a transverse alignment along the pedicle axis causing convergence of screw tips (Figure 8.1). The *positioning* group utilized the same trajectory along the pedicle canal except that the entry point was shifted laterally by approximately 3 mm. Post-implantation x-rays were taken in the axial, antero-posterior and lateral planes to confirm proper implant positioning. Specimens were potted using a custom, simultaneous casting technique (Chapter 6). This created a mold where the clamping force is only transmitted through the upper and lower endplates while ensuring level, parallel surfaces for mounting.

Four different titanium alloy *prototypes* (*pitch1, pitch2, krypton,* and *offset*) of the same outer diameter (5.5 mm) and length (50 mm) were fabricated for testing (Table 8.2). Both the *reference* (tangoRS^{TM}) and K*rypton* screws groups are commercially available from ulrich medical® (Ulm, DE). The *prototypes* were fabricated on-site at ulrich medical®. *Pitch1* and *pitch2* are 1 mm step-wise increases of the pitch of the outer thread from the original tangoRS^{TM} design. The *offset* group utilized a posteriorly placed 'washer' which easily slides onto the reference screw prior to implantation. Table 8.2 provides visual and quantitative overview of the screw designs.

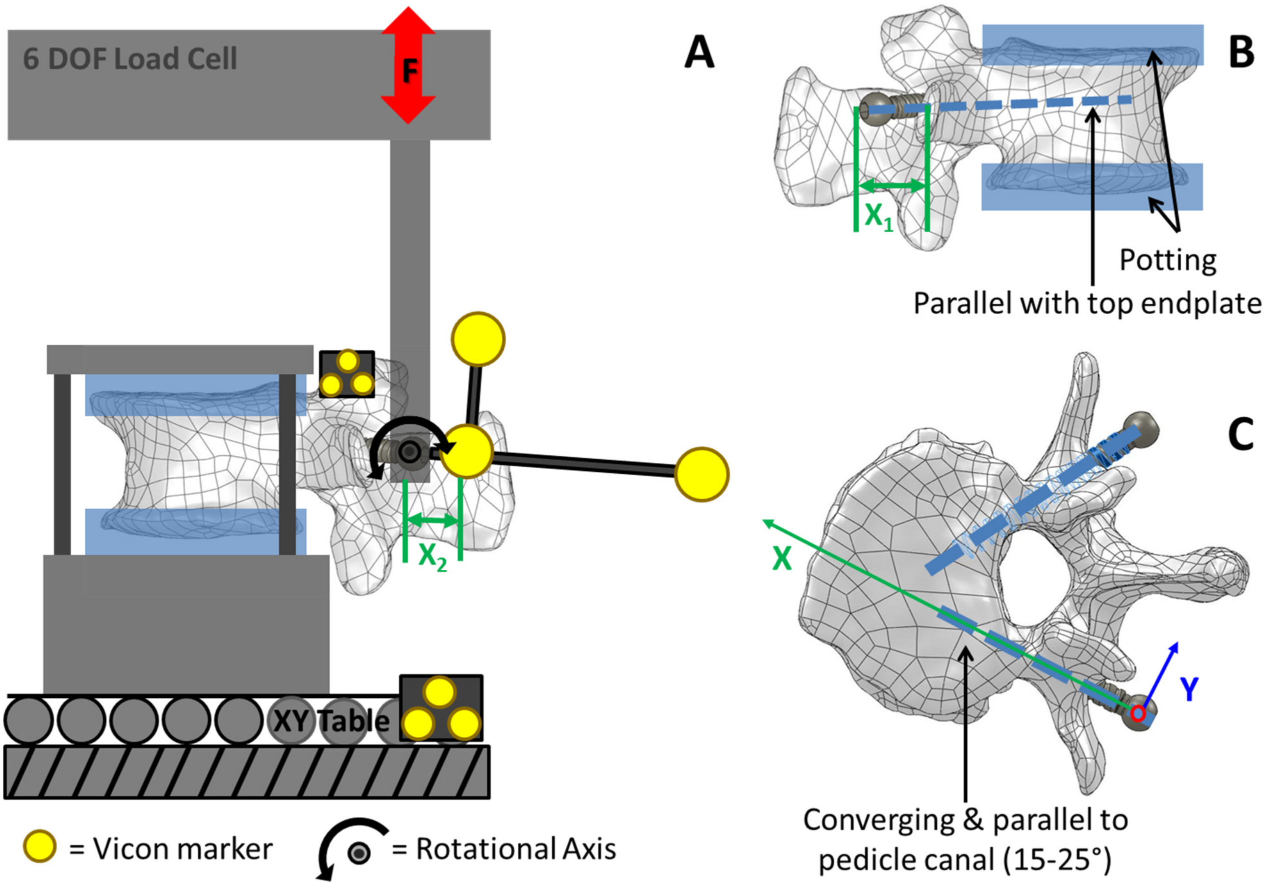
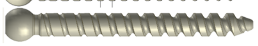
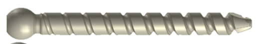


Figure 8.1 A schematic of the test setup (A) and of the primary surgical positioning (B & C) of the pedicle screws.

Table 8.2 Summary of the screw design parameters for each testing group. Pitch is the distance between adjacent thread crests. Area refers to the surface area of the flat crest of the thread which is concentric to the outer diameter. Tapering describes the conicity of the inner core. Crest height is the difference between the inner and outer diameter of the screw.

SpineFX Concepts		N	Length	Diameter	Pitch	Area	Tapering	Crest Height
Design	Name		mm	mm	mm	mm²	°	mm
	*Reference**	39	50	5.50	2.8	262	1.3	0.25 - 1.25
	*Pitch1*	8	50	5.50	3.8	396	1.3	0.25 - 1.26
	*Pitch2*	8	50	5.50	4.8	472	1.3	0.25 - 1.27
	*Krypton*	8	50	5.50	2.0	-	0.0	0.45
	*Offset*†	8	50	5.50	2.8	262	1.3	0.25 - 1.25
NA	*Positioning*†	7‡	50	5.50	2.8	262	1.3	0.25 - 1.25

*The reference group: one screw in each vertebra was a TangoRS screw; †Used TangoRS screws; ‡excluded one specimen due to fracture

8.1.3. Mechanical Setup

After instrumentation the specimens were clamped to a servo-hydraulic testing machine (858 Bionix®, MTS, Eden Prairie, MN, USA). A sinusoidal, cyclic (0.5 Hz) force was applied to the screw head, which was free to rotate around the transverse axis with all other degrees of freedom (DOF) fixed. The specimen attached to the testing machine directly at the screw head by tightening two screws along the rotational axis. Cranial-caudal peak compressive and tensile forces started from ± 15 N and increased linearly by 0.05 N every cycle. Toggle testing was stopped when 5 mm displacement was achieved in either direction. After fatigue failure of one screw, the contralateral screw was loaded with the same protocol.

An optical motion capture system was used (Vicon-460, Vicon Motion Systems, LA, USA) to record (102.4 Hz) the three-dimensional motion of the screw relative to the bone sample. Three, three marker sets were applied (Figure 8.1). The first was attached to the screw being tested and was aligned so as to define the screw axis during testing, the second was on the contralateral screw to record relative vertebral motion, and the last was on the base of the x-y-table.

8.1.4. Measured Parameters

Cycles to failure, *initial stiffness*, *final stiffness*, *pivot point*, *tip motion* and *head motion* were output variables. Stiffness was defined by the slope of the linear best fit to the caudal force-displacement loading curve where 10% of the data under the maximum and minimum displacement for each cycle was discarded. *Initial stiffness* was defined from the average of the first five caudal loading cycles and final stiffness from the last five cycles.

The three-dimensional motion data was transformed from the global coordinates to a local screw coordinate system with its origin at the screw head, y-axis oriented along the screw axis and the z-axis directed cranially. The displacement pattern of the screw axis was then plotted for each data point, assuming the screw to be a rigid body. The height of the screw motion was defined as the maximum z-distance which was calculated continuously along the screw axis (y-axis) in 0.1 mm increments. The motion parameters were calculated by determining the distance along the screw axis with the minimum Z height (*pivot* point), the height at the screw head (*head motion*) and the tip (*tip motion*) of the screw.

The pedicle and vertebral dimensions were measured during specimen preparation using standard calipers. Pedicle dimensions were measured in terms of the major and minor diameters for each side. Length, width and height were recorded for the vertebral body dimensions. The length the screw protruded from the vertebral body (overhang) was also measured. Upon removal of the screw, the torque necessary was measured (Torsiometer 760, Stahlwille, Wuppertal, DE).

8.1.5. Statistical Methods

Statistical evaluations were performed with the software package SPSS Statistics 20 (IBM Corp., Armonk, NY, USA) with a type I error probability set to 5%. Paired-samples t-tests were used to test differences between groups (*pitch1*, *pitch2*, *krypton*, *offset*, and *positioning*) and the *reference* group. The assumption that the sampling distribution of the differences is normally distributed was upheld for the variables: *cycles to failure*, *removal torque*, *initial stiffness*, and *final stiffness*. A two-way Pearson correlation coefficient was used to measure covariance. Pearson's *r* is used to denote effect size magnitude and direction.

8.2. Results

The test setup was confirmed by equal distribution between groups for BMD, vertebral level, and testing order (p>0.87). This allowed for all vertebral (p>0.26, Table 8.1) and pedicle (p>0.58, Table 8.3) dimension parameters to be equally distributed between the groups.

Table 8.3 Averages and standard deviations of the pedicle dimensions, pivot point, overhang and center distance for each testing group.

	Pitch1	Pitch2	Krypton	Offset	Positioning	Reference	Total	p
N	8	8	8	8	7	39	78	
Pedicle Major Ø (mm)	17.3 ± 1.30	16.8 ± 1.78	16.8 ± 2.33	16.6 ± 1.43	16.2 ± 2.03	17.1 ± 1.56	16.9 ± 1.65	> 0.81
Pedicle Minor Ø (mm)	10.0 ± 1.6	9.3 ± 2.2	9.6 ± 2.2	11.9 ± 6.7	9.4 ± 0.9	9.7 ± 1.8	9.9 ± 2.7	> 0.58
Pivot Point (mm)	31.2 ± 3.2	30.9 ± 2.1	30.4 ± 1.9	29.7 ± 1.3	29.9 ± 2.0	30.7 ± 2.2	30.5 ± 2.2	> 0.62
Overhang (mm)	11.6 ± 1.7	12.1 ± 1.9	11.9 ± 1.1	12.7 ± 1.0	12.9 ± 1.8	12.3 ± 1.7	12.3 ± 1.6	> 0.43
Center Distance (mm)	39.1 ± 0.92	39.3 ± 1.16	39.4 ± 0.80	39.4 ± 0.88	39.1 ± 0.75	39.0 ± 0.9	39.1 ± 0.9	> 0.90

8.2.1. Influence of Implant Design

Fatigue fixation results measured in terms of *cycles to failure*, *removal torque*, and both the *initial* and *final stiffness* are shown in Table 8.4 and in Figure 8.2. Overall averages for the loosening parameters between the *prototypes* (n=39) and the *reference* (n=39) groups were extremely similar with differences only ranging from 2.0-7.3% of the *reference* value.

Pitch1 was the only *prototype* group with consistently increased fixation strength compared to the *reference* group for all fixation parameters, the only significant finding was for *final stiffness*. *Pitch1* increased by 6.9% for *cycles to failure* (t(7)=0.751, p=0.48, r=0.27), 12.2% for *removal torque* (t(7)=0.808, p=0.47, r=0.29), 4.4% for *initial stiffness* (t(7)=0.451, p=0.67, r=0.17) and 36.1% (t(7)=3.146, p=0.02, r=0.77) for *final stiffness*. The trend for a fixation strength increase did not continue for the *pitch2* group which experienced fixation reduction in terms of *cycles to failure* (7.0%, t(7)=-0.963, p=0.37, r=0.34), *initial stiffness* (1.3%, t(7)=-0.171, p=0.87, r=0.06), and *final stiffness* (7.9%, t(7)=-0.981, p=0.36, r=0.35) compared to the *reference* group. *Removal torque* increased by 1.7% (t(7)=-0.076, p=0.94, r=0.03).

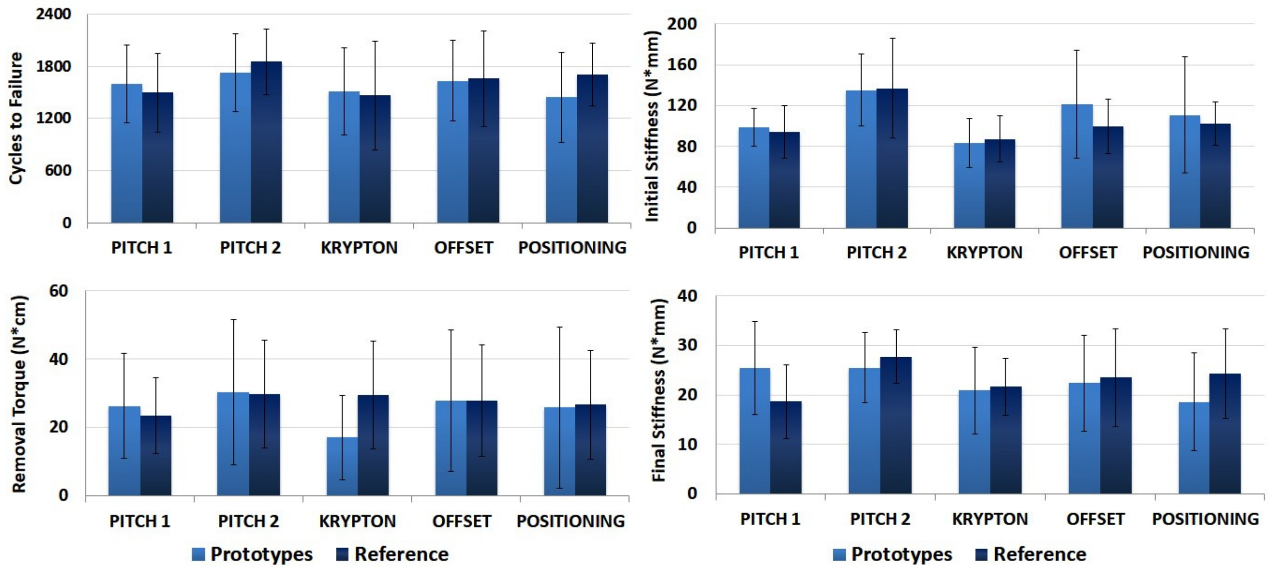


Figure 8.2 Bar graphs of the averages of all four of the measured loosening parameters for each of the *prototype* screws (light blue) compared to their respective *reference* screws (dark blue); note the paired peaks.

Table 8.4 Averages and standard deviations of the four measured loosening parameters for each of the testing groups. The 'Diff' column gives the percentage of the difference of the *prototype* group from the respective *reference* group.

		Cycles to Failure		Removal Torque (N*cm)		Initial Stiffness (N/mm)		Final Stiffness (N/mm)	
Pitch1	Prototype	1599 ± 446		26.4 ± 15.4		99 ± 18		25.4 ± 9.4	
	Reference	1496 ± 454.5		23.5 ± 11.0		94 ± 26		18.7 ± 7.4	
	Difference, p	6.9%	0.48	12.2%	0.47	4.4%	0.67	36.1%	0.02
Pitch2	Prototype	1724 ± 449		30.4 ± 21.3		135 ± 35		25.5 ± 7.1	
	Reference	1854 ± 377		29.9 ± 15.8		137 ± 49		27.7 ± 5.4	
	Difference, p	-7.0%	0.37	1.7%	0.94	-1.3%	0.87	-7.9%	0.36
Krypton	Prototype	1507 ± 499		17.1 ± 12.3		83 ± 24		20.9 ± 8.7	
	Reference	1464 ± 627		29.5 ± 15.8		87 ± 23		21.6 ± 5.7	
	Difference, p	3.0%	0.71	-41.9%	0.16	-4.5%	0.38	-3.2%	0.69
Offset	Prototype	1633 ± 463		27.9 ± 20.6		121 ± 53		22.4 ± 9.6	
	Reference	1656 ± 547		27.9 ± 16.3		100 ± 26		23.5 ± 9.9	
	Difference, p	-1.4%	0.88	0.0%	1.00	22.0%	0.29	-4.9%	0.78
Positioning	Prototype	1440 ± 514		25.9 ± 23.7		111 ± 57		18.6 ± 9.9	
	Reference	1706 ± 360		26.7 ± 15.9		102 ± 21		24.3 ± 9.0	
	Difference, p	-15.6%	0.09	-3.2%	0.91	8.7%	0.68	-23.2%	0.09
Totals	Prototype	1584 ± 459		25.5 ± 18.5		110 ± 42		22.7 ± 8.9	
	Reference	1633 ± 483		27.5 ± 14.4		104 ± 34		23.1 ± 7.9	
	Difference, p	-3.0%		-7.3%		5.5%		-2.0%	

The *krypton* group showed a 3% (t(7)=0.384, *p*=0.71, *r*=0.14) increase in *cycles to failure* compared to the *reference* group; however, all other fixation parameters were reduced (*removal torque* by 41.9%, t(7)=-1.590, *p*=0.16, *r*=0.52; *initial stiffness* by 4.5%, t(7)=-0.940, *p*=0.38, *r*=0.33; and *final stiffness* by 3.2% t(7)=-0.423, *p*=0.69, *r*=0.16). When comparing the *removal torque* of the cylindrical *krypton* group (*n*=8) to all other screw designs which are *conical* (*n*=70) there is a 38.0% reduction (17.1 vs. 27.6 N*cm, *p*=0.09). The *offset* group exhibited small decreases in fixation for *cycles to failure* (3.0%, t(7)=-0.163,

p=0.88, r=0.06), *removal torque* (7.3%, t(7)=0.00, p=1.00, r=0.00), and *final stiffness* (2.0%, t(7)=1.149, p=0.29, r=0.40) and an increase in *initial stiffness* (5.5%, t(7)=-0.290, p=0.78, r=0.11) from the *reference* group.

The *positioning* group had a 15.6% (t(6)=-2.029, p=0.09, r=0.64), 3.2% (t(6)=-0.114, p=0.91, r=0.05) and 23.2% (t(6)=-1.986, p=0.09, r=0.63) loss in *cycles to failure*, *removal torque*, and *final stiffness* respectively from the *reference* group. *Initial stiffness* was increased by 8.7% (t(6)=0.441, p=0.68, r=0.18). The screw positioning did not always reach the desired position: for two samples (S8 L2 & S13 L3) there was no distinguishable difference for the contralateral sides, S15 T12 perforated the canal medially, and two had large perforations (S1 L2 & S10 L1) of approximately half the diameter of the screw (Figure 8.3).

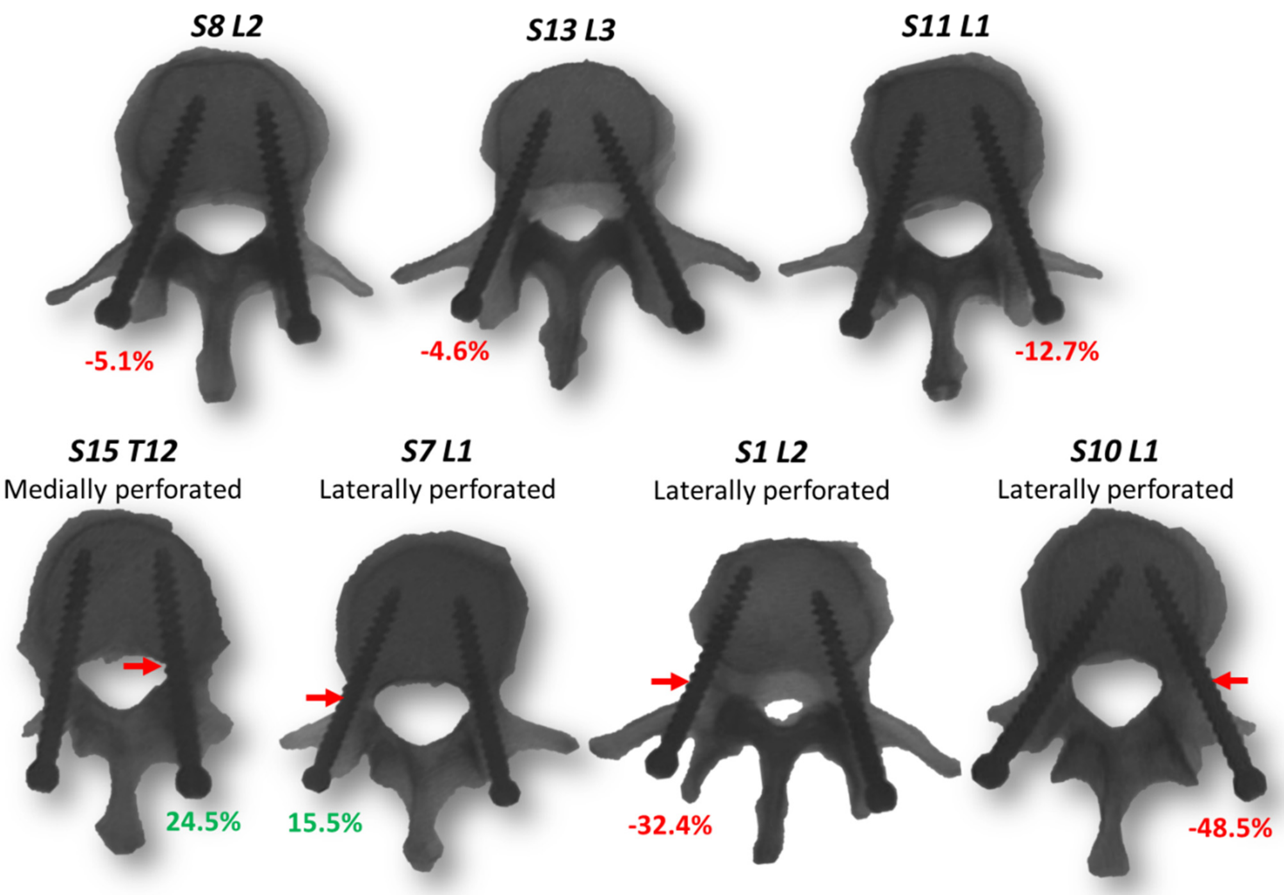


Figure 8.3 The specimens of the *positioning* group showing the variation of screw placement. The percentages given are the amount that the *cycles to failure* of that screw were changed relative to the contralateral *reference* screw. Red arrows highlight areas where cortical perforations occurred. S15 T12 and S7 L1 exhibited mild perforations and S1 L2 and S10 L1 had large perforations (>half the screw diameter).

