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Department of Mechanical Engineering

**Expandable Fasteners for Orthopaedic Applications: Design and
Development of the EXF Screw**

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**This thesis is presented for the Degree of
Doctor of Philosophy
of
Curtin University**

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Declaration

To the best of my knowledge and belief this thesis contains no material previously published by any other person except where due acknowledgment has been made.

This thesis contains no material which has been accepted for the award of any other degree or diploma in any university.

Human Ethics: The research presented and reported in this thesis was conducted in accordance with the National Health and Medical Research Council National Statement on Ethical Conduct in Human Research (2007) – updated March 2014. The proposed research study received human research ethics approval from the Curtin University Human Research Ethics Committee (EC00262), Approval Number # SMEC-51-13.

Signature: .....

Date: 13/07/2017.....

Statement of Contributors

Mrs Intan Oldakowska

Intan is a fellow PhD student and my research colleague who has been involved in the same program of work towards developing the EXF Screw and exploring the performance of expandable fasteners.

Specifically she has been responsible for the mechanical testing literature review to determine the mechanical testing procedures for the pull-out testing (not contained within this thesis), as well as designing experimental testing rigs and conducting some of the mechanical testing of the prototype fasteners in collaboration with the author. She was also responsible for conducting the background IP Search for the second patent (Oldakowski, Oldakowska, Hardcastle, & Kirk, 2015).

Reference to her work has been included as future work, in particular to the mechanical testing in push-in and shear failure modes for the EXF Screw (not contained within this thesis). Intan is a listed inventor on all three patents (Oldakowski, Oldakowska, et al., 2015; Oldakowski, Oldakowska, Hardcastle, & Kirk, 2013) and a co-author on both papers (Oldakowski, Oldakowska, et al., 2016a; Oldakowski, Oldakowska, et al., 2016b).

Mr Philip Hardcastle

Mr Hardcastle, a retired spinal surgeon, was the original inventor of the SZ device concept (see Chapter 2 ('Project background')) and listed as an inventor on the first and second patents (Oldakowski, Oldakowska, et al., 2015; Oldakowski, Oldakowska, et al., 2013). However subsequent work involved significant inventive contributions from the author and other contributors. Throughout the project Mr Hardcastle has provided clinical consultation relating to spinal surgery. Mr Hardcastle was also a co-author on both papers (Oldakowski, Oldakowska, et al., 2016a; Oldakowski, Oldakowska, et al., 2016b).

Prof Brett Kirk

Professor Kirk is the primary academic supervisor and throughout the project has advised the direction of the technical work. He is a listed inventor on the first and second patents (Oldakowski, Oldakowska, et al., 2015; Oldakowski, Oldakowska, et al., 2013). He is a Chief Investigator on the NHMRC Development Grant and a co-author on both papers (Oldakowski, Oldakowska, et al., 2016a; Oldakowski, Oldakowska, et al., 2016b).

Dr Chris Ford

Dr Ford is the academic co-supervisor and throughout the project has advised progress relating to finite element analysis. He is an Associate Investigator on the NHMRC Development Grant and a co-author on both papers (Oldakowski, Oldakowska, et al., 2016a; Oldakowski, Oldakowska, et al., 2016b).

A/Prof Tim Sercombe

Associate Professor Sercombe is a collaborator at the University of Western Australia and throughout the project he has provided advice on Selective Laser Melting (SLM) manufacture and assisted the SLM manufacture of the prototypes. He is a Chief Investigator on the NHMRC Development Grant and a co-author on both papers (Oldakowski, Oldakowska, et al., 2016a; Oldakowski, Oldakowska, et al., 2016b).

Prof Gabriel Lee

Professor Lee is a neurosurgeon and one of the inventors of the gapless EXF Screw patent. Throughout the project he has provided clinical consultation relating to neurosurgery and suggested design modifications to the screw. He is a Chief Investigator on the NHMRC Development Grant and a listed inventor on the third patent (PCT stage).

Prof Markus Kuster

Professor Kuster is an orthopaedic surgeon and one of the inventors on the third patent (PCT stage). Throughout the project he has provided clinical consultation relating to orthopaedic surgery and suggested design modifications to the screw. He is a Chief Investigator on the NHMRC Development Grant.

Mr Rob Day and Mr Alex Hayes

Mr Day and Mr Hayes are collaborators from Royal Perth Hospital. Throughout the project they have provided technical advice on the academic work and helped immensely to guide the work towards rigorous and publishable results as well as helping with practicalities of mechanical testing. Mr Day is a co-author on both papers (Oldakowski, Oldakowska, et al., 2016a; Oldakowski, Oldakowska, et al., 2016b) and a Chief Investigator on the NHMRC Development Grant.

Professor Garry Allison

Professor Allison is an advisor to the project and one of the inventors listed on the third patent (PCT stage), he is a Chief Investigator on the NHMRC Development Grant and he has helped provide governance to the project.

Abstract

Screw fixation failure is a significant clinical problem in many orthopaedic surgeries which can cause severe health complications for the patient and necessitate a costly and technically demanding revision surgery. Expandable screws have previously demonstrated the potential to increase fixation strength, especially in osteoporotic bone. However previous expandable screws have not been extensively adopted. Based on market research and analysis conducted in this thesis, it is hypothesised that this is due to surgeon's concerns about removability, especially during revision surgery when bone has potentially grown into the expansion mechanism preventing the contraction that is required for removal. Additionally there is a paucity of studies in the literature investigating the fundamental science behind expandable fasteners, possibly due to the commercially sensitive nature of developing technology.

The aims of the project were to firstly explore the potential to improve surgical outcomes with removable expandable screws in novel applications such as proximal humerus fracture fixation and posterior cervical fusion and investigate the effect of the expandable fastener design parameters and bone quality on the performance of expandable fasteners. Secondly to develop a novel expandable orthopaedic screw (the 'EXF Screw') that can be removed during revision surgery, optimise the design and perform proof-of-concept testing to demonstrate increased fixation strength, acceptable fatigue strength, the potential for removability and manufacturability.

The Unthreaded Expandable Fastener (UEF) was an early prototype that was designed for lateral mass fixation in the cervical spine and was tested in axial pull-out from ovine thoracic bone samples. This study demonstrated a statistically significant increase in pull-out strength (41%) and failure energy (222%) compared to conventional screws. High Resolution Computed Tomography (HR-CT) was used to analyse the microstructural properties of the bone samples to determine the effect of bone structural properties on fixation strength. This indicated that the UEF samples had a smaller critical volume of bone that affected failure force and that the failure force of the UEF samples was less sensitive to a reduction in cancellous bone quality and cortical thickness than the conventional screws.

HR-CT was also used to analyse human cervical vertebrae to investigate conventional and novel screw trajectories for expandable screws to determine potential limitations of screw expansion size in the cervical spine. Conventional screw trajectories for the lateral mass were demonstrated to be not suitable for expandable screws, as the screw remained adjacent to the cortical shell throughout the trajectory. However the Roy-Camille and Magerl trajectories could be modified to pass through the centre of the lateral mass, providing maximum allowable expansion size and maximum allowable depth of expansion respectively. This study also demonstrated that the vertebral body, through a standard anterior approach, had a much greater potential for expansion than the lateral mass.

Industry and clinical feedback after the above studies were completed, shifted the focus of the project from posterior cervical fusion to trauma fractures. Proximal humerus fracture plate fixation was identified as a commercially viable, unmet clinical need that was suited to the application of expandable screws. New designs of a threaded expandable screw (the EXF Screw) were developed focussing on two objectives. Firstly, on removability by minimising the size of any gaps on the outside of the expanded screw, to prevent bone from growing inside and jamming the expansion mechanism, preventing the contraction required for removal. Secondly, minimising the risk of complicated surgery by reducing the expansion force and ensuring elastic response to the closed orientation for removal. Throughout the project, three patents were filed to protect the intellectual property generated by the project and therefore its commercial viability.

Mechanical testing of the EXF Screw in synthetic bone foam demonstrated that increasing expansion size and increasing the width of the expanding tabs (and therefore the amount of the screw that expanded) increased pull-out force but that expansion angle did not significantly affect failure force for the range of angles tested. Furthermore, for the maximum expansion size to ensure functionally gap-less expansion, it was demonstrated that expansion tab width did not affect failure force. Additionally, increasing the pilot hole size decreased the performance of the expandable screws less than conventional screws, demonstrating that expandable screws may perform better in oversized pilot holes, as found in revision surgeries but may not provide a significant increase in fixation strength in severely undersized pilot holes.

To the author's knowledge, this is the first study to investigate the effect of design parameters on the performance of expandable screws and the first to indicate that the compression at the screw thread and bone interface due to the expansion may be the primary mechanism of increased fixation strength. The prime EXF Screw design demonstrated significantly increased fixation strength of up to 53% and significantly increased failure energy of 175% compared to an equivalent conventional locking screw in synthetic bone using the screw manufacturers recommended pilot hole size.

Mechanical testing also demonstrated that, like conventional screws, the failure stiffness of expandable screws is significantly correlated to the failure force. However, linear elastic Finite Element Models (FEMs) of the fixation stiffness do not take into account the effect of pilot hole size and the subsequent compression of the bone which has a significant effect on performance. Consequently the conventional methodology used in the literature for predicting failure force of screws (by predicting fixation stiffness) is not suitable for assessing the performance of expandable screws.

Finite Element Analysis (FEA) of screw breakage under cantilever bending demonstrated that for most of the EXF designs investigated and for typical worst case proximal humerus screw dimensions and loading conditions, maximum stress occurs at the head of the screw (at the junction of the screw and plate) and not in the expandable section of the screw (the tip). This is due to the increased moment arm at the head of the screw compared to the tip. However for the general case of expandable screws, decreased stress could be achieved by using large radius fillets, decreasing the height and width of the expansion tabs or using a stiffer or higher diameter expansion pin to more effectively share the load across the pin and screw. Multiple expansion levels and staggering the expansions significantly increased the stress in the expandable section of the screw by increasing the effective moment arm of the applied force.

Prototypes for mechanical testing were manufactured from Ti-6Al-4V, a titanium alloy widely used for medical implants, using Selective Laser Melting (SLM). The functional fidelity of geometric test parts was analysed using High Resolution Computed Tomography (HR-CT) to determine the design limitations for geometry specific to the EXF Screw. In particular, thin slots to allow relative movement but prevent bone in-growth between the expansion tabs and the screw body and high tolerance holes for the expansion pin. The thinnest slot with negligible erroneous connectivity across the slot was 90 μm , which had some theoretical potential for bone in-growth. Holes manufactured by SLM required a clearance that ranged between 114-198 μm for the range of hole diameters tested (2.125-2.300 mm).

The above results provide the proof-of-concept for the EXF Screw project. A subsequent study was granted funding (National Health and Medical Research Council Development Grant ID: 1121702) to perform all the benchtop and animal studies required for a first in human clinical test and a regulatory approval submission. The project is also in the process of raising capital to fund business development activities in order to achieve a translational and commercial outcome.

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The Australia New Zealand Orthopaedic Research Society for providing me with a bursary to present my work at their annual conference.

The Australian Microscopy and Microanalysis Society for providing me with a bursary to present my work at their annual conference.

Dedication

This thesis is dedicated to my loving and supportive family.

Especially Intan, the platonic form of an ideal partner, in both life and work, whose patience is unlimited, diligence is unparalleled and without whom there is no possibility this thesis would have been completed or that my life would have half of the joy and happiness that it does. Many times I felt like everything was lost and each time, with her boundless ingenuity and endless enthusiasm, she always showed me the way forward and helped me take the next step.

But also my parents Annette and Peter, who raised me, have always loved and supported me unconditionally and helped me to become the best person that I can be, which I appreciate deeply. And my other parents, Yoyok and Adji who have always shown deep love and affection towards me and allowed me to become a part of their family. Their hard work and enterprising spirit have constantly inspired me to seek out difficult challenges, to never give up in the face of adversity and work hard to create something that I can be proud of.

Lastly, Marcus, who I hope will stay as curious, tenacious and intrepid as he is at three years old. I hope you will always remember that we love you.

Achievements

As a result of this work:

1. two journal publications were published (Oldakowski, Oldakowska, et al., 2016a; Oldakowski, Oldakowska, et al., 2016b);
2. four podium presentations were performed (Australian Orthopaedic Association WA Chapter AGM 2015 & 2016 and Western Australian College for Physical Scientists and Engineers in Medicine WA Annual Scientific Meeting 2012 & 2015);
3. three posters were presented (Oldakowski, Hardcastle, Kirk, Oldakowska, & Medway, 2013; Oldakowski, Oldakowska, Ford, & Kirk, 2016; Oldakowski, Oldakowski, Lee, & Kirk, 2015)
4. three patents were filed, with two in National phase (Oldakowski, Oldakowska, et al., 2015; Oldakowski, Oldakowska, et al., 2013) and one still in the PCT phase;
5. an NHMRC development grant (ID: 1121702) was awarded for \$414,000 over three years (2017-2019); and
6. an MRCF Investment proposal was submitted and progressed to due diligence but was ultimately unsuccessful with capital raising currently in progress with other investors.

This work has won the following awards:

1. Winner of the 2015 Best Presentation Award at the Australasian College of Physical Scientists and Engineers in Medicine (WA) Annual Scientific Meeting;
2. Runner up of the 2013 Curtin Innovation Awards; and
3. Winner of the 2013 Best Presentation Award at the Curtin University School of Civil and Mechanical Engineering Postgraduate Colloquium.

