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A biomechanical comparison of pedicle screw fixation depending on screw material and pilot hole preparation in osteoporotic vertebrae

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Herr PD Dr. med. Stavros Oikonomidis
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Die in dieser Arbeit angegebenen Experimente sind nach entsprechender Anleitung durch Herrn PD Dr. med. Stavros Oikonomidis, Herrn Prof. Dr. med. Max Joseph Scheyerer und Dr. rer. Nat. Johannes Greven. Die Instrumentierung der Wirbelkörper in beiden Studien erfolgte durch PD Dr. med. Stavros Oikonomidis. Die CT-Auswertung in den ersten Teil der Studie und Bestimmung des BMD erfolgte durch Dr. med. Johannes Thüring. Die Präparation der Wirbelsäulen und Wirbelkörper so wie das Einbetten in PMMA und Einbringen in die Test Maschine wurde von mir und PD Dr. med. Stavros Oikonomidis durchgeführt. Die Auswertung der Daten erfolgte durch Dr. med. Stavros Oikonomidis mit IBM SPSS Software (Version 23; IBM Corp., Armonk, New York, USA) und SPSS (Version 25; SPSS, Chicago, IL, USA).

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Abbreviations

ASD	Adjacent Segment Disease
BMD	Bone Mineral Density
BPSS	Bilateral Pedicle Screw Systems
CBT	Cortical Bone Trajectory
CF	Carbon Fiber
CFR	Carbon Fiber Reinforced
CT	Computed Tomography
DEXA	Dual Energy X-ray Absorptiometry
F_{max}	Maximum Force
FSU	Functional Spinal Unit
GPa	Gigapascal
HU	Hounsfield Units
IBM	International Business Machines Corporation
L	Lumbar
MRI	Magnetic Resonance Imaging
N	Newtons
PEEK	Polyether Ether Ketone
PMMA	Polymethyl Methacrylate
ROM	Range of Motion
SD	Standard Deviation
SPSS	Statistical Package for the Social Sciences
Th	Thoracic
Ti	Titanium
WHO	World Health Organization
qCT	Quantitative Computed Tomography

1. Summary

The prevalence of osteoporosis in the population has increased and is projected to continue increasing because of the aging population[1]. Surgery in the osteoporotic spine come with complications such as pedicle screw loosening, pull out and fractures in adjacent vertebrae[2,3], with bone mineral density being a risk factor for screw loosening[4,5]. To reduce the risk of surgery in the osteoporotic spine different techniques and materials have been tested. In this study two experiments were conducted. In the first test series ten osteoporotic fresh-frozen human lumbar spines were instrumented from L3-L4 using titanium or CFR/PEEK rods and screws. Then cyclic loading was conducted with a frequency of 3 Hz, with 500 N for the first 2000 cycles and increased to 950 N for 100,000. The cavity surrounding the screw was measured at 3 points using CT scans. Then the maximum zero-time failure load was measured in a universal testing machine. There was no significant difference in the force to failure or the cavity at the screw base and shaft. However, the CFR/PEEK screws had a smaller total cavity and smaller cavity at the screw tip.

In the second part of the study the use of a thoracic probe and drill for pilot hole preparation in thoracic vertebrae was compared in 12 osteoporotic thoracic vertebrae. The left and right pedicle were alternately prepared with a thoracic probe or drill and instrumented with a standard titanium screw. Cyclic loading was conducted with an initial load of -25N to + 25 N cranio-caudal with an increase of 5N every 500 cycles to a maximum of 10,000 cycles. Loosening was defined as a displacement of the screw head >5 mm. There was no difference in the two preparation techniques with regard to number of cycles to failure or maximum force to failure.

The elastic modulus of CFR/PEEK is closer to that of bone[6], which could result in a more even force distribution through the vertebrae of the axial force applied to the spinal column and reduced microfractures and loosening. However in vivo studies are needed as CFR/PEEK is postulated to reduce stress shielding[7] and may have superior biological properties[8].

Theoretically using a probe compresses the bone in the walls of the pilot hole, however in osteoporotic vertebrae there is less bone substance available for compression. Furthermore, pedicle screw-based instrumentation usually consists of at least 4 rods and screws, whereas this was part of the study was conducted as an intraspecimen unilevel study and could not evaluate a possible summation effect.

There is no standardized protocol for biomechanical testing of spinal instrumentation ex vivo, with different loads, force directions, frequencies and test environments being used[9], which decreases interstudy comparability and applicability in vivo.

2. Introduction

2.1. Spinal Fusion

The human spine is a complex biomechanical construct consisting of vertebral bodies, intervertebral discs, ligaments and muscles[10]. The spine plays an essential role in supporting the weight of the upper body and protecting the spinal cord and nerve roots, while still maintaining flexibility[10]. Changes to the spine can lead to a variety of consequences including back and radiating pain, instability, deformity and further degeneration [2,11-13] .

Spondylodesis has become a routine procedure in clinical practice[14]. The aim of spinal fusion is the creation of a biomechanically stable union between two or more vertebrae[15].

Different spinal devices have been developed to promote fusion by immobilising the motion segment[16]. Examples of spinal devices include screws, wires, plates, rods, bone grafts, fusion cages and prosthetic intervertebral disc replacements[16].

Indications for spondylodesis include the correction of instability and deformity, which may result from trauma, infection, tumours, degeneration, spondylolysis and spondylolisthesis[14,15]. It can also be iatrogenic, occurring after laminectomy or facettektomie[15]. Microinstability may also be a result of segment degeneration. Spondylodesis can be used to recreate a physiological spinal profile in scoliosis or kyphosis. Furthermore, it can be used to decompress nerves or the spinal cord in foramina- and spinalstenosis[15].

There are multiple established surgical approaches to achieving fusion. The surgical access can be posterior, lateral or anterior. There are also different fixation systems on the market and different surgical techniques. It is possible to achieve good results with all techniques, with insignificant differences in fusion and clinical outcome[15,17]. Therefore, the choice of the appropriate operative procedure and implant should be left to surgeon and should be made with regards to the patient's anatomy and pathology, with dorsal pedicle-based fixation systems being the most popular[15].

Spondylodesis was first achieved by inserting autologous spongiosa from the iliac crest into the facet joints or transverse processes[15]. Now it is most frequently conducted using an internal fixator, consisting of pedicles screws and rods, in combination with either an autologous or allogenous bone graft or bone graft substitutes[15]. Bilateral pedicle screw systems (BPSS) have become the gold standard for spinal fusion[18].

The fixation device must have sufficient strength, to provide adequate stabilisation to the spine. The strength of the spinal fixation is dependent on the design of the instrumentation and the anchorage of the screws in the vertebrae[18,19].

2.1.1. Implants

Harrington rods were originally introduced for the treatment of scoliosis achieving good long-term results but have since been used for the treatment of different pathologies[16,20]. Rods have been developed for both anterior and posterior instrumentation of all spinal levels[20]. Rigid rod fixation gained popularity as it led to higher rates of arthrodesis, however it has come under scrutiny for its supraphysiological stiffness[20]. The stiffness places more strain on the adjacent level leading to adjacent segment disease. It has been suggested that a similar rate of bony fusion could be facilitated with a more flexible device whilst also reducing the risk of adjacent segment disease[20].

Semi rigid rod fixation has been developed for dynamic stabilisation to maintain normal motion without applying pressure to the degenerated discs or facet joints[20]. In accordance with Wolff's law, more flexible rods place more pressure on the anterior spinal column and help to facilitate bony fusion[20]. Dynamic stabilisation has reported higher rates of arthrodesis and lower rates of stress shielding [20]. The flexibility of the rods results in more physiological force distribution, placing less pressure on the adjacent motion segments resulting in lower rates of adjacent segment disease[20].

Cages are the most commonly used interbody spacers and are used to create anterior support to facilitate fusion and restore the physiological disc height[15]. The most common materials for cages are titanium and carbon and can be filled with an autologous bone graft from the iliac crest or local bone removed during decompression or a bone graft substitute[15]. The use of interbody spacers in combination with dorsal instrumentation and the use of bone grafts increase the rate of bony fusion[15,16]. In the stand-alone technique a cage is inserted into the intervertebral space without further instrumentation[21]. Preliminary studies have shown acceptable clinical outcomes and fusion[21].

For spinal fusion to be successful the material must be adequately strong to provide initial support while the bone grows whilst also promoting ingrowth[22]. Metals commonly used for screws and rods include alloys of titanium, cobalt chrome, stainless steel, nitinol and

tantalum[22]. The specific properties of each alloy need to be considered to determine its suitability for an indication.

2.1.2. Biomechanical Properties

Fatigue describes how long the instrument can function as intended[22]. The spine is exposed to repetitive stress. Motion can cause cracks in the rods, which aggregate over time, resulting in the rod breaking[22]. Cobalt chrome rods have a longer fatigue lifespan than titanium rods and are being used more frequently[22]. CF/PEEK implants have also been shown to be able to withstand fatigue strain[23].

The stiffness of a material is measured with the elastic modulus, also known as Young's modulus, which is the ratio of stress to strain[6]. The use of softer implants, with a lower elastic modulus, is becoming more popular in spinal surgery. In theory the use of a material with an elastic modulus similar to that of bone leads to less load being transferred from the implant to the bone and less stress shielding[6,22]. The elastic modulus of cancellous bone is 3.78 GPa and cortical bone 14.64 GPa[6]. Pure PEEK is soft with a modulus of 3.84 GPa, whereas CF/PEEK is stiffer at 17.94 GPa but still softer than the conventionally used metals[6,20].

Furthermore, the materials used for implants must be compatible with the internal environment and human tissue, which is described by their biocompatibility. The human body is a corrosive environment consisting of saline solution with sugars, proteins, cells, trace metals and ions[22]. To be considered for implantation materials must have high corrosive resistance as corrosion can reduce the fatigue of implants[22]. This quality is described by the corrosive fatigue strength of a material. Titanium has high corrosive resistance[20] and higher corrosive fatigue resistance than stainless steel and cobalt chrome[22].

Corrosion and wear lead to debris, which causes inflammation by activating macrophages and releasing proinflammatory cytokines[22]. The inflammatory reaction encompasses cell death and osteolysis[22].

There is a correlation between the reported rate of surgical site infection and the material used with titanium comparing favourably to both titanium alloys and stainless steel[22]. The ability of bacteria to create a biofilm on a material is influenced by the surface quality, and the polarity as bacteria can adhere better to rough hydrophobic surfaces[22].

2.1.3. MRI Artifacts

Radiolucency is an important aspect when choosing material for an implant, as imaging is needed for postoperative analysis, for the diagnosis of adjacent segment disease and in the follow up of spinal tumours[24].

Titanium generates fewer artifacts in MRI and CT imaging than stainless steel does[18]. Images containing titanium implants can still be evaluated whereas the artefacts generated by stainless steel render the images uninformative[22]. The ferromagnetic properties of each alloy vary and as such should be evaluated independently[22].

CF/PEEK is already used for cages, rods, interspinous implants and has recently been used in the development of novel pedicle screws[25]. CF/PEEK has the advantage of being radiolucent and generating fewer artefacts CTs or MRIs than the metallic alternatives [23,25-27].

2.2. Complications Related to Pedicle Screw Based Instrumentation

2.2.1. Intraoperative Complications

2.2.1.1 Screw Misplacement

Screw misplacement is the most common complication during pedicle screw insertion[28], with rates depending on instrumentation techniques, pathology and surgeon experience. The reported rates of screw misplacement tend to be higher in scoliosis, ranging from 0-95%, whereas rates in degenerative disease are around 4%[29]. Screw misplacement can lead to a variety of consequences including neurological complications, loss of correction and screw breakage[30,31]. Experienced surgeons can achieve low rates of misplacement when using anatomical landmarks and responding to tactile and visual cues[28]. However the accuracy has been further increased by the introduction of image guidance systems[28].