8.2.2. Influence of Specimen Characteristics

Since no significant differences were found between the groups for the fixation parameters all screws (n=78) were considered together in order to ascertain the influence of specimen characteristics. The average apparent volumetric bone mineral density (BMD) was 106.4 ± 14.1 mgCaHA/cm^3. BMD decreased as the spinal level became more caudal (p=0.01, r=-0.32). BMD decreased with an increase in vertebral height (p=0.004, r=-0.32) and width (p<0.001, r=-0.51). BMD positively influenced the number of *cycles to failure* (*p*=0.04, *r*=0.24), *removal torque* (*p*=0.02, *r*=0.27), and *final stiffness* (*p*=0.03, *r*=0.21) but had no significant influence on *initial stiffness* (*p*=0.14). BMD was not shown to correlate with age (*p*=0.71) and age was not shown to significantly correlate with any fixation strength parameter (*p*>0.09).

The major pedicle diameter increased for T12 vertebrae compared to the lumbar vertebrae (*p*<0.04). An increase in the major pedicle diameter significantly decreased *cycles to failure* (*p*=0.01, *r*=-0.29), *removal torque* (*p*=0.04, *r*=-0.23), and *final stiffness* (*p*=0.005, *r*=-0.32). The minor pedicle diameter was positively associated with the vertebral width (*p*<0.001, *r*=0.47). No linear trend was detected for minor diameter and the four fixation parameters (*p*>0.40). The average overhang for all screws was 12.3 ± 1.6 mm and negatively correlated with vertebra width (*p*=0.002, *r*=-0.34), *cycles to failure* (*p*=0.02, *r*=-0.27) and *final stiffness* (*p*=0.04, *r*=-0.23).

Vertebral length positively correlated with both *cycles to failure* (*p*=0.02, *r*=0.27) and *initial stiffness* (*p*=0.003, *r*=0.33); whereas, vertebral width and height did not correlate with any fixation strength parameter. Vertebra length (*p*=0.03, *r*=0.24), width (*p*<0.001, *r*=0.49), and height (*p*<0.001, *r*=0.51) were found to increase with the vertebral level becoming more caudal. The vertebral dimensions were all interrelated: vertebral length correlated positively with vertebral height (*p*=0.005, *r*=0.31) and width (*p*<0.001, *r*=0.43) as well as height increased with width (*p*=0.04, *r*=0.24).

8.2.3. Inter-relations of Loosening Parameters and Motion Patterns

Cycles to failure was shown to correlate positively with all three other fixation parameters: *removal torque*, *initial* and *final stiffness* (Table 8.5). *Removal torque* further positively correlated with *final stiffness* but not *initial stiffness* (*p*=0.54). *Initial stiffness* increased with an increase in *final stiffness* (*p*=0.05, *r*=0.22).

A butterfly loosening pattern emerged for each testing group with the *pivot points* being 29.4-31.2 mm from the screw head (Figure 8.4). An increase in minor diameter correlated with an increased depth of the *pivot point* (*p*=0.01, *r*=0.29). The *pivot point* was also shown to negatively correlate with *initial stiffness* (*p*=0.02, *r*=-0.27) and positively with vertebral width (*p*=0.03, *r*=0.24). Neither the *head motion* nor the *tip motion* correlated with any of the fixation parameters.

Table 8.5 Summary of the correlations of specimen parameters and loosening parameters to the four loosening measures: *cycles to failure, removal torque*, *initial stiffness* and *final stiffness*.

	Specimen Relations	Loosening Relations
Cycles to Failure	BMD (p=0.04, r=-0.24) Major Pedicle Ø (p=0.01, r=-0.29) Vertebra Length (p=0.02, r=0.27) Overhang (p=0.02,r=-0.27)	Removal Torque (p<0.001, r=0.60) Initial Stiffness (p=0.002, r=0.34) Final Stiffness (p<0.001, r=0.80)
Removal Torque (N*cm)	BMD (p=0.02, r=0.27) Major Pedicle Ø (p=0.04, r=-0.23)	Final Stiffness (p<0.001, r=0.66)
Initial Stiffness (N/mm)	Pivot Point (p=0.02, r=-0.27)	Final Stiffness (p=0.05, r=0.22)
End Stiffness (N/mm)	Vertebral Level (p=0.02, r=-0.28) Major Pedicle Ø (p=0.005, r=-0.32)	

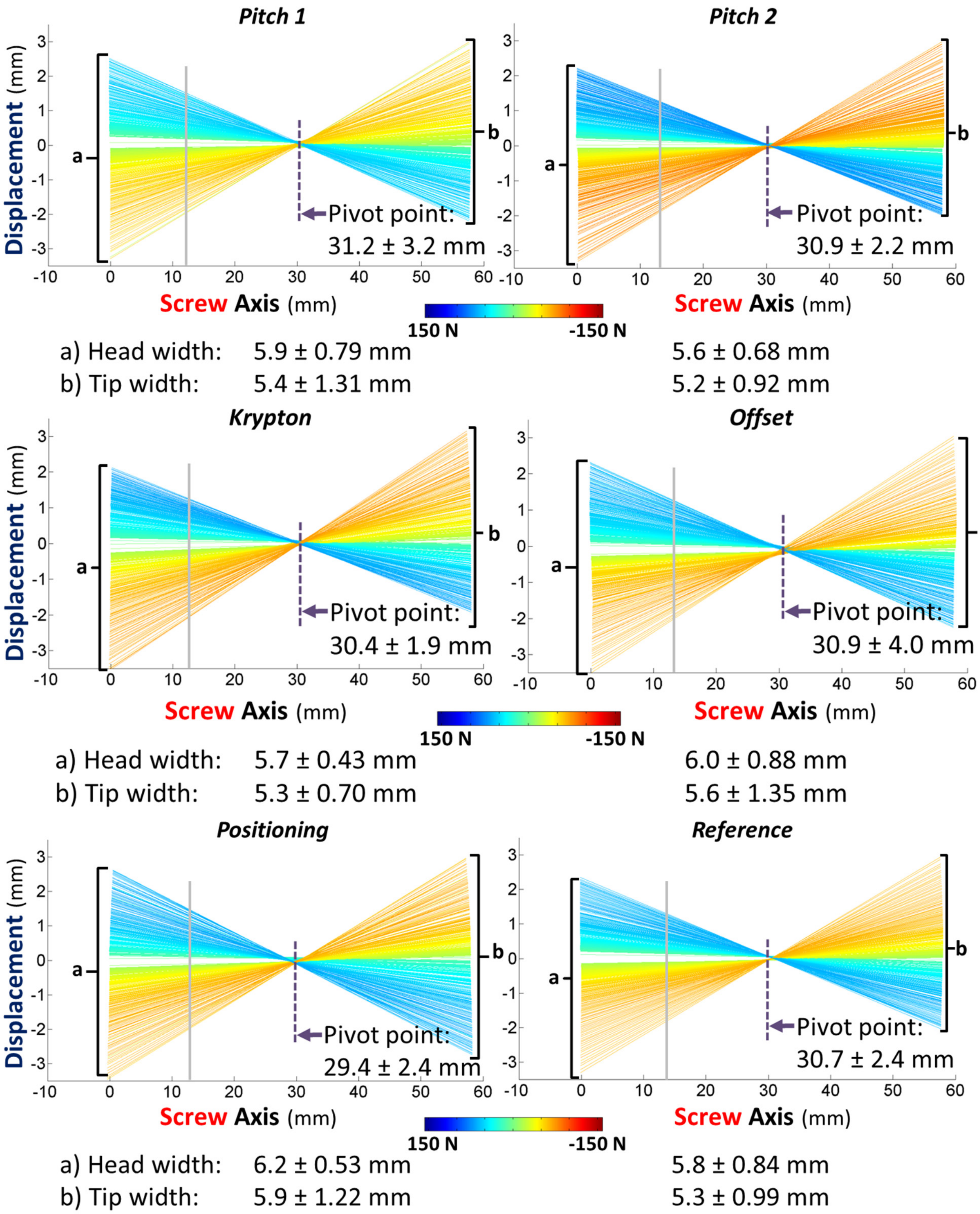


Figure 8.4 The average screw motion patterns for each group. The grey lines represent the average position where the screw entered the vertebral body.

8.3. Discussion

8.3.1. Influence of Implant Design

Variation of the screw thread designs may provide substantial differences in the often tested pullout force[1,6,36,59,121,125,210]; however, these fixation gains did not translate to the more physiologic fatigue loading for the screw designs and setup tested here. The change of screw thread design had little effect for the prototypes compared to the reference screws. No significant differences were found between the *prototypes* compared to the *reference* screws for the loosening parameters of *cycles to failure* (*p*>0.37), *removal torque* (*p*>0.16), and *initial stiffness* (*p*>0.29). If the observed small differences in fixation strength due to screw design reflect actual changes (Table 8.4), it is unlikely that significant results could be obtained with the current test design due to the small sample size and large variance. A sample size greater than 200 would have been necessary to obtain significance between groups with the measured variance.

The study setup was designed to reduce influence of specimen variability as much as possible for an *ex vivo* model. This was done by utilizing a repeated measures design, using specimens of the same gender (male) and of a small age range. Care was also taken for group separation to evenly distribute the specimen number, BMD, vertebral level and testing order to allow between group comparisons. This design allowed for a better chance to see if screw thread difference influences fatigue strength of pedicle screws while limiting generalizations due to the narrow specimen variability. Even with careful study setup, the screw design changes did not result in statistically significant differences of the fixation parameters. The primary measured screw fixation parameters, *cycles to failure, removal torque, initial stiffness*, and *final stiffness* exhibited paired peaks (Figure 8.2). This means that the variance between the *prototype* peak and its corresponding *reference* group peak generally follow the same trends and is smaller than the variance between the different groups of the *reference* screw (*i.e. pitch2 reference* vs. *krypton reference*). This suggests that the values of the fixation parameters are driven more by the specimen grouping than by the screw design parameters.

For pullout testing, a pitch decrease is generally believed to be beneficial[6,121]. However, the groups of *pitch1* and *pitch2* were 1 mm step-wise increases of the pitch from the original reference screw design. It was believed that in the more physiological cranial-caudal toggle loading configuration the number and sharpness of the thread crests might play a larger role in bone damage propagation. The increased pitch caused a decreasing number of threads along the length of the screw. This increased the outer surface area of the screw making it more cylindrical in shape while decreasing the surface area between the thread crests (Table 8.2). It was thought that a more cylindrical screw might be able to distribute the stresses from the fatigue loading more evenly along the length of the implant.

Pitch1 was the only *prototype* which was able to increase all fixation parameters. It saw increases of 6.9% in *cycles to failure* (*p*=0.48), 12.2% in *removal torque* (*p*=0.47), 4.4% in *initial stiffness*, and a significant 36.1% increase in *final stiffness*. However, these benefits did not propagate with the further pitch increase of *pitch2*. *Pitch2* actually saw small decreases of 1.3-7.9% (*p*>0.36) compared to the *reference* group for all loosening parameters except for *removal torque* which obtained a 1.7% increase (*p*>0.94, Table 8.4). On the one hand, the non-consistency of increasing pitch with increasing loosening parameters casts doubt of the non-significant perceived benefits of *pitch1* over the *reference* group. On the other hand, other groups have shown that there is an optimal pitch reduction for axial pullout loading[6,121], once this is exceeded the benefits are non-existent. Perhaps *pitch2* surpasses the upper end of the spectrum for a pitch increase in toggle loading.

The *krypton* group showed similar performance (-4.5-3.0% differences) to the *reference* group for *cycles to failure* and the stiffness values. Although there was a large, non-significant 41.9% reduction of *removal torque* in the *krypton* group, there was also a 3.0% increase in *cycles to failure*. The reduction of the *removal torque* would be expected given that the *krypton* group has a cylindrical core design rather than the conical design of all other screw groups including the *reference* group. Conical cores are designed to increase the screw press-fit by increasing the amount of bone between the screw threads[1,121]. An increase of the volume of trabecular bone between the screw threads has been shown to increase pullout strength and the *removal torque*[121,209,210].

The 'washer' used for the *offset* group was designed to attempt to increase the cortical contact of the implant at the screw entry (Figure 8.5). For simplicity, and consistency of insertion the design uses a symmetric flat surface which is not the reality of the vertebral geometry at the screw entry. The posterior arch often has a large curvature with the facet protruding above and less inferior support at the screw entry point. The only fixation parameter which increased for the *offset* group over the *reference* group was the *initial stiffness* (+22%, p=0.29). The non-significant, *initial stiffness* increase was one of the largest magnitude differences for all groups; however, this possible initial benefit from the washer was not sustained over time with the final stiffness actually being reduced (Table 8.4). On insertion of the *offset* group the superior side of the washer cut into the facet joint (Figure 8.5). The orientation of implant might help the stiffness initially but the sharp edge of the washer might damage the surrounding bone with repeated fatigue loading and thereby reduce the *final stiffness*. The idea for external posterior support conceptually makes sense since the screw entry is a location of peak stress along the bone-screw profile; however, the practice with this particular implant is flawed.

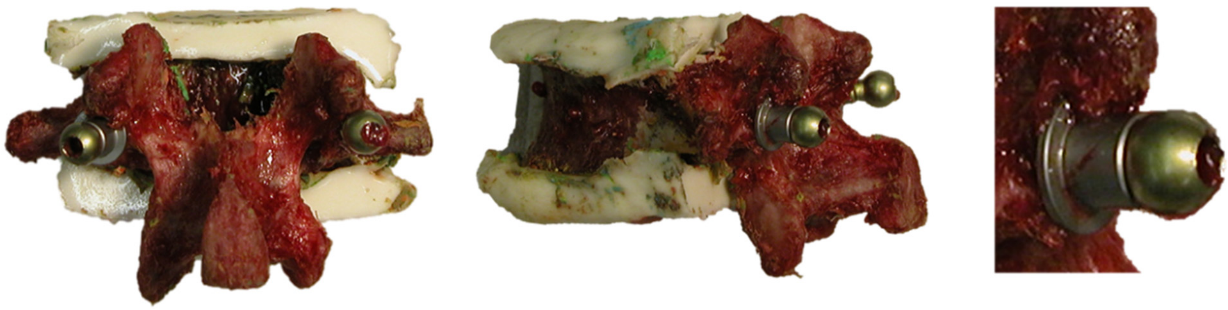


Figure 8.5 Pictures of an example potted *offset* specimen with a close-up (right) of the offset 'washer' showing how the washer cuts into to bone of the facet on the cranial side.

Consistent placement of the screws within the *positioning* group proved difficult. It was intended to displace the screw laterally but stay within or only mild perforate (<2 mm, criteria from Laine et al.[126]) the pedicle. The mild perforations of S15 T12 and S7 L1 (<1 mm) both resulted in higher *cycles to failure;* however, once a perforation of half of the screw diameter was reached a substantial reduction in *cycles to failure* were seen (S1 L2 & S10 L1, Figure 8.3). Similar results were obtained in a porcine model by Costa et al.[49], they found no differences in pullout strength for mildly perforated (<2 mm) screws and said the most important determinant of the pullout strength was the extent of the cortical violation. Relevant alterations of pullout strength were only reached when a 4 mm violation was reached[49]. This 4 mm misplacement distance is also considered a clinical threshold for when neurovascular damage might occur[82]. Conversely, Reichle et al.[174] did not find that screw positioning influenced the primary stability of the screw under cyclic loading. In this study the large variation in the implant positioning and small samples make it not possible to confirm any trends, but as it might be expected it seems large perforations of over half the screw diameter may be detrimental to screw fixation strength.

8.3.2. Influence of Specimen Characteristics

The influence of specimen characteristics, quantified in terms of BMD and major pedicle diameter, played a significant role in the screw fixation strength. A larger major pedicle diameter decreased both the *cycles to failure* and the *removal torque* of the screw; whereas, a higher BMD increased fixation.

The average BMD (106.4 ± 14.1 mgCaHA/cm^3) is rather low considering that all specimens were male and there was a relatively young age range (40-61 years). This is not necessarily bad for what was tested, namely the influence of screw thread design on fixation strength, since larger fixation strength differences of BMD can generally be observed in lower bone quality. Further, the small age range may help explain why there is not the typical correlation between age and BMD, a wider spread of the age range especially on the higher side may be necessary for trend observance. The positive relationship of BMD to the fixation parameters of *cycles to failure* (p=0.04, r=0.24), *removal torque* (p=0.02, r=0.27), and *final stiffness* (p=0.03, r=0.21) was not surprising as bone quality is shown to be one of the best predictors of fixation strength of implants.

An increase in the major pedicle diameter is associated with an increased volume of the cancellous bone within the pedicle. This is because the cortical shell thickness has been shown to stay relatively constant with changes of major and minor diameters; the cancellous core dimensions increase instead [160]. The toggle style loading in this study utilized cyclic forces in the cranial and caudal directions. An increase in the major diameter would then likely be associated with an increase in the volume of the weaker cancellous bone within the pedicle in the direction of loading. The screw is thus more likely to have cancellous bone rather than the desired stronger cortical bone supporting the load in the cranial-caudal direction; this might explain why the reduction in *cycles to failure* (p=0.01, r=-0.29), *removal torque* (p=0.04, r=-0.23), and *final stiffness* (p=0.005, r=-0.32) was seen with an increase in major pedicle diameter. The fact that no linear trend was detected for minor diameter and the four fixation parameters (p>0.40) is not unexpected as the specimens were not loaded in that direction.

The average length of screw outside the vertebra (overhang) for all screws was 12.3 ± 1.6 mm; this was consistent with desire to leave a 12 mm overhang (4 mm plus the 8 mm of the screw head length). Some variation of overhang can be attributed to the necessity of using the same length of screw in different sized vertebrae, as insertion of the screw was always stopped prior to anterior wall perforation. It was believed important not to perforate the anterior cortex because in the spinal region in question (T12-L3) the aorta passes directly anterior to the vertebra. An increase in the overhang can be likened to an increase in the active lever arm, as the screw sees no support until entry into the posterior arch. Therefore, it is not surprising that an increasing overhang correlated with a decrease in the *cycles to failure* (p=0.02, r=-0.27) and *final stiffness* (p=0.04, r=-0.23).

8.3.3. Inter-relations of Loosening Parameters and Motion Patterns

The inter-relations of the four fixation parameter suggest that the fixation parameters do in fact each measure a similar metric. This then begs the question, why report all parameters? Not all metrics are affected the same by the design changes and it is important to know how to manipulate one with a design while ensuring substantial fixation parameters in the others. The end results (-1.4% *cycles to failure*, 0.0% *removal torque*, and -4.9% *final stiffness*) of the *offset* screw seem ordinary. The non-significant increase in *initial stiffness* (+22%, p=0.29) does however catch the attention that the posterior support may help initially but there is a flaw that reduces the effect with time. Perhaps other designs which promote posterior stabilization should be explored.

The loading protocol imposed both tensile and compressive loading in the cranial-caudal plane along the screw axis and accordingly a cranial-caudal butterfly loosening pattern emerged along the screw axis for each testing group (Figure 8.4). The overall average *pivot point* was 30.5 mm from the head of the screw and if the overhang is accounted for the depth of the *pivot point* is in the range of the average length of the pedicle, approximately 18-24 mm[230]. A *pivot point* within but near the end of the pedicle was previously shown in *ex vivo* pedicle screw testing by Tan et al[222], Law et al.[129] and Zindrick et al.[248] as well as within the Screw Augmentation study (Chapter 7). The failure pattern seen here (Figure 8.4) with fanning in the cranial-caudal direction and a *pivot point* near the end of the pedicle is similar to those seen *in vivo*, however, typically the *in vivo* patterns only fan in either the cranial or the caudal direction for the lumbar spine (Chapter 4).

The limitations of this study include the small sample size, an extra freeze-thaw cycle for the specimens, and large variance for the measured fixation parameters. Furthermore, use of osteoporotic vertebrae would have been more appropriate; as loosening is much more problematic in the osteoporotic spine.

8.4. Conclusions

Neither increasing the thread pitch nor adding posterior support to pedicle screws was able to significantly alter the fatigue fixation strength. The variation of specimen characteristics likely drove differences in fatigue fixation more than changes to the screw thread or the addition of posterior support.

The relationship of the pitch to the fatigue fixation strength is not clear and further investigations in a controlled parametric manner (such as Finite Element analysis) might be useful in determining the optimal pitch range before further laboratory investigations. Agreeing with literature[1,121], a conical core tended to non-significantly increase the *removal torque*.

Large perforations of the cortical shell (>4 mm) are likely to substantially reduce the fatigue fixation strength of pedicle screws. This has been shown with pullout testing[49] as well as here with the two screws with large perforations. A higher BMD and a smaller major diameter of the pedicle significantly increased fatigue fixation. Further, implanting the screw with less length outside the vertebra improved the *cycles to failure*.

Chapter 9.

Bone Damage

In general, numerical simulations can provide deeper insight into the bone-screw interface stability by allowing a quantitative look into the stress, strain and damage patterns within the bone. This can help identify areas where loosening will likely progress and provide key parameters which can be targeted for optimization. Moreover, it is believed that the application of numerical simulations could eventually lead to a reduction in the number of experimental tests required for testing relative differences in systematically altered variables. Once established, the simulations can become a useful tool for prediction of relative costs/benefits of utilizing specific design changes. This may be taken a step further and optimization routines can be performed to determine the most probable best values for the design variations of interest. In this way, FE can be used to identify the primary design variations of interest and then to further predict the probable, optimal values for those parameters. Therefore, FE modelling could potentially provide a useful tool in the optimization of pedicle screw design.

Although FE is theoretically very promising, the processes to obtain these benefits are often extremely time-consuming and tedious with many required assumptions for the model creation. In order to utilize these models they must first be verified to the known clinical situation and validated to results seen by particular experimental testing. The process of verification and validation is an intensive endeavour in terms of both man-hours and cost. Ultimately, either the verification or validation is often the first critique of any computational simulation, even after intensive methods are applied.

Loosening of a pedicle screw in the vertebra is an observable occurrence which is believed by some to involve the progressive collapse of trabecular bone due to the experienced stresses or strains of everyday activity[42,129]. The much stiffer screw is believed to transfer the stresses/strains produced by the repeated everyday motion[17] to the bone[42]. Once a threshold of approximately 1-2% nominal strain is surpassed the struts of the trabecular bone collapse. This collapse is characterized by inelastic buckling, formation of plastic hinges and increasing contact of the trabecular rods or plates[37,95]. The trabecular buckling is also associated with a sharp decrease in both the bone's load carrying capacity and its stress (known as stress softening). The bone's collapse results in irreversible material damage which can materialize in the form of a loosening void surrounding the screw. For modelling of mechanical loosening at the bone-screw interface it is, therefore, essential to have a complex material model for trabecular bone which can reflect this irreversible material damage.