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List of Abbreviations

ACCF	Anterior Cervical Corpectomy and Fusion
ACDF	Anterior Cervical Discectomy and Fusion
AO/ASIF	Association for Osteosynthesis/Association for the Study of Internal Fixation
ASTM	American Society for Testing and Materials
AVN	Avascular Necrosis
BS/TV	Bone Surface Area
BVF	Bone Volume Fraction
BMD	Bone Mineral Density
CAD	Computer Aided Design
CMCA	Centre for Microscopy, Characterisation and Analysis
CT	Computed Tomography
EXF Screw	Product name
FDA	Food and Drug Administration (American regulatory body)
FEA	Finite Element Analysis
FEM	Finite Element Modelling
HA	Hemi-Arthroplasty
HR-CT	High Resolution Computed Tomography
IAF	Investment Application Form
IM	Intramedullary
IP	Intellectual Property
LAF	Large Animal Facility

MRCF	Medical Research Commercialisation Fund
NHMRC	National Health Medical Research Council
ORIF	Open Reduction Internal Fixation
PCT	Patent Cooperation Treaty
PIP	Preliminary Investment Proposal
PMMA	Poly Methyl MethAcrylate
RPH	Royal Perth Hospital
rTSA	Reverse Total Shoulder Arthroplasty
SFDA	Chinese State Food and Drug Administration
SLM	Selective Laser Melting
SMA	Shape memory alloy
SMI	Structural Model Index
Tb.N	Trabeculae Number
Tb.Sp	Trabeculae Spacing
Tb.Th	Trabeculae Thickness
TSA	Total Shoulder Arthroplasty
TSF	Thread Shape Factor
UEF	Unthreaded Expandable Fastener
UWA	University of Western Australia
VOI	Volume Of Interest

Chapter 1 Introduction

Orthopaedic screws are used in most orthopaedic surgeries to attach implants, such as rods and plates, to bone in order to fixate fractures or fuse joints. However if the bone quality is too poor due to osteoporosis or a severe fracture, screw fixation can fail causing the screw to loosen, cut-out or pull-out of the bone, usually necessitating a revision surgery. In some surgeries, such as proximal humerus fracture fixation with plate and screw systems, screw fixation failure related complications are the most common reason for a revision surgery (Sproul, Iyengar, Devcic, & Feeley, 2011) and consequently, in these surgeries, increasing fixation strength can reduce complications and the subsequent revision rate for these patients.

Expandable screws have previously demonstrated increased fixation strength leading to a reduction in patient complications (Wu et al., 2012) and several devices have CE Mark regulatory approval and are therefore commercially available in Europe, including Osmium (Rohl, Ulrich, Huber, & Morlock, 2009), X-Ped (Chen et al., 2014), Osseoscrew (Vishnubhotla, McGarry, Mahar, & Gelb, 2011) and X-Bolt (O'Neill et al., 2013). However these expandable screws have only been adopted by a minority of surgeons and are typically only used for severely osteoporotic cases or as a 'rescue screw' in revision surgery after previous screws have failed. Advice from surgeons, informally and through surveys (Appendix A) and implant manufacturing companies, through discussion and formal support letters (Appendix B) suggest that the slow uptake of this technology is due to concerns about removability.

The author conducted a written survey of 11 surgeons that were not connected with the project to better understand clinician's attitudes to expandable fasteners in the primary application for the EXF Screw, proximal humerus fractures. Table 1 below summarises the results, with the full results detailed in Appendix A.

Table 1 A summary of the critical results from the EXF Voice Of Customer Surgeon survey

Questions	Yes or likely		maybe		unlikely or no	
	Increased fixation strength improves surgical outcome?	7	63.6%	2	18.2%	2
Increased fixation strength reduces the rate of revision?	6	54.5%	4	36.4%	1	9.1%
Increased fixation strength reduces screw overpenetration risk?	5	45.5%	4	36.4%	2	18.2%
Would you consider using an expandable screw with positive pre-clinical data?	10	90.9%	0	0.0%	1	9.1%
Would expandable screws improve rehabilitation?	4	36.4%	4	36.4%	3	27.3%
Would using expandable screw allow you treat more patients with ORIF?	4	36.4%	5	45.5%	2	18.2%
	Critical or important		Neutral		Unimportant or irrelevant	
How important is removability?	8	72.7%	3	27.3%	0	0.0%

Six surgeons said that removability was ‘critical’ and two said it was ‘important’, with the remaining three saying that it was ‘neutral’. Removal of existing expandable screws is especially difficult during revision surgery after bone has grown into the expansion mechanism, preventing the contraction of the expandable screw that is required for removal. There have been documented cases of the screw breaking during failed contraction or removal whilst partially expanded and the bone fracturing during removal (Wu et al., 2012). Furthermore the X-Bolt, a commercially available expandable screw, has a procedure detailed the surgical technique guide in case the X-Bolt breaks during removal (X-Bolt Orthopaedics, 2014).

These concerns could be addressed by creating an expandable screw with minimal gaps for the bone to grow into, that can consequently contract automatically after the expansion pin has been removed (either under elastic response or under a removal torque) even after it has been in the bone for a long period of time. Consequently an expandable screw that increases fixation strength with only minimal change in operating procedure (screwing in and screwing out the expansion pin during implantation and removal) will be an attractive proposition to surgeons and can potentially improve surgical outcomes for patients who currently have a high risk of screw fixation related complications.

In the survey, 10 of 11 surgeons responded 'yes' or 'likely' to the question of 'would you consider using a *removable* expandable screw with positive pre-clinical data?' The other surgeon responded 'unlikely' due to a lack of confidence that increased fixation strength would significantly improve surgical outcomes due to the confounding influence of fracture types and bone quality in proximal humerus fractures.

In this dissertation the central thesis is that removable expandable fasteners can reduce risk of fastener fixation failure in a large number of orthopaedic surgeries that have a significant unmet clinical need in a way that can be commercially attractive to both implant manufacturers and payers (insurance companies and health systems) and functionally attractive to surgeons. Consequently the aim was to explore the potential of expandable fasteners in different orthopaedic applications, understand the design, manufacturing and performance constraints and develop such an expandable fastener towards commercialisation.

Developing a novel orthopaedic fastener is a complex project comprising a series of diverse investigations which must be completed to reduce the risk involved in a project and demonstrate to potential investors and ultimately commercial implant manufacturers that the fastener has the potential to measurably improve clinical outcome (i.e. lower revision rate, reduce cost, etc.). This provides the justification that the cost of taking the project through detailed development, regulatory approvals and clinical trials is worth the potential reward in terms of increased market size or share or the ability to charge a product premium. These investigations include:

1. Generating enforceable intellectual property;
2. Determining the primary application;
3. Defining the competitive advantages;
4. Determining surgical technique;
5. Refining manufacturing process;
6. Optimising the design; and
7. Demonstrating proof-of-concept.

Generating enforceable intellectual property

Any novel medical device must be supported by robust Intellectual Property (IP) to ensure that an implant manufacturing company is able to have exclusive use of the technology for a substantial period. This is required to offset the significant development cost which includes the extensive clinical trials necessary to gain reimbursements from insurance companies and health departments, the cost of redesigning the implants and surgical tools and setting up new manufacturing processes. Although there are other methods of IP protection (trademarks, industry secrets, etc.), in the orthopaedic industry patents are the most robust method of protection. In order to be patented the IP must be both inventive and novel. During the course of this project three patents have been filed, two of which are in the national phase (Oldakowski, Oldakowska, et al., 2015; Oldakowski, Oldakowska, et al., 2013) with the PCT recently filed for the third patent but is not yet published (Appendix G). A patentability analysis can be found for each design process iteration in Chapter 4 ('Design of the EXF Screw').

Determining the primary application

Determining a suitable primary surgical application for a novel medical device is critical. However, because the EXF Screw is a platform technology that can potentially be applied to many orthopaedic procedures, it is a complex decision that depends on many factors (which may vary for each application) including:

1. Attractiveness of the competitive advantage;
2. Size of the market;
3. Risks in regulatory approvals process and clinical trials; and
4. Competition and market trends.

Preliminary work in this thesis investigated screw fixation in the lateral mass of the cervical spine and for the anterior cervical discectomy and fusion procedure as the main indications. However, the feedback that was received through consultation with a range of surgeons, biomedical engineers and industry experts indicated that the clinical problem is not significant enough and that spinal surgeries are high risk for novel technology (risk of neural damage and mortality) and involve long clinical trials (to determine the long term outcomes of the spinal procedure) which makes a less attractive investment opportunity.

Throughout the project suggestions were received from a number of industry and academic sources that proximal humerus fracture fixation surgery has a significant clinical unmet need, with a 14% revision rate in the general population (Sproul et al., 2011). Additionally, there is a solid market size (approximately US\$332M in the United States based on the calculation in Chapter 3 ('Literature review') in Section 3.4 ('Orthopaedic screw failure modes')), creating a potentially attractive investment opportunity. Subsequently, the project changed focus to proximal humerus fracture fixation for commercialisation. Detailed discussion on the potential applications and their suitability to expandable fasteners can be found in Section 11.4.4 ('Future potential indications').

Defining the competitive advantages

Defining the competitive advantages of the EXF Screw is also a complicated decision, in that the increasing fixation strength can be used to:

1. Reduce the risk of fastener fixation failure;
2. Reduce fastener length;
3. Reduce fastener diameter;
4. Vary the screw trajectory into weaker bone; or
5. A mixture of the above.

The decision as to which aspect of potential advantage to pursue depends on the magnitude of the performance increase of the expandable fastener compared to conventional screws, the primary surgical application, the target patients (elderly patients, elite athletes, etc.) and surgeon and implant manufacturer preference. Surgeon surveys (Appendix A) and literature on the incidence of various complications (see Chapter 3.2 ('Literature review: Proximal Humerus Fracture Fixation')) were used to determine which competitive advantage to pursue for the primary applications.

For the initial spinal fixation application, axial pull-out strength was the main parameter to define competitive advantage as this is the main mode of screw failure clinically and reducing the screw length to minimise the risk of over-penetration was the main competitive advantage. However for the subsequent primary indication of proximal humerus fracture fixation, resistance to push-in and shear through the bone are the main parameters to define competitive advantage as these modes of failure are the main cause of screw related complications and revision surgery. The design and testing methodology developed within this thesis are based on optimising the performance in these modes of failure and demonstrating the competitive advantage.

Determining surgical technique

Expandable screws may require alternative screw trajectories and therefore surgical implantation procedures depending on the design of the screw, especially where the length or diameter are different to conventional screws and the expansion is large. This was the case in the preliminary applications (cervical anterior and lateral mass fixation) and so the possible entry points and angulations throughout the cervical spine were investigated using High Resolution Computed Tomography (HR-CT) to analyse cleaned, human bone specimens in Chapter 9 ('Feasible expansion size for expandable screws in the posterior cervical spine'). This work was done in collaboration with Professor Gabriel Lee, a neurosurgeon at St John of God Hospital, Subiaco.

Refining manufacturing process and selecting a material

Manufacturability is a challenge for the EXF Screw due to its innovative design and unconventional manufacturing method. Consequently significant work was done within the thesis to evaluate the ability of Selective Laser Melting (SLM), a 3D printing process, to create the functional geometry required for the EXF Screw designs including minimising the width of functional slots and minimising the clearance around holes. This work can be found in Chapter 8 ('Design constraints for selective laser melting manufacture of the EXF Screw') and was done in collaboration with Associate Professor Tim Sercombe at the University of Western Australia using the Realizer100 SLM.

Optimising the design

Given that the surgical application, the competitive advantage and the surgical technique have been chosen, then suitable designs must be selected based on the design constraints and then optimised based on the design criteria. The final design was determined in the design process detailed in Chapter 4 ('Design of the EXF Screw'). Design optimisation was performed based on data provided by mechanically testing design variants in synthetic bone foam in Chapter 6 ('Effect of design parameters on mechanical performance of the EXF Screw') and using Finite Element Analysis in Chapter 7 ('EXF Screw breakage strength') to determine the effect of design variation on predicted fatigue strength.

Demonstrating proof-of-concept

In order to demonstrate Proof-of-concept, the EXF Screw must have superior mechanical performance to an equivalent screw whilst still being removable and sufficiently strong to survive physiological loading. Superior mechanical performance was demonstrated by testing the EXF Screw in synthetic bone in Chapter 6 ('Effect of design parameters on mechanical performance of the EXF Screw') and testing an early unthreaded prototype in ovine bone samples in Chapter 5 ('Preliminary UEF pull-out strength testing').

Suitable static strength was investigated using Finite Element Analysis in Chapter 7 ('EXF Screw breakage strength'). Finally, the feasibility of removability was investigated by empirical testing in Chapter 8 ('Design constraints for selective laser melting manufacture of the EXF Screw') to determine whether a high fidelity gap could be created that had no potential, theoretical bone in-growth.

The competitive advantage of the EXF Screw is its anticipated performance in poor quality, osteoporotic bone. Also because the screw may be implanted in different screw trajectories, the bone quality may vary. For this reason it was critical to investigate the effect of bone morphology parameters, related to osteoporosis, on the fasteners mechanical performance. This work can be found in Chapter 5 ('Preliminary UEF pull-out strength testing').

Many of the investigations conducted within this thesis were designed to address and minimise risk identified in the commercialisation of the EXF Screw. However literature on the basic science of expandable screws in orthopaedic is sparse. This is possibly due to the commercially sensitive nature of the work performed on potential orthopaedic products. The literature on expandable screws in orthopaedics is reviewed in Chapter 3 ('Literature review') in Section 3.7 ('Expandable orthopaedic fasteners'). However the following questions are not adequately addressed by the literature and so consequently were investigated and are reported in this thesis:

1. How does the failure mode of expandable fasteners and expandable screws vary compared to conventional screws and what consequence does this have for their application?
2. How do generic design parameters affect the pull-out force of expandable screws?
3. Are finite element methods previously used to determine screw pull-out force appropriate for expandable screws?
4. Do screws with expandable screw have significantly decreased fatigue strength and what design parameters effect fatigue strength?

5. What are the potential anatomical limits for the expansion size of expandable screws?

Chapter 2 Project background

SZ Dynamic Stabilisation

The project was initiated in early 2012 when Professor Philip Hardcastle, a retired orthopaedic spinal surgeon and adjunct Professor at Curtin University, contacted Professor Brett Kirk (the primary academic supervisor for the project) with an idea for a novel orthopaedic implant that would provide dynamic stabilisation in the cervical spine. Dynamic stabilisation is a method whereby a spinal joint is stabilised without eliminating movement, as is typically the case in the conventional spinal fusion surgery (Ianuzzi et al., 2010; St-Pierre, Jack, Siddiqui, Henderson, & Nataraj, 2016). Prof Hardcastle noted that although there were dynamic stabilisation devices in the lumbar spine such as the Dynesys system (Figure 2-1) there was not yet a device that could provide dynamic stabilisation to the cervical spine through a posterior approach. The Dynesys system (Figure 2-1) is composed of an inner polymeric cable and an outer polymeric tube. Under flexion (forwards movement of the back) the cable provides a small stretch and under extension (backwards movement of the back) the tube compresses allowing limited movement (Ianuzzi et al., 2010).