Screw misplacement can be asymptomatic if adjacent structures are not damaged[28]. The rates of neurological injury reported vary[31] and complications can range from transient to permanent neurological deficits and pain[28]. Revision surgery may be necessary following screw misplacement, for example in patients who experience radiculopathy[28].

2.2.1.2. Pedicle Fracture

There is a risk of pedicle fracture during pedicle screw insertion. In lumbar fusion the rate of pedicle fracture is low (1.1%), usually occurring as a result of using a screw with a too large diameter for the patients anatomy[28]. The reduced bone mineral density in the cortical,

subcortical and trabecular bone and the thinner cortex make osteoporotic patients more vulnerable to pedicle fracture during screw insertion[32]. The rate of pedicle fracture during transpedicular pedicle screw instrumentation is higher in patients with poor bone quality[29].

2.2.2. Postoperative Complications

2.2.2.1. Infection

Surgical site infection is a serious complication of spinal surgery with reported rates from 0.7-12%[33]. Infection increases mortality, morbidity and healthcare costs. Wound infection can be subcategorized in deep and superficial surgical site infection. Independent risk factors for developing an infection are diabetes, estimated blood loss of over 1 litre, previous surgical site infection and a posterior surgical approach[33]. However multiple other cofounding factors may also increase the risk of infection. Amongst others the rate of infection also shows a correlation with the duration of the surgery[31]. Infection can be successfully treated with antibiotics and debridement[30].

2.2.2.2. Adjacent Segment Disease

Adjacent segment disease (ASD) refers to pathological changes in the motion segment next to spinal fusion, the most common of which is disc degeneration[34]. Radiographic degenerative changes are common, however there is no direct correlation to clinical symptoms[34,35]. The rates of symptomatic adjacent segment disease are much lower, ranging from 5-18%[34].

ASD may be an iatrogenic complication of spondylodesis, caused by alteration of the spine's biomechanics[34,35]. However, ASD can also reflect the progression of the underlying spinal disease or natural degeneration experienced during aging[34].

From a biomechanical standpoint adjacent segment disease may be caused by increased mobility in adjacent segments to compensate the rigidity of the instrumented section. Hypermobility can increase the load on the facet joint and the intradiscal pressure[34]. Increased intradiscal pressure can alter the discs metabolism leading to changes in the biochemical composition and accelerating disc degeneration[34,35]. The increase in intradiscal pressure correlates with the length of fusion[35].

2.2.2.3. Hardware Failure

Hardware failure usually occurs in the first 6 months after surgery[29] before the bone fuses. Metal fixation should not be seen as a permanent solution in achieving stabilisation, as hardware failure is a continuous risk. The primary target should be achieving fixation long

enough to facilitate bone fusion. Poor bone healing leads to a longer dependence on the metal instrumentation and may encourage pedicle screw loosening[29]. The rate of bone union can be increased by using autogenous bone graft from the iliac crest[29]. The incidence of hardware failure, mainly pedicle screw breaking but also loosening, increases with the number of spinal segments instrumented[29,30].

Rod failure can occur in the form of rod loosening or breaking. The rates of rod loosening a fracture in the first year following transpedicular screw fixation with loosening being more common in degenerative instability and breaking more in traumatic injury[29]. Another possible form of implant failure is component-component junction failure, leading to disconnection of the screw and rod[31] or rod migration[30]. Junction failure can be caused by insufficient nut tightening[30].

In non-osteoporotic patients pedicle screw breaking is a more frequently described complication than screw loosening, with some authors naming it as the most frequent form of hardware failure[29]. However the reported rates have a high variety, ranging between 2.6% to 60%[29]. Screw fracture is a result of metal fatigue. A larger force acts on the screws when there is more pressure in the spinal column, which can result from delayed fusion, pseudarthrosis[28] and a lack of anterior support[30]. This could be caused by an increase in pressure in the dorsal spinal column leading to the screws experiencing more force. Screw breaking usually occurs in more caudal screws[29], presumably as these are exposed to a higher mechanical load. Furthermore the rate of screw breaking is also higher when the sacrum is instrumented, most commonly affecting the screws inserted in the sacrum itself[30].

Pedicle screw loosening may not be clinically relevant in non-osteoporotic patients, with reported rates in thoracolumbar stabilisation ranging from <1% to 15%[36]. Stress shielding has been suggested as a mechanism leading to pedicle screw loosening. In stress shielding the spinal load is shifted to the screw-rod construct, reducing stress on the bone leading to remodelling and bone resorption[36,37].

In non-osteoporotic vertebrae screw loosening can be caused by higher local strain on the screws, wear debris and infection[4]. Strain on the pedicle is caused by inadequate distribution of the spinal load, with a disproportional force being applied to the posterior spinal column. If the centre of gravity after posterior stabilisation is anterior of the physiological centre more strain is placed on the screw. This can be caused by insufficient correction of the spinal axis[38] or by inadequate anterior support[4,36] which can be due to poor bone healing or insufficient

ventral stabilisation. Wear debris can stimulate osteolysis[36], creating a hollow around the screw. Although infection may facilitate screw loosening, the evidence is lacking[36].

2.3. Osteoporosis

Osteoporosis is characterized by a low bone density and microarchitectural deterioration of bone mass, leading to increased fragility and fracture risk[39]. The World Health Organisation (WHO) definition of osteoporosis is a bone mineral density at least -2.5 standard deviations below the mean of young women in the population[40]. These values were established in 1994 by assessing bone mineral density scores associated with fragility fractures in the wrist, spine and femur[41].

Osteoporosis is a common disease in the elderly, with the risk increasing with age[1]. The aging population makes osteoporosis an increasing concern. In Germany 15% of the population will be over 80 years old by 2050 and the prevalence of osteoporosis is projected to reach 15%, a 50% increase from 2007[1]. The relevance of osteoporosis is particularly important in orthopaedic patients, including spinal surgery, as rates of osteoporosis in female spinal surgery patients have already reached 51.3%[42].

2.3.1. The Osteoporotic Spine

Osteoporosis is a common comorbidity in elderly patients and can increase spinal instability and deformity, making it a growing concern in the in the surgical care of orthopaedic patients[43].

Osteoporotic changes on a local level in the spine can alter the entire spinal profile because the vertebrae all act as a functional unit. The back muscles are also weaker in osteoporotic patients resulting in less posterior support of the spine[44]. The combination can result in a pronounced kyphosis. Kyphosis shifts the spinal load further anterior and places additional pressure on the already weakened vertebrae. The spinal deformities resulting from osteoporosis can impair the cardiorespiratory, gastrointestinal and entire skeletal system[44].
Osteoporosis can also accelerate degenerative processes[45]. Osteoporosis results in endplate thinning with decreased endplate vascularisation and consecutive malperfusion of the adjacent discs, increasing disc degeneration[45]. Degeneration reduces the discs ability to absorb shock and can lead to instability of the motion segment, which may result in lower back pain[46].

Spinal deformity, instability, degeneration and diminished bone quality increase the risk of fractures. Vertebral fractures are the most common osteoporotic fracture[18] and can often be the first clinical manifestation of osteoporosis[47]. Osteoporotic fractures can cause a significant reduction in quality of life and an increase in morbidity and mortality[5,39].

2.3.2. Treatment of Osteoporotic Spinal Fractures

The surgical treatment of osteoporotic patients requires special attention. Osteoporotic patients have an above average age, which corresponds with more comorbidities[48]. The management of osteoporotic patients must take these risks into account. Osteoporotic fractures present a surgical difficulty as osteoporotic bone has poor capacity for regeneration, high rates of refracture and poor fixation[5]. The postoperative results in osteoporotic patients have shown higher rates of comorbidity, pseudarthrosis, additional vertebral fractures and hardware failure[2].

Most osteoporotic spinal fractures are stable compression fractures and receive conservative treatment[5]. Vertebral compression fractures place osteoporotic patients at a high risk of developing secondary complications including changes in the spine structure, such as progressive kyphosis, stenosis, sagittal imbalance and degeneration[2,3].

Indications for surgery in osteoporotic patients include instable fractures, a neurological deficit or paralysis and kyphotic deformity. Surgery can also be performed to reduce spinal instability due to degenerative spinal disease, tumours or infection[5,47].

However multiple complications can occur when using pedicle screws in osteoporotic vertebrae. The most common complications of posterior instrumentation are pedicle screw loosening, pedicle screw pull out and fractures in adjacent vertebrae[2,3].

Early complications of pedicle screw based instrumentation in osteoporotic vertebrae include pedicle fractures and compression fractures[48]. The pedicles are already vulnerable to fracture during screw insertion.

In the long-term osteoporotic patients are also more susceptible to adjacent level degeneration, pseudarthrosis and progressive kyphosis[2,48]. The original spinal disease can also progress.

Low bone mineral density is a predisposing factor to instrument failure[2]. Pedicle screw loosening is a common complication in osteoporotic vertebrae, with reported rates as high as 60%[47]. The screw fixation correlates with bone mineral density resulting in osteoporosis being a major risk factor for screw loosening[4,5,49]. Screw loosening leads to instability throughout the construct, resulting in non-union and loss of correction[19].

Stress shielding has been described as a possible mechanism of screw loosening, the load is carried by the implants and less load is transferred through the bone causing remodelling of the surrounding bone tissue, microfractures and decreasing the anchorage[36]. The high fragility of the osteoporotic bone makes it more vulnerable to micro-injuries and excessive force at the bone-metal boundary, resulting in higher rates of hardware pull out[18].

Furthermore, fusion can be more difficult to achieve in osteoporotic bone because of the excess of osteoclast activity relative to the osteoblast activity. This creates the risk of delayed fusion or pseudarthrosis[2]. The longer duration of loading before fusion increases the risk of pedicle screw failure, as the instrumentation is only intended to provide temporary stabilisation[2,50]. Although higher rates of delayed union were reported in osteoporotic vertebrae, there was no significance difference in the rate of fusion. A definite correlation between the rate of fusion and clinical outcome or deformity correction has not been proven[48].

2.4. Improving Pedicle Screw Anchorage in Osteoporotic Vertebrae

The increasing life expectancy and incidence of osteoporosis will continue to lead to more spinal operations being performed in osteoporotic patients[42]. The associated complications, especially screw loosening, have resulted in a demand for the development of appropriate techniques[18]. The aspects being explored to improve pedicle screw anchorage in osteoporotic vertebrae include the screw design, the material, the instrumentation technique, the screw trajectory and cement augmentation.

2.4.1. Screw Design

Screw design influences the anchorage of pedicle screws. The surface area of the screw in contact with the surrounding bone has been named as a significant predictor of screw fixation in some studies, however others did not find a significant correlation[18]. Approaches to increasing the surface area include; screw length, diameter, thread type and shape[18].

The role of using a larger screw diameter to improve pull out strength has been shown in both cadaver testing and clinical trials[44]. It has been suggested that the outer diameter is the screw design feature with the highest influence on the pull out strength[51]. A larger diameter increases the screw purchase and improves fixation[18]. Pedicle anatomy can limit the screw diameter because a larger diameter increases the risk of pedicle fracture during screw insertion[32]. The poorer bone quality in osteoporotic patients makes the pedicle more vulnerable to fracture during instrumentation, further limiting the screw diameter and requiring extra care[18,44].