After the initial trabecular buckling of the bone at 1-2% nominal strain, there has been demonstrated a second phase of densification around 25-40% nominal strain[84,95]. This densification is attributed to the increasing contact of the broken trabecular rods or plates and is characterized by increases in both the load carrying capacity and in the microstructure stiffness.

Bone damage was first parameterized in mechanical testing by comparing force-displacement curves to materials with similar behaviour or by comparing the energy absorption capacity to the *in vivo* fracture behaviour of bone[34,35]. An early FE model from 1994 included material damage which was based on the principles of crack propagation and creep fracture[91]. It used a two-dimensional model with a honeycomb like structure of linear elastic beam elements. Once a predefined level of crack length was reached the element was considered fractured and removed; the overall material modulus was then recalculated. In 2000, the concept was continued but once the tissue yield strain was reached the element was not removed but it did have its effective modulus reduced by 95%[152]. The material model was used in a three-dimensional model with unifom but asymmetric tensile and compressive strains. This material model was found to allow for sufficient prediction of the apparent strength of cubes of vertebral trabecular bone. This material model has been built upon to attempt to predict vertebral fracture strength from clinical CT images of entire vertebral bodies[51].

Other CT-based homogenized finite element models have been created which have anisotripic elasticity and can account for the bone volume fraction (BV/TV) and the orientation of the trabecular which is often termed the bone's 'fabric'[159,249]. However, the elastic and post-yield behaviour of these models can only account for small strains[40]. Hosseini et al.[100] then introduced a bone material model that is able to include large compressive strains (up to 80% nominal strain) by the inclusion of a densification mechanism. The densification was modelled in an independent post-yield function as a non-linear spring which is enacted once a certain threshold of negative volumetric change is reached. In this model a viscous term was also introduced in the yield function of bone (an inviscid material) in order to allow the hardening and softening behaviour of the model to take into account the loading rate and to overcome the numerical instabilities which are shown to exist due to softening[15]. The damage variable is modelled as an inverse exponential function and is based on the cumulated plastic strain. The material model presented by Hosseini et al.[100] was able to predict the damage localization and densification of trabecular bone within whole vertebrae and is, therefore, a fitting model for use in the study of loosening at the interface between the vertebra and the screw.

In the previous chapters, the accepted idea that different patient, surgical and screw design parameters can influence the fixation of the bone-screw interface was introduced and sometimes quantified. The purpose of this present study was to create a FE model containing basic geometry which could also reflect bone damage in order to be parametrically altered to comparatively investigate the relative influences of defined patient, surgical, and screw design parameters. The investigated patient parameters were the cortical shell thickness and the material properties. The screw placement was altered via the angle, offset, and depth of insertion for the surgical parameters. The diameter and the angle of the screw core were changed for the screw design parameters. Due to its ability to capture and quantify the damage localization of trabecular bone, the material model introduced by Hosseini et al.[100] was used to model bone in this comparative analysis of loosening at the bone-screw interface. A rough verification to the clinical situation was performed by comparing the patterns of the damage induced from the applied *in vivo* style loading in the FE model to both a FE model with patient specific geometry and to loosening patterns seen *in vivo*.

9.1. Methods

Predefined patient, surgical and pedicle screw design parameters were investigated for their effect on the magnitudes and distribution of bone damage. In order to quantify the irrecoverable plastic damage in trabecular bone, a complex material model was used for bone [100]. The material model was applied to a simplified geometry of a lumbar vertebra instrumented with a pedicle screw with an applied loading of a typical *in vivo* loading pattern for walking. Comprehensive details about the construction and the performance of the models are given in Bünning[27] and Wagner[232].

9.1.1. Geometry of the Basic Model

The simplified geometry was created in SolidWorks 2011 (Dassault Systèmes S.A.,Vélizy, FR) to roughly mimic a pedicle screw inserted into a vertebra (Figure 9.1). All dimensions were derived from the anatomical[24] and surgical positioning[230] studies performed on the osteoporotic lumbar vertebrae in the Screw Augmentation study (Chapter 7). The pedicle screw was represented by a cylinder with a length of 60 mm and a diameter of 5.5 mm; screw threads were not modeled. The vertebra was represented by a merging of two cylinders; a smaller one (Ø=10.5 mm, length= 19.65 mm) to simulate a pedicle and a larger cylinder (Ø=23.5 mm) to simulate the vertebral body. A cortical shell was represented by a 1 mm thick wall in the area of the pedicle with a 0.4 mm shell for the vertebral body. The screw was inserted to a depth of 45 mm leaving 10 mm from the screw tip to the anterior wall. The geometry was then meshed with 2nd order hexahedral elements (n=29116) in HyperMesh (Version 11.0, Altair Engineering, Troy, MI, USA). This model will hence forth be referred to as the *basic model*; all other models used in the parametric analysis are slight variations with the alterations to the *basic model* described in the following section.

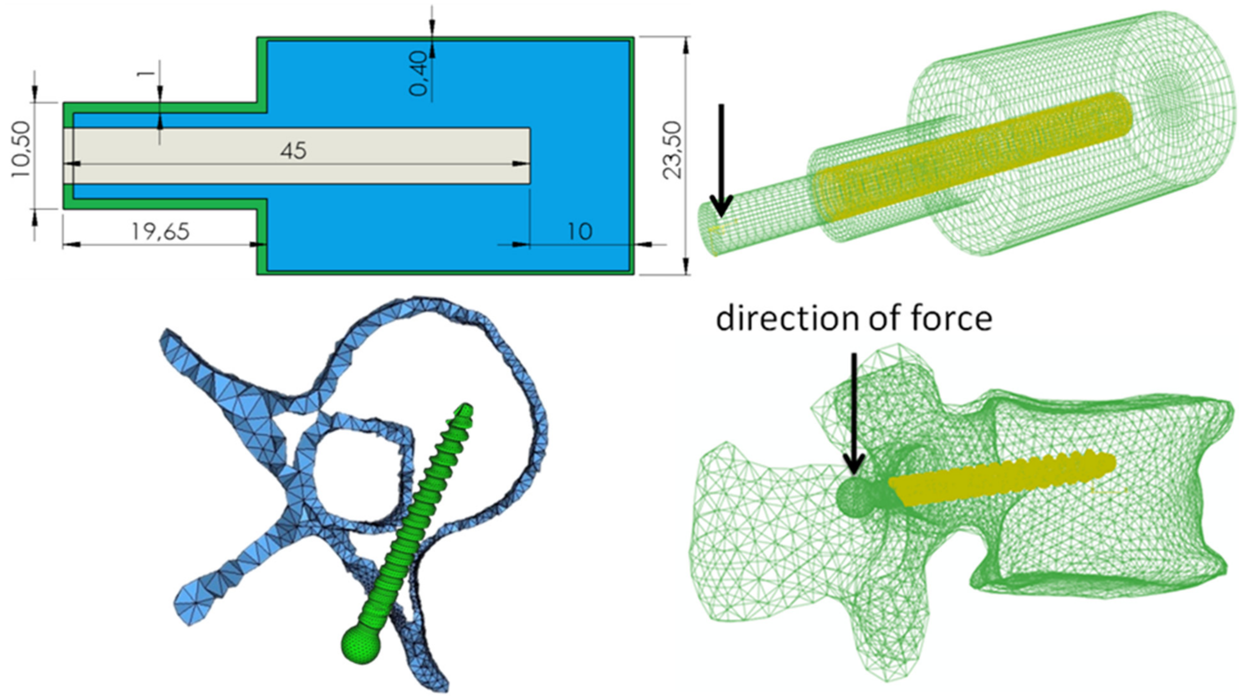


Figure 9.1 Geometry and mesh overview of the basic model (top) and the patient specific model (bottom). [Altered from Bünning[27] (top) and Wagner[232] (bottom)]

9.1.2. Parametric Alterations to the Basic Geometry

Patient

Two basic concepts were altered to encompass changes related to the patient: the first is the material property parameters and the second is the cortical shell thickness. The *material property models* (*n*=2) used material properties which were chosen to mimic a reduction in bone quality as it is believed to progress from osteopenia to osteoporosis. The lowest values of BV/TV from the study of Rincon et al.[178] were chosen as a *worst case* quality since the study used solid methods and included specimens with an age up to 89 years old (Table 9.1). Additionally, a *low bone quality* model was created by calculating the midpoint between the normal quality and the *worst case* quality. The *cortical shell* models (*n*=3) involved a 50%, 100%, and 150% thickness increase of the vertebral cortex. The 150% increase resulted in a cortical shell which completely surrounded the screw throughout the length of the pedicle.

Table 9.1 The bone material parameters used for the *bone quality* models[40,170,178].

	Normal			*Low Quality*			*Worst Case*		
	BV/TV	EV1	EV2	BV/TV	EV1	EV2	BV/TV	EV1	EV2
Cortical Bone	0.940[1]	0.9[3]	0.9[3]	0.911	0.9[3]	0.9[3]	0.883[1]	0.9[3]	0.9[3]
Trabecular Bone	0.100[2]	0.9[3]	0.9[3]	0.066	0.9[3]	0.9[3]	0.033[2]	0.9[3]	0.9[3]

1) Qiu et al. 2) Ricón-Kohli et al 3) Chevalier et al.

Surgical

Three basic concepts were parametrically changed to encompass alterations which can be influenced by the surgeon: the depth of screw insertion, the angle of screw insertion, and the offset of the entry point. For all models the ideal positioning of the screw in the basic model was altered relative to the vertebra. The *depth of insertion* models (*n*=2) changed the depth the screw was inserted in the vertebra directly along the screw axis by ±5 mm. The distance of the loading point to the screw entry into the vertebra remained consistent; therefore, the screw length was either 55 mm or 65 mm. For the *angle of insertion* (*n*=4) models, a 2° and 4° insertion angle was applied in the sagittal planes from the screw entry point for both the ascending and the descending directions. The *offset of insertion* models (*n*=4) were altered by either a 1 or 2 mm parallel offset of the screw from the midline in both the cranial and the caudal directions.

Screw Design

Two basic screw features were altered: the outer diameter and the angle of the inner core. The *diameter* models (*n*=3) were altered with respect to the trabecular core diameter; the included diameters were 50% (4.25 mm), 75% (6.375 mm), and 100% (8.500 mm) of the trabecular core. The *angle of core* models (*n*=2) started with a diameter of 5.5 mm at the screw entry then a taper angle of either 1.66° or 2.49° was introduced. The 1.66° model was chosen to mimic the taper in the commercially available tangoRS™ screw (ulrich medical®, Ulm, DE).

9.1.3. Patient Specific Geometry

A patient specific geometry (Figure 9.1 bottom) was obtained of an osteoporotic lumbar vertebra by segmenting (Avizo version 5.1, Mercury Computer Systems, San Diego, CA, USA) a CT scan of a specific specimen (S16 L2) from the Screw Augmentation experiment (Chapter 7). The tangoRS™ screw geometry (Ø=5.5 mm, length=50 mm) was provided by ulrich medical®. The positioning of the screw was aligned to the vertebra on the basis of the CT scans[230]. The vertebral and screw geometries were then meshed using second order tetrahedral elements (C3D10, *n*=74,005 for the vertebra, *n*=24,683 for the screw) in HyperMesh (Version 11.0, Altair Engineering, Troy, MI, USA). The mesh utilized smaller elements near the screw location to allow for modeling of screw threads; the element size was allowed to grow as the distance from the screw increased. A cortical shell was distinguished by selecting the outermost layer of elements.

9.1.4. Loading and Boundary Conditions

Basic Model

A standard loading protocol (SLP) was created from publicly available, *in vivo* measurements of the forces (F_x, F_y, F_z) and moments (M_x, M_y, M_z) of an internal spinal fixator for a specific patient (NFL) during walking[17]. The data curves came with a corresponding video which was used to distinguish four complete, two step walking cycles. Six stages of gait were then identified for each cycle (Figure 9.2). The average number of data points was determined for each individual stage; the data was then resampled to have the same number of points as the average for each walking stage (MATLAB 2012b, MathWorks, Natick, MA, USA). The data was then averaged from each phase (*n*=6) of each cycle (*n*=4) and concatenated to obtain one data curve for each F_x, F_y, F_z, M_x, M_y, and M_z. The forces and moments were then transformed from the recorded location in the middle of the implant to the values as they would appear at the screw head (Table 9.2).

Table 9.2 The maximum forces and moments seen in the SLP and the SLP after transformation to the screw head, compared to the average magnitudes recorded from five patients. Data for the SLP derived from four complete gait cycles from patient NFL[17].

	F_x	F_y	F_z	M_x	M_y	M_z
SLP Max	-31.4	-24.9	-287.9	-1.14	-1.55	0.18
SLP Max (screw head)	-31.4	-24.9	-287.9	-0.47	-5.00	0.41
Max Magnitude (Ave. of 5 Patients)	21.7	24.6	135.6	4.02	1.18	0.26

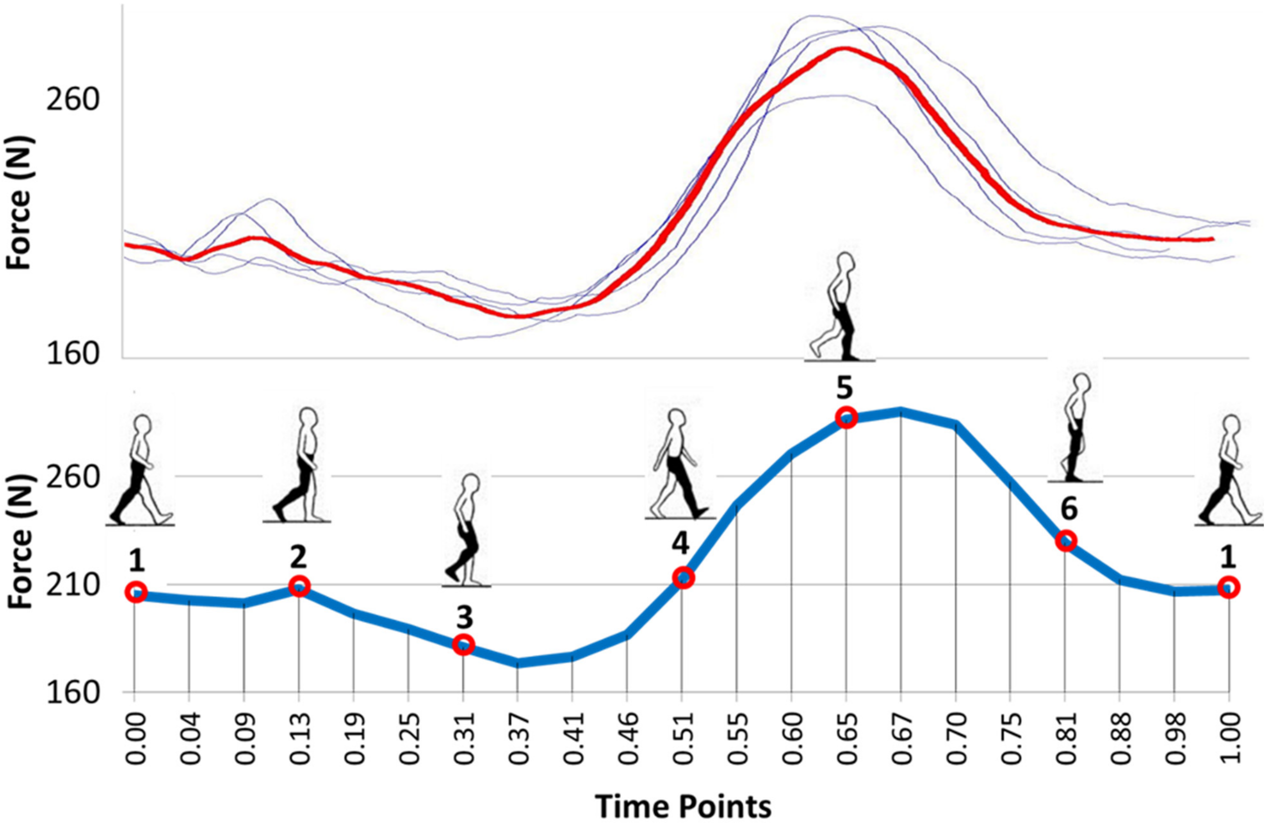


Figure 9.2 The SLP used the above total force curve of a full gait cycle acquired from an *in vivo* loading data set from a single patient. The top graph shows the averaged total force (red) derived from the four individual walking cycles (black). The bottom graph shows the developed standard loading protocol (SLP) as implemented in ABAQUS. The stages of gait are indicated along the force curve and consist of: left foot: 1-heel strike, 2-opposite toe off, 3-passing and right foot: 4-heel strike, 5-opposite toe off, 6-passing (walking figures modified from[251]). The 20 time points shown in the SLP correspond to the points where data was output. [Altered from Bünning[27]]

The mesh of the screw and vertebra were then imported into the commercial software ABAQUS (6.11.-1, Dassault Systèmes S.A., Vélizy-Villacoubaly, France) for implementation and data analysis. The nodes on the outside of the vertebral shell were constrained in all six degrees of freedom (Figure 9.3). The SLP was applied to a node in the center of the screw, located 4.5 mm ventrally from the screw head. The node was tied to the elements 3.5 mm in every direction to simulate the clamp used in the internal fixator[182,184,188]. Hard contact was modeled at the bone-screw interface using a pure penalty formulation with separation allowed. Isotropic Coulomb friction was assumed for the bone-screw interface with a coefficient of friction set to 0.35[206].

Patient Specific Model

The *patient specific* model utilized two different loading regimes: (1) a ramp loading with similar magnitudes as *ex vivo* testing (2) the SLP to enable comparisons to the *basic model*. The first loading protocol consisted of a ramp loading starting from -25 up to -350 N. Twelve time steps were used to gather data at the different loading levels which were applied in the *ex vivo* testing (Chapter 7).

The outer vertebral shell was constrained in all six DOF to roughly mimic the cement encasing of the vertebral body (Figure 9.3). In accordance to the mechanical test setup, the load was applied to two circular areas on the lateral faces of the screw head. Contact was modeled at the bone-screw interface by using the same settings of the *basic model*.

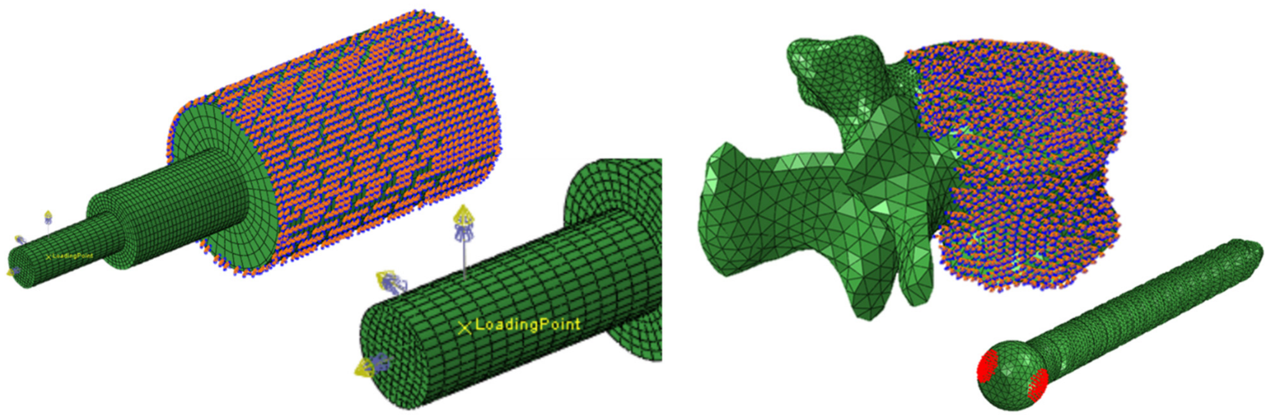


Figure 9.3 Boundary conditions for the basic model[27] (left) and the patient specific model[232] (right). The orange and blue symbols represent the nodes constrained in all six degrees of freedom. The red areas on the screw head are the areas where the force was applied in the patient specific model. [Altered from Bünning[27] (left) and Wagner[232] (right)]

9.1.5. The Material Models for the Bone and Screw

The material model used for both the trabecular and cortical bone in this study was introduced by Hosseini et al.[100] and was implemented as a user material within ABAQUS. It builds upon prior material models[40,249] and uses previously defined material constants[178,250]. The model is characterized as rate-independent, elastic, plastic and coupled damage. The model captures both the softening and the densification regions of the characteristic bone curve and quantifies damage with a parameter based on the cumulated plastic strain. The bone material model also incorporates anisotropic elasticity and the ability to account for the bone geometry parameters of bone volume fraction (BV/TV) and fabric.

The BV/TV and the fabric could not be assigned to each element since the *basic* vertebral geometry is not based on CT images and the *patient specific* geometry is based on clinical qCT data (which does not have the necessary µm resolution). Therefore, the BV/TV and fabric were assumed homogeneous (parameters used are given in Table 9.1). The trabecular architecture is captured by the fabric tensor (M) which is described by three eigenvalues (EV1, EV2, and EV3). EV1 and EV2 describe the orthogonal directions of the trabecular struts in the axial plane. When using a transverse isotropic formulation, these can be approximated by EV1=EV2=0.9 for models with an assumed homogeneous fabric[40]. The third eigenvalue of the fabric tensor is calculated by setting the trace of the fabric tensor equal to three (tr(M) = EV1+ EV2+ EV3 = 3). The screw was modelled as a linear elastic material with the material properties representative of a typical titanium alloy (Ti-6Al-4V) used in medical devices (E=110 GPa, v=0.3)[21].

9.1.6. Output Measures

The displacements at the screw head and tip, damage, cumulated plastic strain, stress, and elastic strain energy were the compared output parameters. Maximum displacement is reported for both the screw head and tip. Damage and von Mises stress were compared on the basis of their maximum values as well as by analyzing the overall patterns within the trabecular bone. Reducing displacement, damage, cumulated plastic strain, stress, and the elastic strain energy was considered beneficial for reducing the possibility of screw loosening for the SLP.