Figure 2-1 The Dynesys system, a dynamic stabilisation device for the lumbar spine (Ianuzzi et al., 2010)

Professor Hardcastle hypothesised this was due to the small size of the cervical spine, thus increasing the design complexity, and the reduced market size compared to the lumbar spine due to smaller surgical volume. Furthermore he understood that a cervical dynamic stabilisation device would need high fixation strength to resist the dynamic loading, which is higher than fusion loading (Meyers et al., 2008) and so he also described a conceptual ‘expandable bollard’ which he suggested may be able to provide higher fixation strength than conventional screws. Prof Hardcastle’s preliminary sketches can be found in Figure 2-2 below. The provisional name for the device and the project was the SZ device, coming from the ‘S’ or ‘Z’ shape that Prof Hardcastle envisaged for the elastic element between the screws that provided dynamic stabilisation.

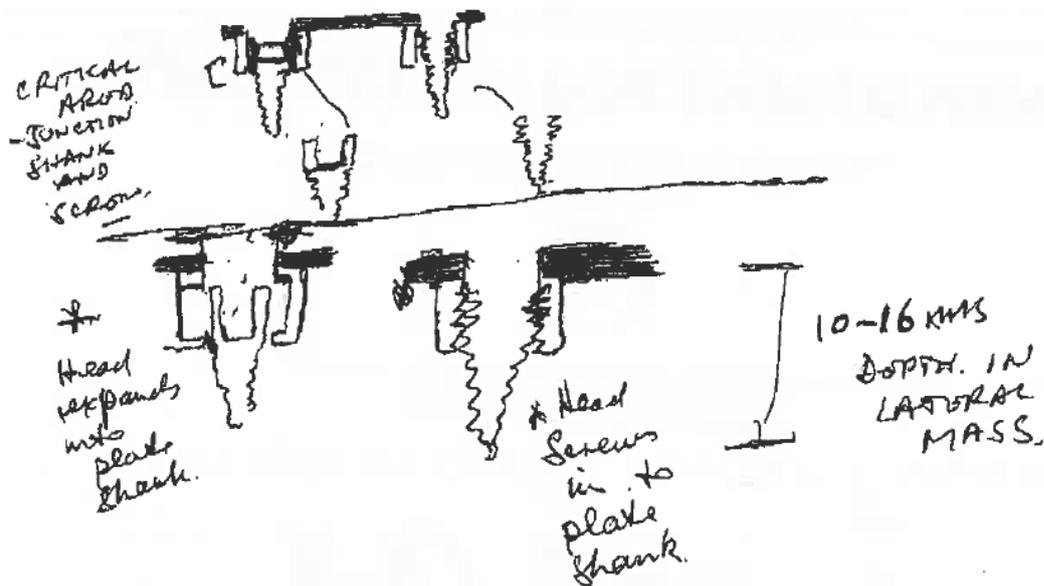


Figure 2-2 Professor Hardcastle’s initial design

After going through extensive concept design and then evaluating the intellectual property landscape, it was determined that several novel design features had been invented. This resulted in a patent submission (Oldakowski, Oldakowska, et al., 2013). The central claims of this patent were that with integral expandable fasteners the SZ device could be a single-part unit that might reduce the complication of surgery (Figure 2-3 left) and that the SZ device could provide an adjustable range of dynamic motion during stabilisation by allowing the surgeon to control the range of motion by adding or removing end-stop pins (Figure 2-3 right).

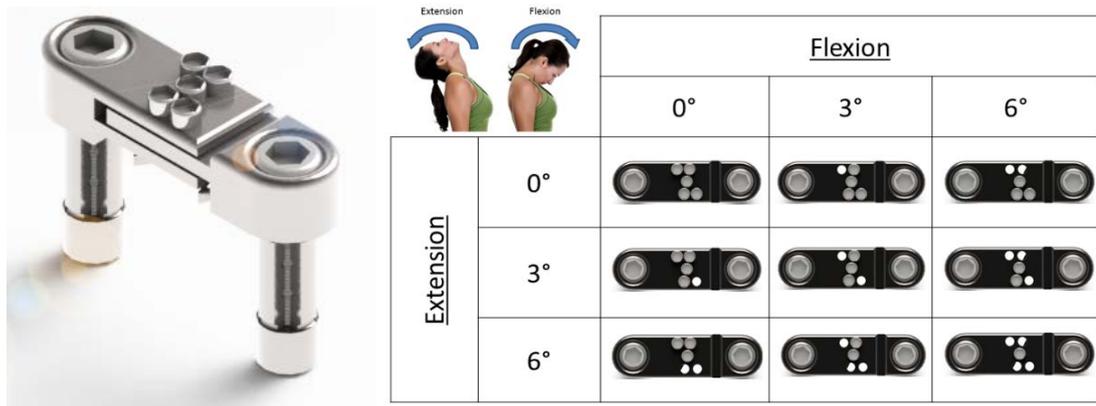


Figure 2-3 A prototype of the SZ device demonstrating the integral one-part construction (left) and the adjustable range of motion mechanism using a pin-in-slot system, where the surgeon can control the range of motion in flexion and extension by adding or removing end-stop pins (right)

A postal survey was mailed out to a number of senior, orthopaedic surgeons in Perth to obtain feedback on the concept of the device (Appendix C). The feedback received was on balance positive (three answered ‘yes’, three answered ‘maybe’ and two answered ‘no’ to the question “Is dynamic stabilisation advantageous for the cervical spine?”), demonstrating that some surgeons were receptive to dynamic stabilisation in the cervical spine. However surgeons were concerned and sceptical about the removability of expandable fasteners in general.

In 2013 Mrs Intan Oldakowska, another PhD student, joined the project initially to develop the expandable fasteners for the SZ device and later focusing on the mechanical testing of the EXF Screw. All subsequent commercialisation work was done in collaboration with her. Her work is explicitly outlined in the Statement of Contributors and referenced in the text where appropriate.

In 2013 the SZ project was presented to the Curtin Commercialisation Advisory Board for the innovation awards and was awarded runner-up with a \$7500 prize and \$5000 of in-kind commercialisation services. The in-kind services were used to create a Commercialisation Australia ‘Skills and Knowledge’ grant application which was never submitted due the federal program being discontinued without notice.

Whilst presenting a poster (Oldakowski, Hardcastle, et al., 2013) (see Appendix D) about the SZ device concept (Figure 2-3) at the International Society for Technology in Arthroplasty (ISTA) conference in 2012, feedback was obtained from several industry experts that dynamic stabilisation was currently commercially unattractive because of lack of support for the technology from the Food and Drug Administration (FDA) in the United States. Stryker, a large implant manufacturing company, revealed that they had invested heavily in IP surrounding dynamic stabilisation which was not commercially viable to develop because of the regulatory hurdles imposed by the FDA. This sentiment was further supported by the Medical Research Commercialisation Fund (MRCF), who were pitched the SZ concept, gaining external advice about dynamic stabilisation and declining to continue the investment process because of the significant commercial risk involved. Detailed discussion of the design of the SZ device can be found in Chapter 4 ('Design of the EXF Screw') in Section 4.1 ('SZ – Dynamic Stabilisation Device').

UEF – Unthreaded Expandable Fastener

As the technical work up to this point had focused mostly on the expandable fastener aspect of the SZ device, the expandable fasteners as a stand-alone device became the focus of the project going forward. Since the filing of the first patent (Oldakowski, Oldakowska, et al., 2013) additional novel features had been developed for the fastener specifically, and so consequently another patent was filed in order to ensure robust IP protection and continued commercial viability of the project (Oldakowski, Oldakowska, et al., 2015).

In 2014 Professor Gabriel Lee, one of the surgeons that had participated in the postal survey, contacted the team to get more information about the project. After a preliminary meeting with Professor Lee, a collaboration was established and he suggested that the majority of modern posterior fusions used polyaxial screws and fusion rods rather than screws and plates. This was because of the variability of the screw insertion points precluding the use of a plate or integrated device where the fastener points were rigidly defined, as was envisaged for the modified fusion SZ device. Professor Lee also suggested that anterior cervical or the lumbar spine might be a more suitable location for the expandable fasteners.

With the help of Professor Lee, a meeting was organised with Dr Hassan Serhan, a Distinguished Engineering Fellow of DePuy Synthes who provides technical advice to the major implant manufacturing company. The expandable fastener project was presented to him and he confirmed in a support letter (see Appendix B) that:

1. the expandable fastener meets an area of unmet need in the cervical spine;
2. a device which achieves better fixation, possible with reduced dimensions can improve clinical outcomes and reduce complications of screw misplacement;
3. although there were other expandable fasteners on the market, none of them were removable and this limits surgical uptake; and
4. Depuy Synthes would be interested in an on-going relationship or research collaboration in the future.

Consequently DePuy Synthes provided 25 lateral mass screws for comparative testing at a market value of approximately US\$25,000.

With the support of a number of additional clinicians as well as industry support, an NHMRC Development Grant was submitted to secure funding for future pre-clinical development of the EXF Screw. Feedback was received on the grant proposal and the main criticisms were that the team lacked the necessary academic and commercial experience. As per the protocol, a rebuttal was written to address these concerns but was ultimately unsuccessful.

In August 2015 the project was presented to the Australian Orthopaedic Association (WA) annual scientific meeting and unanimous feedback was received that in general surgeons were unwilling to use expandable fasteners that increased the difficulty of removal. Although removal using elastic response and a hypothetical un-expansion tool were discussed with them, they asserted that once bone had grown into the mechanism of the fastener, it would no longer be able to be fully contracted for removal. This was confirmed by reports of other expandable fasteners that are already in the market not being fully removable, even though they are able to be contracted outside of the bone (Chen et al., 2014; X-Bolt Orthopaedics, 2014). Detailed discussion of the design of the UEF can be found in Chapter 4 ('Design of the EXF Screw') Section 4.2 ('UEF – Unthreaded Expandable Fastener').

EXF Screw

Based on further discussions it was decided that the primary hurdle to adoption for expandable screws in the orthopaedic applications was removability and that consequently to be successfully adopted, expandable screws needed to prevent the in-growth of bone into the fastener through some mechanism. This led to the invention of a 'gapless expandable' screw (the EXF Screw), whereby the screw expands but without leaving any gaps for bone to grow into. This resulted in the submission of a third patent (PCT publication date September 2017 with full text in Appendix G).

In late 2015, Professor Markus Kuster, an orthopaedic surgeon with an extensive history of commercial achievement joined the team. Although he was unable to comment on the use of the fastener in the spine, he supported the use of the expandable fasteners in proximal humerus and proximal femur fractures.

Based on the renewed commercial potential of the project Curtin provided funds to engage Ian Brown, a commercialisation consultant to work on the project. Through his contacts the team met with Professor Philip Proctor, an ex-Stryker executive who suggested proximal humerus fractures as an ideal primary application for the project given the solid market size, strong unmet clinical need related to poor fixation and the reduced follow-up time required for a clinical trial. The attractiveness of the proximal humerus application was also supported by a number of orthopaedic shoulder surgery specialists in Perth. Additionally the team contacted Professor Gordon Blunn and Professor Allen Goodship, world experts on orthopaedic implants from the University College London and they confirmed that fragility fractures (shoulder, wrist and hip fractures) were ideally suited to the EXF Screw.

EXF Screw Project Future Funding

Based on the new 'gapless' EXF Screw, with further commercial support and a team with the required academic and commercial experience, the NHMRC development grant was resubmitted for the EXF Screw with gapless expansion focusing on proximal humerus fractures and anterior cervical corpectomy and fusion applications (see Appendix E) in March 2016. This grant was successful and funding commenced in 2017 for three years to fund the pre-clinical testing of the final EXF Screw design. Details of this grant scope of works can be found in Chapter 11 ('Future work') in Section 11.4 ('EXF Screw project').

With the new EXF Screw direction, contact was reinitiated with the MRCF and based on meetings with their representative in Perth, Dr Kath Giles. The project was then invited to submit a preliminary investment proposal (PIP) which was presented at the national board meeting. Based on the positive feedback on the PIP we were invited to submit a full Investment Application Form (IAF) and present to the board for investment (see Appendix F). To support the commercial and technical work necessary to prepare for this pitch the project was awarded \$53,000 from the Curtin Commercialisation Advisory Board. The team submitted the IAF and presented the project to the board of investment on the 30th August 2016 and were successful in progressing to the due diligence phase. However ultimately the MRCF declined to invest and so the project is currently seeking funding from other sources.

Chapter 3 Literature review

This chapter aims to provide an overview of concepts relevant to novel orthopaedic fixation technology. The review begins with the aetiology of bone fractures and the orthopaedic surgeries used to treat them, focussing on proximal humerus fracture fixation through Open Reduction Internal Fixation (ORIF), the primary indication of the EXF Screw. Further detailed discussion about the choice of applications of the EXF Screw can be found in Chapter 11 ('Future work') in Section 11.4.4 ('Future potential indications'). This is followed by a summary of the effect of screw design parameters on orthopaedic screw failure modes and common methods of augmenting screw fixation. Finally, previous scientific and commercial work on orthopaedic expandable fasteners is described and all known previous expandable fastener orthopaedic products and development projects are catalogued and discussed.

Orthopaedic screws are used to attach implants such as rods, plates, nails and sutures (Figure 3-1) to bone in orthopaedic surgery. These implants are commonly used to fixate fractures, fuse joints and repair or replace damaged tendons and ligaments. Although these implants may be external (outside the body), the majority are internal (inside the body).