By increasing the screw length, the insertion depth also increases. In non-osteoporotic bone inserting the screw through 80% of the vertebral body is enough to achieve fixation[18]. However, pull out testing in osteoporotic vertebrae only showed an insignificant increase in fixation with increasing insertion depth, suggesting that the same fixation can be achieved when only penetrating 50% of the vertebral body[18,50]. A significant increase in pull out strength was achieved by penetrating the anterior cortex in bicortical fixation[50]. Moreover, increasing the insertion depth also reduced loosening under cranio-caudal cyclic loading, possibly due to the angular stiffness[50].

Another aspect being explored to increase purchase is the thread type. When pedicle screws are pulled out the bone between the threads is removed as well, therefore the pull out is influenced by the quality and quantity of the bone between the screw thread[51]. Altering the thread type to compress the bone may improve the anchorage more than increasing the contact area between the screw and bone[18]. The optimal thread type for a particular patient

maybe dependent on the pedicle anatomy. The thread pitch is the distance between the crests of two screw threads. The thread depth is height from root to crest. From a mechanical view point a small thread pitch and depth are beneficial when the pedicle size is a limiting factor whereas a large pitch and depth improve purchase in soft materials[18]. This presents a challenge in instrumentation of osteoporotic spines, as a compromise must be made between the fracture risk and soft bone substance.

2.4.2. Material

The material properties of the screws influence the fixation. Stainless steel is often used to make pedicle screws due to its high strength and biocompatibility[18]. However, titanium has become more commonly used because it may have superior mechanical and biological properties to stainless steel. Titanium has a lower modulus of elasticity, making it more flexible than stainless steel. The higher flexibility may reduce stress shielding[18] which would make titanium more suitable for use in osteoporotic vertebrae. In addition to being biocompatible, titanium is bioactive[18]. The combination of flexibility and bioactivity may further facilitate osteointegration[52].

The modulus of elasticity also influences peri-implant remodelling, with a modulus more similar to that of bone promoting osteointegration and bone on growth. In a series of pull out tests comparing titanium pedicle screws and screws made out of a titanium alloy, with a lower elastic modulus, the alloy showed more bone on growth[18]. The full benefit of a lower elastic modulus requires time for the bone to grow and therefore will not be detected in ex vivo studies. This is a possible explanation for CF/PEEK and titanium screws showing not significant difference in anchorage in ex vivo cyclic loading[25].

2.4.3. Instrumentation Technique

There are different approaches to pilot hole preparation. Both the diameter and the pilot hole preparation technique are being explored to optimise instrumentation. Typically the pilot hole is 71.5% of the screws diameter[18]. A larger diameter pilot hole reduces the purchase of the screw. However, a smaller diameter leads to more pressure having to be applied to the screw during insertion and higher insertion torque. Insertion torque presents a fracture risk in osteoporosis[18] and should be kept to a minimum during instrumentation.

The instrument used to prepare the pilot hole may also impact the mechanical relationship between the pedicle screw and the surrounding bone. The pilot hole can be created with a probe or a drill. The use of a drill removes tissue whereas the probe compacts the spongy bone tissue to the walls of the pilot hole. Theoretically this compacted bone tissue should increase the anchorage of the pedicle screw, as there is more material to be integrated in the screw thread. Some studies have found a that the use of a probe increased the pull out strength of screws[53], however others did not find a significant difference[53,54].

Another aspect to consider is whether to pretap the pilot hole or to use self-tapping screws. On insertion self-tapping screws encounter more resistance, resulting in higher insertion torque. Self-tapping screws have shown mixed results, especially in osteoporotic bone because of the afore mentioned fracture risk related to insertion torque in low bone density[18].

Bicortical fixation has been shown to increase pull out strength in the thoracic and lumbar vertebrae and sacrum[2,18]. The cortex is stronger than cancellous bone in both healthy and osteoporotic vertebrae[2]. However the cortex is thinner in osteoporotic vertebrae[51]. The increase in pull out strength achieved through bicortical fixation varies with the degree of osteopororsis[18], the screw dimensions and the screw type[2]. Penetrating the anterior cortex risks damaging the structures anterior of the spine in particular vascular injury[18]. Bicortical fixation is not routinely preformed in the thoracic and lumbar spine because the risk of damaging the anteriorly located aorta and vena cava is too severe[2,18]. It is implemented in the sacrum, where structures at risk of damage include the nerve root, the colon, and the sacral and iliac arteries[2].

From a biomechanical stand point bicortical fixation may lead to a windshield wiper motion of the screw, which increased the risk of pedicle fracture and screw bending[18].

Hubbing refers to inserting the pedicle screw deeper into the vertebral body, so the head is in contact with the outer cortex. Forces are constantly acting on the screws resulting in the screw toggling and loosening the surrounding bone. Theoretically hubbing shortens the lever and an applied forced would result in a smaller torque. Biomechanical testing showed that hubbing reduced the pull out strength after cranio-caul cyclic loading and led to higher rates of pedicle fracture[18]. Therefore hubbing is not a recommended technique to increase pedicle screw fixation[18].

2.4.4. Cement Augmentation

Cement augmentation of pedicle screws increases the pull-out strength. The degree, to which cement augmentation decreases pedicle screw failure, depends on the bone mineral density. Cement augmentation showed a stronger positive effect in osteoporotic than in osteopenic bone, and no significant improvement in healthy bone[4]. Cement presents risks such as cement leakage and embolisms[4].

Polymethyl methacrylate (PMMA) cement is commonly used, however it cannot integrate into bone. Also the exothermic reaction, which occurs during hardening, can damage surrounding tissue[2]. Cement augmentation may also complicate infections, as infected screws can be difficult to extract[2].

Calcium phosphate may increase the pull out less than PMMA[2] but it may show superior biological qualities[2]. Calcium phosphate is bioactive and can be remodelled by osteoclasts and eventually replaced by bone[2]. This results in a closer simulation of the physiological spine.

2.4.5. Screw Trajectory

Pedicle screws are traditionally inserted into the junction of the transverse process and the lateral wall of the facet and follow a transpedicular lateral to medial trajectory[55]. A new cortical bone trajectory (CBT) has been suggested in which the pedicel screw is inserted lateral in the axial plane and caudocephalad in the sagittal plane, without penetrating the trabecular space in the vertebral body[55]. In the CBT the screw has more thread contact with the cortex[56]. In the traditional trajectory the screw end point is in the cancellous bone of the mid-vertebral body but in CBT it is in the bone cortex[57]. The cortex maintains its density longer during aging and osteoporosis whereas the cancellous bone quality diminishes more, which makes the screws less vulnerable to toggle[57].

Radiological comparisons showed that the bone mineral density of CBT was significantly higher than in the traditional trajectory. Further assessment showed that the BMD of the fixation points of CBT was also significantly higher than in the traditional trajectory[57]. The difference between the BMD was more pronounced when comparing osteoporotic and elderly with normal vertebrae, indicating that osteoporotic patients could benefit from use of the CBT[57].

The traditional method for pedicle screw placement is associated with longer operating times, larger incisions, more soft tissue damage, more blood loss and wider retraction[56]. The reported rates of superior facet joint violation and symptomatic adjacent segment degeneration are also higher[56]. Dissecting the spinal muscles and violating the superior facet joint both lead to instability and could result in the increase the rate of adjacent segment degeneration. However the rates of fusion, revision surgery and complications, such as wound infection, dural tear, screw malposition and hematoma were not significantly different between CBT and traditional placement[56].

2.4.6. Changes to the Screw-Rod Construct to Improve Pedicle Screw Anchorage

2.4.6.1. Instrumentation Length

The length of the spinal instrumentation and the levels instrumented also have to be considered in preoperative planning as osteoporotic patients are at increased of developing postoperative kyphosis and vertebral fractures[3]. Instrumentation should not be ended in a kyphotic segment, as it can cause sagittal imbalance, especially in osteoporotic spinal deformities[2]. Sagittal imbalance places additional stress on the pedicle screws. Primary long segment instrumentation has shown better clinical outcomes than inserting a longer rod during revision surgery[2] and avoids the operative risk. To avoid junctional kyphosis it is sometimes necessary for the instrumentation to span over more levels[18]. Extending the instrumentation over multiple spinal levels can also reduce the screw failure because the applied forces are spread throughout the construct; thereby a lower force acts on each individual screw[3].

2.4.6.2. Material

The modulus of elasticity influences the force distribution throughout the implant and at the bone-implant-interface. This is true for the choice of material for rods and screws. CF/PEEK has an elastic modulus closer to that of bone than either titanium or stainless steel[25]. A similar modulus of elasticity leads to a more homogenous stress distribution between the screw and the bone, resulting in less micromotion[25] and therefore should decrease screw loosening.
Rods with an elastic modulus closer to that of bone can help to recreate the physiological load sharing between the spinal columns. A stiffer construct places more stress on the posterior column, thereby straining the anchorage points. Increased anterior column load sharing helps to facilitate bony fusion and decreases the risk of adjacent segment disease[25].

Rods with a lower elastic modulus may transfer less stress on to the screw and surrounding bone, resulting in lower rates of screw loosening and pull out. This was demonstrated in

titanium rods with a low elastic modulus[3]. However, the rigidity of the rods is also influenced by their diameter and length.

2.5. Hypothesis

Studies on the influence of the elastic modulus on pedicle screw anchorage are lacking. The development of CFR/PEEK and its possible application in spinal surgery must be explored further. Our hypothesis is that CFR/PEEK pedicle screws will have better fixation than the currently used titanium screws as an elastic modulus more similar to bone should result in a more even force distribution and reduce stress shielding.

There have been several biomechanical studies comparing the use of a probe and drill for pilot hole creation, however the reported results are inconsistent[53,58,59]. Furthermore, the experiments were not conducted in osteoporotic spines. Theoretically the drill will remove bone substance whereas the probe will compress bone against the wall of the pilot hole, leaving more substance available for anchorage. Our hypothesis is that the use of a probe will result in better anchorage than the drill.

3. Materials and Methods

3.1. Biomechanical Comparison of CF/PEEK and Titanium Pedicle Screws

3.1.1. Study Design

The biomechanical study was done in cooperation with the Department of Trauma and Reconstructive Surgery, the Department of Diagnostic and Interventional Radiology, the Department of Dental Materials and Biomaterials Research and the Institute of Molecular and Cellular Anatomy, RWTH Aachen University Hospital. The experiment complies with the principles of the Declaration of Helsinki (2013) and was approved by the local ethics committee (17-248) of our institution. The study received funding through Icotec AG, Altstätten, Switzerland.

3.1.2. Specimen

The study was conducted on ten fresh-frozen human cadaver lumbar spines from L1 to L5. Prior to inclusion in the study, the cadavers were stored at -20℃ in triple sealed bags. All donors were over 50 years old. After the soft tissue was removed from the spines, they were inspected for elimination criteria including fractures, tumours, scoliosis deformity more than 20°, T-score > -1.5, and prior lumbar instrumentation. The bone mineral density of each vertebra was determined with a quantitative computed tomography (qCT).

3.1.3. Implants

The instrumentation utilised CF/PEEK poly-axial pedicle screws (Icotec AG, Altstätten, Switzerland.) with CF/PEEK rods, and titanium poly-axial pedicel screws with titanium rods.
Group A: In group A 6.5 mm × 45 mm standard titanium (Ti6Al4V ELI) pedicle screws (Icotec Pedicle System Titanium, Icotec ag, Altstätten, Switzerland) and lordotic 5.7 mm x 40 mm rods (Icotec Pedicle System Titanium, Icotec ag, Altstätten, Switzerland) were used.
Group B: In group B 6.5 mm × 45 mm carbon fiber-reinforced polyetheretherketone (CF/PEEK) pedicle screws (VADER® Pedicle System Carbon/PEEK, Icotec ag, Altstätten, Switzerland) and lordotic 5.5 mm x 40 mm rods (BlackArmor® Carbon/PEEK, Icotec ag, Altstätten, Switzerland) were used.