9.2. Results

The SLP produced similar damage and stress patterns for all models. Maximum damage and stress within the trabecular core generally presented at the cranial screw tip. Damaged zones expanded around the cranial screw tip and at the caudal portion of the screw where the screw enters the vertebral body (Figure 9.4). A third damage localization occurred away from the screw at the cranial pedicle entry to the vertebral body.

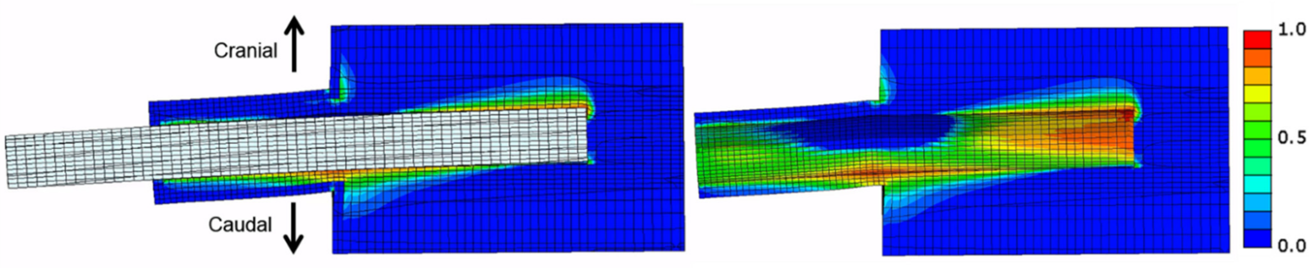


Figure 9.4 The damage pattern is shown with a sagittal cross section of the *basic model* along the midline of the screw after undergoing one walking cycle (SLP). The left picture shows the screw and the cortical shell. Since the cortical shell underwent little damage and the screw was unable to (modeled as linear elastic) the cancellous core alone is shown (right). [Altered from Bünning[27]]

9.2.1. Relative Influence of Patient, Surgical, or Screw Design

The results of the *basic model*, the *patient specific* model and the comparative differences of the other fifteen completed models are reported in Table 9.3 and shown in Figure 9.5. Five models did not converge to a solution when undergoing the SLP loading profile. These models included the *low quality* and *worst case* scenarios from the *bone quality* models, the 1 mm and 2 mm caudally offset screws in the *offset of insertion* models, and the 4° descending *angle of insertion* model. Due to the large influence of the bone quality on fracture found in the literature, the *bone quality* models were then run with a caudal ramp displacement to 3 mm applied at the screw head (results in Table 9.4). The other three non-converged models were not investigated any further.

Table 9.3 The overall results of the *basic model* separated by their alteration groups. The absolute values for the *basic model* and the *patient specific model* are given. For all other models the percentage difference from the *basic model* is displayed; green values represent improved performance and red values stand for reduced performance.

		Differences from the *Basic Model*	Disp. Screw Head mm	Disp. Screw Tip mm	Max Damage	Cumulated Plastic Strain	Max von Mises Stress MPa	Elastic Strain Energy N mm
	Basic	NA	**2.32**	**0.39**	**0.95**	**1.44**	**14.1**	**183**
	Patient Specific	real specimen and screw geometry	**1.08**	**0.12**	**0.97**	**0.52**	**7.3**	**151**
Patient	*Cortical Shell*	+ 50% cortical shell thickness	-23%	-35%	-3%	-31%	-17%	-12%
		+ 100% cortical shell thickness	-38%	-56%	-3%	-43%	-19%	-19%
		+ 150% cortical shell thickness	-59%	-91%	-32%	-87%	-60%	-21%
Surgical	*Depth of Insertion*	- 5 mm insertion, 40 mm depth	38%	77%	14%	83%	38%	-10%
		+ 5 mm insertion, 50 mm depth	-43%	-44%	-4%	-35%	-21%	12%
	Angle of Insertion	2° Ascending	2%	2%	0%	12%	5%	1%
		4° Ascending	-5%	-8%	-2%	-5%	4%	1%
		2° Descending	3%	4%	-4%	-2%	-3%	1%
	Offset of Insertion	1 mm cranially offset from midline	4%	4%	3%	120%	66%	0%
		2 mm cranially offset from midline	9%	14%	3%	540%	201%	1%
Screw Design	*Diameter*	Ø = 4.25 mm	93%	34%	4%	117%	52%	144%
		Ø = 6.375 mm	-31%	-24%	-4%	-31%	-17%	-39%
		Ø = 7.5 mm	-80%	-80%	-22%	-81%	-53%	-78%
	Angle of Core	1.66° taper	80%	-4%	0%	0%	49%	65%
		2.49° taper	174%	-40%	2%	28%	58%	136%

The *low quality, worst case,* 1 and 2 mm caudal *offset of insertion*, and 4° decending *angle of insertion* models did not converge.

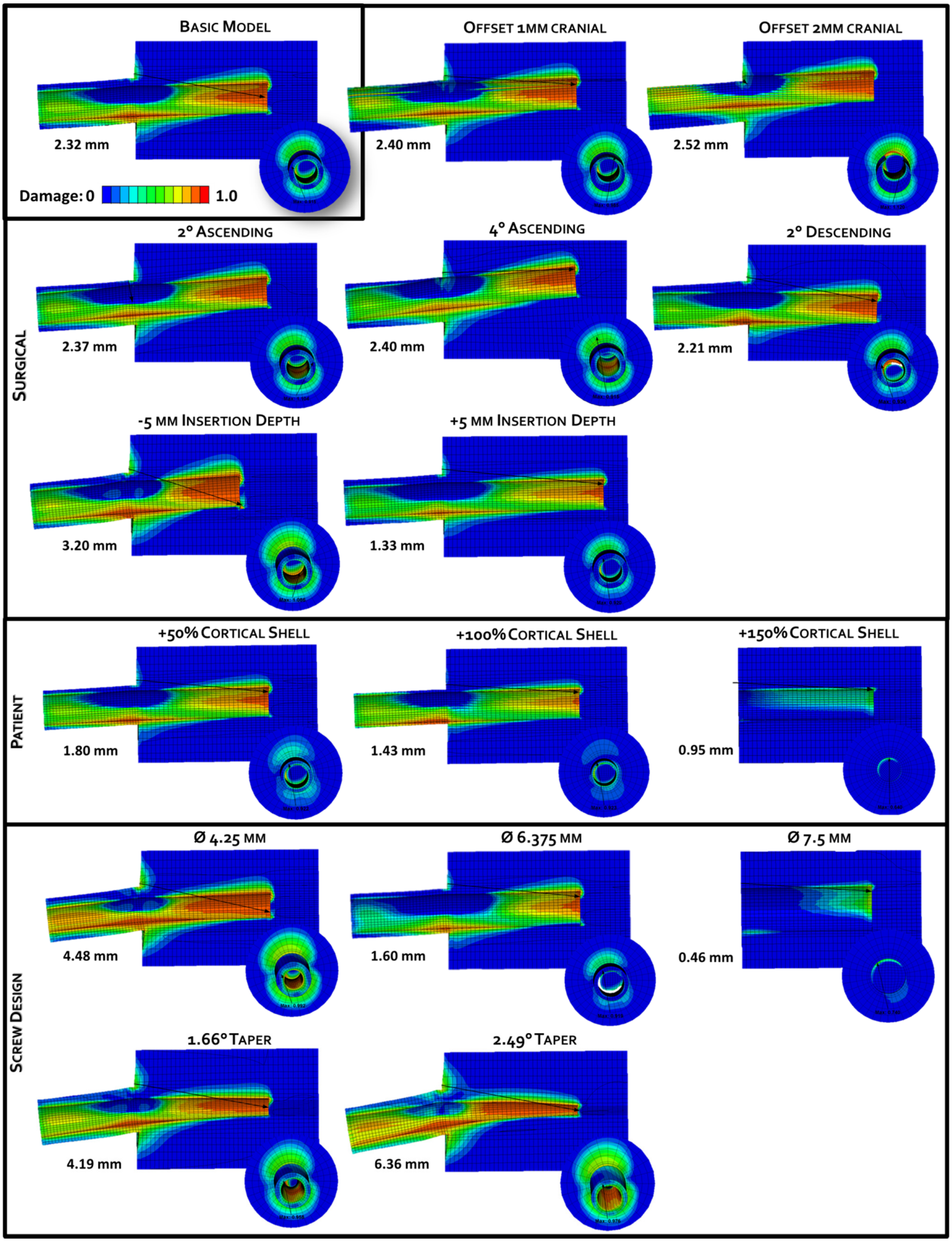


Figure 9.5 The damage distribution patterns in the trabecular bone around the screw in the sagittal plane for all of the models completing a loading protocol of one gait cycle (SLP). The numbers given are the screw head displacement. [Altered from Bünning[27]]

Patient

The *bone quality* models were the only models which underwent a 3 mm ramp displacement at the screw head. The reduction of the material properties of the bone led to a larger screw tip displacement (29-65%), maximum damage (1-2%) and cumulated plastic strain (39-102%, Table 9.4). While the reaction force at the screw head, maximum von Mises Stress and the total elastic strain energy of the models all decreased. The *cortical shell* models saw a reduction in the displacement, damage, plastic strain, stress and strain energy with an increasing cortical shell thickness (Table 9.3). The 150% cortical shell thickness led the largest reductions of screw tip motion (-91%), damage (-32%), plastic strain (-87%), and von Mises stress (-60%).

Table 9.4 The results from the *bone quality* models are shown for a loading of a 3 mm displacement from the screw head. The values are given for the *basic model* and then the percentage difference from the *basic model* are given for the step-wise reduction in material properties for the *low quality* and *worst case* models.

3 mm Disp. Loading	Reaction Force at Screw Head N	Disp. Screw Tip mm	Max Damage	Cumulated Plastic Strain	Max von Mises Stress MPa	Elastic Strain Energy N mm
Basic Model	31.6	0.522	0.885	0.715	8.27	132.7
Low Quality	-13%	29%	1%	39%	-25%	-53%
Worst Case	-26%	65%	2%	102%	-62%	-88%

Surgical

The *depth of insertion* models showed a reduction of screw motion, damage, cumulated plastic strain and maximum von Mises stress with an increased depth into the bone (Table 9.3). The total elastic strain energy increased with an increase in screw depth. A reduction in length of 5 mm led to a 38%, 77%, and 83% increase in screw head motion, screw tip motion and cumulated plastic strain respectively. The *angle of insertion* models showed little difference from the *basic model* with differences tending to be within 5%. An angle of insertion in an ascending direction led to an increasing displacement while the descending direction lead to a decreased displacement (changes between 3-5%). The *offset of insertion* models tended to increase the screw motion, damage, cumulated plastic strain and maximum von Mises stress with an increased cranial offset. The cumulated plastic strain and the maximum von Mises Stress showed large increases (540% and 201% respectively) with a 2 mm cranially offset insertion point.

Screw Design

With increasing screw diameter there was a substantial decrease in displacement, damage, plastic strain, stress and strain energy. The 7.5 mm model exhibited the largest reduction in head motion (-80%) and total strain energy density (-78%) while having the second highest reduction in tip motion (-80%), damage (-22%), cumulated plastic strain (-81%), maximum stress (-53%). Increasing the screw taper angle (*angle of core* models) caused increasing damage to the trabecular bone in terms of increasing damage, plastic strain, stress and strain energy. The screw head was shown to have greater displacement (80-174%) with increasing taper angle; whereas, the screw tip showed less displacement (-4 to -40%) with increasing core angle.

9.2.2. Verification of the Basic Model Behavior

Similar features were exhibited for displacement and for damage all along the SLP loading pattern when comparing the *basic model* to the *patient specific* model (Figure 9.6). For both the *basic* and the *patient specific* models the highest peak displacements, stresses and strains occurred at the highest applied force. This force was located just after 5th stage of gait when the patient would be in single leg stance on the same side in which the telemerized implant was located. The magnitude of the displacement of the *basic model* consistently stayed between 115 and 130% of the *patient specific* model with both models showing peaks where peak loading existed in the SLP (Figure 9.6 left).

The maximum damage value the *patient specific* model was found at the location of the self-tapping screw feature. This feature is an extremely sharp edge at the tip of the screw and stress concentration at this edge is likely the reason for the sharp increase in damage shown at such an early time point (Figure 9.6 Right). Due to this stress concentration, a node with high damage which fell on the outer cylindrical surface of the tip of the real screw was chosen as a more representative comparison to screw of the *basic model*. A damage curve with similar features throughout the loading cycle was then observed between the *basic* and the *patient specific* models. Since damage is cumulative the maximum damage occurs once loading is ended.

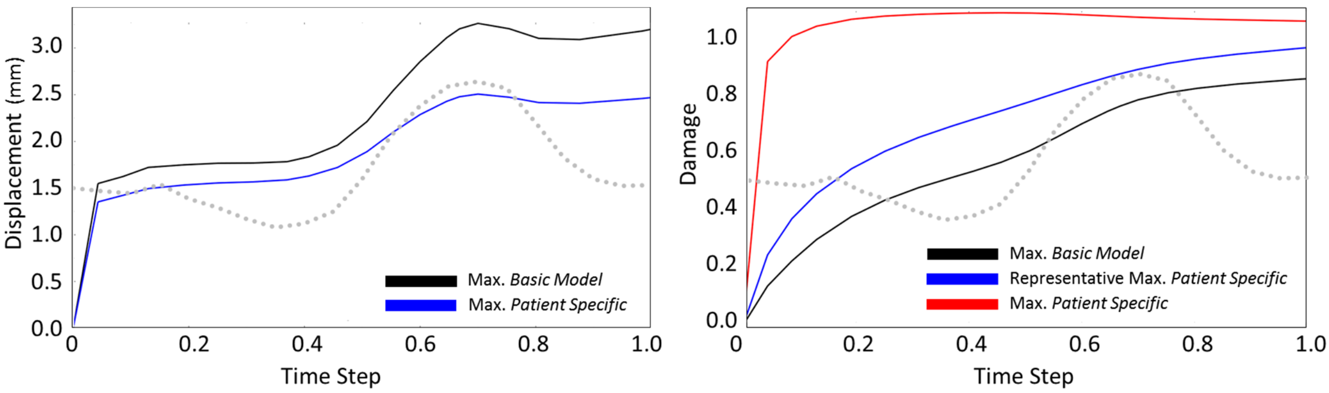


Figure 9.6 The trend of the maximum displacement and the damage through the entire gait loading cycle for the *basic* and the *patient specific* models. To illustrate how the variables developed with loading magnitude the total force profile which was applied with the SLP is represented as a grey dotted line.

The *patient specific* model had a reduction in the screw head motion (-53%), tip motion (-69%), plastic strain (-64%), von Mises stress (-48%), and strain energy (-18%) and a slight increase in damage (1%) when compared to the *basic model* (Table 9.3). The damage and stress distribution patterns show maximum magnitudes at the screw tip (Figure 9.7). Spreading of the damage and stress patterns was seen at the screw tip and at the sharp corners where the screw enters the vertebral body in the *basic model*. The *patient specific* model showed less damage spreading at the tip than the *basic model* and more on the caudal side near the screw entry to the vertebra.

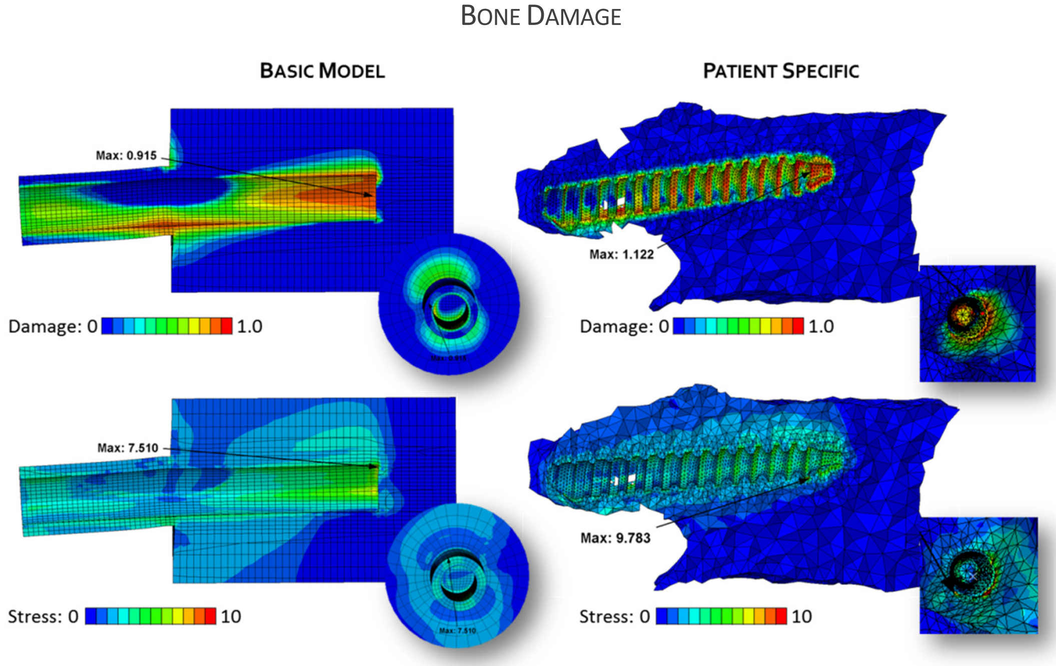


Figure 9.7 Damage (top row) and von Mises stress (bottom row) patterns are shown for the *basic* (left) and the *patient specific* (bottom) models after the complete SLP loading protocol. [Altered from Bünning[27]]

The segmented damage pattern exhibited along the screw axis in the *basic* and the *patient specific* models are compared to two loosening patterns which occurred *in vivo* (Figure 9.8). These clinical failure patterns are the sagittal cross sections along the screw axis of a segmented loosening halo as seen in a CT scan (Chapter 4). Clinical loosening patterns from an L2 vertebra (67 years old, female, instrumented from L2-S1) were chosen for comparison to *in silico* damage patterns because the *patient specific* model is based on the geometry of a L2 vertebra. The *basic model* captures the cranial toggle at the screw tip but has damage localizations at the pedicle entry to the vertebral body. The *patient specific* model captures the widening and the toggle at the posterior end of the screw but it does not capture the slight cranial toggle at the tip. Conversely, this tip widening is seen in the stress distribution patterns of the *patient specific* model (Figure 9.7).

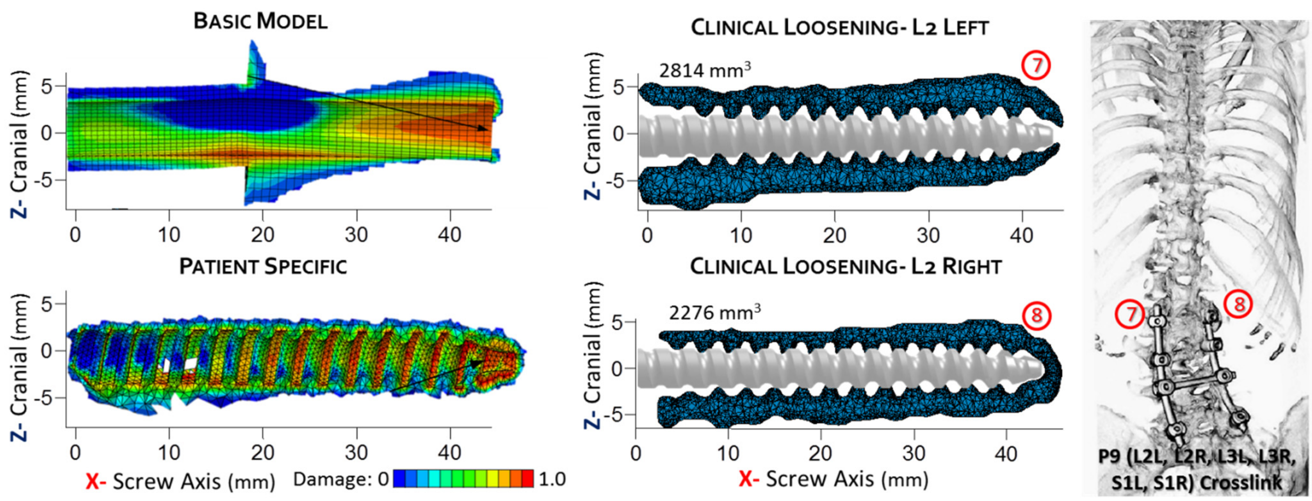


Figure 9.8 A comparison of the *in silico* damage propagation patterns for the *basic model* and the *patient specific* model compared to the loosening failure patterns observed *in vivo* for a L2 vertebrae (Chapter 4).

9.3. Discussion

9.3.1. Parameters and Material Model Selection

The material model from Hosseini et al.[100] was utilized because it is the first material model for bone which simulates the collapse of trabecular bone. The trabecular buckling is also associated with a sharp decrease in both the bone's load carrying capacity and its stress (known as stress softening). The load carrying capacity is important because the bone's ability to transmit load should correspond to the stability of the implant. If you reduce the load carrying capacity of the bone surrounding the screw, the ability of the bone to resist the repetitive loading is lost and; therefore, motion is likely introduced. Motion is detrimental to pedicle screws because in order for the screws to be clinically useful they must maintain their fixation with bone to either stabilize the spine for fusion or to keep the surgically corrected alignment. For these reasons, it is believed that the motion at the screw head and tip have a high clinical relevance. Damage is also extremely relevant because it represents plastic damage and, therefore, the permanent loss in stiffness of the bone. If the bone is permanently less stiff it will lead to this clinically detrimental implant motion.

9.3.2. Comparative Influence of Patient, Surgical, and Screw Design Parameters

While undergoing a standard walking load the largest influences of damage and motion of the screw were seen with changes in the cortical shell thickness, to the diameter of the screw, and in the length of insertion. When not considering bone quality, this matches very well with pre-clinical testing reported in the literature[41] as well as with the current clinical opinion (Chapter 3). Although the diameter and the screw insertion length were classified as either a screw design or a surgical factor respectively; in the end, it is the patient geometry which limits these factors. The screw diameter cannot be wider than minor outer pedicle diameter or the pedicle canal will be perforated. If the perforation is substantial enough (typically considered >4 mm), it can cause instability of the screw[49] or neurological damage to the patient[82]. The screw insertion length is limited by the vertebral body dimensions because in many regions of the spine the screw should not perforate the anterior wall due to the proximity of important neurovascular structures. Therefore, all of the primary influential categories studied here are driven by the initial situation as it presents to the surgeon either in terms of bone material quality or the vertebral dimensions (cortical thickness, pedicle dimensions, or vertebral body size). It is therefore imperative that the surgeon utilizes these patient dimensions to the fullest.