Figure 3-1 Orthopaedic screws can be used for rod-based systems (left, Zimmer Biomet Virage rod system for Lumbar Fusion (Zimmer GmbH, 2014)) or plate-based systems (right, DePuy Synthes' Philos plate for proximal humerus fracture fixation (Synthes, 2002))

3.1 Fracture fixation

Studies suggest a total global incidence of bone fractures to be between 9-23 per 1000 people per year (Court-Brown & Caesar, 2006). Bones can fracture due to trauma under a high impact load (e.g. car crash, fall from height, etc.) or due to a low impact load (e.g. fall from standing). Low impact fractures are usually caused by bone degeneration, typically associated with aging (Baron, Barrett, & Karagas, 1996). However only 13% of patients hospitalised with fractures have normal bone density (Baron et al., 1996) and approximately 30% of fractures in men, 66% of fractures in women and 70% of inpatient fractures overall are potentially due to osteoporosis (Court-Brown & Caesar, 2006). Furthermore after the age of 55 most fractures occur under 'moderate load' due to a fall from standing (Baron et al., 1996).

Once fractured, the bone no longer fulfils its mechanical function and must be fixed by the biological mechanism of bone healing. Partial fractures or non-displaced, stable fractures can be treated without surgery if immediate mobilisation is not required, as there is no need to reduce (anatomically align) or stabilise the fracture. However, unstable fractures or fractures that have been anatomically displaced usually need to be fixed through a surgical procedure and typically require the use of orthopaedic screws to attach an implant to the bone (Colton, Buckley, & Camuso, 2011). Reduction can be achieved through a non-surgical, closed procedure (a combination of manipulation and traction) however this is not common for proximal humerus fractures (Twiss, 2015).

Internal fixation to stabilise fractures can be achieved surgically by using either plates or intramedullary nails. Plates are attached, by orthopaedic screws, to the outside of the bone to bridge the fracture gap. Whereas intramedullary nails are inserted into a hole drilled at the end of the long bone and pushed along to the intramedullary canal to bridge the fracture gap internally. Screws are then placed through the threaded holes within the nail to lock it in place. The preference for rods or plates varies depending on the fracture type and the regional preference of the surgeons (Jaeger, Leung, & Li, 2011).

Although fractures can occur in the diaphysis (middle) of the bone, fractures in the metaphysis (ends) are more at risk for screw fixation failure, especially in older patients (Baron et al., 1996). This is because typically fixation strength in diaphyseal screws is very strong, due to the strong anchorage provided by the thick cortical bone that is found there. However metaphyseal fractures often have low fixation strength because the cortex is thin at this point and fixation all the way through the bone (bi-cortical fixation) is not possible if the distal cortex is an articular joint, as is often the case and the cancellous bone is low density or non-existent. For this reason fractures of the proximal humerus, proximal femur, distal radius and other metaphyseal fractures often have high screw complications and associated revision rates. This problem is highlighted by the number of screws used in these surgeries. For proximal humerus fractures often seven or more screws are used to maximise fixation strength and minimise the risk of screw failure (Zimmer GmbH, 2015).

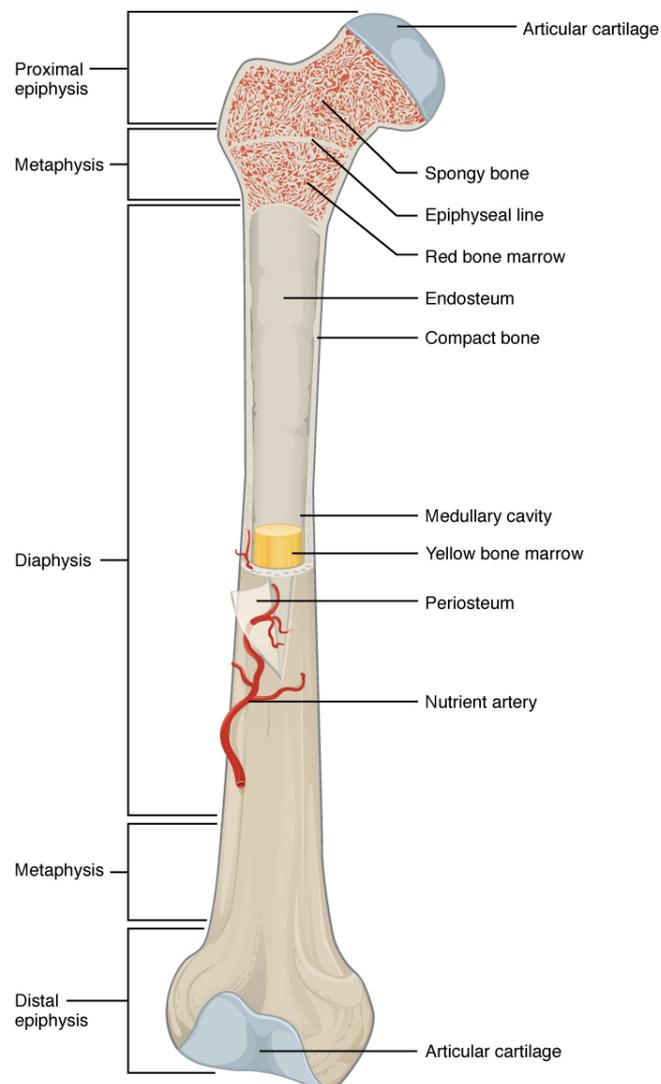


Figure 3-2 Long bone anatomy

(Source: https://commons.wikimedia.org/wiki/File:603_Anatomy_of_a_Long_Bone.jpg)

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3.2 Proximal humerus fracture fixation

Proximal humerus fractures are the third most common fracture (Court-Brown & Caesar, 2006; Erasmo, Guerra, & Guerra, 2014) accounting from 4.0-11.7% of total fractures and 45-50% of all humeral fractures (Burke, Kennedy, Green, Dodds, & Mullett, 2012; Kim, Szabo, & Marder, 2012). They occur at a rate of between 63-129 fractures per 100,000 population per year (Court-Brown & Caesar, 2006; Twiss, 2015). However this rate is significantly higher for women over 60 years as indicated by Figure 3-4. Consequently, the current population rate is expected to increase three-fold over the next 30 years with the aging population (Baron et al., 1996). This fracture is one of the leading causes of excessive mortality in the elderly (Kim et al., 2012).

Between 75-87% of proximal humerus fracture cases are due to a low impact fall from standing (Figure 3-3) coupled with the presence of osteoporosis (Court-Brown, Garg, & McQueen, 2001) and females account for 70-80% of cases (Twiss, 2015). Consequently patients with proximal humerus fractures are typically older (average age 62 (Sproul et al., 2011)) and female. Women over the age of 60 have an 8% lifetime risk of a proximal humerus fracture (Lauritzen, Schwarz, Lund, McNair, & Transbøl, 1993).

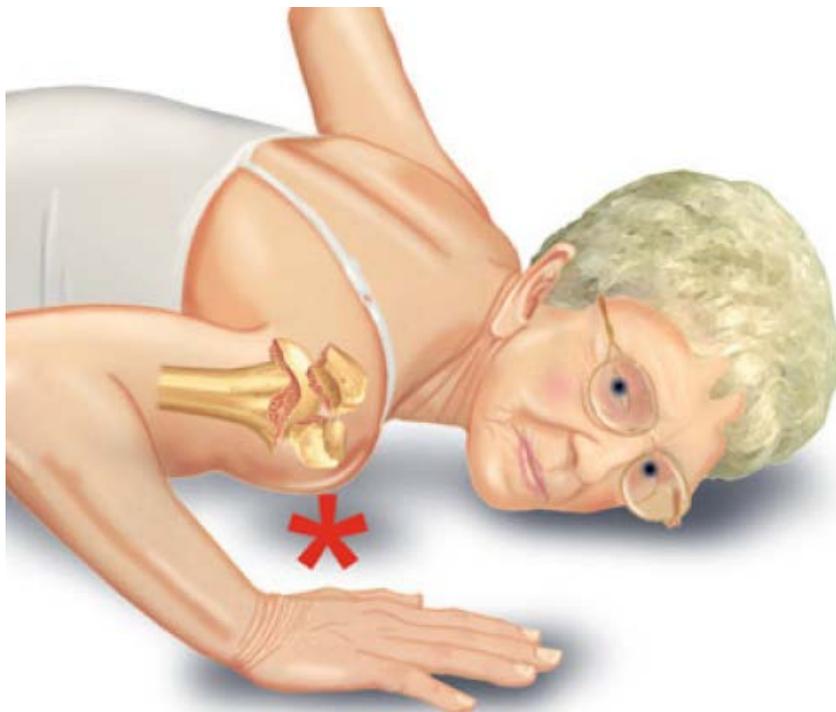


Figure 3-3 Typical proximal humerus fractures are caused by a fall from standing and are due to age-related osteoporosis (Twiss, 2015)

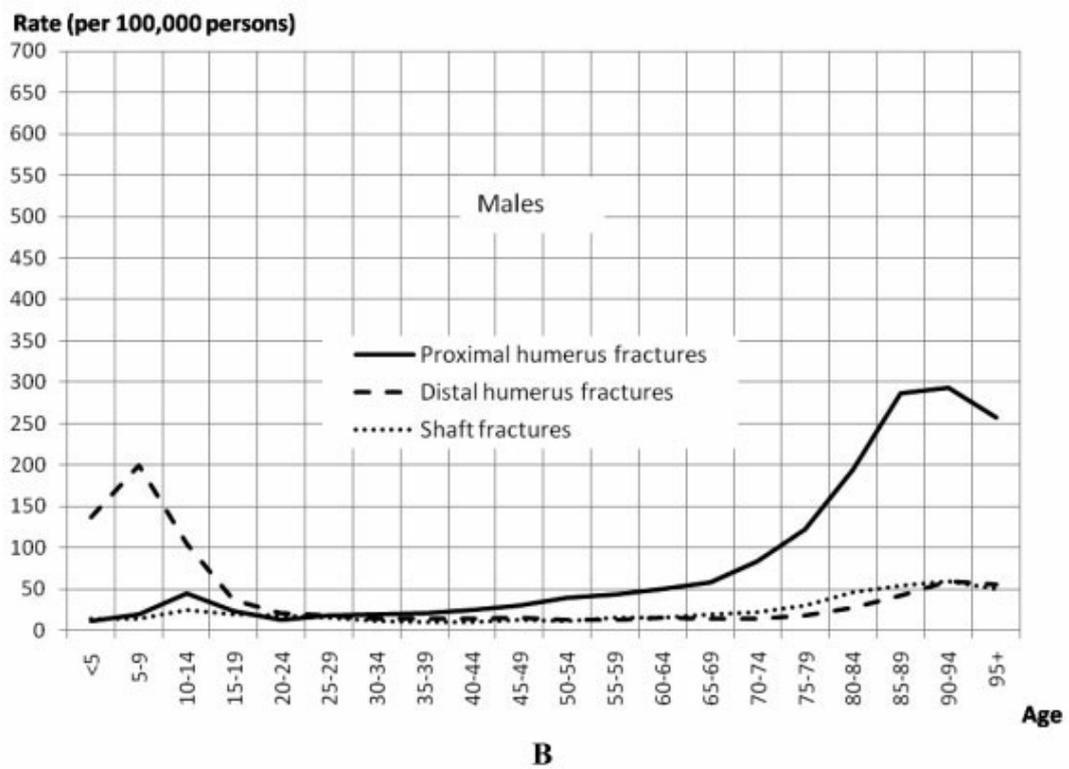
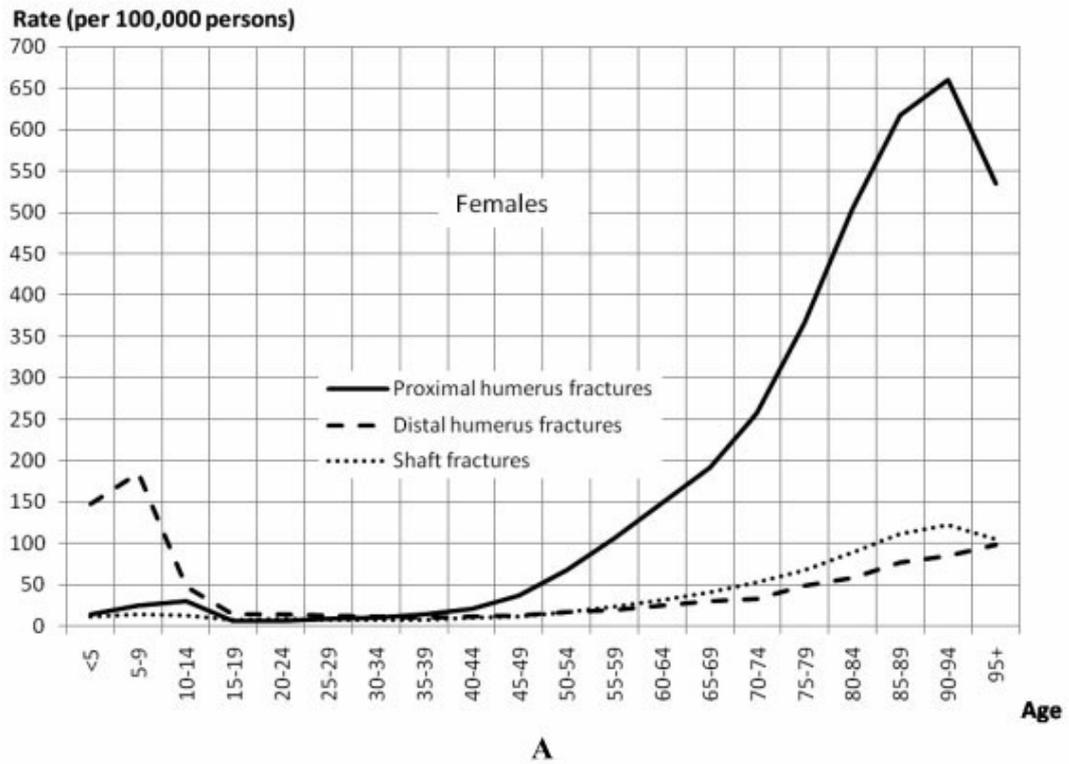


Figure 3-4 The rate of humeral fractures for women (A) and men (B) over different age groups in the United States of America (Kim et al., 2012)

Based on the Neer classification, Court-Brown et al. (2001) found that 49% of proximal humerus fractures are minimally displaced, 37.5% are 2-part fractures, 9.5% are 3-part fractures and 4% are 4-part fractures, as shown in Figure 3-5. Patients with minimally displaced fractures are commonly treated conservatively, which typically involves early protection, with a sling for the first 7-10 days and gradual mobilisation with physical therapy (Twiss, 2015). Although conservative treatment has favourable outcome in the majority of these patients, some experience fracture non-union which then requires surgical intervention to ensure long term fracture reduction and union. Some displaced fractures can be treated by closed reduction without surgery (by manipulation and traction), however most will require surgical intervention (Twiss, 2015). Patients with two part fractures had better surgical outcomes than three part fractures and that four part fractures had the worst surgical outcomes (Sproul et al., 2011).