3.1.4. Experimental Set-Up and Protocol

The lumbar spine specimens were thawed at 4 ℃ for 16 hours following the testing protocol of Panjabi et al.[60]. The muscle, fat tissue and cranial and caudal intervertebral discs were removed, while preserving the spinal ligaments, facet joints and intervertebral discs. The soft tissue was removed using chisel, gouges, forceps and scalpels. The lower half of the fifth

lumbar vertebrae and the upper half of the first lumbar vertebrae were embedded in a polymerising two component liquid-powder System (PMMA, Technovit 4004, Heraeus Kulzer GmbH, Hanau, Germany). The embedding process used a custom-made rigid fixation system and a water level to ensure that the embedding blocks were parallel.

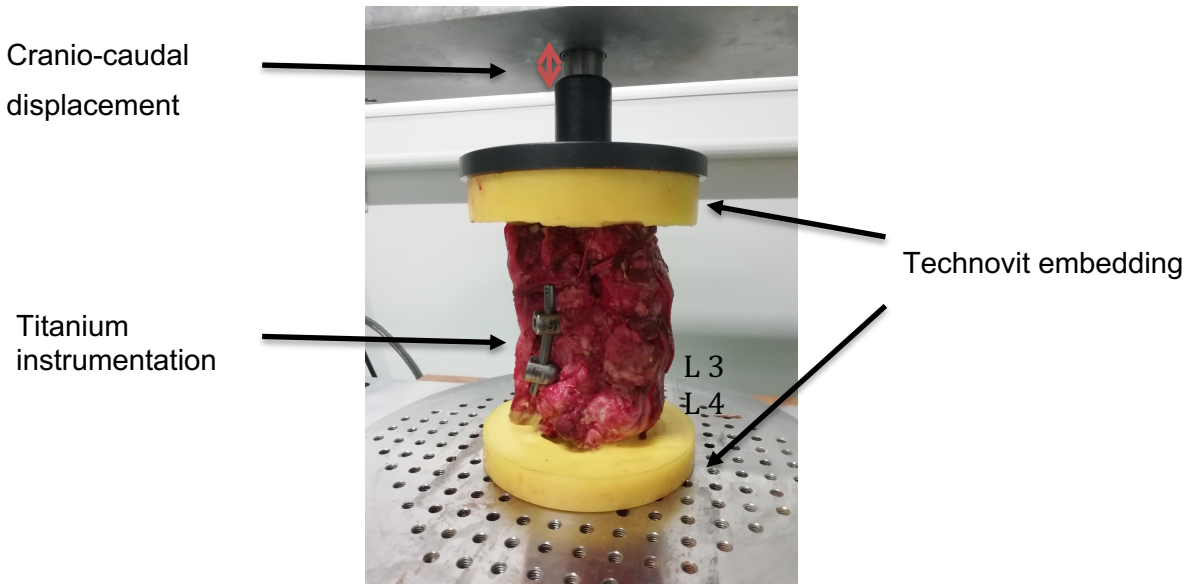
The spines were paired regarding to bone mineral density and each matched pair was randomly divided into two groups, A (n=5) and B (n=5). The spines in Group A were instrumented with CF/PEEK screws and rods and Group B with titanium.

Monosegmental dorsal pedicle screw instrumentation was performed in the third and fourth lumbar vertebrae by an experienced spinal surgeon. The pedicle screws were inserted in an intrapedicular trajectory using anatomical landmarks and fluoroscopic guidance. The pilot hole was prepared the pedicle awl provided by the manufacturer for each system (Titanium/CFR/PEEK, Icotec ag, Altstätten, Switzerland). A ball-tipped probe was used to rule out a violation of the medial, lateral, cranial and caudal wall. The pedicle screw was inserted manually with the hand-driver provided for each system. The lordotic bended rods were inserted into the pedicle screws following the anatomical curve of the lumbar spine. No additional rod bending was performed.

The pedicle screw placement was evaluated in a CT using the Zdichavsky Classification by a radiologist[61].

The spines were inserted into the Test machine (Dyna-Mess, Stolberg, Germany) as shown in Image 1.

Image 1: Experimental set up for cyclic loading in the Dyna-Mess



Cyclic loading was performed using a vertical servo-pneumatic actuator (Dyna-Mess, Stolberg, Germany). The embedded and instrumented specimen were loaded into the actuator so that the axial force was applied to the middle spinal column.

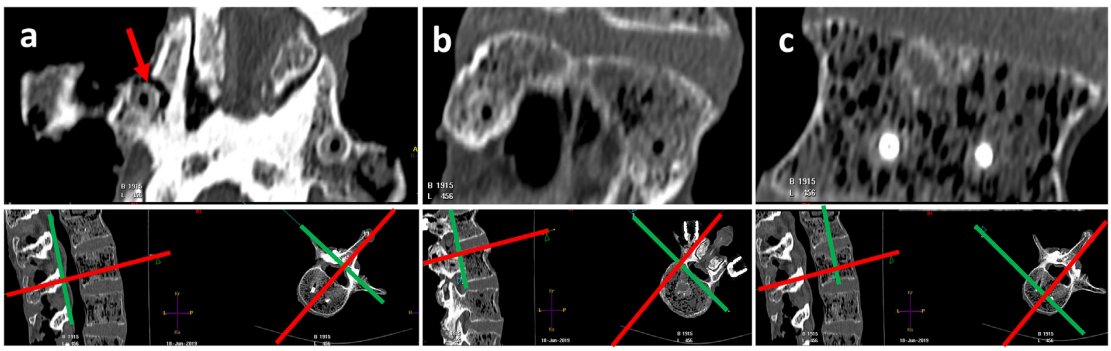
The specimens were axially loaded with 5 kg for 15 minutes to reduce the hydration level of the intervertebral disc and to level the spine.

Then cranial-caudal cyclical loading was carried out at a frequency of 3Hz for 100.000 cycles. The initial 2.000 cycles were conducted with a peak of 500 N and increased by 50 N every 2.000 cycles to a maximum of 950 N.

After cyclic loading a further CT scan was performed and the cavity surrounding the pedicle screw was measured at the three previously defined points (point 1: screw tip, point 2: mid-shaft of the screw, point 3: entry point). The total volume of the cavity was calculated.

Image 2: CT scan showing the cavity surrounding the pedicle screw at 3 points

a: point 3, entry point, b: point 2, mid-schaft, c: point 1: screw tip [62]



Pull out testing was conducted in a universal testing machine. The failure load was determined through pull out testing and defined as the maximum axial force resulting in a loss of resistance of 80% F_{max}.

3.1.5. Statistical Analysis

The statistical analysis was performed using IBM SPSS software (version 23; IBM Corp., Armonk, New York, USA).

Demographic data including age, gender, grade of osteoporosis (T-Score) and bone mineral density was collected (Tables 1 and 2) and the corresponding means and standard deviations

were calculated (Table 3). The average and standard deviation of the failure load (N) and the number of cycles was also calculated (Table 3).

The averages of cavity at each point and of total cavity were calculated for each group.
The Mann-Whitney Test was used to compare the groups due to the small sample size (5 specimen per group) with a significance set at $p<0.05$. Adjustment for multiple testing was not made because all testing procedures were explorative.

3.2. Biomechanical Evaluation of Pilot Hole Preparation

3.2.1. Study Design

The biomechanical testing was done in cooperation with Center for Anatomy at the University of Cologne.

The study was approved by the ethics committee of our institution (file number: 17-248) and complies with the principles of the Declaration of Helsinki (1996). Prior to death the donors gave their informed consent for their bodies to be used for scientific and educational purposes.

3.2.2. Specimen and Preparation

The study was conducted on twelve fresh frozen thoracic vertebrae (Th9-Th12) from three donors (two males, age 61 and 68 years, and one female, age 92). The spines were stored in tripled sealed bags at -20℃. The spines were inspected for tumours, fractures and deformities, scoliosis > 20°, and previous spinal surgery as these would have exclusion criteria. CT-scans were performed on all vertebrae prior to testing to determine the Housefield Units (HU) and estimate the bone mineral density (BMD) to ensure all vertebrae were osteoporotic. The mean BMD was 107.9 HU (SD 41.9), which is osteoporotic[63].

In accordance to the experimental protocol established by[60], the fresh frozen thoracic spinal segments were defrosted at 4℃, 16 hours prior to testing. The preparation was partially conducted during the thawing process. The spinal segments were separated into individual vertebrae. The ligaments, intervertebral discs, muscles and fat tissue were removed. The vertebral bodies were embedded in a polymerising two-component methyl methacrylate resin (PMMA Technovit 4004, Heraeus Kulzer GmbH, Wehrheim, Deutschland), leaving the vertebral arch exposed for instrumentation to facilitate rigid fixation at a perpendicular angle in the testing machine.

After the embedding hardened, lateral and anterior-posterior x-rays were done of each vertebra, to ensure the bone had not suffered any damage during the preparation.

3.2.3. Instruments

The pilot hole was prepared using either a curved thoracic probe (CD Horizon Solera spinal system, Medtronic, Dublin, Ireland) or a 3,2 mm drill. A standard 5,5 mm x 45 mm titanium multi-axial pedicle screw (CD Horizon Solera spinal system, Medtronic, Dublin, Ireland) was manually inserted into each pilot hole.

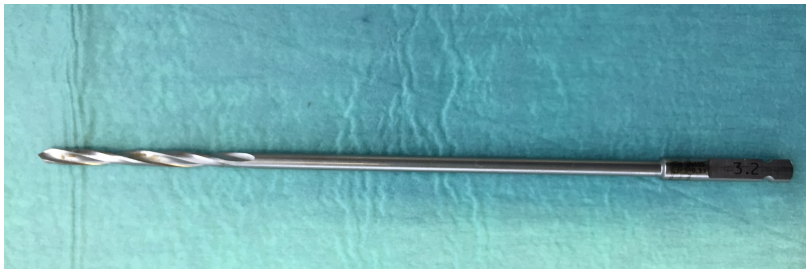


Image 3: 3.2 mm Drill

Image 4: Curved thoracic probe

3.2.4. Pedicle Screw Instrumentation

The first pilot hole was alternately created with the thoracic awl and the drill. An intrapedicular trajectory for the pilot holes was achieved through the use of anatomical landmarks and fluoroscopic guidance in lateral and anterior posterior orientation. The pedicle screw was manually inserted into the pilot-hole and the placement was controlled fluoroscopically. Then cyclic loading was conducted following the below described protocol.

After biomechanical testing the pedicle screw was removed from the vertebrae and the contralateral pedicle of each vertebra was prepared using the second preparation technique to facilitate a direct comparison. The pilot holes prepared with the curved thoracic probe were assigned to Group 1 and those prepared with the drill were in Group 2.