Bone quality is largely determined to be an influential parameter in bone-implant fixation strength[47]. The stress softening behavior of the material model led to the reduced bone quality models undergoing higher tip motion (65%), while sustaining less reaction force (-26%) and stress (-62%). The *bone quality* models were not able to be evaluated with the standard walking loading protocol but only with a displacement control. Direct comparisons to the other groups of altered parameters were thus not possible and, disappointingly, no clear statement on the most influential factor for fixation can be made across all altered parameters.

The 7.5 mm *diameter* and the 150% *cortical shell* thickness models contained the largest reductions of both damage and screw motion (Figure 9.5). The fact that these models had such large reductions is not surprising due to the incredibly ideal nature of their fixation: the cortical shell was in contact with the screw for the entire length of the pedicle. It is, however, interesting that they exhibited different damage patterns. The cortical shell model had a larger damage area, although it was more evenly spread manifesting itself in lower maximum damage (0.64 vs. 0.74) and lower cumulated plastic strain (Figure 9.5). It has been shown[122] that the ideal profile for implant stability would be the creation of an even distribution of the stresses along the complete implant profile. With that in mind, for the investigated pedicle diameters it would theoretically be better to have the cortical shell meet the screw rather than the screw diameter enlarge to the cortical shell. A screw placement which utilizes the full inner pedicle minor diameter with purchase into the cortical shell would likely the most key aspect for proper surgical placement of a pedicle screw.

A diameter decrease to 4.25 mm caused more displacement at the screw head (4.48 mm) but less screw tip displacement (0.40 mm) in comparison to the screw length decrease (3.20 mm and 0.57 mm respectively). The higher screw head displacement for the smaller diameter model is likely due to the fact that there was more trabecular bone between the screw and the cortical shell, and since the trabecular bone is substantially softer the pedicle region was less stiff and was allowed to deform more easily. This allowed more head motion but similar damage. For the shorter screw, most of the increased motion was expressed at the screw tip. This is because when compared with the *basic model* it had the same stiffness in the pedicle region but less area to dissapate the forces within the vertebral body. This caused a increase in the bredth and the peak magnitudes of the damage patterns at both the screw tip and the enrty to the vertebral body.

Interestingly, the *angle of insertion* models showed very little variation, generally less than 5%, from the *basic model*. A trend was found that a change in the angle of insertion for both ascending and descending directions reduces the maximum bone damage with higher reductions for the descending direction. A caudal offset to the screw entry point caused an increase of the damage, but a decrease in the displacement. Both the reduction of the bone damage in the angle models and the decreasing displacement in the offset model can likely be attributed to the closer proximity of the cortical shell allowing the stress dissipation and relief of the softer trabecular bone. In comparison to the other screw and patient parameters, the surgical positioning effects of the *angle* or the *offset of insertion* had only a slight influence on both the motion and on the maximum trabecular bone damage. This corresponds well to *ex vivo* investigations: one which shows no effect of surgical placement[174] and another which shows little influence of screw positioning on fixation strength until a 4 mm cortical perforation was achieved[49] (no perforations were modeled in the present study). This suggests that obtaining a more appropriate diameter and screw length is of more consequence to screw fixation than the proper surgical alignment.

9.3.3. Other Observations

For all simulated pedicle models, a damage distribution originating at the bone-screw interface was observed in the trabecular bone (Figure 9.5). Therefore, it appears that irreversible damage can be invoked on normal quality trabecular bone by only one standard gait cycle. A typical pattern with damage spreading at the screw tip was observed (Figure 9.8). This roughly matches the clinically observed radiographic loosening patterns from Chapter 4. These facts reinforce the perception that repetitive daily loading of the pedicle screw could be a mechanism for pedicle screw loosening.

With the large increases in screw head motion (80%- 174%) for the *angle of core* models it was initially surprising that the damage was only slightly influenced (0-2%). However, when considering that a tapered implant with uniform material properties behaves similarly to an implant with a continually reduced stiffness along the core[122] the relationship becomes clearer. The decrease in the screw stiffness allowed more screw bending rather than large increases in permanent bone damage or screw tip displacement. This in turn allows for more motion at the screw head which is not considered good for rigid implant fixation. When inspecting the damage pattern of the 2.49° taper angle (Figure 9.5) the peak width of the damage pattern does not occur at the screw tip as it does in every other model. The damage pattern width is spread more evenly along the length of the screw. For implants which are not necessarily for the rigid fixation of the spine, the often termed dynamic stabilization, the increase in screw head motion may not be a problem because motion is actually desired and the extremely even distribution of damage would be ideal.

Chen et al.[39] created a FE model with six varying screw lengths (12 mm to 39 mm) and a similar contact definition as in this study in order to investigate the load transfer mechanism at the interface of the pedicle screw and the vertebra. They identified that with increasing screw length the displacement and the stress decrease; these findings correspond well with this study. Additionally, the study by Chen et al.[39] states that the influence of screw length on the stress became negligible when the screw surpassed a certain depth into the vertebra. For this current model further varying screw lengths would be necessary to investigate this trend representatively; nevertheless, initial similarities were shown because between the 55 mm and 60 mm screw the stress decreased 27%, while it decreased only 21% between the 60 mm and 65 mm.

9.3.4. Verification of the Model Behavior

The *basic* and the *patient specific* models were able to capture similar trends all through the various stages of gait for both of the two primary parameters of interest, displacement and damage (Figure 9.6). The *basic model* can further capture the cranial toggle pattern as it is seen at the screw tip *in vivo* (Figure 9.8). The *basic model* does, however, introduce areas of stress concentration at the pedicle entry to the vertebra. These corners act to both localize damage in non-realistic areas as well as to increase the dispersion of damage (Figure 9.7). The reduced cumulated plastic strain (-64%), von Mises stress (-48%), and strain energy density (-18%) for the *patient specific* model compared to the *basic model* likely occur because of these stress concentrators. The reduced motion at the screw tip (-69%) for real geometry is likely due to the decreased distance from the screw tip to the cortical shell (Figure 9.7). This decreased distance means there is less of the softer trabecular bone and; therefore, the stiffness is increased. Importantly, the *basic model* can capture general trends of motion as well as damage. For purely comparative testing the same magnitude of results is not necessary, it is more important that the model can capture similar trends.

9.3.5. Limitations

It should be appreciated that a very simplified model of the screw and vertebra geometry has been utilized. The *basic model* was chosen to exhibit symmetry while roughly mimicking the sagittal cross-section of a typical lumbar pedicle screw and vertebra complex because this plane has been shown to be the primary loading plane of the pedicle screw[17,181]. However, the model used explicitly neglects the presence of the screw threads and importantly it also introduces sharp stress concentrating corners. These corners exist at the transition between the pedicle and the vertebra as well as at the tip of the cylindrical screw. These stress concentrators can have a large influence on the propagation of the stress and damage patterns. This said, it has been found by Huiskes and Boeklagen[103] that general trends that are found using a simple model will most-likely be retrieved in more elaborate models as well.

Both a homogenous material and fabric were utilized for these models. The material model used is designed for use with µCT data sets in order to be able to capture the distribution of these parameters throughout the model. Use of material mapping has been shown to increase the models ability to capture densification of trabeculae[40].

A Boolean subtraction of the screw was used with no modeling of the damage which is imparted upon screw insertion. Screw insertion, especially for a conical core (*i.e. angle of core* models), has been shown to compress the screw and µCT studies have shown breakage of trabecular struts around the screw making the area around the screw have a higher BV/TV[1,49,121,165]. Peyker and Pahr[165] then used the scans to make FE voxel models to see the influence of modeling these extra trabecular struts on the screw fixation. They found a higher strength was seen for the models which included the broken bone rather than only doing a Boolean subtraction.

The goal of the present study was to obtain comparative rather than absolute differences between models for the damage propagation and screw motion in pedicle screw fixation. The model used was not chosen to try and predict happenings but rather to investigate trends due to parametric changes to the primary aspects of fixation as determined in the literature. Symmetry within the comparative geometry of the basic model was consequently important.

9.4. Conclusions

Screw diameter, patient cortical shell thickness and the screw depth into the bone are the most influential parameters of the models tested. In the end, these factors are all limited by patient vertebral dimensions. Pre-operative planning which would allow for the utilization of the largest length without anterior wall perforation and a diameter which slightly penetrates the inner cortical shell of the pedicle shell could be ideal for pedicle screw placement.

The surgical placement parameters of *angle of insertion* (2-5%) and *offset of insertion* (4-9%) had much less comparative influence on fixation when compared to the diameter (31-93%) and length of the screw into the vertebral body (38-43% for screw head displacement). Extra care should be used for determining screw diameter and length.

The introduction of a tapered core reduced the width of the damage pattern along the screw profile while substantially increasing the screw head motion. For dynamic systems where motion at the screw head is not problematic, the small, even damage distribution along the screw axis may be ideal.

The material model used in this study was quite robust in terms of convergence and computational cost while producing visualization and quantification of permanent bone damage at the screw-bone interface. This makes it an ideal material model for further investigations implant interface damage.

The study showed that irreversible damage can be invoked on normal quality trabecular bone surrounding a pedicle screw by only one standard gait cycle. This supports the notion that repetitive everyday loading of the pedicle screw may in fact be a mechanism for pedicle screw loosening.

Chapter 10.
General Discussion

Studies in this thesis investigated factors which affect the fixation between a pedicle screw and the vertebral bone in which it is implanted. The primary goals were to determine the clinical pedicle screw loosening pattern and the primary influential factors of loosening in order to ultimately identify potential avenues to mitigate this failure mode. In order to identify possible avenues to reduce screw loosening, a series of studies was performed within this thesis to determine the clinical failure pattern, the most important determinants of fixation, and to identify an experimental setup to enable the parameterization of screw loosening. The current chapter aims to synthesize the results and conclusions from the individual studies and speak about them in the terms of the more comprehensive research questions.

Pedicle screw fixation is the gold standard for posterior spinal stabilization surgeries[80]. The fundamental aim of rigid pedicle screw fixation is to reduce motion in order to allow healing (bone growth for fusion) and/or to stop painful motion[148,163]. Pedicle screw loosening is the most common clinical failure mode of this surgical fixation technique. A loss in fixation between the bone and the screw is clinically important because it has been associated with pseudarthrosis, detrimental motion of the entire spinal construct, loss of the corrected spinal alignment, and can subsequently lead to the necessity for screw removal[61,64,128,173]. These side effects can require a revision surgery which increases the rate of infection while often requiring a longer instrumentation and, thereby, placing a higher demand on the patient[63,211].

The two primary research questions forming the foundation of this thesis are admittedly broad; however, they were investigated within the framework of seven experimental studies which contained more specific questions and investigated parameters (Table 10.1). The first research question of the thesis pertains to the quantification of the loosening zone around the pedicle screw. Investigations of failure patterns can be useful when attempting to mitigate a failure mode or to ascertain the proper testing methods. The details from failure pattern analysis can provide insight into the failure mechanisms, the regions of failure, and may lead to useful clues on where to direct changes in design. Within the biomechanical literature, there is a paucity of studies on the clinical appearance of pedicle screw loosening. One study described the histology of the tissue surrounding the screw[199] and others gave very broad, qualitative descriptions from radiographs[57,115,229]. From the relevant literature and a consideration of fundamental mechanics, the hypothesis was made that clinical and *ex vivo* loosening patterns will exhibit the most motion in the primary *in vivo* loading plane as well as peak displacements at the screw tip and screw entry to the vertebra.

Studies relevant to the second research question investigated the primary influential factors of pedicle screw fixation. Knowing which factors have the highest relative influence on a failure mode helps to identify the most relevant aspects of a design and identify in which situations the design should be used. There is a plethora of studies on pedicle screw fixation which employ heterogeneous methodological techniques and output measures to investigate individual aspects of patient characteristics, surgical techniques or screw design. This heterogeneity precludes the comparison and synthesis of results which leads to difficulties in discerning the most influential factors of pedicle screw fixation. The ways that the current thesis attempts to overcome the deficiencies in the current literature include: (1) an attempt to discern the most important influential factors within one study to enable quantitative comparison (2) the use of comparable output parameters and testing methodologies to facilitate the synthesis of results. Based on the results from the available literature, the hypothesis was formulated that patient attributes, especially related to bone quality and pedicle dimensions, will be the most important factors influencing pedicle screw fixation.

Table 10.1 A tabular representation of the connections between the parameters investigated, the research questions and the chapters including relevant data.

Research Questions	Investigated Parameters	Relevant Chapters
(1) Pattern of Loosening	**Clinical Loosening Pattern** (quantifying loosening zones, clinical observation)	Chapter 3: Current Clinical Opinion Chapter 4: Clinical Appearance
	Pre-clinical Screw Motion (pivot point, screw tip motion, screw head motion)	Chapter 5: Test Method Comparison Chapter 6: Atlas Chapter 7: Screw Augmentation Chapter 8: Design Concepts Chapter 9: Bone Damage
(2) Primary Aspects of Fixation	**Patient Attributes** (bone quality, vertebral dimensions)	Chapter 3: Current Clinical Opinion Chapter 5: Test Method Comparison Chapter 6: Atlas Chapter 7: Screw Augmentation Chapter 8: Design Concepts Chapter 9: Bone Damage
	Surgical Variables (angle of screw insertion, depth of screw insertion, cement augmentation of screws)	Chapter 3: Current Clinical Opinion Chapter 6: Atlas Chapter 7: Screw Augmentation Chapter 8: Design Concepts Chapter 9: Bone Damage
	Implant Attributes (thread design, diameter, length)	Chapter 3: Current Clinical Opinion Chapter 7: Screw Augmentation Chapter 8: Design Concepts Chapter 9: Bone Damage

10.1. Research Question 1: The Pattern of Pedicle Screw Loosening

10.1.1. The Clinical Pattern of Pedicle Screw Loosening

The features of the pedicle screw loosening pattern quantified from the clinical CT scans (Chapter 4) along with the opinion of the surgeons (Chapter 3) corroborate the first hypothesis, that the loosening patterns will exhibit the most motion in the primary *in vivo* loading plane as well as peak displacements at the screw tip and screw entry to the vertebra. The clinically quantified patterns (Chapter 4) were characterized by the following features:

- A distinct fulcrum located near the pedicle end.
- The volume of loosening increased from cranial to caudal down the spine.
- A higher volume of loosening at the marginal construct ends when compared to mid-construct loosening.
- A bimodal distribution of loosening volume with peaks either towards the screw tip and entry in 74% (17 of 23) of loosening patterns in both the sagittal and transverse planes.
- Distinct failure patterns in the different spinal regions (classified according to Figure 4.5):
    - cervical region: cranial toggle
    - thoracic region: primarily widening patterns with no sharp cranial or caudal peaks
    - lumbar patterns: 30% were cranial toggle + widening (L2 or L3), 20% were pure widening (L3), 40% were caudal toggle (all in L4 or L5), and one was a butterfly (L4)
    - sacral region: 7 of 9 were caudal toggle + widening and two were pure widening

The clinically determined loosening patterns corresponded well with previous *in vivo* loading data[17] as well as with the typical locations of peak stresses and strains for medical implants[122]. Although non-significant, the loosening peaks in the sagittal plane were larger than the peaks in the transverse plane suggesting there is greater loading in the cranial-caudal direction as had been shown *in vivo*. The loosening volume peaks localized at the screw entry and tip matched the previously recorded areas for peak bone-implant interface stresses/strains[122], as well as the peaks in the bone damage patterns in both the simplified *basic* geometry and in the *patient specific* FE models (Chapter 9). Reducing or more evenly distributing the loading along the screw axis might be a key to reducing these damage peaks and improving screw stability within the bone. Perhaps the implementation of an optimized stiffness gradient along the screw axis would be useful in this case.

An inference that pedicle screw loosening typically presents first at the marginal ends of the construct is based on a combination of findings from the quantified clinical loosening patterns investigated in Chapter 4. (1) Corresponding with previous findings[57,115,229], a higher incidence of loose screws occurred at the cranial or caudal ends of the construct compared to the mid-construct screws. (2) Mid-construct screw loosening was only present if marginal loosening existed. (3) Loosening volumes on the construct ends were significantly larger than volumes of mid-construct loosening within the same patient (p=0.02). Taken together, these results indicate that loosening may begin on the marginal construct ends and, as the loosening zone increases in size, the construct is likely to have decreased stability. In turn, decreased stability may then induce loosening in subsequent levels.

The increased screw dimensions, vertebral volume, curvature and the spinal loading in the caudal spine may lead the lumbosacral region to being particularly susceptible to high rates and volumes of pedicle screw loosening. The lumbosacral region was determined as having the highest rates of screw loosening from both the screening in the clinical CT study (Chapter 4) and via surgeon observation (Chapter 3). The higher rates of screw loosening may derive from the coupled facts that (1) caudal spinal regions experience higher loading and (2) that larger vertebral dimensions mean there is a higher likelihood that the more compliant trabecular bone surrounds the screw[160]. These factors would, theoretically, lead to less resistance to screw displacement. In addition to high loosening rates, the loosening volumes grew by a factor of ten from the cranial to the caudal spinal regions. While larger screw dimensions are shown to increase screw stability in the spine (Chapter 7 & 9), they also mean that the same amount of cranial-caudal displacement will result in larger loosening volumes. Larger screws are used in the caudal spine due to the larger vertebral dimensions; therefore, the loosened screws included in this study should have a higher loosening volume with a similar total displacement.

10.1.2. Mechanisms of Pedicle Screw Loosening

There are many possible explanatory mechanisms underlying the loosening of pedicle screws. Within the literature, the predominate belief for the pedicle screw loosening failure mechanisms is boney failure due to repeated loading either as either cranial-caudal toggling or micromotion[19,39,42,112,129,155,156,199]. Both of these mechanisms are corroborated by findings within this thesis.

Results from both the surgeon survey (Chapter 3) and the clinical CT study (Chapter 4) suggest that the predominate loosening mode is repeated cranial-caudal loading on the spinal implants. For the surgeon survey (Chapter 3), the observed length of time to loosening, observed patterns of failure, the relative importance given to cranial-caudal wear and micro-motion as failure mechanism suggest repeated loading. When considering the results of the clinical CT study, the presence radiographic halo suggests fatigue failure of bone occurred. The primary loading direction is suggested to be in the cranial-caudal direction because there was the first quantitative evidence of a fulcrum near the end of the pedicle with the greatest volume of loosening in the cranial-caudal plane. When considering the indications of fatigue and the cranial-caudal failure pattern together, the indicated failure mode would be cranial-caudal fatigue overload at the bone-screw interface.

Mechanical loosening of a pedicle screw in the vertebra is believed to involve the progressive collapse of trabecular bone due to the stresses or strains of everyday activity[42,129]. The much stiffer screw is believed to transfer the stresses/strains produced by the repeated everyday motion to the bone[42]. Once a threshold of approximately 1-2% of nominal strain is surpassed, the struts of the trabecular bone collapse. After the initial collapse, a second phase of densification occurs around 25-40% of nominal strain[84,95]. The densification is attributed to the increasing contact of the broken trabecular struts and is characterized by increases in both the load carrying capacity and in the microstructure stiffness. The densification via compacting and bone remodelling of the trabecular struts could be a possible explanation for the appearance of the double halo. The double halo is a dense radiopaque rim of compacted trabecular bone surrounding the screw and is sometimes used for the visual confirmation of screw loosening[57,115]. Fatigue at the bone-screw interface could be indicated by the presence of this double halo. Such an opaque rim surrounding the loosening halo is not seen around unloaded screws with induced infection. The halo/rim is, therefore, hypothesized here to form from the repeated compaction of the cancellous bone by the loading of the screw.

Findings from a FE model from Guo et al.[91] suggest that that the primary failure mechanism for low-stress, high-cycle fatigue of trabecular bone is crack growth and propagation. Daily activities of typical spinal loading would fall in the low-stress, high-cycle fatigue category suggesting crack growth and propagation to be a likely failure mechanism. The FE study presented here (Chapter 9) supports the notion that low-stress everyday activities may contribute to screw loosening. The FE model showed that irreversible damage can be invoked on normal quality trabecular bone surrounding a pedicle screw by only one standard gait cycle. However, bone remodeling and other biological responses may help to repair damaged bone.

Micromotion is also believed to be a clinically relevant failure mechanism. The clinical observation of a reversal of screw loosening around a broken screw tip suggests motion may be a relevant loosening mechanism and that radiographic loosening may be reversed if the interface motion is terminated. This is corroborated by the disappearance of clinical loosening halos surrounding screws after radiographic fusion was achieved[229] and by a study which showed that if motion at the screw interface is stopped than cancellous bone can grow into the screw threads[199].

10.1.3. Appropriateness of Pre-clinical Testing Methods

Although axial pullout testing is the standard screw fixation test for the spine[8], pullout has not often been reported to be a clinically relevant failure mechanism (Table 2.4) nor is it typically considered to be a probable mechanical mechanism of screw loosening[58,112]. Results within this thesis raise further questions about clinical efficacy of pullout testing. An axial pullout failure pattern presents radiographically as a stripping of the screw threads along the screw axis[49]. In the clinical screening of CTs in Chapter 4, no screws produced a pullout failure pattern. Surgical opinion (Chapter 3) also demonstrated that surgeons believed that pullout was the least likely loosening pattern (*p*s<0.001). Importantly, when results from both pullout and fatigue testing of the spine were compared between four treatment groups, a significant interaction of the treatment group and the testing method was found (p=0.001, η_p^2=0.4, Chapter 7). This finding casts serious doubt that significant results from pullout testing can correspond to increases in the more physiologic fatigue testing in a controlled experimental setting, let alone in the even more complex clinical situation. It is, therefore, believed that pullout testing of pedicle screws is not an appropriate method to clinically screen potential screw design alterations.

To ascertain the clinical appropriateness of a testing method, it is useful to compare the mechanical loading and the modes of failure to those observed *in vivo*. There were four various testing configurations used within this thesis. When ordering them in increasing complexity, these methods included: (1) axial pullout, (2) toggle (cranial-caudal loading directly at the screw head), (3) moment (a moment arm attached to single screw), (4) a setup similar to the ASTM 1717 standard (4 screws, 2 rods, 2 vertebrae). When excluding axial pullout testing, all of the other three setup configurations utilized a cranial-caudal cyclic loading and produced failure patterns characterized by a fulcrum and a peak displacement at the screw tip, thereby capturing the features seen in *in vivo* failure patterns. These failure pattern features had been reported previously in *ex vivo* testing[129,222,248], and were the observed clinical loosening pattern according to clinical opinion (Chapter 3) and via the quantification of clinical CT scans (Chapter 4). Even though all three methods produced the characteristic fulcrum and peak at the screw tip, different patterns were observed. When a moment was applied in the ASTM 1717 and moment test setups the tip moved in the caudal direction, whereas, the tip displaced cranially in the toggle setup (no moment arm). The introduction of a moment would be considered more physiologically appropriate as it mimics the loading which is seen *in vivo*[17] to a higher degree. Even though this is the case, there cannot be any definitive conclusion made as to whether or not the introduction of the moment improves the clinical relevance compared to the toggle setup due to the variability in the clinical loosening patterns produced (Appendix C). Therefore, in order to replicate a clinically relevant failure mode it is important to have loading in the cranial-caudal direction rather than in the axial direction; however, the necessity of an applied moment is remains unconfirmed.