	2 PART	3 PART	4 PART	
Anatomical Neck	2  0.3% 50yrs			Minimal Displacement 1  49% 63yrs
Surgical Neck	3  28% 70yrs			
Greater Tuberosity	4  4% 67yrs	8  9% 73yrs	12  2% 72yrs	
Lesser Tuberosity	5  0%	9  0.3% 65yrs		
Fracture-Dislocation	6  5% 59yrs	10  0.1% 77yrs	13  1% 73yrs	Articular Surface 15  0.7% 73yrs
Anterior				
Posterior	7  0.2% 54yrs	11  0.1% 51yrs	14  0.1% 68yrs	

Figure 3-5 The Neer classification showing the incidence and average age for each category (Court-Brown et al., 2001)

Surgical options for proximal humerus fracture cases are percutaneous pinning, Open Reduction Internal Fixation (ORIF) either with locking plate and screw system or an intramedullary (IM) nail, hemiarthroplasty (HA) (see Figure 3-6), Total Shoulder Arthroplasty (TSA) and reverse Total Shoulder Arthroplasty (rTSA) (Jaeger et al., 2011).

Although percutaneous pinning (using individual screws to hold the fracture together, as shown in Figure 3-6 Left) can provide additional stability to minimally displaced 2-part fractures, the majority of 2-part and 3-part surgical cases are treated by ORIF using locking plate and screw system as it provides adequate reduction and stabilisation and not as invasive as HA or TSA. 4-part fractures and other severe fracture types that cannot be adequately treated by ORIF are treated by the more invasive and expensive HA or TSA procedures. Revision surgery after a failed ORIF where the shoulder joint has been damaged generally require a HA procedure where the shoulder ball joint is replaced with a prosthesis. Extensive damage to the shoulder joint will require a TSA or rTSA where both the ball and socket of the shoulder joint is replaced with prosthesis (Jaeger et al., 2011).

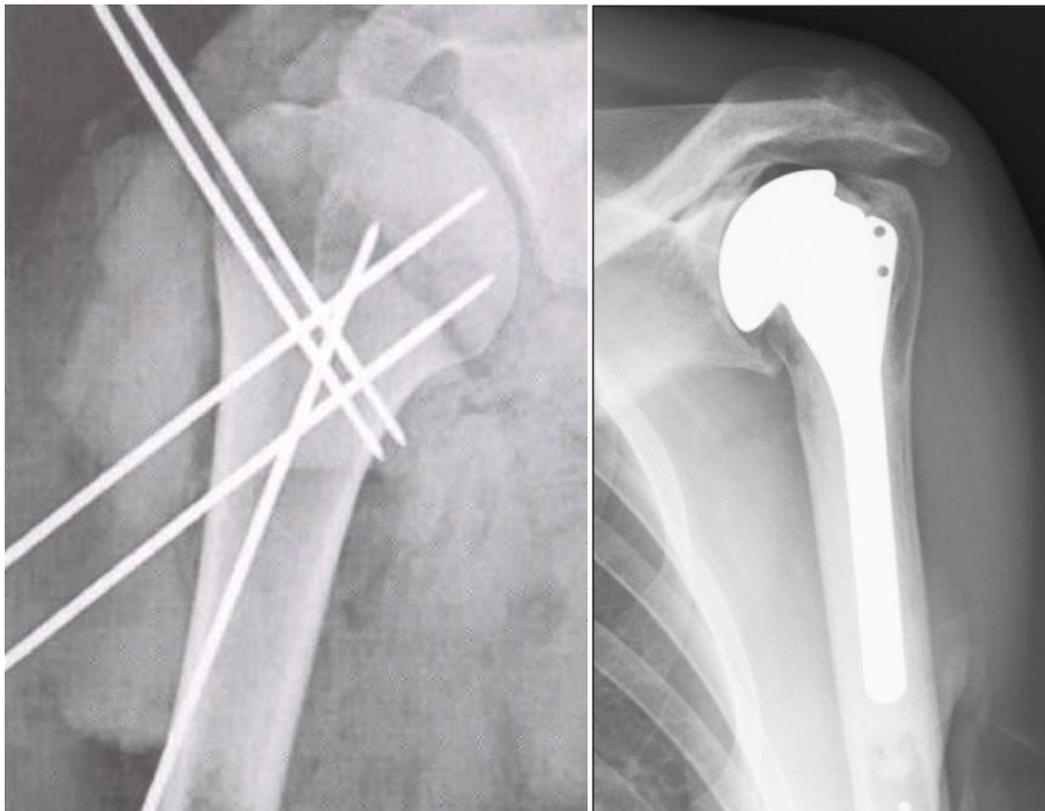


Figure 3-6 Percutaneous pinning (left, (Rowles & McGrory, 2001)), Hemiarthroplasty (right, (Geervliet, Somford, Winia, & Van Den Bekerom, 2015))

The primary indication for the EXF Screw is proximal humerus fracture fixation by ORIF using locking plate and screw system. As previously mentioned, this is the surgical procedure of choice for the majority of displaced 2-part and 3-part fractures, as it is less invasive than arthroplasty and provides better patient outcomes (Sproul et al., 2011). However, as screw related complications are still a significant problem leading to revision surgery, improving the fixation strength of the screws can subsequently reduce this revision rate. This surgery can be done percutaneously (minimally invasively) but is more commonly performed with an open incision. The conventional ORIF procedure is outlined below (Figure 3-7), based on the Zimmer NCB polyaxial locking plate system (Zimmer GmbH, 2015).

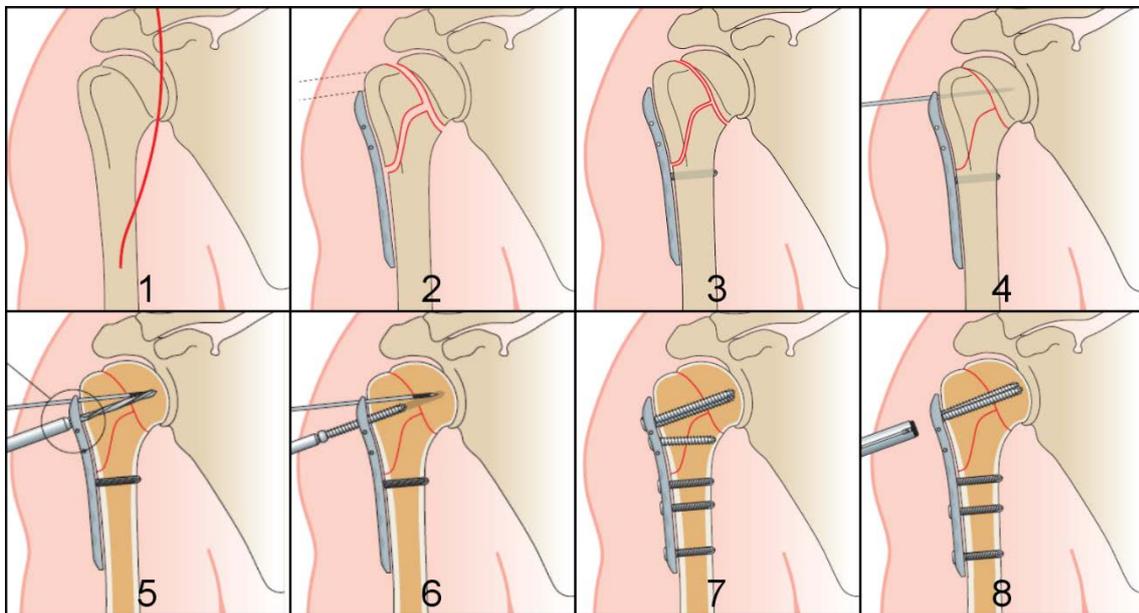


Figure 3-7 The basic steps involved in a conventional open proximal humerus fracture fixation surgery using a plate (Zimmer GmbH, 2015)

1. A delto-pectoral (or less commonly a deltoid split) incision is made, attempting to preserve the blood supply to the bone fragments
2. The plate is inserted into the incision and lined up with anatomical markers
3. A distal (bottom) screw is placed just below the fracture line, holding the plate to the lower bone.
4. Using the plate and a Kirschner wire (K-wire) through the proximal holes of the plate the fracture fragments are reduced (pulled together to form a continuous bone surface).

5. Holes in the bone are drilled through the holes in the plate using a drill guide. Implant manufacturers typically recommend using image intensifier and aiming to stop approximately 5 mm before the subchondral bone adjacent to the shoulder joint. Screw lengths for each hole are measured using a screw depth gauge.
6. Self-tapping proximal (top) screws are placed into the head of the humerus to secure the reduction. The surgeon can choose the number of screws and, using the NCB system, can angulate them to maximise fixation strength. More screws and larger diameter (typically 4.5 mm) cancellous screws are recommended for osteoporotic cases.
7. The remaining distal screws are placed, usually with bicortical fixation.
8. With the Zimmer NCB system, all screws are locked using locking caps to achieve angular stability. Other systems have uniaxial locking screws that don't require locking (DePuy Synthes Philos) or else are older non-locking plates.

The revision rate of proximal humerus fracture fixation, treated by locking plate and screw system, is reportedly between 13.7-19% for the general population (Sproul et al., 2011; Südkamp et al., 2009; Thanasas, Kontakis, Angoules, Limb, & Giannoudis, 2009). The most common reason for revision surgery is screw cut-out or perforation, whereby the screw fixation fails under load and the tip of a screw is forced through the sub-chondral bone of the humeral head into the glenohumeral joint (Südkamp et al., 2009). This complication reportedly occurs with rates of between 7.5-11.6% in the general population (Sproul et al., 2011; Thanasas et al., 2009) and accounts for 31% of revision surgeries (Thanasas et al., 2009). However the complication rate of screw cut-out increased to 43% for patients older than 60 (Owsley & Gorczyca, 2008), supporting the hypothesis that this is due to low screw fixation strength which is affected by the bone quality.

The most common complication, occurring in 16% of patients in the general population, was varus malunion (Sproul et al., 2011), where either the bone fragments are not sufficiently reduced during surgery or becomes displaced after surgery, which can occur due to insufficient screw fixation strength. This complication can limit active abduction or forward flexion (Benegas et al., 2007). Although older or less active patients may accept restricted mobility, younger and more active patients may opt for a valgus osteotomy of the surgical neck of the humerus to correct the deformity (Benegas et al., 2007). With increasingly active older patients the proportion of patients willing to tolerate restricted mobility will reduce over time and consequently this complication will have more of an effect on the revision rate than it does currently.

Damage to the shoulder joint due to primary screw penetration which occurs during the surgery due to surgical error is another complication. Südkamp et al. (2009) reported intraoperative screw perforation of the humeral head to be 14% of patients and that this was the most common complication to cause revision surgery. The high risk of this complication is due to the number of screws placed in the humeral head (up to seven) and the importance of engaging the higher density subchondral bone immediately below the joint surface and maximising screw length to reduce the risk of screw failure. Consequently implant manufacturers suggest a 5-8 mm buffer between the end of the screw and the joint surface (Synthes, 2002; Zimmer GmbH, 2015). Because of the risk of over-penetration, implant manufacturers recommend that the surgeon perform the operation under an image intensifier (Zimmer GmbH, 2015) although this is not standard practise. As trauma procedures, typically these surgeries are performed by less experienced, orthopaedic registrars, further increasing the risk of surgeon error.

Another complication is Avascular Necrosis (AVN), where a discontinuity in the fracture can de-vascularise a bone fragment. Without blood supply to the fracture site, fracture healing cannot occur which can lead to non-union. This complication can develop as long as five years after injury and can result in pain, decreased range of motion, and glenohumeral joint arthritis (Sproul et al., 2011). Some AVN patients will have a revision surgery to a shoulder arthroplasty. However radiographic AVN does not necessarily require revision surgery, depending on whether it is symptomatic or not.

The complication rate in older patients with osteoporosis is higher than in the general population due to low quality bone. Owsley and Gorczyca (2008), observed a much higher percentage of complications overall in the group of patients older than 60 years, 57% compared to 22%. In the majority of cases, complications due to screw cut-out or varus malunion and the resulting revision surgery may be addressed by increasing fixation strength. A number of methods of augmenting orthopaedic screws have been suggested in the literature including using bone cement (Blazejak, Hofmann-Fliri, Buchler, Gueorguiev, & Windolf, 2013) and expandable screws (Gibson, Keogh, & Morris, 2012; Lei & Wu, 2006; O'Neill et al., 2013; Wu et al., 2010; Wu et al., 2012). Details of these alternative methods will be discussed in more detail in Section 3.6 ('Orthopaedic screw fixation augmentation').

In Australia, the cost of proximal humerus fracture fixation surgery ranges from approximately AU\$13,000 for ORIF to AU\$29,000 for a TSA. Consequently, based on an average proximal humerus fracture incidence of 100 per 100,000 people per year (Court-Brown & Caesar, 2006; Twiss, 2015) and an average 16% revision rate (Sproul et al., 2011; Südkamp et al., 2009; Thanasas et al., 2009) reported in the literature, it is estimated that revision surgeries cost the Australian health care system \$24m per year, without considering the loss of time and trauma to the patient related to revision surgery or if a more expensive and invasive revision to a TSA is required (Handschin, Cardell, Contaldo, Trentz, & Wanner, 2008; Kim et al., 2012). Improved fixation strength can also potentially allow earlier rehabilitation, as was the case for the introduction of locking plates (Handschin et al., 2008), which would reduce economic burden for athletes and patients with work-preventing injuries. In the surgeon survey (see Appendix A) 4 of 11 surgeons said 'yes' or 'likely' when asked whether expandable screws would positively affect patient rehabilitation. Of the remaining surgeons four responded 'maybe' and three responded 'unlikely' or 'no'.