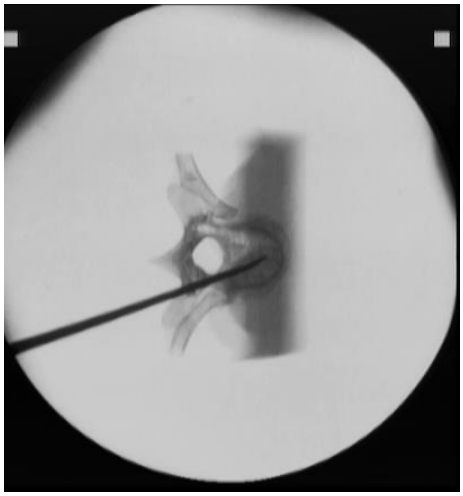


Image 5: An axial fluoroscopic image depicting the creation of a pilot-hole with the **t**horacic probe

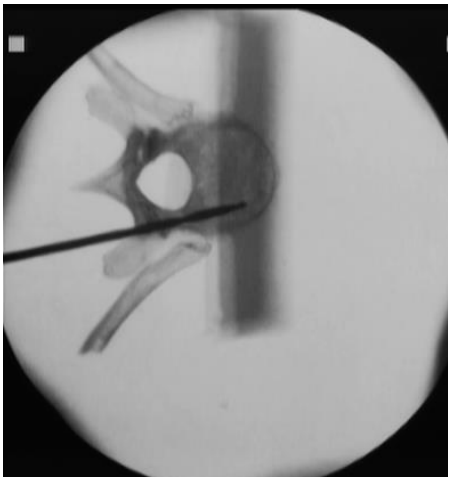


Image 6: An axial flouriscopic image showing the creation of the pilot hole with the drill

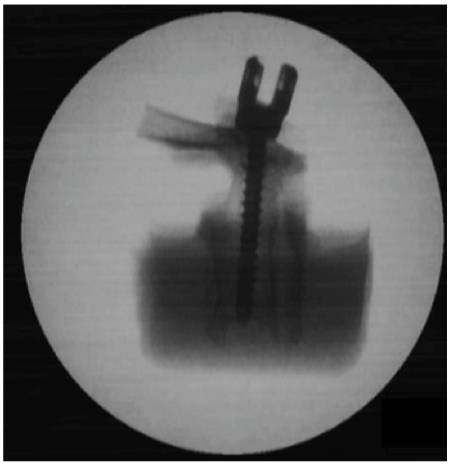


Image 7: Pedicle screw in axial fluoroscopic image

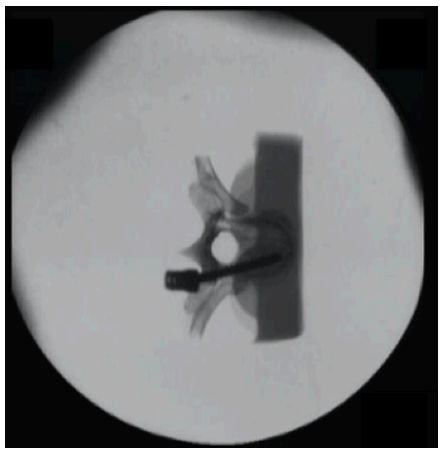
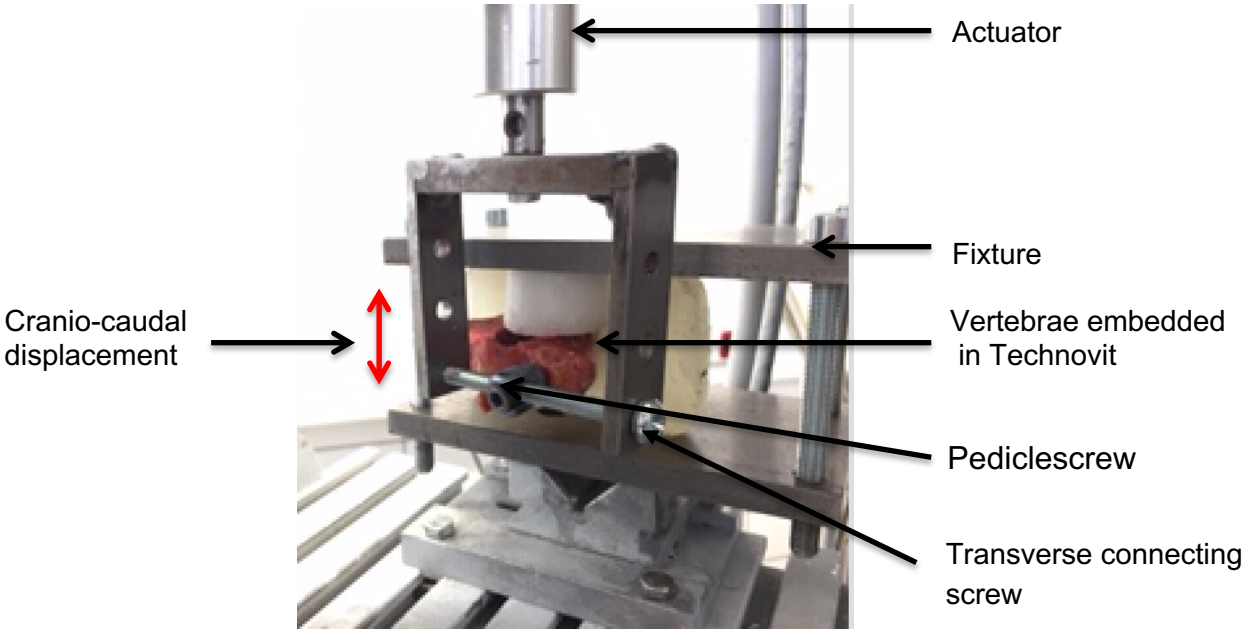


Image 8: Pedicle screw in lateral fluoroscopic image

3.2.5. Experimental Set-up and Protocol

The embedded and instrumented vertebra was clamped into a specifically made rigid fixation system, consisting of a xy-table. The construct was inserted into the material testing machine (Zwick/Roell Z010, Fa. Zwick Roell, Ulm, Germany). The pedicle screw head was connected to the actuator via a transverse set screw, according to the instructions provided by the manufactured. The head of the pedicle screw was set in the axis of the actuator of the testing machine to ensure a tension free starting position. The set screw was fixed according to the instructions of the manufacturer. The set up is shown in Image 9.

Image 9: Experiment setup for cranio-caudal cyclic loading



Fatigue testing was conducted through cranio-caudal cyclic loading. The initial 500 cycles were done with a load ranging from +25 N (compression) to - 25N (tension) at a frequency of 5mm/s. The load was increased by 5N every 500 cycles. The cyclic loading was ended after 10 000 cycles or pedicle screw failure. For the purpose of this study pedicle screw failure was defined as displacement of 5 mm in the axial plane or by reaching the switch-off threshold, which was defined as 40% Fmax.

The Zwick/Roell recorded the Force and Displacement throughout testing and generated Force-Displacement graphs.

3.2.6. Statistical Analysis

Statistical analysis was conducted using SPSS (version 25; SPSS, Chicago, IL, USA). Demographic data, Hounsfield units and biomechanical properties were collected for all specimens. The two groups were compared regarding maximum number of cycles and maximum force until loosening. Normal distribution was tested for using the Kolmogorov-Smirnov (0.000: not normally distributed). The mean values of the 2 groups were compared using the Mann-Whitney test because of the small sample size (N=12). P-values < 0.05 were considered statistically significant.

4. Results

4.1. CF/PEEK vs. Titanium

Demographic data was provided by the donor records of the Institute of Molecular and Cellular Anatomy, RWTH Aachen University Hospital. The grade of osteoporosis (T-score) and BMD were measured with CTs. The failure load and completed number of cycles during biomechanical testing were recorded.

Table 1: Demographic and specific data and overview of the grade of osteoporosis and BMD for Group A: Titanium based pedicle screws

Specimen	Age (years)	Gender *	Grade of osteoporosis (T-score)	BMD (mg Ca-HA/ml)	Failure load (N)	Count of completed cycles (950 N/cycle)
#1	95	F	-4.82	46.9	2281.000	100 000
#2	70	M	-2.41	110.9	3876.529	100 000
#3	79	F	-3.38	85.1	2378.424	100 000
#4	88	F	-1.69	130	4470.196	100 000
#5	79	F	-3.49	82.3	2025.699	100 000

Table 2: Demographic and specific data and overview of the grade of osteoporosis and BMD for Group B: CFR/PEEK pedicle screws

Specimen	Age (years)	Gender *	Grade of osteoporosis (T-score)	BMD (mg Ca-HA/ml)	Failure load (N)	Count of completed cycles (950 N/cycle)
#6	77	F	-2.99	95.5	3637.491	100 000
#7	71	M	-5.98	16.2	2976.394	100 000
#8	81	M	-4.36	59.1	2191.713	100 000
#9	74	F	-4.93	44.1	3039.364	100 000
#10	84	F	-3.68	77.3	1474.89	100 000

* In the gender column f represents females and m represents males.

Tables 1 and 2 show that all specimen withstood the full 100 000 cycles and all specimen had a T-Score < -2,5 and were therefore classified as osteoporotic according to the WHO-definition[40].

Table 3: Average demographic data by group and in total

	Age (years)	Grade of Osteoporosis (T-score)	BMD (mg Ca-HA/ml)	Failure load (N)
Total (average)	79.8±7.70	-3.77±1.28	74.74±33.91	2835.17±936.81
Group A (average)	82.2±9.58	-3.16±1.19	91.04±31.51	3006.37±1093.41
Group B (average)	77.4±5.22	-4.39±1.15	58.44±30.50	2663.97±840.12

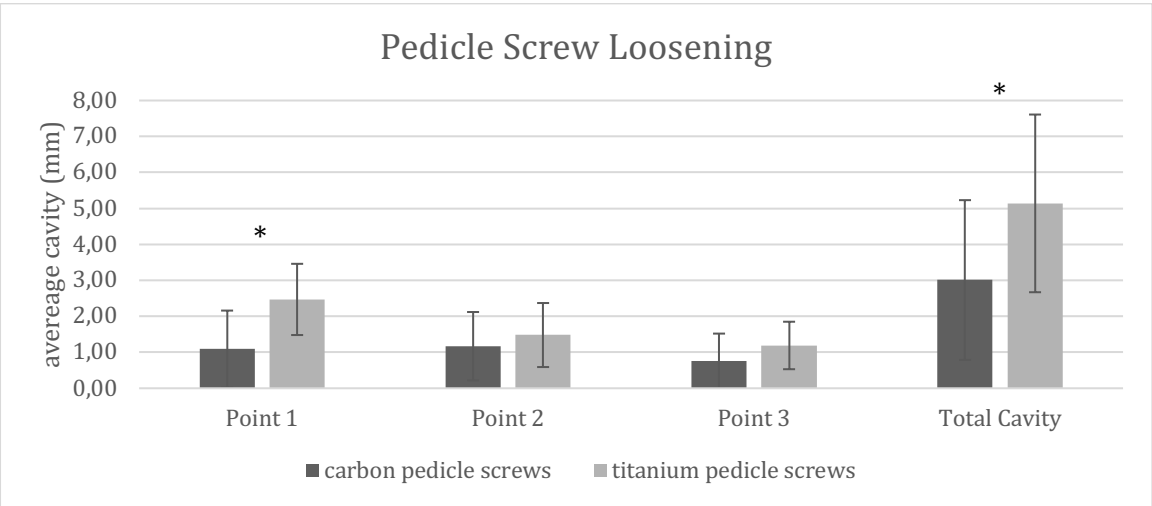
There was no significant difference between both groups regarding the T-score and BMD (p=0.135).

Table 4: The averages of the total cavity and cavity at each point in mm for either Group A (CFR/PEEK pedicle screws) and Group B (titanium pedicle screws) and p-values

	CFR/PEEK pedicle screws	Titanium pedicle screws	p-value
Point 1	1.09±1.07	2.47±0.99	<0.001
Point 2	1.17±0.95	1.48±0.89	0.286
Point 3	0.76±0.76	1.19±0.66	0.183
Total Cavity	3.01±2.22	5.14±2.47	0.007

Table 4 shows the mean and standard deviations of the cavity surrounding the three previously defined points and the total cavity surrounding each screw. The CFR/PEEK pedicle screws had a statistically significant smaller mean cavity at Point 1 ($p < 0.001$) and a statistically significant smaller mean total cavity ($p < 0.007$) than the titanium pedicle screws. These results are summarized in Graph 1.