A recommended testing method would be similar to that of the moment setup in Chapter 5. This setup utilizes a sinusoidal, cyclic sweeping force applied through a moment arm attached directly to the screw head. Using this setup, a physiological loading range can be applied which was also shown to produce a failure pattern with similarities to those seen *in vivo* (Figure 5.10). This method further enables the use of a repeated measures design, with different screws or methods able to be tested on the contralateral sides of the vertebra. This is a critical testing design feature because the specimen characteristics can be the most influential aspect of pedicle screw fixation even after careful group allocation. It is also important that the loading pattern should be run to level where loosening is clear; because, if loosening is not obtained, the fatigue parameters measured are less likely to parameterize loosening.

10.2. Research Question 2: Primary Factors Influencing Pedicle Screw Loosening

The surgeon begins with a pre-determined set of initial conditions which are different for every patient. Surgeons are, therefore, presented with a challenge to determine the best way to approach each individual case. This involves the complex matching of the surgical technique (*e.g.* surgical positioning or cement augmentation) and the choice of screw design features (*e.g.* size and shape) to the patient attributes (*e.g.* bone quality and dimensions). The choices made form a delicate interdependency between the patient, the surgeon, and the implant. Knowing the extent and the direction of influence of each these various factors may improve pedicle screw fixation by allowing for more informed surgical decisions which focus on the aspects of greatest importance.

The primary findings from the surgeon survey (Chapter 3) and the comparative FE model (Chapter 9) supported the hypothesis that patient attributes related to bone quality and pedicle dimensions are the most important factors influencing fixation. By and large, the surgeon opinion favored (1) bone quality as the most important aspect of fixation, distantly followed by (2) surgical techniques and finally (3) by screw design characteristics (Chapter 3). The *in silico* models (Chapter 9) produced similar findings to the surgeon survey; however, caution must be taken in their interpretation as they were derived from extremely simplified geometry and the fact that the models simulating *bone quality* changes were unable to be compared. From the *in silico* models (Chapter 9), the patient cortical shell thickness, the screw depth, and the screw diameter were the most influential parameters to reduce bone damage while undergoing a full standard walking loading cycle. All three of these influential factors essentially stem from patient attributes because the possible screw depth and the diameter are both limited by patient vertebral dimensions. When combined, these findings suggest that the utilization of the largest screw length without anterior wall perforation and a diameter which slightly penetrates the inner cortical shell of the pedicle shell could be ideal for pedicle screw placement. Pre-operative planning would help inform the decisions regarding the screw dimensions and position given the limiting patient attributes.

10.2.1. Patient Parameters

The fact that bone quality was ranked as having the highest importance (Chapter 3) emphasizes the initial challenge a surgeon with osteoporotic patients faces; if a surgeon is given a poor quality material to work with, poor outcomes will likely ensue. This belief is widely supported in the biomechanical and clinical literature, especially in relation to the notion that bone quality, often quantified in terms of BMD and fabric descriptions, drive patient outcomes and bone fracture prediction[71,141,207]. Confirmation of the influence of material parameters was found in the *ex vivo* studies on the lumbar spine with a lower bone quality (*i.e.* BMD) being associated with lower fatigue fixation parameters (Chapters 7 & 8).

Throughout the experimental studies (Chapters 6-8), the vertebral dimensions were shown to be associated with changes in measured pedicle screw fixation parameters. The pedicle size in terms of cross sectional area and major diameter correlated negatively with fatigue force and stiffness (Chapter 7 & 8). In the cervical spine study, the specimen height correlated positively with initial stiffness (Chapter 6). In the atlas vertebra, there is no pedicle per se; therefore, the specimen height is the closest estimate of the major pedicle diameter. An increase in the major pedicle diameter is likely to be associated with an increased volume of the cancellous bone because the cortical shell thickness has been shown to stay relatively constant[160]. Since screw diameters were held constant during all testing presented in the presented studies, an increase in the major diameter or pedicle area would then likely be associated with a higher chance of the weaker cancellous bone supporting the cranial-caudal loading. In the parametric FE model, the least damage and strain was imparted in the two models in which the cortical shell was in contact with the screw for the entire length of the pedicle (150% cortical shell thickness and 7.5 mm screw diameter). These findings through both *ex vivo* and *in silico* testing suggest that it is desirable to fill the cancellous core of the pedicle as much as possible with the screw diameter in order gain as much support as possible from the ever desirable cortical contact.

10.2.2. Surgical Technique

The surgical technique is believed to have a substantial impact on the fixation of pedicle screws. According to surgical opinion (Chapter 3), it is the second most important determinant of screw fixation after patient attributes. Surgeons believe that the type and amount of anterior support as well as the location and alignment of the screws were the important surgical technique parameters. Spinal surgeries are known to have a particularly wide-ranging discretion in their planning[63], high regional variation of surgery choice[225], and it has been shown that the individual surgeon preferences can outweigh patient and disease characteristics when choosing spinal surgical procedures[233]. These factors create a tough environment for the adoption of new methods and standardized techniques after initial training, adding a particular emphasis for the need of consistency in teaching from an early point in surgical training.

Surgical Positioning

Results from Chapter 6 highlight the effect that surgical positioning has on screw fixation strength. In this study, only the screw entry point was altered which enabled the screw path to traverse the narrow canal of the posterior arch of the atlas vertebra and to obtain a longer screw depth. This change in surgical positioning resulted in a significant 33% increase in fatigue force and a 65% increase in final stiffness. An increased depth of the screw was also associated with an increased fatigue strength in the *ex vivo* lumbar spine study (Chapter 7) as well as a reduction in head motion and bone damage in the parametric FE model (Chapter 9). These consistent, significant findings highlight the importance of achieving the maximal screw depth into the vertebra.

When compared to the screw depth and the screw diameter, the surgical positioning parameters of the angle of insertion or the offset of insertion had little influence on screw fixation (Chapters 6, 7, and 9). This was shown in the *ex vivo* cement augmentation experiment (Chapter 7) where there was no correlation between sagittal or transverse angle and the fatigue fixation parameters. Furthermore, results from the comparative FE model showed small, 2-5%, screw head displacement changes were associated with the largest angles (Chapter 9). These findings correspond well to other *ex vivo* investigations which show little influence of screw positioning angles on fixation strength when no major cortical shell perforations exist[49,174].

Large perforations of the cortical shell (>4 mm) are likely to substantially reduce the fatigue fixation strength of pedicle screws. This has been shown with pullout testing[49] as well as within this thesis with the two screws with large perforations in Chapter 8.

The length of the screw protruding from the vertebra (overhang) could mechanically be considered as adding to the length of the acting lever arm. An increasing overhang correlated with a decrease in the fatigue fixation in the design concepts *ex vivo* study (Chapter 8). In the screw augmentation study (Chapter 7), the lever arm length (overhang + pedicle length) negatively correlated with fatigue force and stiffness. Implanting a pedicle screw with the minimal length outside the vertebra is, therefore, another possible technique to mitigate loosening.

When considering all the surgical positioning factors together, it can be concluded that the screw depths (the depth into the vertebra and length outside) seem to have the larger comparative influence on the fatigue fixation when compared to the angle of insertion. From the results presented in this thesis, the recommended surgical positioning would be to reduce the length of the screw outside the vertebra while directing the screw down the pedicle axis. The alignment down the pedicle axis would allow the maximal screw diameter to be used and also minimize the length within the pedicle while allowing the achievement of a similar, maximal vertebral depth.

Cement Augmentation

The presence and the distribution method of the cement augmentation was shown to impact screw fixation. Surgeons believed that augmentation with cement was important for pedicle screw fixation for both normal and osteoporotic bone in particular (Chapter 3). Surgeons felt that cement with a continuous distribution along the screw length would be the best for fixation; however, this was contradicted in the literature[43] and in the cement augmentation study (Chapter 7). In Chapter 7, two augmentation techniques were investigated and the screw injected group, which exhibited a more posterior cement dispersion pattern, had higher fatigue and pullout strength than the continuously distributed prefilled group. This difference is likely influenced by the significant seven-fold increase in the cortical contact, since cortical contact was also associated with a higher fatigue force and stiffness. These findings suggest that if a patient presents with osteoporosis then cement augmentation through the screw should be considered to help improve pedicle screw fixation. Furthermore, this method is considered safe and almost routine in Germany, with 80% of surgeons augmenting pedicle screws and two thirds of these surgeons utilizing the screw injected technique[88].

10.2.3. Screw Design

When considering the fixation of pedicle screws, the major screw dimensions are consistently found to be the most influential screw design parameter in both the biomechanical literature[41,58,59,98,120] as well as in the results of this thesis. The surgical opinion (Chapter 3) ranked the major dimensions to be the most influential screw design parameters and the *in silico* model showed extensive reduction of bone damage and screw head motion when the screw dimensions increased. The major screw dimensions were only altered in one *ex vivo* study presented in this thesis (Chapter 7). The diameter increase of one millimeter increased all fatigue fixation parameters and was associated with a 24% increase in pullout force and a 5% increase in fatigue force while inducing the least loss in stiffness. These consistent findings combined with the knowledge that screw dimensions are limited by vertebral dimensions in clinical practice, place a substantial emphasis on utilizing the patient's anatomical dimensions to their fullest.

When omitting the major screw dimensions, the remaining screw design features do not exhibit a consistent impact on the pedicle screw fixation strength. Despite high variability in the rankings, surgeons believed that the screw thread profile, core type and pitch were all important determinants of screw fixation (Chapter 3). Modifications to the screw thread design (Chapter 8) did not substantially alter the *ex vivo* fatigue fixation strength parameters. An *in silico* model would be an ideal testing environment to identify the potential influence of these minor design features; however, the geometry of the model included in this thesis (Chapter 9) was too rudimentary for investigation of these fine features. Future models should utilize a more refined geometry and, ideally, an optimization routine in order to determine the parameters most favorable for fixation. The non-substantial and non-consistent findings suggest these minor parameters have less influence on screw fixation when compared to major screw dimensions or patient attributes.

The introduction of a tapered core had diverse responses across the conducted studies. Surgeons believed that the core shape was important for fixation but they did not distinguish significant advantages between conical *vs*. cylindrical cores (Chapter 3, Question 19). The *ex vivo* study (Chapter 8) found that a conical core tended to non-significantly increase the screw removal torque. This result has previously been shown and studies suggest this increase may be attributed to the initial press-fit[1,121]. In the parametric FE model (Chapter 9), the introduction of a tapered core reduced the width of the damage pattern along the screw profile while substantially increasing the screw head motion. The tapering of the thickness of the screw introduces a stiffness gradient down the screw axis resulting in the small, even damage distribution. The combination of the press-fit established by a conical core and the tapering stiffness along the screw axis may potentially be ideal for promoting pedicle screw fixation.

The addition of posterior support could be another possible path to help reduce screw loosening. Within the confines of an *ex vivo* study (Chapter 8), the design which introduced a posterior spinal support exhibited initial stiffness benefits. However, these benefits were not maintained throughout testing, potentially due to a design flaw which introduced sharp corners and bone damage. Other options for stabilization such as radiopaque UHMWPE sublaminar wires[176,189] or filling the posterior arch with cement could be pursued. The sublaminar wires are currently being investigated for a growth guidance system for early onset scoliosis and are showing promising fixation results[189]. These wires might also be utilized in patients with osteoporotic bone as they might be able to reduce the stiffness gradient at the marginal ends of the construct or dissipate the strain peaks better than metal screws[176]. This is due to the fact that the wires are less stiff and would only surround cortical bone rather than relying on an interface with the extremely fragile osteoporotic trabecular bone. Filling the posterior arch with cement could also be beneficial as it would give initial support at the screw entry where stresses are shown to be high. Furthermore, distributing cement here might incur less leakage than when filling the vertebral body as there are no large blood vessels that allow an easy path for leakage.

10.3. **Future Work**

As with any empirical research, there are opportunities in the current thesis to improve the analytic and methodical approaches as well as extending the present work in future studies. For example, in the clinical CT study (Chapter 4), a validation study of the method is needed to ensure the dark volume around the screw can be determined within an acceptable error. Furthermore, the patient numbers and parameters should be expanded in order to determine whether surgical positioning or device parameters might influence the loosening volume. The prediction of the effect of the measured parameters on long-term clinical outcomes could be enabled by a longitudinal study pairing each patient with radiographic loosening to a control patient without loosening. In this way, the most important factors of fixation could be ascertained from clinical data.

The design concepts study (Chapter 8), utilized a relatively large number of specimens (*n*=38; when considering the availability of specimens for biomechanical testing) and tested them using the same screw and same loading protocol. If this approach could be extended to a study using an even larger number of vertebrae from the various *ex vivo* tests, it would be interesting to perform more sophisticated data analyses (*e.g.* multiple regression or random decision forests) to more definitively investigate the impact of patient parameters, surgical positioning parameters, and screw design features on fatigue fixation.

The bone material model used in the FE study (Chapter 9) was quite robust in terms of convergence and computational cost while enabling visualization and quantification of permanent bone damage at the screw-bone interface. Furthermore, with repeated loading on the same load level, the damage pattern grew. These properties make it an ideal material model for further investigations of implant interface damage. Use of this model in combination with optimization routines could help in the isolation of new promising prototypes before their production and use pre-clinical *ex vivo* testing.

A typical medical screw is made of a titanium alloy and is much stiffer than normal trabecular bone and especially osteoporotic trabecular bone. Optimizing the stiffness profile of the screw could maximize the ability to evenly distribute the load (minimize peak loading). This is a potential future avenue of research to minimize loosening, especially in low quality bone which cannot withstand large peak forces. A first step towards this goal would be to identify the regions and levels of optimal stiffness and this could initially be determined numerically using FE models and optimization routines. The second step would be to use methods to alter the physical profile of the screw such as introducing mechanical struts, cuts, or grooves (which could also allow for bone ingrowth), or to utilize a material which can be processed with selective regions of hardening.

10.4. Addition to Literature and Clinical Significance

The current body of work includes novel findings which have implications for both clinical practice and for research in this field. For purposes of clarity, the major results which, to the author's best knowledge, have not been shown before are presented once more in a synthesized form in this section.

Firstly, a clinical survey was conducted (Chapter 3) to establish meaningful rankings of 122 factors for their influence on pedicle screw fixation. Despite the importance of ascertaining the most common experiences from those directly in clinical practice, such a study does not currently exist in the literature. It was also found that surgical experience, specialty and region of training all influence surgical opinion on pedicle screw fixation. A need for a consistent, easy to access reference to guide the best practices for pedicle screw fixation using evidence based practices was also identified.

According to a clinical screening of CT scans (Chapter 4) as well as clinical opinion (Chapter 3), the lumbosacral region is considered especially susceptible to pedicle screw loosening. Furthermore, it was identified as the region with the highest loosening volume with the sacral region having over ten times the loosening as the cranial region. These results indicate that this region should be the first to be targeted for design optimization.

The clinical presence of a fulcrum was found in the patterns of pedicle screw loosening segmented from CT scans (Chapter 4). This confirmed the previous postulations of its existence. Furthermore, this fulcrum provides further evidence of the ecological validity of toggling fatigue pre-clinical testing methods, since all of the toggling fatigue methods utilized in the current work contained this fulcrum (Chapter 5). Furthermore, the osteoporotic, composite foam models tested here could be a potential comparative testing material for pedicle screws since they were able to reflect quantifiable material damage after sustaining loading within the *in vivo* ranges while producing clinically relevant failure patterns (Chapter 5).

The loosening volumes at the marginal ends of constructs was greater than loosening volumes within the same construct (Chapter 4). When combined with the fact that mid-construct loosening was only present if marginal loosening existed, this suggests that the construct ends become loose first and loosening then progresses to mid-construct screws. The implication of this result is that reduction of the loading gradient at the construct end should be targeted as an area for design optimization.

Across multiple studies, the screw depth into the bone was shown to have a substantially larger influence than the angle of the screw insertion on the stability of pedicle screws (Chapters 3, 6, 7, & 9). This was especially evident in the finite element model (Chapter 9) and indicates that more attention should be placed on maximizing screw depth rather than obtaining a specified angle.

For the atlas vertebra, the pedicle screw trajectory is comparatively more biomechanically stable in toggling fatigue than the massa screw trajectory (Chapter 6). Use of the pedicle screw technique could, therefore, potentially provide fixation benefits over the more established massa screw technique.

The unique design of the study in Chapter 7 provides the first direct experimental evidence to substantiate the notion that pullout testing alone is not clinically sufficient and should not be used for pre-clinical testing of pedicle screw fixation. The results obtained in the pullout testing were not transferable to the comparatively more physiologic fatigue testing. Therefore, caution should be taken when attempting to extrapolate previous pre-clinical pullout testing results to perceived clinical benefits.

Cement augmentation injected through the screw increased pedicle screw fixation when considering both toggling fatigue and pullout (Chapter 7). Therefore, it is a good option to enhance biomechanical stability in the osteoporotic spine. The volume of cement in contact with the cortical shell linearly correlated to the fatigue strength of pedicle screws. The seven-fold increase in cortical contact which is obtained by the screw injected technique may, therefore, be the reason for its fixation benefits.

It is commonly believed that the pedicle screw loosening failure mechanism is via repeated loading either from cranial-caudal toggling or from micromotion. These suppositions are supported by the results of the finite element analysis which showed that one walking cycle permanently mechanically damaged the trabecular bone surrounding the screw (Chapter 9).

10.5. **Conclusions**

In order to ultimately mitigate pedicle screw loosening, it is important to have information on the potential failure modes and mechanisms. Investigation into the failure patterns of mechanical devices can often lead to inferences on their underlying failure modes and mechanisms. For this reason, one of the primary aims of the thesis was to quantify the clinical failure pattern of pedicle screws from CT scans. Clinically loosening presented with the highest volume within the cranial-caudal plane as well as with loosening volume peaks at the screw tip and the entry to the vertebral body. The locations of the volume peaks were also areas of peak damage and strain within the finite element models. Targeting ways to more evenly distribute the strain distribution along the screw may help to reduce trabecular damage and, therefore, screw loosening. The trough between the loosening volume peaks was identified as a fulcrum. This fulcrum has been found in *ex vivo* fatigue testing with loading in the cranial-caudal direction both previously[129,222,248] and within all of the *ex vivo* studies presented here. The *ex vivo* location of this fulcrum was associated with fatigue fixation: altering the device design to move this fulcrum from the entry to the vertebral body to safely within the confines of the pedicle canal may provide a more stable environment and help to mitigate loosening. The loosening volume also increased from cranial to caudal down the spine. This increase is likely influenced by increased loading, screw dimensions, and vertebral size in the caudal spine. In the current samples, there was always a loosened screw at either the cranial or caudal ends of the pedicle screw and rod construct. These marginal screws showed significantly higher loosening volumes than the screws which loosened mid-construct. Reducing the loading gradient and movement at the marginal ends of the construct may help to reduce the prevalence of screw loosening.

The second aim of the thesis was to utilize new methodological approaches to enable direct comparisons of various aspects of pedicle screw loosening in order to identify the most influential ones. Patient parameters, specifically bone quality and vertebral dimensions, were shown to be the largest determinant of pedicle screw fixation strength. Poor quality bone allows the screw to permanently damage the bone under low loading conditions while the vertebral dimensions limit the most influential screw design characteristics: length and diameter. Surgeons are left with a challenge to match the optimal screw design and the proper surgical techniques to achieve the best fixation possible. A surgical technique which would position the pedicle screw directly along the pedicle axis while reducing the length of the screw outside the vertebra is recommended. This would allow for a minimization of the lever arm, the use of a maximal screw diameter, while enabling a similar, maximal vertebral depth. If the patient has poor quality bone than cement augmentation injected through the screw should be considered. This technique was shown here to be the best osteoporotic fixation method according to both pullout force (+92%) and fatigue force (+28%). The fixation benefit of augmentation injected through the screw is likely due to the more posterior cement distribution pattern which was associated with a seven-fold increase of cement contact to the vertebral wall. For fatigue fixation of pedicle screws, both the screw thread design as well as the angles of the screw insertion were found to have comparatively less effect than the other patient and positioning parameters measured. Greater awareness should, therefore, be directed to obtaining the optimal surgical screw depths and the largest screw diameter.

The predominate belief in the literature is that pedicle screw loosening failure mechanisms are due to low-stress, high cycle repeated loading either in the form of cranial-caudal toggling or from micromotion[19,39,42,112,129,155,156,199]. Loosening from repeated daily loading is supported by the results of the finite element analysis and potentially by the appearance of the dense, radiopaque rim known as the double halo. The FE model showed that mechanically irreversible trabecular bone damage can be invoked by the loading of one standard walking cycle. It is plausible that the repeated loading can thus break the trabecular struts and displace the bone fragments until the motion is small enough to allow bone remodeling to form a continuous boney rim surrounding the loosened area. The *in vivo* bone growth around a broken screw tip suggests that motion may be a relevant loosening mechanism and that the radiographic appearance of loosening may be reversed if the interface motion is terminated.

Multiple experimental test configurations were employed in the current thesis to evaluate their biomechanical and clinical appropriateness. Thorough pre-clinical testing of medical devices is necessary in order to reduce patient risk by allowing the development of medical devices with the best chance to succeed *in vivo*. The most commonly used pre-clinical testing method for pedicle screws, axial pullout testing, produced results which did not correspond to those determined via the more physiologic toggling, fatigue loading. Furthermore, pullout testing had the least ecological validity since it did not fail by the probable pedicle screw failure mode, cranial-caudal fatigue. All of the methods which utilized cranial-caudal fatigue loading were able to produce failure patterns similar to those seen *in vivo*. A testing method which utilizes a force controlled, cranial-caudal fatigue loading with the chance of a repeated measures design is recommended for *ex vivo*, pre-clinical testing of pedicle screws. Pre-clinical testing using axial pullout is not sufficient and should not be performed for pedicle screws.