Furthermore according to Court-Brown et al. (2001), a proximal humerus fracture "often occurs in a fit elderly independent patient who is a net contributor to society but who might well be converted to a degree of social dependency by the fracture." They found that nine out of ten patients lived at home, approximately two thirds by themselves with only one fifth requiring social support demonstrating the social and economic cost of proximal humerus fractures outside of the direct costs of surgery. Therefore improving the clinical outcome of shoulder surgery is important to improve the quality of life and independence for patients with proximal humerus fractures.

The above findings establish that proximal humerus fracture fixation, using ORIF with a plate, is a strong, unmet clinical need, suited to the application of expandable fasteners. There are very high rates of revision due to screw related failure that can be addressed by increasing screw fixation strength in push-in (to prevent secondary penetration) and shear (to prevent varus malunion). Furthermore the alternative to this procedure, joint replacements, are more expensive and invasive. Lastly an aging population with an increasingly active lifestyle means that the magnitude of this problem will increase in the future.

3.3 Bone microstructure

Understanding the structure of bone is critical to understanding the factors that will cause fastener fixation failure. Bones can be divided into two structural units. The thick, dense outer layer of bone, the ‘cortical’ bone (or ‘compact bone’) and the inner volume of lower density, spongy bone composed of a network of struts or ‘trabeculae’, this bone is called ‘trabecular’ or ‘cancellous’ bone (Rogers, 2011).

The bulk material properties of bone are strongly dependant on structure, especially cancellous bone which is composed of a lattice of trabecular struts. Investigation into various parameters such as the number of trabeculae, trabecular thickness and the rodness/plateness of the trabeculae has demonstrated that cancellous structure significantly affects bone mechanical properties (Ab-Lazid, Perilli, Ryan, Costi, & Reynolds, 2014; Poukalova et al., 2010). Cortical bone is dense, with small voids, which can also be quantified with CT scanning (Nishiyama, Macdonald, Buie, Hanley, & Boyd, 2009).

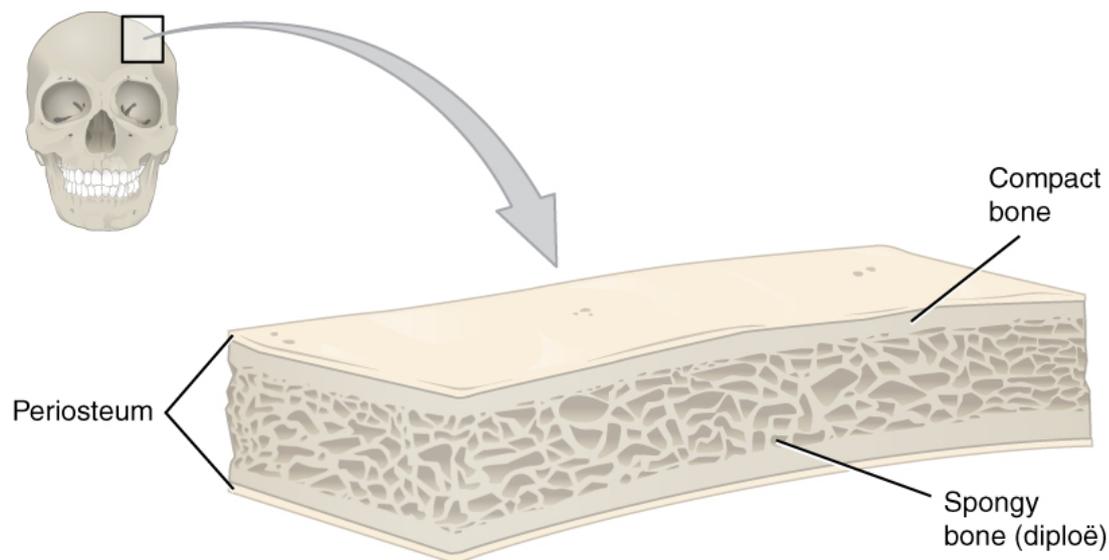


Figure 3-8 Bone structure can be divided into cortical bone (or ‘compact bone’) and cancellous bone (or ‘Spongy bone’)

(Source: <https://commons.wikimedia.org/w/index.php?curid=30131423>)

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Osteoporosis is a disease of decreased bone density, most commonly found in older patients (see Figure 3-9). However in osteoporosis reduced bone density is usually accompanied by other degradations such as increased anisotropy (with the preferential resorption of horizontal struts), deterioration of plate-like trabecular structures into rod-like structures and cortical thinning (Montoya et al., 2014; Seeman, 2003). This degradation results in drastically reduced strength, increasing the risk of bone fracture (Bell, Dunbar, Beck, & Gibb, 1967).

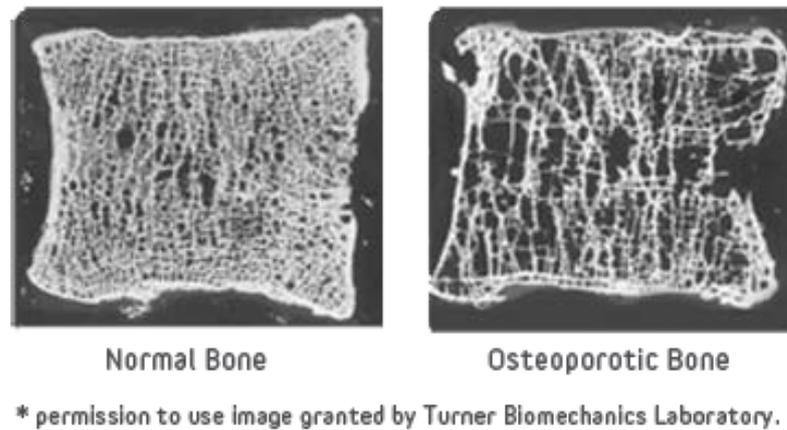


Figure 3-9 Bone degeneration (Source: <http://www.osseon.com/osteoporosis-overview/> used under creative commons license)

Many clinical studies have demonstrated the correlation between Bone Mineral Density (BMD) and screw failure force. Okuyama et al. (2001) demonstrated that patients with screw loosening have a significantly lower BMD and Katonis et al. (2011) found that a screw failure in their 225 large subject cohort occurred only in elderly patients, mostly with severe osteoporosis.

Many ex-vivo studies have investigated the correlation between BMD and screw pull-out force with varied success. Barber, Feder, Burkhart, and Ahrens (1997) centred an arbitrary 1 cm³ volume of interest (VOI) on various screw attachment points on cadaveric human humeral heads but found no correlation between BMD and failure force. Goradia, Mullen, Boucher, Parks, and O'Donnell (2001) divided the humerus into wedges to form VOIs for various screw attachment locations and found a correlation for the cortical BMD but not the trabecular BMD. Seebeck et al. (2004) demonstrated correlation for both cortical thickness and cancellous BMD by measuring density along the screw axis in human tibial bone. However, Thiele, Eckhardt, Linke, Schneider, and Lill (2007) reported only correlation with cortical properties (thickness, volume and BMD) and no significant correlation with trabecular properties when testing in human osteoporotic femoral bone with a 15 mm diameter VOI.

Wirth et al. (2011) used Finite Element Analysis (FEA) to assess the pull-out stiffness of the screws, which is a good predictor of failure force. They demonstrated that a better correlation was found when considering only the peri-implant bone volume fraction, indicating that the specific VOI that is measured is critical in assessing correlation. This explains why earlier studies which used larger, non-specific VOIs (Barber et al., 1997; Goradia et al., 2001) failed to demonstrate significance where studies with more relevant and smaller VOIs did (Seebeck et al., 2004) and studies with a large but screw specific VOI demonstrated partial significance only (Thiele et al., 2007).

Using FEA, Wirth et al. (2011) also demonstrated a higher correlation for calculated Young's Modulus than for bone volume fraction, demonstrating that the structure of the bone affects the screw performance beyond just the influence of the bone volume fraction.

More recently researchers have begun to assess the effects of trabecular bone morphology on screw pull-out strength. Poukalova et al. (2010) investigated how the trabecular bone structure immediately adjacent to screws affected their pull-out strength and demonstrated significant correlations with some microstructural properties. Ab-Lazid et al. (2014) investigated the effect of bone microstructure, using a VOI centred on the screw and demonstrated a strong relationship between most of the microstructural properties examined. The diameter of the VOI for their study was taken from the deformed area during pull-out loading in the FEA study by Wirth et al. (2011).

Both studies found that Structural Model Index (SMI) was the most strongly correlated parameter, followed by Bone Volume Fraction (BVF) and Trabeculae Thickness (Tb.Th) (Ab-Lazid et al., 2014; Poukalova et al., 2010). In addition, Ab-Lazid et al. (2014) also found correlation for Trabeculae Spacing (Tb.Sp), Trabeculae Number (Tb.N) and Bone Surface Area (BS/TV).

No previous study has investigated the effect of bone quality on expandable fastener failure force. However, some authors have suggested that expandable fasteners may perform better, relative to screws, in low quality osteoporotic bone (Cook, Salkeld, Whitecloud III, & Barbera, 2000; McKoy & An, 2001). Consequently, to better understand expandable fasteners and identify which orthopaedic applications they are most suited for, the effect of microstructural properties on the performance of an early, unthreaded expandable fastener prototype (the UEF) was investigated.

This work is described in Chapter 5 ('Preliminary UEF pull-out strength testing'). Based on the findings and recommendations of the literature described above, this study used a small cylindrical VOI and the microstructural properties that were investigated where those that have been previously demonstrated to have statistically significant correlation with screw failure force.

3.4 Orthopaedic screw failure modes

According to Bennani Kamane (2012), close to one million orthopaedic screws fail each year. The mechanical performance of orthopaedic screws is critical as failure to function can cause significant injury or discomfort to the patient and serious failures can necessitate a revision surgery. Revision surgeries are typically more technically difficult for the surgeon, involve additional surgical risks to the patient and represent a significant financial burden to the healthcare system.

For example revision of proximal humerus fractures alone accounts for \$US332M worth of revision surgeries in the United States, based on a 14% revision rate (Sproul et al., 2011), a cost of \$US1547 for the implant, \$US5852 for the surgery (Coe et al., 2012), a 2017 US population of 312M and a fracture incidence of 100 per 100,000 (Court-Brown & Caesar, 2006; Twiss, 2015). This figure does not take into account intangibles such as work productivity loss (estimated to be \$US3935 per patient (Coe et al., 2012)) and reduced quality of life for the patient and conservatively assuming that revisions were to hemiarthroplasty rather than a reverse total shoulder joint replacement, which is roughly twice as expensive (Coe et al., 2012).

Orthopaedic screws can be considered failed when they cease to provide the mechanical function of attaching the implant rigidly to the bone or they injure the patient. Orthopaedic screw failure modes include:

1. Pull-out, where the screw pulls out of the bone along the axis of the screw;
2. Cut-out, where the bone surrounding the screw breaks under shear loading allowing the screw to penetrate out of the bone;
3. Over-penetration during screw placement in surgery (primary penetration);
4. Over-penetration due to screw push-in under compressive physiological loading (secondary penetration);
5. Screw loosening where the screw moves inside the bone and allows an unacceptable degree of movement between the implant and the bone;
6. Screw back-out, where the screw turns out of the hole under cyclic torsional loading;
7. Screw breakage, usually caused by screw loosening; and
8. Screw induced infection.

Screw pull-out occurs when the axial force is excessive and the screw breaks out of the bone. The bone either fails in layers with each layer starting at the tip of the screw thread (King & Cebon, 1993) or failure can occur due to shear failure of the bone between the threads resulting in the removal of a 'bone plug' (Mueller, Basler, Müller, & van Lenthe, 2013; Zdero, Shah, Mosli, Bougherara, & Schemitsch, 2010). Pull-out is the typical failure mode for soft tissue anchors which can only create tension on the screw and multi-level Anterior Cervical Corpectomy and Fusions (ACCFs) and Anterior Cervical Discectomy and Fusions (ACDFs) where the bending moment across the plate is translated into a primarily axial pull-out force during flexion and extension of the spine, in a similar manner to a crow-bar levering out a nail.

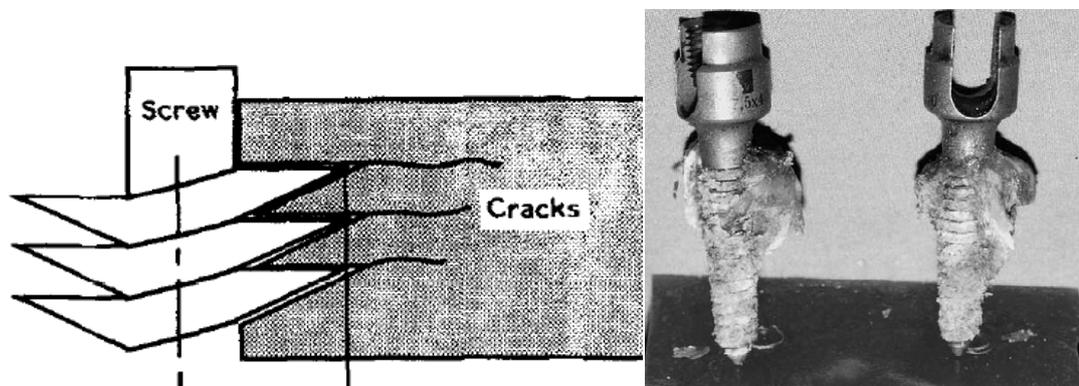


Figure 3-10 Screw pull-out can result in the bone breaking in layers around the screw, allowing the screw to come loose (King & Cebon, 1993) or shear failure of the bone to allow a bone plug to be removed (Abshire, McLain, Valdevit, & Kambic, 2001; Zdero et al., 2010)

Although pull-out is not the most common failure mode clinically, it is by far the most commonly evaluated measure of screw fixation strength due to uncomplicated methodology, the direct correlation between pull-out strength and screw design and the fact that pull-out is a good predictor of failure on other modes (Abshire et al., 2001).