Graph 1: Average cavity (mm) at each point and total cavity for carbon and titanium pedicle screws[62]



4.2. Effects of Pilot Hole Preparation

Table 5: Summary of results

Vertebral Body	Group	Maximum number of cycles	Maximum Force (Newtons)
1	1	500	25
	2	536	25
2	1	1291	35
	2	582	30
3	1	1555	40
	2	970	30
4	1	2540	50
	2	1055	35
5	1	2286	45
	2	1575	40
6	1	1973	40
	2	1162	45
7	1	2565	50
	2	2116	45
8	1	3709	60
	2	3362	55
9	1	2208	45
	2	2500	45
10	1	9020	115
	2	10000	120
11	1	10000	120
	2	6158	85
12	1	8180	105
	2	10000	120

Table 5 shows the results of each trial. Group 1 was prepared with a thoracic probe and Group 2 with a drill. There was no clear difference between the number of cycles until failure or the maximum force for loosening between the two instrumentation techniques.

Table 6: Evaluation of the Results

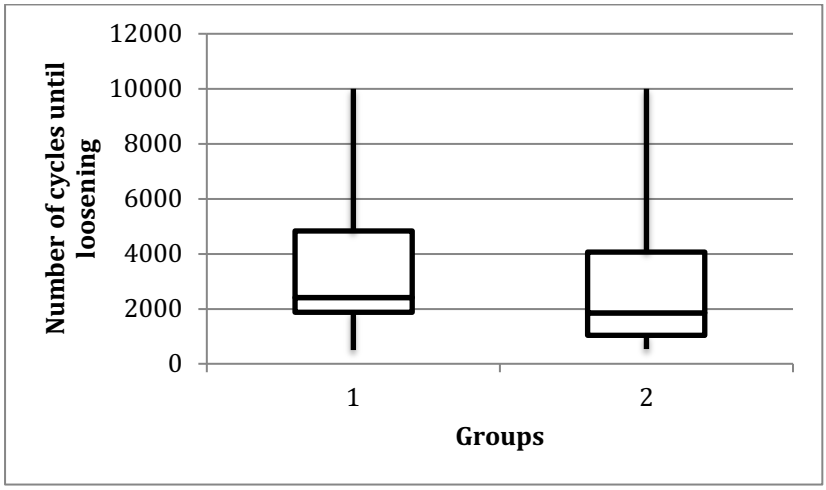
	Group 1	Group 2
Average Maximum Number of Cycles	3819	3335
Minimum number of Cycles	500	536
Maximum number of cycles	10000	10000
Average Maximum Force (N)	61	56
Minimum maximum force	25	25
Maximum maximum force	120	120

In both groups the maximum number of cycles withstood was 10.000, one screw in Group 1 and two screws in Group 2 achieved this. 21 of the 24 pedicle screws used in instrumentation loosened within the 10.000 cycles. The minimum number of cycles to loosening was 500 in Group 1 and 536 in Group 2.

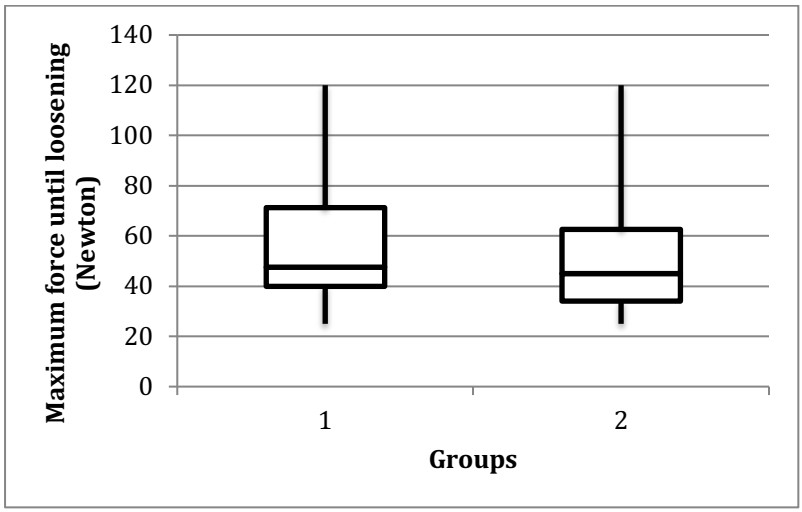
The screws in Group 1 withstood an average of 3819 cycles until failure with a standard deviation of 3281, and in Group 2 3335 cycles with a standard deviation with of 3477. Although Group 1 withstood a higher number of cycles than group 2, the results not statistically significant (P=0.797).

The average maximum force to failure in Group 1 was 61N (SD 33) and in Group 2 56N (SD 34) however these results were also not statistically significant (P= 0.791).
The minimum force to loosening (25 N) and the maximum force to loosening (120 N) were the same in both groups.

Graph 2: Box plots comparing the distribution of the number of cycles until loosening for both instrumentation techniques. Group 1 was instrument using a probe and Group 2 with a drill.



Graph 3: Box plots comparing the distribution of the maximum force until loosening for both instrumentation techniques. Group 1 was prepared with the thoracal probe and group 2 with the drill.



5. Discussion

5.1. Biomechanical Evaluation of CFR/PEEK and Titanium Instrumentation

Rigid rod fixation has been used since the introduction of the Harrington rod in 1962 to achieve high rates of fusion[20]. The elastic modulus of the rods used in posterior spinal instrumentation affects the biomechanics of the spine and the success of fusion[64]. A stiff spinal implant may result in adjacent segment degeneration (ASD), implant failure, stress shielding and pseudoarthrosis. A too flexible rod may not provide the stability needed for union to occur also resulting in pseudoarthrosis.

To circumvent the complications related to excessively stiff materials, such as Titanium, new materials are being developed. Desirable properties for implant materials are high strength with a low Young's modulus[65]. The elastic modulus of PEEK can be modified by adding carbon fibre (CF/PEEK) to more closely resemble the elastic modulus of cortical bone[66] than Ti and stainless steel[25]. This may help to recreate the physiological biomechanics of the spine.

The results of this study indicate that CFR/PEEK pedicle screw-rod constructs have similar biomechanical properties, regarding the failure load, as the standard titanium alloy pedicle screw-rod constructs. All specimen successfully completed the full 100,000 cycles without loosening or breaking and there was no significant difference in the failure load. The endurance of CF/PEEK should be equal to that of titanium.

Biomechanical trials have found that both PEEK and titanium rods could withstand forces exceeding the physiological load of the spine[67]. PEEK rods were found to have the same endurance as clinically used metallic implants in dynamic testing[7]. Furthermore the observed mode of failure was rotation of the screw head, rather than PEEK fracture, which corresponds with the current trials findings[7]. The rods showed different strain patterns, with the lowest strain in Titanium, followed by CF/PEEK and finally PEEK. Lower strain in CF/PEEK rods could reduce the implant fatigue at the implant interface, however was not able to definitively show this as multiple cycles would be needed to evaluate the failure pattern over time[66]. The PEEK and rigid constructs demonstrated the same endurance. Again PEEK did not fail through rod fracture but through rotation of the screw tip[66]. This should address the concern that the less rigid PEEK rods could result in more long-term failure.

The results suggest that CF PEEK rods can restrict the range of motion (ROM) under axial compression enough to allow fusion to occur. This corresponds to the findings of multiple

biomechanical trials, which have shown that PEEK, CF/PEEK and titanium rods do not have a significant difference in the restriction to the ROM[7,66,67]. Although the current trial only applied axial compression, Gornet et al did not find a significant difference in the ROM in PEEK and titanium instrumentation in flexion-extension, rotation and lateral bending[7].

However, a cadaveric trial found that PEEK reduced the ROM in the instrumented level significantly more than titanium under extension. The authors suggested, that this could be due to the PEEK rods being more tightly compressed into the interbody spacer than the titanium rods before placing the set screw, thereby reducing motion within the construct[68]. The flexibility of PEEK rods allowing tighter placement in the spacer could be another advantage in their clinical application.

The volume of the cavity surrounding the CF/PEEK screws was significantly lower than that of the titanium screws. The elastic modulus of the CFR/PEEK screws more closely resembles that of bone[6]. Therefore, the axial force, which was applied to the spinal column, can be distributed more evenly. A more homogenous load distribution should reduce microfracture. The accumulation of microfractures may have led to larger cavity formation around the titanium screws. Titanium rods have been found to result in higher stress at the screw bone interface[7,68,69].

An ex vivo cadaver biomechanical trial comparing the screw loosening of CF/PEEK and titanium pedicle screws also stipulated that the lower modulus of elasticity would result in a more homogenous stress distribution and less micro-motion thereby preventing screw loosening[25]. However, it did not find a significant difference in the screw loosening, failure load or the angular motion measured using stress fluoroscopy[25]. However, the lower modulus may not have reduced screw loosening because the lower modulus has a larger effect on the long-term viability through osteointegration and bone remodelling rather than the primary stability[25].

However the trial was conducted in non-osteoporotic bone, which has a higher elastic modulus and therefore might not benefit from the lower elastic modulus of CF/PEEK[70]. Furthermore, the cranio-caudal axial load was applied directly on the screw base, which is in the dorsal spinal column, and only 10,000 cycles were performed. The current trial applied the load to the middle column and conducted 100,000 cycles. The load application to the middle column, which is the centre of rotation of the lumbar spine, is more representative of the compressive forces in vivo and the increased number of cycles of the long-term effect.

The current study found that the cavity was smallest around the entry point and largest in the screw tip for both titanium and CFR/PEEK instrumentation. The difference in cavity formation at each point measured between CFR/PEEK and titanium was only significant at the screw tip, which was placed in the mid-vertebral body. The anchorage of the pedicle screw was better at the entry point, in the cortical bone. The trabecular bone in the vertebral body contributes less to the anchorage than the cortical shell [50,71]. Although the cortical shell thins in osteoporosis it still has a large influence on the pull-out stiffness[71]. The larger screw cut out indicates that the loosening was initiated at the screw tip.

This is in contrast to an investigation into pedicle screw fixation under non-axial loading, which found that the cavity was conically shaped with the largest cut out at the entrance point[72]. The force was applied to the screw base leading to a cranial-caudal toggling motion of the screw within the vertebrae. Initiating the movement at the screw base may have resulted in the observed ploughing effect. Kinematic tracking was conducted using a high-speed camera and tracers to portray the movement of the screw in the vertebrae. The kinematic tracking showed a rotational movement with the fulcrum being anterior of the screw tip. However, the current trial applied force directly to spinal column, which resulted in the load being distributed along the length of the screw rather than using the screw as a lever. Therefore, the mechanism of loosening was different.

To improve on the current trial kinematic tracking could have been done to better portray the movement of the pedicle screws and allow further insight into the mechanism of the screws loosening.

The current trial focused on screw loosening and not on force distribution in the spine as a whole unit. But in clinical application the spine should be seen as a whole unit because of postoperative complications such as ASD and bone remodelling.