The work presented here is only a small step in the understanding of the complex inter-relations of the major influences on pedicle screw loosening. Obtaining the optimal pedicle screw fixation remains a complex task involving the balancing of patient, surgeon and screw design characteristics.

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Appendices

Appendix A Pedicle Screw Loosening Mechanisms from Literature (Chapter 2)

Table A.1 The proposed mechanisms of pedicle screw loosening; quotes are taken directly from journal articles to reduce interpretation bias[19,39,42,58,112,115,129,155,156,199].

Class	Quote
General	"Clearly, the important failure mode is loosening" (Dawson, Boschert et al. 2003)
	"Although the precise failure mechanism is unclear, it is believed to be related to the excess bending stress, improper position, cyclic loading, or delayed bone union."(Chen 2003)
	"The most frequent mode of failure of pedicle screw constructs in osteoporotic spines is cranial or caudal cutout of screws (not axial pullout), which is why biomechanical pullout tests cannot provide a reliable assessment of implant anchorage in these situations." (Birkenmaier 2011)
Micromotion	"The fibrous tissue, the synovial like lining cells, the cartilage nests and the marked osteoclastic activity, are not the result of bone death stemming from the screw insertion, but are the result of micro-movement. This is a gradual process requiring time...The clinical significance of these findings is that the appearance of a halo about a screw signifies resorption which is either due to movement or infection. In either instance, fixation is lost and a revision has to be carried out to prevent non-union and/or fatigue failure of the implant." (Schatzker, Horne et al. 1975)
	"Our impression is that stabilization of multiple segments necessitates immobilization of each constitent segment. This is particularly so because repeated micro-movements, which may be responsible for a localized bone resorption at the screw/bone interface resulting in screw loosening, are probably accentuated when multiple segments are not stabilized individually." (Ohlin, Karlsson et al. 1994)
Pullout	"In sudden failures, the result of massive overload rather than movement, pull out of the screw with the surrounding cone of bone occurs because of bone failing in bending" (Schatzker, Horne et al. 1975)
Cyclic Loading/ Toggle	"Loading a pedicle screw in caudal and cephalad directions produced a typical pattern, as shown in Figure 5. The screw toggles around a fulcrum, which is located at the base or narrowest diameter of the pedicle. The moment generated by a force applied at the screw head is resisted by cancellous bone in the pedicle and vertebra. When excessively loaded, this cancellous bone crushes, and a butterfly-shaped void is formed in the vertebra along the axis of the pedicle screw. Because there is less engagement of the screw threads with bone, loosening results." (Law, Tencer et al. 1993)
	"Screw loosening was caused mainly by cyclic caudo- cephalad toggling at the bone–screw interface, and screw breakage was caused by cyclic axial stress concentration at the base of the pedicle screw.[2,15]" (Okuyama, Abe et al. 2000)
	"Cyclic loading of instrumentation constructs is a useful and valid mechanism to test fixation constructs and is a more clinically relevant parameter than pull out strength." (Kiner, Wybo et al. 2008)
	"Clinically, screw loosening-pullout usually presents itself a number of days/months postoperatively, implying that cyclic load induced pedicle screw-bone interface fatigue is the predominant clinical cause of failure in osteoporotic patients instead of a single-cycle catastrophic overload...We hypothesize that clinical pedicle screw loosening is not the result of the classic tensile stress-induced material fatigue fracture, but rather due to localized irreversible compressive yield or viscoelastic creep of the osteoporotic bone and/or shear slip between interface or fracture surfaces that progressively propagates each loading cycle that reaches or exceeds a threshold force, as the patient increases activity postoperatively. An analogy would be that augmentation acts like a snow-shoe with osteoporotic bone being the snow." (Choma, Frevert et al. 2011)
Dynamic	"Dynesys stabilization system offers more biomechanical flexibility than the rigid fixation system, which minimizes the incidence of broken screws.[18] On the other hand, more flexibility may translate the shearing force onto the vertebral body, resulting in screw loosening. " (Ko, Tsai et al. 2010)

Appendix B The Distributed Surgeon Survey (Chapter 3)

Fragebogen zu Fixierungstechniken in der Wirbelsäule

Dieser Fragebogen ist Teil eines internationalen Forschungsprojektes (http://www.spinefx.eu) und wurde von der Technischen Universität Hamburg Harburg (TUHH) mit Unterstützung von ulrich medical erstellt. Für unsere wissenschaftliche Arbeit spielt die Erfahrung von im Bereich der Wirbelsäulenchirurgie tätigen Operateuren/-innen eine große Rolle. Ihre Meinung und Ihr Wissen können uns helfen, neue Wege in der Forschung mit Schwerpunkt auf die Wirbelsäulenchirurgie zu erschließen. Wir wären Ihnen sehr dankbar, wenn Sie uns hierbei unterstützen und sich die Zeit nehmen würden, diesen Fragenbogen auszufüllen.

Wer wir sind:

SpineFX ist auf die Ausbildung und Forschung in den Fachbereichen der Biomechanik und Medizintechnik im Bereich der Wirbelsäule spezialisiert. Dieses Projekt ist Teil des „Marie Curie Initial Training Network (ITN)" und eine Kooperation von vier in diesem Fachbereich führende Universitäten und drei Firmen aus insgesamt sechs Nationen.

Kernpunkte dieses Fragebogens:

Ziel dieses Fragenbogens ist, die aktuellen Meinungen und Erfahrungen aus der Wirbelsäulenchirurgie in Bezug auf folgende Punkte zu ermitteln:

1) Faktoren, die für die Verbesserung der dorsalen Stabilisierung eine wichtige Rolle spielen
2) Die Ursache für eine Schraubenlockerung
3) Wann und wie eine Lockerung von Pedikelschrauben auftritt

Diese Informationen sollen genutzt werden, um das Interface von Fixierungsvorrichtungen durch neuartiges Implantatdesign und weiterentwickelte Materialien zu verbessern.

Wir wissen, dass Ihre Zeit sehr wertvoll ist und wären Ihnen sehr dankbar für Ihre Hilfe. Bitte senden Sie den Fragebogen an Rebecca Kueny oder füllen Sie die Online-Version unter https://www.socialsci.com/s/73891547-d980-42d2-9fa4-d61aee396f50 (Deutsch) & https://www.socialsci.com/s/a1ad4411-543f-4781-8583-e6c939f94942 (Englisch) aus. Falls Sie noch weitere Fragen haben sollten, können Sie uns jederzeit unter der u.g. Adresse kontaktieren.

Vielen Dank im Voraus für Ihre Hilfe!

Hochachtungsvoll,

Rebecca Kueny
ITN Fellow & PhD Candidate
TUHH-Technical University of Hamburg
Denickestr. 15
21073 Hamburg
Email: rebecca.kueny@tuhh.de
Tel: (Germany) +49 (0)40 428 78 3712
Tel: (USA) +1 660 851 1790

Fragebogen zu Fixierungstechniken in der Wirbelsäule

I. Operative Erfahrungen und Beobachtungen

A) In diesem Abschnitt bitten wir Sie, anhand Ihrer klinischen Beobachtungen und Erfahrungen die vorgegebenen Antwortmöglichkeiten, welche sich auf verschiedene Aspekte der Stabilisierung einer Wirbelsäule beziehen, auf einer Intervallskala bezüglich Ihrer Wichtigkeit oder Häufigkeit zu bewerten. Bitte kreuzen Sie nur das Ihrer Meinung nach zutreffende Kästchen (bitte nur ein „X" pro Antwort) an.

1) Inwieweit beeinflussen die nachfolgend aufgelisteten Faktoren die Verankerung von Pedikelschrauben?

	Kein Einfluss	2	3	4	5	6	7	Sehr großer Einfluss
Zementaugmentation								
Bioaktive Beschichtung der Schraube								
Knochenqualität								
Querverbinder								
Computernavigation								
Tiefe der eingebrachten Schrauben im Wirbelkörper								
Gebrauch von Bohrer oder Pfriem beim Einbringen								
Hohes Drehmoment / press fit								
Hohe Steifigkeit der Konstruktion								
Intraoperative Durchleuchtung								
Länge des Konstrukts (z.B. S1-L3)								
Tragfähigkeit der vorderen Säule (z.B. Knochendichte)								
Zusätzliche Stabilisierung von anterior (durch z.B. Cage, Knochenspan oder Platte)								
Platzierung der Schrauben (konvergierend etc.)								
Andere:								

2) Wie wichtig sind folgende Punkte beim Nachweis einer Schraubenlockerung?

	Nicht Wichtig	2	3	4	5	6	7	Sehr Wichtig
CT								
Symptombeschreibung des Patienten								
Körperliche Untersuchung des Patienten								
Röntgen								
Andere:								

3) Inwiefern beeinflusst der Wirbelsäulenabschnitt das Auftreten von Schraubenlockerungen?

	Höchste Inzidenz	2	3	4	5	6	7	Niedrigste Inzidenz
Zervikal								
Zervikothorakaler Übergang								
Thorakal								
Thorakolumbaler Übergang								
Lumbal								
Lumbosakraler Übergang								

4) Wie sehr beeinflusst die Länge der Versorgung das Auftreten von Schraubenlockerungen?

	Höchste Inzidenz	2	3	4	5	6	7	Niedrigste Inzidenz
Langes Konstrukt (≥4 Segmente)								
Mittellanges Konstrukt (2-4 Segmente)								
Kurzes Konstrukt (1 Segment)								

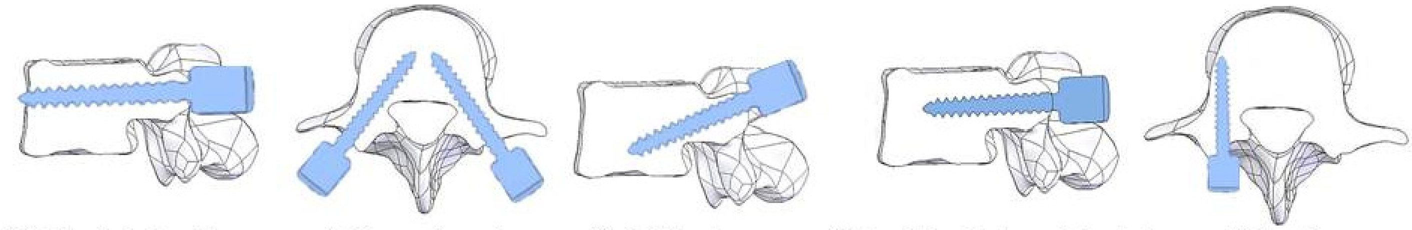


Abb. 1. Mögliche Positionierungen von Pedikelschrauben in der Lendenwirbelsäule.

5) Welche Positionierung (s. Abb. 1) nutzen Sie, um eine bestmögliche Fixierung in der Lendenwirbelsäule zu erreichen?

	Niemals	2	3	4	5	6	7	Immer
(A) Bikortikale Ausrichtung								
(B) Konvergierend in der Transversalebene								
(C) Abfallend zur Grundplatte								
(D) Parallel zu Deck- und Grundplatte								
(E) Gerade								
Andere:								

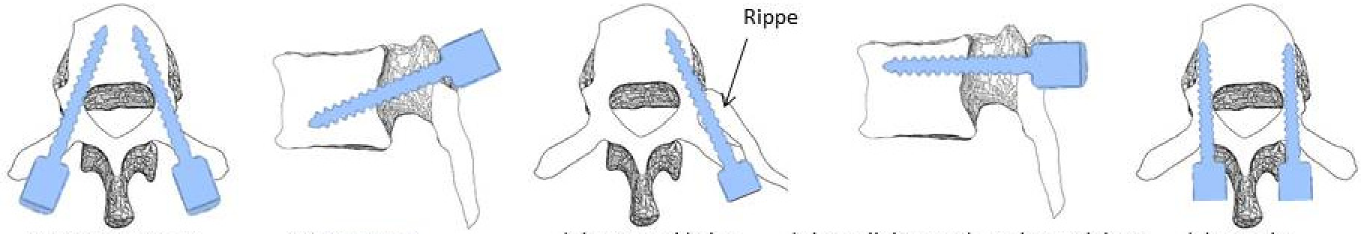


Abb. 2. Mögliche Positionierungen von Pedikelschrauben im Bereich der Brustwirbelsäule .

6) Welche Positionierung (s. Abb. 2) nutzen Sie, um eine bestmögliche Fixierung in der Brustwirbelsäule zu erreichen?

	Niemals	2	3	4	5	6	7	Immer
(A) Konvergierend in der Transversalebene								
(B) Abfallend zur Grundplatte								
(C) Extrapedikulär (auch Trikortikale oder "outside in" Technik genannt)								
(D) Parallel zu Deck- und Grundplatte								
(E) Gerade								
Andere:								

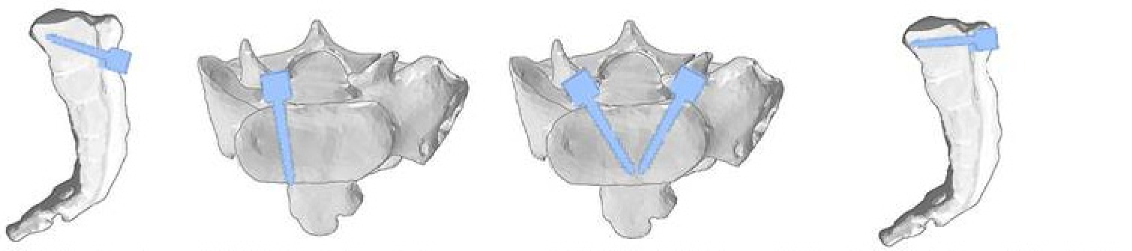


Abb. 3. Mögliche Positionierungen von Pedikelschrauben im Bereich der Kreuzbeinregion.

7) Welche Positionierung (s. Abb. 3) nutzen Sie, um eine bestmögliche Fixierung in der Kreuzbeinregion zu erreichen?

	Niemals	2	3	4	5	6	7	Immer
(A) Aufsteigend								
(B) Bikortikale Ausrichtung								
(C) Konvergierend in der Transversalebene								
(D) Parallel zu den Endplatten								
Andere:								

8) Wie beeinflusst die Benutzung folgender Werkzeuge die Verankerung der Pedikelschrauben?

	Schlechteste Fixierung	2	3	4	5	6	7	Beste Fixierung
Ahle								
Bohrer								
Gewindeschneider								
Andere:								

9) Wie beeinflusst der Durchmesser der benutzten Instrumente beim Einbringen einer Schraube die Fixierung von Pedikelschrauben?

	Schlechteste Fixierung	2	3	4	5	6	7	Beste Fixierung
Oversize (Instrumentendruchmesser größer als Schraubenkerndurchmesser)								
Gleicher Durchmesser wie der Schraubenkern								
Undersize (Instrumentdurchmesser kleiner als Schraubenkerndurchmesser)								

10) Inwieweit spielen die genannten Faktoren Ihrer Meinung nach eine Rolle bei der Schraubenlockerung?

	Nicht Wichtig	2	3	4	5	6	7	Sehr Wichtig
Kräfte entlang der Schraubenachse (posteriorer Ausriss)								
Kräfte am Schraubenkopf nach kranial und kaudal								
Mikrobewegungen der Schraube gegen den Knochen								
Initial schlechter Halt der Schraube beim Einbringen								
Rotationskräfte (Momente am Schraubenkopf)								
Andere:								

Kommentare zu Abschnitt I:

B) In diesem Abschnitt geht es um die Häufigkeit der unten aufgeführten Komplikationen in Prozent. Wir bitten Sie, diese Frage mit einer bestmöglichen Schätzung aufgrund Ihrer Erfahrung zu beantworten. Bitte kreuzen Sie das am ehesten zutreffende Kästchen an.

11) Wie viel Prozent der Pedikelschrauben sind von Ihnen aus den folgenden Gründen entfernt worden?

	Nie (0%)	1-14	15-28	29-42	43-57	58-71	72-85	86-99	Immer (100%)
Schraubenbruch									
Cut out									
Subjektive Beschwerden									
Lockerung									
Keine Notwendigkeit mehr									
Andere:									

12) Wie hoch ist die Wahrscheinlichkeit einer Schraubenlockerung? Bitte geben Sie eine geschätzte Prozentzahl innerhalb des angegebenen postoperativen Zeitraums an:

	Nie (0%)	1-14	15-28	29-42	43-57	58-71	72-85	86-99	Immer (100%)
Während des initialen Krankenhausaufenthaltes									
Nach Entlassung - 3 Monate									
4-12 Monate									
> 12 Monate									

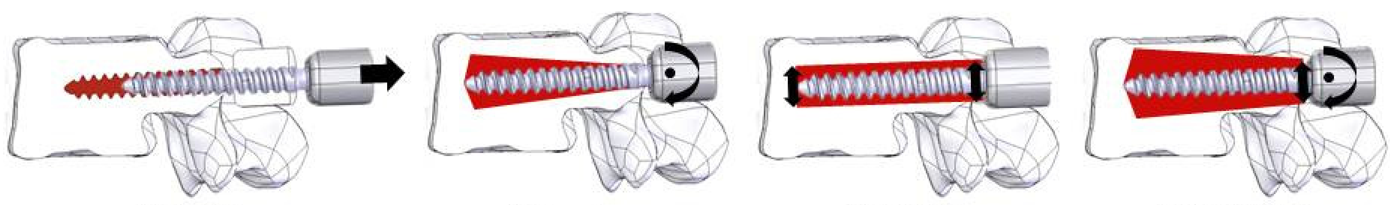


Abb. 4. Mögliches Schraubenversagen im Wirbelkörper.

13) In wie viel Prozent der Fälle versagen die Schrauben nach folgendem Muster? (s. Abb. 4):

	Nie (0%)	1-14	15-28	29-42	43-57	58-71	72-85	86-99	Immer (100%)
(A) Ausriss: Dislokation der Schraube nach posterior									
(B) "Toggle": fächerförmiger Lockerungssaumen um die Schraube									
(C) Weitung: Lockerung des Schraubengewindes kranial nach kaudal									
(D) Kombination aus B und C									
Andere:									

14) Wo tritt in einer multisegmentalen Fixierung am ehesten eine Lockerung auf? Bitte geben Sie eine Schätzung für die folgenden Höhen an:

	Nie (0%)	1-14	15-28	29-42	43-57	58-71	72-85	86-99	Immer (100%)
Kraniales Ende									
Mittlere Schrauben der Instrumentation									
Kaudales Ende									

II. Schraubendesign

A) In diesem Abschnitt bitten wir Sie, anhand Ihrer klinischen Beobachtungen und Erfahrungen unterschiedliche Eigenschaften in Bezug auf das Schraubendesign auf einer Intervallskala zu bewerten. Bitte kreuzen Sie nur das Ihrer Meinung nach zutreffende Kästchen (bitte nur ein „X" pro Antwort) an.

15) Wie wichtig sind die folgenden Schraubeneigenschaften, um eine Schraubenlockerung zu verhindern?

	Nicht Wichtig	2	3	4	5	6	7	Sehr Wichtig
Schraubendurchmesser								
Gewindesteigung der Schraube								
Schraubenlänge								
Form des Schraubenkerns (konisch oder zylindrisch)								
Art des Schraubenkopfes (monoaxial oder polyaxial)								
Andere:								

16) Wie wichtig sind die folgenden Eigenschaften in Bezug auf das Schraubendesign im osteoporotischen Patienten, um eine Schraubenlockerung zu verhindern?

	Nicht Wichtig	2	3	4	5	6	7	Sehr Wichtig
Augmentation mit Zement								
Bikortikale Schraube								
Bioaktive Beschichtung der Schraube								
Schraubendurchmesser								
Expandierbare Schrauben								
Gewindesteigung der Schraube								
Schraubenlänge								
Form des Schraubenkerns (konisch oder zylindrisch)								
Schraubengewinde (Form des Gewindes)								
Verlauf der Schraube im Wirbelkörper								
Art des Schraubenkopfes (monoaxial oder polyaxial)								
Andere:								

17) In welchem Maß verhindert die Art der Schraube (monoaxial oder polyaxial) eine Schraubenlockerung?

	Gar Nicht	2	3	4	5	6	7	Sehr
Monoaxial								
Polyaxial								

18) Wie oft benutzen Sie:

	Nie	2	3	4	5	6	7	Immer
Nur monoaxiale Schrauben								
Nur polyaxiale Schrauben								
Kombination aus mono- und polyaxialen Schrauben								

19) In welchem Maß verhindert die Schraubenform (konisch oder zylindrisch) eine Schraubenlockerung?

	Nicht Hilfreich	2	3	4	5	6	7	Sehr Hilfreich
Konisch								
Zylindrisch								

20) Welches ist die optimale Schraubengröße (relativ zum Pedikel)?

	Pedikelende	2	3	4	5	6	7	Bikortikal
Schraubenlänge im zervikalen Wirbelsäulenbereich								
Schraubenlänge im thorakalen Wirbelsäulenbereich								
Schraubenlänge im lumbalen Wirbelsäulenbereich								
	3,5 mm < Pedikel Ø	-3	-2,5	-2	-1,5	-1	-0,5	Ø Pedikel
Schraubdurchmesser (Ø) im zervikalen Wirbelsäulenbereich								
Schraubdurchmesser (Ø) im thorakalen Wirbelsäulenbereich								
Schraubdurchmesser (Ø) im lumbalen Wirbelsäulenbereich								

21) Wie bestimmen Sie den richtigen Schraubendurchmesser?

	Nie	2	3	4	5	6	7	Immer
Intraoperatives Gefühl beim Einbringen der Schraube								
Präoperative Messungen im CT								
Präoperative Messungen im Röntgen								
Navigation								
Andere:								

22) Wie bestimmen Sie die richtige Länge der einzubringenden Schraube?

	Nie	2	3	4	5	6	7	Immer
Intraoperatives Gefühl beim Einbringen der Schraube								
Präoperative Messungen im CT								
Präoperative Messungen im Röntgen								
Navigation								
Andere:								

Kommentare zu Abschnitt II:

III. Weitere beeinflussende Faktoren

A) In diesem Abschnitt bitten wir Sie, anhand Ihrer klinischen Beobachtungen und Erfahrungen verschiedene Aspekte bzgl. Knochenzement und der Beschichtung von Schrauben auf einer Intervallskala zu bewerten. Bitte kreuzen Sie nur das Ihrer Meinung nach zutreffende Kästchen (bitte nur ein „X" pro Antwort) an.

23) Wie hilfreich sind die folgenden Beschichtungen, um eine Schraubenlockerung zu verhindern?