Screw cut-out occurs when the bone is loaded nominally transverse to its axis, causing localised crushing around the bone as shown in Figure 3-11. This failure mode can occur with proximal femur fractures leading to damage of the hip joint and proximal humerus fractures which leads to varus malunion and potential sub acromial impingement (Teague & Gorman, 2014). This failure mode is a major cause of revision surgery and it is dependent primarily on the shear resistance of the screw. Unlike other failure modes (pull-out and push-in) this failure mode is not theoretically affected by the design of the screw thread. Consequently some implants (shown in Figure 3-12) that aim to prevent cut-out eliminate the thread altogether, including the DePuy Synthes DHS Blade (DePuy Synthes, 2015) in the proximal femur and the Zimmer Biomet S³ Proximal Humerus Plating System (Biomet Trauma, 2014). This failure mode is more difficult to mechanically test than pull-out due to the complexity of the loading and often requires a more elaborate methodology (Sommers et al., 2004).

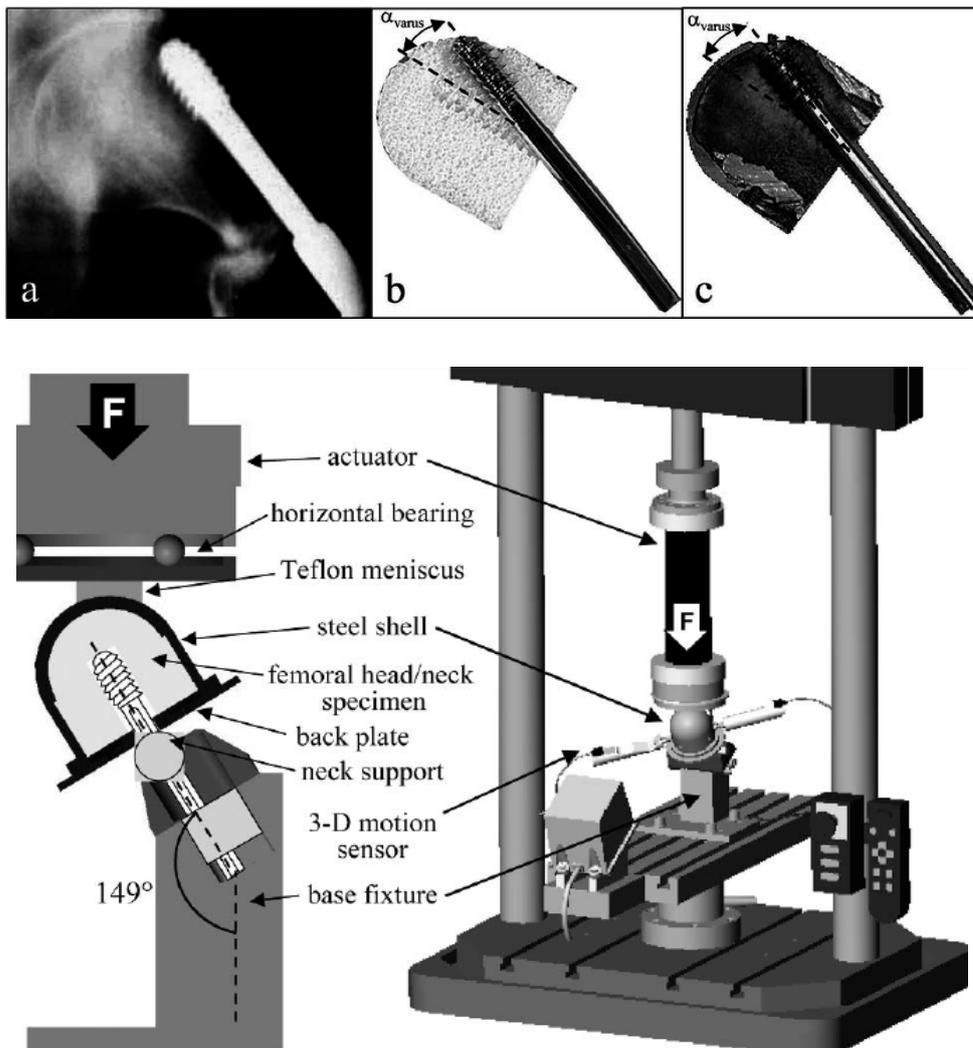


Figure 3-11 Screw Cut-out in hip fractures (above) and the elaborate test rig for evaluating cut-out of proximal femoral screws (below) (Sommers et al., 2004)



Figure 3-12 The Biomet S3 Proximal humerus system (Biomet Trauma, 2014) and the DePuy Synthes DHS Blade (DePuy Synthes, 2015) both eliminate the screw thread to improve shear performance in the proximal humerus and the femur respectively

Screw over-penetration occurs when the screw penetrates the distal cortex and damages the anatomical structures beyond. This can occur during pilot hole drilling or when the screw is being introduced in surgery (primary over-penetration) or after implantation under physiological push-in loading due to screw fixation failure (secondary over-penetration) (Sproul et al., 2011). In proximal humerus fractures over-penetration damages the shoulder joint, which usually leads to a shoulder replacement surgery. This injury is not uncommon, due to the number of screws used and the importance of engaging the subchondral bone immediately below the joint surface (Sproul et al., 2011).

Clinically, the loading of screws holding together fractures will typically be a combination of axial and transverse force. Furthermore the case of proximal humerus fractures, with a large number of angularly stable screws holding together the fracture, for one screw to fail in cut-out, another screw must fail axially and so clinical failure is often a mixed mode failure even if in systematic review it is reported as a single failure.

If screws loosen, undesirably high movement across the fracture gap may prevent bone healing (Burr & Allen, 2013) and in cases of radiculopathy in the spine cause re-impingement of nerves, causing recurrent pain. Furthermore excessive movement and the absence of bone healing will increase the likelihood of screw, plate or rod breakage through fatigue. Screw loosening can be caused by a mechanical process (through fatigue failure of the bone) or through the biological process of bone resorption around the screw-bone interface (Kim et al., 2008).

Biological failure is usually termed osteolysis and referred to in the literature as the halo phenomena (Kang, Kim, Park, & Kim, 2011; Kim et al., 2008) after the halo of less dense bone surrounding the implant in an x-ray (see Figure 3-13). The cause of this loosening has not been conclusively demonstrated but previous authors have suggested that heat during drilling, detaching particles of bone during screwing or the screw toggling effect inside the bone could lead to screw loosening (Kang et al., 2011; Kim et al., 2008). However not all radiographic loosening is symptomatic, Risso Neto et al. (2016) found no correlation between radiographic loosening and quality of life. Screw loosening is a relatively common screw failure mode clinically but is less commonly tested directly ex-vivo due to the difficulty in replicating cyclical loading and interpreting the results.

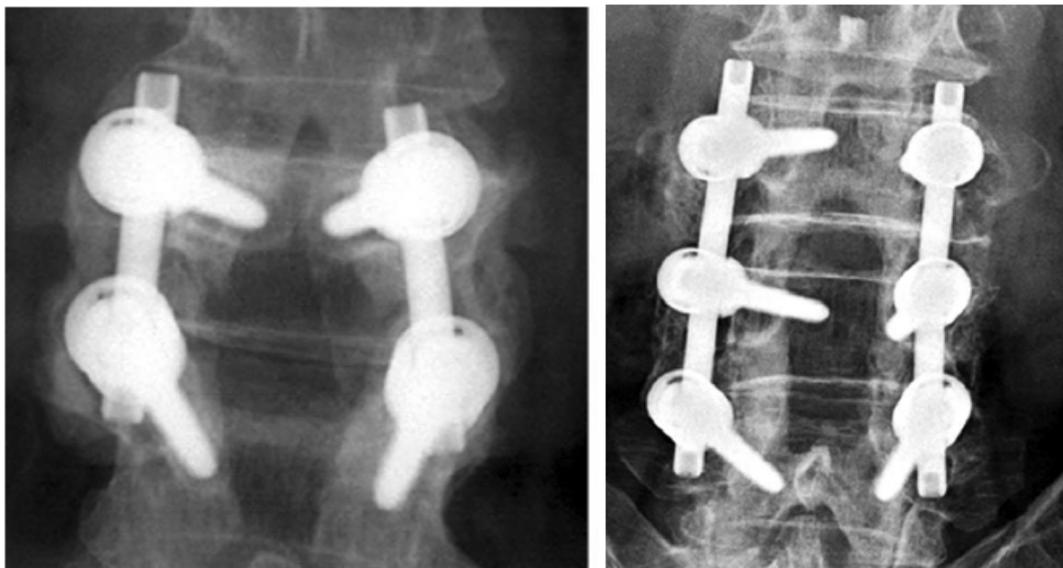


Figure 3-13 The halo phenomenon in lumbar pedicle fixation shown in the left image, but not in the right (Kim et al., 2008)

Screw back-out is where the screw over time slowly backs out of the threaded hole by turning. This failure mode is more common with conical screws, that are typically used in the lumbar spine to suit the tapering profile of a normal pedicle and maximise engagement with the cortex (Abshire et al., 2001).

Screw breakage is a failure mode encountered in the lumbar spine (Cho, Cho, & Wu, 2010) but can occur elsewhere usually due to non-union of the fracture (Giannoudis et al., 2013; Rancan, Dietrich, Lamdark, Can, & Platz, 2010). Typically breakage occurs at the junction of the screw head and the screw core (Figure 3-14) which is often, but not always, the point of maximum stress (Cho et al., 2010).



Figure 3-14 A pedicle screw that has broken at the junction between the screw and the polyaxial head (Kuklo, Rosner, & Polly Jr, 2004)

Consequently some thread designs remove the thread at this location (to eliminate the stress raiser) and increase the diameter fillet applied, to further reduce stress concentration (see Figure 3-15). Additionally, as shown in Figure 3-15 some screws are designed to be thicker at the head (conical) to minimise the likelihood of this occurring (Abshire et al., 2001).

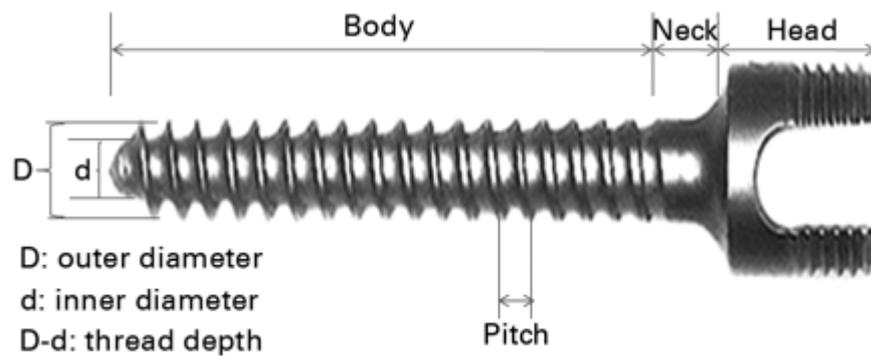


Figure 3-15 The ‘neck’ of the screw is usually unthreaded and a large diameter fillet is applied. especially in applications where screw breakage is common (Cho et al., 2010)

Infection can also occur around the screw site and the screw will need to be removed. Typically a ‘spacer implant’ is implanted that has antibiotic properties. For this reason, removability of screws is critical if infection occurs (Kienapfel, 2009).

In the current primary application of proximal humerus fracture fixation, screw over-penetration is the most common cause of revision surgery (7% of revisions (Sproul et al., 2011)). Screw cut-out and screw pull-out also occurs which can cause fracture displacement post-surgery and potentially malunion (accounting for 5% of revisions (Sproul et al., 2011)). However, in this thesis the author have focussed on screw pull-out failure, as this is the most globally applicable and commonly studied failure mode. However concurrent to the work of this thesis, in collaboration with the author, Intan Oldakowska has investigated the performance of expandable fasteners in other failure modes including push-in, shear and rotation.

3.5 Orthopaedic screw design

Although there is significant variation across surgical applications and manufacturers, conventional screws can broadly be defined as:

1. Cortical Screws, with a relatively fine pitch to maximise engagement with the cortex and consequently a relatively low thread depth. Typically used for fixation in the diaphysis of long bones;
2. Cancellous screws, with a high thread depth to maximise engagement with the cancellous bone and consequently a relatively coarse pitch. Typically used for reducing fractures; or
3. Locking screws, with a very low thread depth and a very fine pitch to suit a conventional threaded locking head. Several angularly stable locking screws are typically used in the epiphysis for holding a reduced fracture together.

There are a number of design parameters that compose a screw design and have demonstrated to have an effect on pull-out force including:

1. screw diameter;
2. thread proximal half angle;
3. thread depth;
4. thread pitch; and
5. screw length.

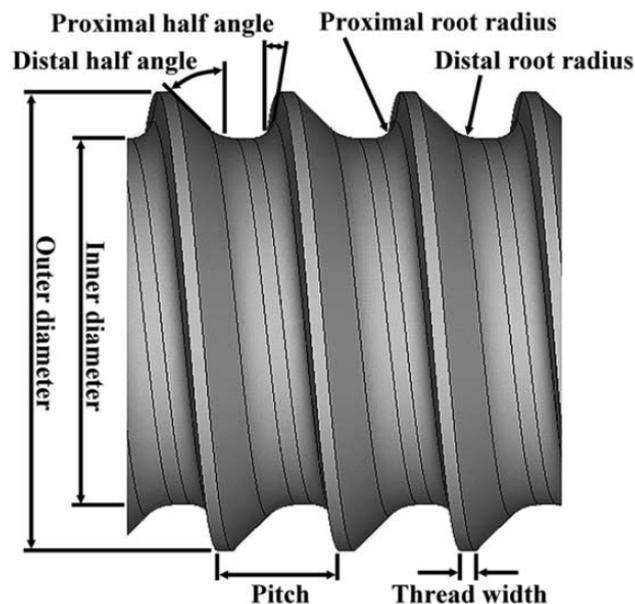


Figure 3-16 A diagram describing some of the critical design parameters for orthopaedic screws (Hou, Hsu, Wang, Chao, & Lin, 2004)

Screw Diameter

Asnis et al. (1996) determined that external diameter of the screw was the most important parameter, followed by the thread pitch and then thread depth. In a Taguchi Factorial Analysis, Hou et al. (2004) agreed that the outer diameter was the most important parameter, accounting for 46% of variation for length corrected failure force, followed by pitch (29.01%), half angle (16.39%) and lastly thread depth (4.52%). Other parameters such as thread width and root radius did not demonstrate significant effect on the failure force in the study by Hou et al. (2004) or elsewhere.