Stiff dorsal instrumentation leads to stress shielding, which is often discussed as a mechanism of pedicle screw loosening[36]. In stress shielding the stress is shifted to the pedicle-rod system and away from the vertebral bodies[37]. Reducing stress on the bone leads to reconstruction and absorption resulting in pseudoarthrosis and screw loosening[37]. The lower modulus of elasticity of CF/PEEK should increase the stress on the vertebral bodies and reduce stress shielding[52]. A literature review of PEEK rods found that anterior load sharing was higher in the PEEK than in the titanium rods[64]. Anterior column load sharing should reduce stress shielding by increasing the pressure on the interbody spacer and allowing for a more physiological

recreation of the spine[67]. A finite element model showed that PEEK instrumentation had a slightly higher pressure in the instrumented level than titanium in all applied motions; flexion-extension, lateral bending and rotation[7].

The more flexible rods also facilitate micro-motion[69]. Micro-motion and increasing the pressure on the interbody spacer both promoted interbody fusion in accordance to Wolffs' law[20]. The potential benefits of CFR/Peek over Titanium rods in spinal instrumentation may not be revealed in cadaver trials, as the reaction of the bone and interbody spacer to the altered strain patterns will not be seen.

There are concerns, that the higher load placed on the pedicle screws in dynamic stabilisation could increase screw loosening in the immediate post-operative period before fusion has occurred[36]. However, the current findings did not find a significant difference in the failure load and CF/PEEK compared favourably to titanium in cavity surrounding the screws.

The use of PEEK instrumentation results in a more physiological load in adjacent segments, which should reduce adjacent segment disease[20,68,69]. A gauged spacer was used to measure more physiological interbody pressures in the instrumented and subadjacent level in PEEK rod constructs compared to titanium rod constructs[68]. The intradiscal pressure in the instrumented and adjacent levels following PEEK instrumentation is similar to that of intact spines and lower than in Titanium instrumentation[64]. PEEK instrumentation also results in a more physiological range of motion in adjacent levels than titanium[68]. A cohort study did not find a significant difference in ASD between PEEK and Titanium posterior instrumented fusion, but PEEK did how lower rates of nonunion and hospital readmission in a 90 day period[73].

The potential advantage of PEEK rods in reducing adjacent segment disease cannot be demonstrated in cadaveric trials. However, it is difficult to evaluate ASD in clinical trials, as the radiological degeneration may not correlate with the symptoms, leading to a wide range in rates of adjacent segment disease reported by clinical studies[34,35]. Furthermore, ASD may also be caused by normal degenerative processes consistent with aging as well as the altered biomechanics of the spine[34,64].

As previously mentioned, the clinical application of this trial is limited by being conducted in ex vivo. A lower modulus of elasticity may affect the long-term stability of the screws. The implant modulus effects peri-implant remodelling with lower modulus promoting

osteointegration and bone on growth[74]. Therefore, the long-term success of fixation cannot be evaluated in an ex vivo trial.

An in vivo trial in osteoporotic sheep comparing the fixation of expandable pedicle screws made of Titanium-alloys with different elastic moduli, found that the low elastic modulus expandable pedicle screws compared favourably in histological, biomechanical and Micro-CT observations. The low elastic modulus expandable pedicle screws had more bone formation and histological analysis showed more direct bone contact and less fibrous tissue which resulted in a higher pull out strength[74]. Titanium-alloy implants with a higher Young's modulus resulted in higher rates of bone atrophy and less remodelling[65]. The lower modulus of CFR/PEEK implants should result in a more even load distribution and further decrease stress shielding. These findings correspond to the current experiment, as the cavity formation was larger in the higher elastic modulus Titanium screws.

However another in vivo trial found that although titanium alloys had more bone on growth than stainless steel in histomorphological analysis, this did not result in a difference in maximum load to failure, energy to failure or bone volume[52]. Therefore, assumptions about the impact of bone on growth on pedicle screw fixation maybe overstated.

In addition to being mechanically successful, the bio-viability of a material must be considered before application in clinical practice. Titanium and its alloys have been shown to be inert, fatigue resistant, non-toxic and to promote osteointegration. However corrosion remains a threat and Titanium implants result in poor MRI imaging[75].

There is need for further study into the viability of CFR/PEEK in implanted devices. PEEK has been shown not to be harmful for the spinal cord and safe for use in spinal implants[76]. CFR/PEEK promoted osteoblast differentiation more than unfilled machined PEEK, however CFR/PEEK, PEEK and Ti supported cell adhesion and proliferation to similar extents[75]. Furthermore CFR/PEEK has been found to have better wear resistance than PEEK[25] and to result in less wear debris than titanium implants[23]. Wear debris results in higher osteoclast activity and increasing the risk of consecutive screw loosening[77,78]. This is may be particularly influential in osteoporotic patients, as the osteoclast activity outweighs the osteoblasts in osteoporosis, leading to bone resorption[79]. Therefore the in vitro application of the CFR/PEEK implants should have an advantage over Titanium screws, which cannot be evaluated in cadaver models.

Another benefit of the clinical application of CFR/PEEK over titanium instrumentation is fewer imaging artefacts in both CT and MRI[26]. An in vivo study comparing MRI artefacts following lumbar spondylodesis with CF/PEEK or titanium pedicle screws in degenerative spinal disorders found that the CF/PEEK screws had fewer artefacts within the vertebral body and the surrounding structures such as the spinal cord and neuroforamina, which allowed for better assessment of the structures[27]. The reduction of imaging artefacts is beneficial in radiation planning and the assessment of post-operative residual or recurrent tumours[24,26].

It is difficult to compare the findings of different biomechanical trials, as there is no standard protocol, resulting in different testing methodologies. Preconditioning was conducted to reduce the hysteresis of the intervertebral disc in order to increase the reproducibility by reducing the effect of load history.

In cyclic loading in the lumbar spine the frequency rates vary, however rates from 0.5-5 Hz have been shown to have a small impact on disc stiffness[9]. The frequency of 3 Hz used in this trial fits within this range.

Many biomechanical trials work under the assumption that the spine completes 1-3 million cycles over a year, therefore 100,000 cycles represents 2 weeks of mobilization[80]. However a review of spinal testing methodologies suggested that cyclic loading should be carried out until displacement reaches a plateau[9]. By extending the duration of cyclic loading instrumentation failure may have occurred.

The axial compressive force on the lumbar spine in vivo is caused by the weight of the upper body, the load in L4/5 is 60% of the body weight[9]. The in vivo load on the lumbar spine is also dependent on the motion and position[9]. The applied load ranging from 500-950 N is representative of sitting relaxed to holding < 20 kg close to the body[9].

This study only applied axial force to the instrumented lumbar spine. The direction and magnitude of axial compression effects the mechanical and kinematic properties of motion segment[9]. A finite element study comparing load distribution following spinal osteotomy in healthy and osteoporotic bone found that the stress on vertebrae and instrumentation depended on the motion[81]. Therefore, no assertion can be made regarding the screw fixation under the full range of motion and forces which they would be exposed to in vivo. The differences in load distribution between instrumentation and bone were more pronounced as the degree of osteoporosis increased. Under each working condition (axial, lateral bending,

extension, flexion) overall the stress on the screws and rods was higher and on the vertebrae lower in osteoporotic bone than in healthy bone[81]. Therefore, there may be a higher risk of instrumentation failure and fracture in osteoporotic vertebrae. A combined loading protocol applying axial compression with lateral bending or axial rotation has been suggested to be more representative of in vivo motion[9].

However, an in vitro mechanical evaluation of a CFR/PEEK system applying force in compression, bending and torsion found that the rods withstood all directions. CFR/PEEK demonstrated superior endurance compared to the titanium system. Failure was observed under compression and static torsion due to slippage of screw rod link[82]. Further mechanical trials found that the stability and endurance of PEEK instrumentation was not significantly different to titanium instrumentation in any mode. The rods remained intact and attached to the screw. The leading cause of failure was rotation of the screw[7].

The biomechanical properties of the spine may change ex vivo. The human spine has been shown to with stand up to four freeze-thaw cycles without change to the mechanical properties[9]. However air exposure can result in tissue dehydration during biomechanical testing[9]. There have been attempts to reduce the effect of air exposure by wrapping specimen in saline soaked gauze, submerging or spraying specimen but there is no universally accepted protocol[9].

5.2. Biomechanical Evaluation of Pilot Hole Preparation

The preparation of the pilot hole influences the bone-screw interaction and the fixation of the pedicle screw in the vertebrae[18,59]. Different aspects of the pilot hole and instrumentation technique, such as diameter[18], tapping, insertion angle and depth[83] as well as inserting a pedicle screw without prior pilot hole creation[84] have been investigated.

Theoretically the use of a probe compresses the cancellous bone in the walls of the pilot hole, whereas the use of a drill removes bone. It is postulated that the increased amount of bone substance could improve the anchorage of pedicle screws. However the pedicle in osteoporotic vertebrae have a thinner cortex and significantly lower bone mineral density in the trabecular, subcortical and cortical bone[85]. Therefore, there may be less material available for compression in the pilot hole wall, which would reduce the theoretical benefits of using a probe.

The purpose of this investigation was to compare the effect of pilot-hole preparation using a curved thoracic probe or a 3.2 mm drill on pedicle screw fixation in the thoracic osteoporotic

spine through cranio-caudal cyclic loading. On average the pedicle screws inserted in pilot holes created with the thoracic probe withstood a higher number of cycles and had a higher maximum pull-out force to failure than those inserted in pilot holes created with the drill, however these results were not statistically significant. Therefore, the results do not support the hypothesis, that the use of a probe would increase pedicle screw fixation in comparison to a drill in osteoporotic vertebrae.

Pedicle screw fixation following pilot-hole creation with either a probe or drill has been compared through pull out testing in multiple biomechanical studies. But this was the first study to compare the influence of pilot-hole preparation with either a drill or a probe on pedicle screw fixation in osteoporotic vertebrae. A series of pull-out tests on transpedicular pedicle screws in thoracolumbar vertebrae (Th 10- L2) was conducted to compare the influence of the pilot-hole preparation with a probe or a drill. The two insertion techniques were investigated through an intraspecimen comparison, prior to instrumentation the vertebrae were inspected for bone disease, however BMD was not measured. The pull out strength of pedicle screws implanted in the pilot-holes, which were created by a probe, was 1.4% higher, but the difference was not statistically significant[58]. These findings correlate with the current study.

However a series of pull out tests in 10 non-osteoporotic thoracolumbar vertebrae (Th2-L5) found that 8 out of 10 pedicles inserted with a probe withstood a higher pull out force than those inserted with a 3.2 mm drill[86]. A one tailed paired t-test showed that probing had a significantly higher pull-out resistance than drilling ($p \leq 0.04$). The study received criticism for not using a two-tailed t-test, which would be better suited, and would have resulted in $p \leq 0.08$, which is generally considered not to be a significant difference[58].

A series of mechanical essays conducted in wooden, polyurethane and bovine bone test bodies found that the pull out strength was higher when drilling with a probe rather than a burr[53]. The bovine bone model used the femur and had the cortical bone removed, which may weaken the clinical application of the results, as the removal of the cortex reduces pedicle screw anchorage[87] and therefore limits is practical application. Furthermore, the models were non-osteoporotic.

A review of pedicle screw insertion techniques found that drills and probes are both routinely used during pedicle screw instrumentation, although the benefits and drawbacks of each technique have not been clearly established and therefore recommends using the technique the surgeon is more familiar with[59].

Biomechanical experimentation involving pedicle screw instrumentation often use pull out strength as a measure of fixation. However, pull out testing does not accurately represent the tridimensional forces acting on spinal instrumentation in vivo. Furthermore, pedicle screw pull out is a rarely observed failure mechanism in vivo, therefore the clinical application of the results obtained through pull out testing should be critically evaluated[88,89]. Stress shielding has been suggested as a screw loosening mechanism in non-osteoporotic[36] and osteoporotic[47] vertebrae. A more physiological way to investigate screw loosening may be cyclic loading with cranio-caudal loading representing flexion and extension[88].