	Nicht Hilfreich	2	3	4	5	6	7	Extrem Hilfreich
Hydroxylapatit (HA)								
Raue Oberfläche zur Osteointegration (z.B. Plasmapore)								
Andere:								

24) Was hilft Ihnen, sich für oder gegen eine Schraubenaugmentation zu entscheiden?

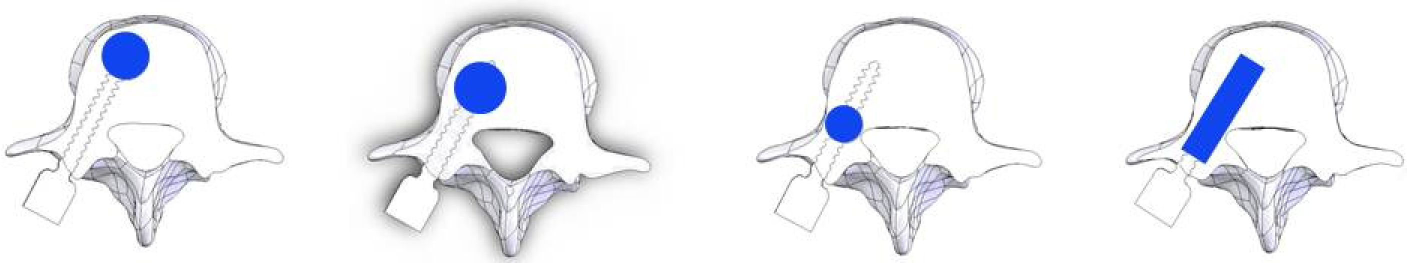
	Immer	2	3	4	5	6	7	Nie
Intraoperatives Gefühl beim Einbringen der Schraube								
Präoperativ bekannte Risikofaktoren (z.B. Osteoporose oder Chemotherapie)								
Präoperative diagnostische Maßnahmen								
Andere:								

25) Welche Zementart ist ideal zur Augmentation von Schrauben?

	Schlecht	2	3	4	5	6	7	Ideal
Bioaktiver								
Bioresorbierbarer								
Nicht bioaktiver Standardzement (z.B. PMMA)								
Andere:								

26) Wie viel Zement injizieren Sie durchschnittlich in eine Schraube zur Augmentation (ml)?

0,0 – 0,5:	0,5 – 1,0:	1,0 – 1,5:	1,5 – 2,0:	2,0 – 2,5:	2,5 – 3,0:	> 3,0:



(A) Zementblase an der Spitze

(B) Zementblase entlang des distalen Endes der Schraube

(C) Konzentriert entlang des Schraubenkopfes im Verlauf des Pedikels

(D) Kontinuierliche Verteilung im gesamten Verlauf der Schraube

Abb. 5. Zementverteilungsmuster im Wirbelkörper.

27) Welche Zementverteilung um die Schraube (s. Abb. 5) führt zu einer guten Fixierung?

	Schlechteste Fixierung	2	3	4	5	6	7	Beste Fixierung
(A) Zementblase an der Spitze (z.B. wie bei Augmentation mit einer kanülierten Schraube)								
(B) Zementblase entlang des distalen Endes der Schraube (z.B. wie Augmentation mit einer perforierten und kanülierten Schraube)								
(C) Konzentriert entlang des Schraubenkopfes im Verlauf des Pedikels								
(D) Kontinuierliche Verteilung im gesamten Verlauf der Schraube								
Andere:								

28) Bei welcher Art von Zementverteilung ist das Auftreten einer Leckage am Unwahrscheinlichsten?

	Höchstes Risiko	2	3	4	5	6	7	Niedrigstes Risiko
(A) Zementblase an der Spitze								
(B) Zementblase entlang des distalen Endes der Schraube								
(C) Konzentriert entlang des Schraubenkopfes im Verlauf des Pedikels								
(D) Kontinuierliche Verteilung im gesamten Verlauf der Schraube								
Andere:								

Kommentare zu Abschnitt III:

IV. Ihr Profil:

A) In diesem Abschnitt würden wir Sie bitten, noch ein paar Fragen zu Ihrem klinischen Hintergrund auszufüllen. Diese Fragen helfen uns, die erhobenen Daten genauer zu analysieren. Personenbezogene Daten werden Dritten nicht zugänglich gemacht und alle Ergebnisse werden ausschließlich in anonymisierter und zusammengefasster Form untersucht und veröffentlicht.

In welchem Fachbereich arbeiten Sie? (Bitte kreuzen Sie zutreffendes an):

Neurochirurgie:	Orthopädie:	Unfallchirurgie:	Andere:

Wie lange arbeiten Sie schon als Chirurg? ______________________

Wie viele Jahre arbeiten Sie schon im Bereich der Wirbelsäulenchirurgie? __________

Welche Bereiche der Wirbelsäule behandeln Sie? (bitte kreuzen Sie die entsprechenden Regionen an):

Zervikal:	Thorakal:	Lumbal:	Keine:

In welchem Land arbeiten Sie? ______________________

In welchen Ländern wurden Sie ausgebildet? ______________________

Wie viele thorakolumbale Instrumentationen führen Sie pro Jahr durch? __________

Die zukünftigen wissenschaftlichen Projekte werden auf der Grundlage der erhobenen Daten der klinischen Erfahrungen basieren. Daher sind Ihre Meinung und Erfahrung sehr wertvoll für den Erfolg dieses Projektes. Bitte fügen Sie jede Art von Kommentar und Verbesserungsvorschläge an:

Bitte kreuzen Sie die entsprechenden Kästchen an, wenn Sie die Ergebnisse der Studie erhalten möchten oder bei einer Veröffentlichung berücksichtigt werden wollen:

☐	Ich möchte einen Bericht über die Ergebnisse und die daraus abgeleiteten Schlussfolgerungen dieser Studie erhalten.
☐	Ich möchte bei einer wissenschaftlichen Veröffentlichung, die Daten aus dieser Studie verwenden, gewürdigt werden (z.B. Vorträge und Abstracts).
☐	Ich möchte mich an weiteren Teilbereichen dieses SpineFX-Projekts beteiligen.

Wenn Sie weitere Informationen erhalten möchten, hinterlassen Sie bitte Ihre Emailadresse oder Postanschrift, damit wir Sie kontaktieren können.

Name:

Email:

Vielen Dank für Ihre Unterstützung!

Bitte senden Sie den vollständig ausgefüllten Fragebogen entweder 1. per Email (rebecca.kueny@tuhh.de) 2. per Post an Rebecca Kueny, TUHH-Technische Universität Hamburg-Harburg, Denickestr. 15, 21073 Hamburg 3. per Fax 040 428 78 2996.

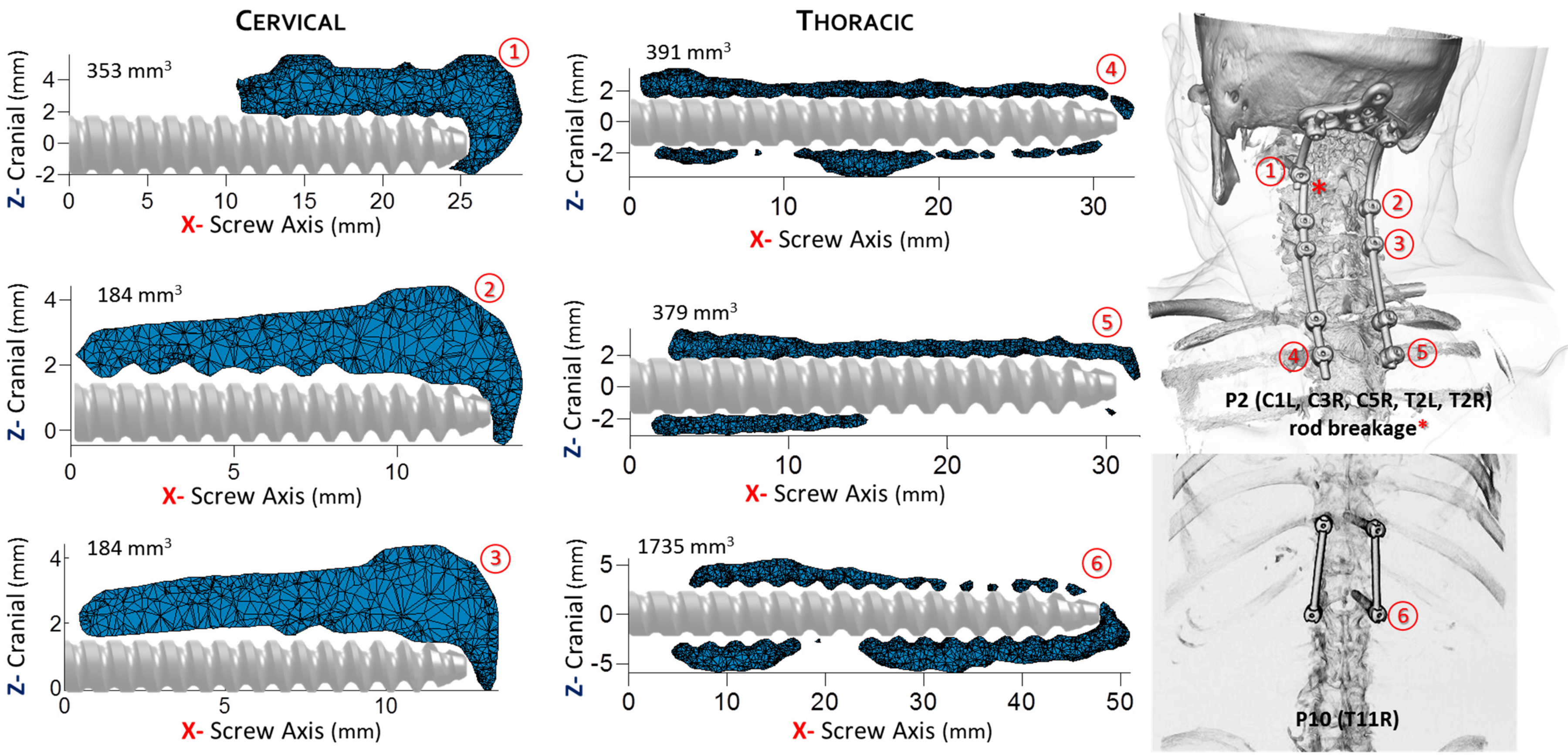


Figure C.1 The loosening patterns of the cervical (left column) and the thoracic spine (middle column) along with the rendered CT scans of the corresponding patients. A representative screw has been inserted to facilitate visualization. The red numbers indicate which halo corresponds to which screw.

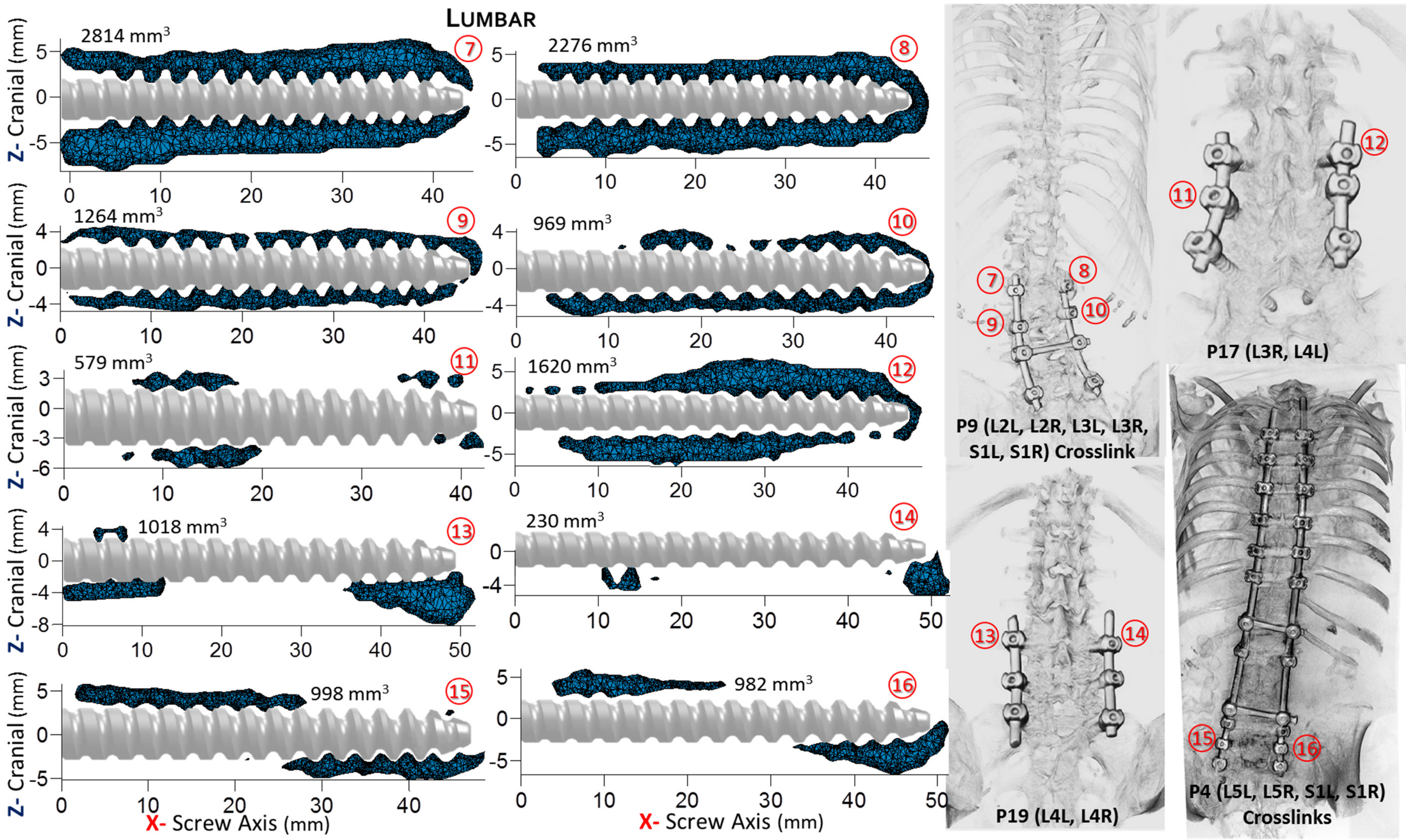


Figure C.2 The ten loosening patterns of the lumbar spine (left and middle columns) along with the rendered CT scans of the corresponding patients. A representative screw has been inserted to facilitate visualization. The red numbers indicate which halo corresponds to which screw.

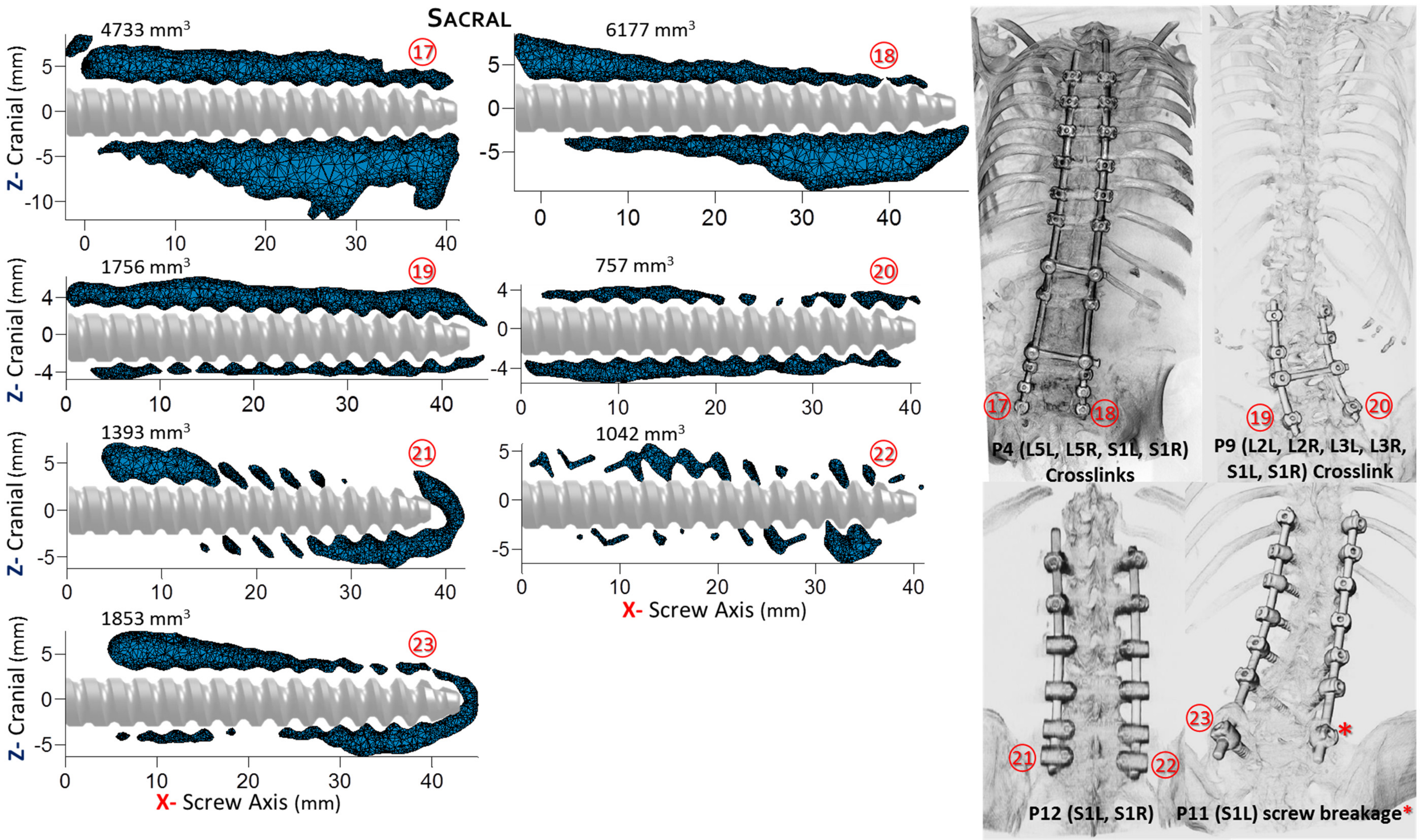


Figure C.3 The seven loosening patterns of the sacral spine (left and middle columns) along with the rendered CT scans of the corresponding patients. A representative screw has been inserted to facilitate visualization. The red numbers indicate which halo corresponds to which screw.

Curriculum Vitae

Rebecca Anne (Kueny) Murray

Born December 4th, 1984 in El Dorado, Kansas, USA

EDUCATION

2010 –2013	*Dr.-Ing. Doctoral degree*: "Pedicle Screw Fixation," TUHH Hamburg University of Technology, Germany
2008 -2009	*MSc. Masters degree* [Distinction]: Biomedical Engineering, "*Why Femoral Neck Fracture Occurs in Hip Resurfacing: A Finite Element Analysis,*" University of Oxford, Oxford, England
2003 -2008	*B.S. Bachelors degree* [Summa Cum Laude]: Ceramic Engineering. Missouri University of Science and Technology (S&T), Rolla, Missouri, USA
1999 -2003	*High School Diploma* [Valedictorian, Honors]: Boonville High School, Boonville, Missouri, USA

WORK

2010-2014	*Research associate*, TUHH Hamburg University of Technology, Biomechanics Institute. Supported by a Marie Curie Research Fellowship within the SpineFX network.
2009 – 2010	*Biomedical Engineer,* Pfeiffer Engineering, LLC, Boonville, MO, USA
2004 – 2007	*Undergraduate Research,* Missouri University of Science & Technology, Rolla, MO, USA Projects: ▪ *Titanophosphate Glasses for Biomedical Applications* ▪ *Bioactive Glass Fiber Scaffolds for Tissue Engineering* ▪ *Bioactive Glass Coatings for Titanium Hip Replacements*
Summer 2005	*Quality Control Assistant,* Internship with Saint-Gobain Containers, Pevely, MO, USA

Publication List

Journal Articles

J Kolb†, **RA Kueny†**, K Püschel, A Boger, JM Rueger, MM Morlock, G Huber, W Lehmann; 'Does the Cement Stiffness Affect Fatigue Fracture Strength of Vertebrae After Cement Augmentation in Osteoporotic Patients?' *Eur Spine J.* 2013; 22(7):1650-6. doi: 10.1007/s00586-013-2809-2.†share first-authorship

F Fensky†, **RA Kueny†**, K Sellenschloh, K Püschel, MM Morlock, JM Rueger, W Lehmann, G. Huber, N Hansen-Algenstaedt; 'Biomechanical Advantage of C1 Pedicle Screws over C1 Lateral Mass Screws –A Cadaveric Study' *Eur Spine J.* 2014; 23(4):724-731. †share first-authorship

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M Reichl, **RA Kueny**, R Danyali, P Obid, H Übeyli, K Püschel, MM Morlock, G Huber, T Niemeyer, A Richter, 'Biomechanical Effects of a Dynamic Topping off Instrumentation in a Long Rigid Pedicle Screw Construct' *J Spinal Disord and Tech* [submitted August 2014]

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RA Kueny, R Danyali, B Nowak, K Püschel, W Lehmann, MM Morlock, G Huber; 'Influence of Pedicle Screw Design on the Fatigue Fixation Strength in the Human Lumbar Spine' *ORS Conference,* New Orleans, LA, USA; March 2014

RA Kueny, F Fensky, MM Morlock, K Sellenschloh, JM Rueger, K Püschel, W Lehmann, N Hansen-Algenstaedt, G. Huber; 'Surgical Technique Effects on the Screw Fixation Strength in the Upper Cervical Spine' *German Society of Biomechanics meeting*, Ulm, Germany; May 2013

RA Kueny, J Kolb, M Niebuhr, K Püschel, W Lehmann, MM Morlock, G Huber; 'How Diameter and Cement Augmentation Technique Influence the Fixation and Motion of Pedicle Screws' *EORS Conference,* Amsterdam, Netherlands; September 2012

RA Kueny, J Kolb, K Püschel, W Lehmann, MM Morlock, G Huber; 'Effect of Cement Augmentation Technique on the Fatigue and Pullout Strength of Pedicle Screws' *European Society of Biomechanics (ESB) Congress*, Lisbon, Portugal; July 2012

RA Kueny, J Kolb, K Püschel, W Lehmann, MM Morlock, G Huber; 'Effect of Cement Augmentation Technique on the Fatigue and Pullout Strength of Pedicle Screws' GRIBOI Conference, Uppsala, Sweden; May 2012

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