Several of the afore mention biomechanical essays were conducted in non-osteoporotic vertebrae. Bone mineral density influences the biomechanics of pedicle screw instrumentation[19,49,90]. A correlation between BMD and pedicle screw stability has been observed in biomechanical trials using under cyclic loading[49] and pull out testing[83]. One trial found a correlation between BMD and pedicle screw stability under cyclic loading in the thoracolumbar spine and suggested that under a BMD of 80 mg/cm^3 the pedicle may be instable and additional stabilisation should be considered[4,49]. A biomechanical trial comparing the influence of various factors, such as BMD, insertion depth and insertion angle, found that BMD had the highest influence on pull out strength of pedicle screws[83].

The stability of pedicle screws was shown to be lower in vivo in osteoporotic vertebrae, with significantly higher rates of screw loosening in patients with lower BMD[19]. This clinical study also found that screw loosening was more common than screw pull out, further supporting that pull-out strength is not an accurate method for portraying pedicle screw fixation in vitro.
When applying pull out force to the rods in 4 different posterior fixation systems the pull-out resistance of screws in osteopenic vertebrae (BMD < 150 mg/ml) was lower than in normal bone (BMD> 150 mg/ml), with the different fixation systems achieving an average pull out strength approximately a quarter as high as the value in normal bone[90].

The influence of pilot hole preparation technique found in studies conducted in non-osteoporotic vertebrae may not be comparable to the results found in our trial, as the influence of BMD may surpass the effects of instrumentation technique.

DEXA is generally seen as the gold standard in diagnosing osteoporosis. However, it has been suggested that degenerative disease, vascular calcification and compression fractures lead to falsely elevated BMD measurements[63,91]. HU have been shown to correlate with T-

Scores in DEXA measurements, however the correlation is influenced by the devices used so there remains uncertainty about the cut-off values for osteoporosis[63,92].

The mean BMD in this mechanical trial was 107.9 HU. A retrospective study found that 110 HU and 135 HU at L1 had a specificity of 90% in determining osteoporosis and osteopenia respectively[93]. A systematic review suggested using 112.4 HU for osteoporosis and 118 HU for low BMD at L1[63], by these definitions the vertebrae used in the current trial would be osteoporotic. However, another study found different cut-off values for diagnosing osteoporosis for each lumbar vertebral body (L1 ≤ 110HU or L2 ≤ 100HU or L3 ≤ 85HU or L4 ≤ 80HU)[91] , which would not make the vertebral bodies used in this trial osteoporotic.

Furthermore, HU have been found to be effective at predicting the occurrence of osteoporosis related complications, such a screw loosening, cage sintering and postoperative fractures after ventral fusion[92]. A second further retrospective study found that patients with pedicle screw loosening had a mean BMD of 116,2 compared to 132 HU in patients without loosening[63]. It was suggested that HU should be considered in preoperative planning with further screw augmentation at HU < 120 and further stabilisation of Cages such endplate augmentation at HU < 180[92]. These studies support, that the vertebrae used in this trial had a reduced BMD and were there at greater risk of pedicle screw loosening.

Other techniques based on the theory, that compression of the surrounding cancellous bone would increase screw purchase have also been investigated, with varying results. Using a pedicle screw with a conical core and constant diameter compressed the bone between the threads and improved anchorage more than increasing the contact area between the screw and the bone[18]. Furthermore not tapping or under-tapping the pilot hole leaves more cancellous bone available to compress and was shown to be effective in improving pull-out in the osteoporotic lumbar spine but not in the thoracic spine[94]. Silva et al found that pilot-hole tapping reduced the pull out in healthy thoracic sheep vertebrae and polyurethane models[95].

A series of biomechanical tests examining the relative contribution of the pedicle and vertebral body to screw stability in normal and osteoporotic bone found that 60% of the pull-out strength and 80% of the cranio-caudal stiffness depend on the pedicle with the trabecular bone of the vertebrae only providing 15-20% of the pull-out strength[85]. This suggests that the contribution of the cancellous bone in the vertebrae to pedicle screw fixation may have been over estimated and provides a possible explanation as to why compressing the cancellous bone

may not significantly improve fixation. The cancellous bone mass lost by drilling may also not be a significant, because the cortex is more influential on fixation.

The influence of compacting the trabecular bone in the pilot hole may not be significant because the cortical bone has a higher influence on pedicle screw fixation. A series of pull-out tests and cranio-caudal and medial-lateral loading conducted in a finite element model of thoracic vertebrae supports the importance of the cortex for fixation[87]. Although the screw diameter had the largest influence on pull out, the fixation strength was also increased when less cortical bone was removed from the entry point and the screw threads started closer to the cortex[87]. This also correlates with the results of another series of pull-out tests, which found that although the technique used to prepare the pilot hole did not have a significant influence on pull out strength, damaging the perpendicular cortex did weaken pedicle screw fixation without significantly lowering it[58].

A computational model showed that the cortical bone has a large influence on the pull-out stiffness, with a large decrease in pull out strength when the cortex is removed. The stress in trabecular bone is concentrated in the bone surrounding the screw tip[71].

The importance of the cortex for achieving screw fixation is further supported by multiple biomechanical trials, which explored bicortical fixation. Bicortical fixation has been found to increase fixation in multiple studies[18,50,87]. A biomechanical trial found that increasing screw insertion depth increased the pull-out strength and decreased loosening under cyclic loading and that fixation was significantly better when the anterior cortex was engaged through bicortical fixation[50].

The cortical bone trajectory was developed to utilise the fixation of the cortical bone. The cortical bone trajectory achieved higher pull out and toggle resistance compared to the traditional trajectory[55].

5.3. Limitations

In general, there is not standardized protocol for biomechanical testing for instrumentation of the spine. This has resulted in different testing protocols being used[96]. A standardized protocol would increase the interstudy comparability. Often the protocols are based more on consensus rather than data.

The frequency and number of cycles conducted should be chosen to accurately represent a set period in vivo. The protocols used in these studies only apply to the short-term properties of the implants. The 100,000 cycles used in the first part of the study were assumed to represent two weeks of mobilization[80]. However, the 10,000 cycles of the second part would represent approximately 1.4 days. Other studies have suggested conducting 60,000 cycles to represent walking 1,000 steps/day in the first two months postoperatively until bony union occurs[88].

A further discrepancy between different protocols for cyclic loading in the spine is the frequency used. The average walking pace is between 1.4-2.1 Hz, which should be doubled as the spine is loaded during both foot strikes[9].

Ex vivo trials conducted using axial compression have used a wide range of loads[9]. The load applied to the pedicle screws should represent the physiological load experienced in normal daily activities, such as walking, in the post-operative period until bony fusion occurs to increase the clinical application. A review suggested using axial compressive loads of 460-530N in long term static testing[9]. The initial loads used in the first part of this study falls within this range, however there is a lack of consensus on the actual loads experienced in vivo.

During walking the spine experiences an axial fore and bending moment[88]. In both test series forces were only applied in the axial plane. Cranio-caudal force was used to represent flexion and extension[88,89], however it does not consider rotational or translational forces. When applying the forces experienced by screws during walking, most screws loosened by rotation or toggling, defined as a combination of translation and rotation[88]. This suggests that translation and rotation may be more important than axial strain to accurately portray pedicle screw failure in vivo. A review off spinal testing protocols suggested using combined loading protocols such as compression with bending or rotation during cyclic loading[9]. Nonetheless cranio-caudal loading is a more physiological representation of forces in vivo than pull out strength.

Pull out testing is generally seen as less accurate representation of the forces on the spinal instrumentation than loading protocols, as it does not accurately represent the tridimensional forces acting on spinal instrumentation in vivo and is a rare failure mechanism in vivo[88,89].

Most studies are conducted in multiple FSU, most frequently from L1-L5 and instrumenting the same levels in throughout the trial. However, some trials are conducted using single FSU[96]. The use of multiple FSU increases the number of variables; but it is also a better replication of the application in vivo.

Pedicle screw based spinal instrumentation consists of at least 4 screws connected via rods. However, the biomechanical testing in the second trial was conducted on individual vertebrae and applied force directly to each screw, not a screw-rod construct. It does not consider the vertebrae in context of the spine or the distribution of force within spinal instrumentation. Although the difference between the preparation techniques was not significant for individual screws, the summation within a construct was not calculated.

Furthermore, the motion at the tip of the screw is not equal to the motion of the head. The motion of the screw tip was 1.5 times larger than at the head, which reflects the clinical windshield wiper effect, which has been suggested as a mechanism for screw loosening in vivo[18,88]. An optical measurement system with optical markers can be utilized to measure screw displacement to further examine the loosening mechanisms of the screw[88].

Cadaver studies cannot fully replicate in vivo conditions. The biomechanical properties, such as ROM, neutral, hysteresis and stiffness, of the spine are also affected by temperature and humidity[9]. To reduce the influence of dehydration in in vitro testing specimens can be wrapped in saline soaked gauze, irrigated or conducted in 100 % humidity[9]. The material properties of spinal segments may be altered and impacted by freezing, however there is no significant difference in the material properties of spinal segments after freezing or in the 13 days following thawing[60].

The effect of osteointegration cannot be evaluated in ex vivo experiments. These results represent primary stability in the immediate post-operative time before osteointegration occurs and does not show the long-term viability of the implants. Post-mortem biomechanical and histological experiments have reported more bone on growth on more flexible titanium alloy screws than steel screws[52]. This correlation could be extrapolated to CF/PEEK screws, but the effects cannot be monitored ex vivo. Furthermore it, could also be seen as a worst-case scenario in which osteointegration does not occur.

The effect of stress shielding can also not be evaluated in ex vivo experiments. This is particularly important in the first trial as the CFR/PEEK has been stipulated to compare favourably to titanium regarding stress shielding due to its lower elastic modulus[64].

5.4. Conclusion

Achieving good results in osteoporotic patients remains a problem. Due to the increasingly aging population with corresponding higher rates of osteoporosis, the surgical treatment of osteoporotic patients is becoming more frequent. The associated difficulties include implant loosening, peri-implant fractures and poor bone healing.

With the advent of new materials such as CFR/PEEK there is an opportunity to create implants with superior biomechanical properties by adjusting the elastic modulus and improving osteointegration. The potential advantages of the mechanical properties were tested and shown to lead to a significant reduction in the cavity formation at the base of the screw and the total cavity but not at the tip or screw shaft. The osteointegration could not assessed in the ex vivo trial.

An effect of osteoporosis is the loss of bone substance. By creating the pilot hole with a probe, the bone substance is compressed rather than removed as it is with a drill. However, the single level intraspecimen trial did not show a significant difference in the rates of screw loosening when using a probe or drill.

Both mechanical trials used different protocols which shows weakness in the field of inconsistent methodologies. In general, a consistent protocol would increase the comparability between studies and help in the creation of guidelines for safety and efficacy recommendations for in vivo usage.

The use of CFR/PEEK needs further study in particular regarding the biological properties and in vivo application. The osteointegration and stability in osteoporotic bone should also be studied in further in vivo trials.

6. References

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7. Appendix

7.1. List of Figures

7.2. List of Tables

8. Previous Publications of the Data

Oikonomidis S, Greven J, Bredow J, et al. Biomechanical effects of posterior pedicle screw-based instrumentation using titanium versus carbon fiber reinforced PEEK in an osteoporotic spine human cadaver model. *Clinical Biomechanics* 2020; **80**: 105153.

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