Proximal Half Angle

Chatzistergos, Magnissalis, and Kourkoulis (2010) reported a weak but strongly linear correlation with lower proximal half angles (more severe) providing marginally increased failure force. However Wang, Mori, Ozoe, Nakai, and Uchio (2009) found that a proximal half angle of 30° provided significantly increased failure force compared to 0° or 60°. This finding is supported by an FEA study which found an increase in computed reaction force when the lower proximal half angle was modified from 5° to 30° (Piper, 2016). This increase was on average 8.4% and this advantage depended on both the thread pitch and thread depth, varying from 0.6% to 28.6%.

Thread Depth and Pitch

Chapman et al. (1996) suggested the theoretical Thread Shape Factor (TSF) which increases fixation strength proportionally:

$$TSF = 0.5 + 0.57735 \times d/p$$

Where p is the pitch and d is the thread depth to optimise failure force. However current orthopaedic screws do not maximise the thread pitch according to this relationship. For example the Zimmer NCB locking screw has a thread depth of 0.3 mm and a pitch of 0.875 mm (TSF=0.698) and the NCB cancellous screw has a thread depth of 0.65 mm and a pitch of 1.75 mm (TSF=0.714) (Zimmer GmbH, 2015). Furthermore the American Society for Testing and Materials (ASTM) standard for bone screws (ASTM F543-07) defines two standard screw geometries HA and HB, which have TSFs of 0.923 and 1.19282 respectively (*ASTM F543 - 17 - Standard Specification and Test Methods for Metallic Medical Bone Screws*, 2017). Asnis et al. (1996) confirm that reducing the pitch of currently available orthopaedic screws will increase fixation strength, however the optimal pitch depends on the bone density and the external diameter of the screw.

Chapman et al. (1996) provided the equation below to approximate failure force from a synthetic bone model. Compared to their empirical testing data, they reported an R^2 value of 0.95 and this was independently verified with an R^2 value of 0.90 (Brown, McCarthy, Bourgeault, & Callahan, 2000). Note that this equation does not take into account the effect of proximal half angle and cannot be applied to tapered screws.

$$F_{pull\ out} = S_{shear} \times \pi L D_0 \times \left(\frac{1}{2} + \frac{1}{\sqrt{3}} d/p \right)$$

However the relationship between pitch, proximal half angle and thread depth is complex and inter-dependant. For example Chatzistergos et al. (2010) reported that for deep thread depths (0.75 mm and 1 mm) the pull-out force was independent of the pitch, whereas for lower thread depths (0.5 mm) coarser threads results in a reduced failure force.

Screw Length

Chapman et al. (1996) confirmed that, as expected theoretically, fixation failure force is linearly dependant on screw length. However Chatzistergos et al. (2010) reports that screws with coarser thread pitch are more sensitive to screw length, varying the gradient of the line of best fit.

Pilot hole

Screw fixation strength is decreased significantly by tapping screws before they are implanted into cancellous bone, with reportedly 8% reduction for tapped screws in synthetic cancellous bone (Chapman et al., 1996). Consequently the Association for Osteosynthesis/Association for the Study of Internal Fixation (AO/ASIF) technique manual recommends not tapping holes in cancellous bone. Chapman et al. (1996) demonstrated that, in synthetic bone foam, tapping increases the hole size significantly (average increase of 27%) which they hypothesise may account for the reduction in failure force. Furthermore, decreasing the pilot hole size for self-tapping screws provides increased fixation strength. Steeves, Stone, Mogaard, and Byrne (2005) reported increased fixation strength for lower than recommended diameter pilot holes in human cadaveric cancellous bone at a number of different insertion points across the skeleton.

Recommended pilot hole size varies for different screws, especially between cancellous and locking screws. For example, in the Zimmer NCB range, the recommended pilot hole for the 4 mm locking screw is 3.3 mm (0.1 mm smaller than the core diameter) whereas the recommended pilot hole for the 4.5 mm cancellous is 2.5 mm (0.7 mm smaller than the core diameter) (Zimmer GmbH, 2015). Clearly this can artificially increase the performance of the high thread depth screws (cancellous screws) and allows them to ‘out-perform’ the locking screws, contrary to the literature based on tapped holes. This is because the recommendations are for different patients (locking threads for normal bone and cancellous screws for osteoporotic bone) and different applications (locking threads for preventing cut-out and cancellous threads for preventing pull-out or allowing high reduction force via a lag screw). A previous study has demonstrated that screw tightening torque significantly correlates with pull-out strength (Ab-Lazid et al., 2014).

All the design parameters above are the basis of the design optimisation process. Mechanical testing to determine the effect of these parameters on the EXF Screw can be found in Chapter 6 (‘Effect of design parameters on mechanical performance of the EXF Screw’) and the final design decisions are detailed in Chapter 4 (‘Design of the EXF Screw’) in Section 4.3.6 (‘Final design’).

3.6 Orthopaedic screw fixation augmentation

For screw fixation in the spine and the epiphysis of long bones, surgeons traditionally used bi-cortical fixation to augment fixation strength, where the screw goes all the way through the bone into the distal cortex, maximising screw purchase. However, this creates a risk of over-penetration of the distal cortex and drilling into the soft tissues on the other side such as the nerve root, the spinal cord or the vertebral artery in the spine. Consequently, bi-cortical fixation is no longer standard practise for these applications. However bi-cortical fixation is still widely used for fixation in the diaphysis of the long bones as there are no critical surrounding soft tissues.

Bone cement augmentation is another way to increase fixation strength in severely osteoporotic and low density bone (Deb, 2008). Poly Methyl MethAcrylate (PMMA) bone cement is composed of a monomer and polymer which, when combined, creates a free radical polymerisation. Under exothermic conditions the mixed bone cement transitions from an initial fluid state that can be injected into the trabecular voids within the bone and fills the small gaps on rough surfaces, such as titanium to interdigitate and form a strong surface bond, to a putty which can be manipulated by the surgeon and pressed into macro bone voids (Deb, 2008). Finally the mixture hardens into Plexiglas, a strong but relatively brittle material (Lubansu, Rynkowski, Abeloos, Appelboom, & Dewitte, 2012). Other bone cement systems include hydroxyapatite composite resin which has demonstrated superior mechanical properties (Saito, Maruoka, Mori, Sugano, & Hino, 1994).



Figure 3-17 Bone cement augmentation using fenestrated pedicle screws whereby the fenestrated screw is implanted (left) bone cement is injected down the fenestration (centre) filling up the bone around the screw thread (right) (Lubansu et al., 2012)

Although bone cement significantly increases the fixation strength (Burval, McLain, Milks, & Inceoglu, 2007; Costa et al., 2016; Elder et al., 2015) it has some disadvantages that usually limit its use to patients with significant risk of screw fixation failure. These disadvantages include:

- extravasation or cement leakage into the surrounding soft tissues (Lubansu et al., 2012; Pare et al., 2011) including the shoulder joint in proximal humerus fractures fixation surgeries or the spinal cord in spinal fusion surgeries;
- difficulty in removing the fasteners during a revision surgery with risk of bone fracture if the bone-bone cement junction fractures before the bone cement-screw junction (Pare et al., 2011);
- thermal necrosis during curing damaging the bone and adjacent soft tissues, such as nerves, arteries and joints (Boner, Kuhn, Mendel, & Gisepp, 2009); and
- the proposed bone cement implantation syndrome which may cause an increased risk of embolism (Donaldson, Thomson, Harper, & Kenny, 2009).

Removability of bone cement augmented screws has been demonstrated in an ex-vivo human model after cyclical loading in the axial direction (Goetzen, Windolf, & Schmoelz, 2014). In this study the removal torques for the bone cement augmented screws were not significantly higher than conventional screws. The authors hypothesise that this was due to the axial cyclical loading, performed as part of another experiment, which may not be representative of in-vivo loading. Consequently removal may be more difficult in-vivo after bone in-growth in the absence of mechanical axial cyclical loading. However, in another study, fenestrated pedicle screws augmented by bone cement had almost 2.5 times the removal torque of the standard pedicle screw in cadaveric bone and 2 out of 17 of the removals created pedicle enlargement (Pare et al., 2011).

A recent study has indicated that in the proximal humerus injection of a small amount of bone cement through tip-fenestrated screws may not reach the critical threshold of temperature and time for thermal necrosis (47°C for one minute (Eriksson, Albrektsson, & Magnusson, 1984) with a maximum recorded temperature of 43.5°C (Blazejak, Hofmann-Fliri, Büchler, Gueorguiev, & Windolf, 2013). Another study, investigating the potential for thermal necrosis of bone cement augmented hip screws, indicated that the risk of necrosis was affected by the amount of bone cement used with no risk of necrosis with a cement layers that was less than 3 mm thick, but risk of necrosis for 5 mm thickness and greater (Boner et al., 2009).

Hydroxyapatite coating of screws seek to increase the rate and extent of osseointegration, thus increasing the fixation strength over time (Sandén, Olerud, Petren-Mallmin, & Larsson, 2002). Unfortunately this does not increase fixation strength immediately post-surgery, when many screws fail, and is consequently not a complete solution to the problem of screw failure.

Previous studies have demonstrated that expandable fasteners can increase fixation strength significantly whilst avoiding some of the additional risks associated with bone cement (Shea et al., 2014). However this comes with the disadvantage of difficulty in removing them during a revision surgery. The next section aims to provide a review of other expandable fasteners in the literature and commercially available.

3.7 Expandable orthopaedic fasteners

Previous academic work on expandable fasteners is relatively sparse due to the confidential nature of developing potential intellectual property. Furthermore the majority of expandable fastener literature relates to lumbar pedicle fixation with only a small number of studies looking at the potential use of expandable fasteners in long bones. There are a number of expandable fastener products in the market and several active research projects, summarised in Table 2 below.

Table 2 Summary of other expandable fastener projects and products

<u>Name</u>	<u>Company</u>	<u>Application</u>	<u>DIA</u> <u>(mm)</u>	<u>Stage of</u> <u>Development</u>	<u>Removability</u>
Appian Fx	KFx Medical	Biceps tenodesis implants- arthroscopic	5.5	FDA 510(k) approved, commercially available in US	Not removable.
Morphix	Medshape	Suture anchors for upper and lower limbs	2.5, 3.5, 4.5, 5.5	FDA 510(k) approved, commercially available in US	Not removable.
Osmium	Ulrich Medical	Anterior cervical spine plate fixation	5	CE Mark certified, commercially available in EU	Passively removable before bone in-growth
XPed	Expanding Orthopedics	Lumbar Pedicle screw system	6.5	CE Mark certified, commercially available in EU	Actively removable before bone in-growth
Osseo- screw	Alphatec Spine	Thoracic/lum bar pedicle screw system	6.5	CE Mark certified, commercially available in EU	Actively removable before bone in-growth

<u>Name</u>	<u>Company</u>	<u>Application</u>	<u>DIA (mm)</u>	<u>Stage of Development</u>	<u>Removability</u>
X-Bolt	X-Bolt Orthopaedics	Hip fracture	9	CE Mark certified, commercially available in EU	Actively removable before bone in-growth
EPS	Sofamor- Weigao Orthopaedic Device Co., Limited	Lumbar Pedicule screw system	6.5	Chinese SFDA approved, commercially available in China	Passively removable before bone in-growth
EBI Omega- 21	Electro- Biology, Inc	Lumbar Pedicule screw system	6.5	FDA 510(k) approved in 1998. No longer commercially available	Passively removable before bone in-growth
Active	Intelligent implant systems	Orthopaedic and spine	3-7.5	FDA 510(k) approved in 2012.	Possibly removable after bone in- growth
SMArt	University of Toledo, USA	Pedicule screw		Research	Unremovable
EPEEKS	TOBB University, Turkey	Pedicule screw	7.5	Research	Unremovable

3.7.1 Long bones

One of the earliest publication found describing a type of expandable fixation device as an alternative to screw fixation for use in long bone is by King and Cebon (1993). They found that their purpose-built device outperformed screws in osteoporotic long bones, but not in normal long bones, indicating that perhaps expandable fasteners are more suited to osteoporotic bone.

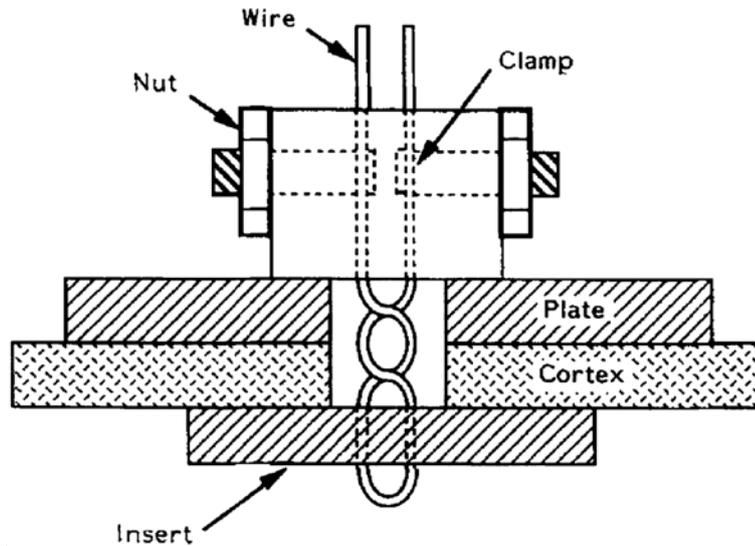


Figure 3-18 A purpose-built device built by King and Cebon (1993) to investigate the potential increase in fixation strength of expandable fasteners

Drew and Allcock (2002) described a method of fixation in osteoporotic long bones with stripped screw hole using a nylon cavity plug which expands underneath the cortical bone layer to provide increased fixation strength. The nylon plug demonstrated 270% greater push-out strength than the control screw in a synthetic model bone.

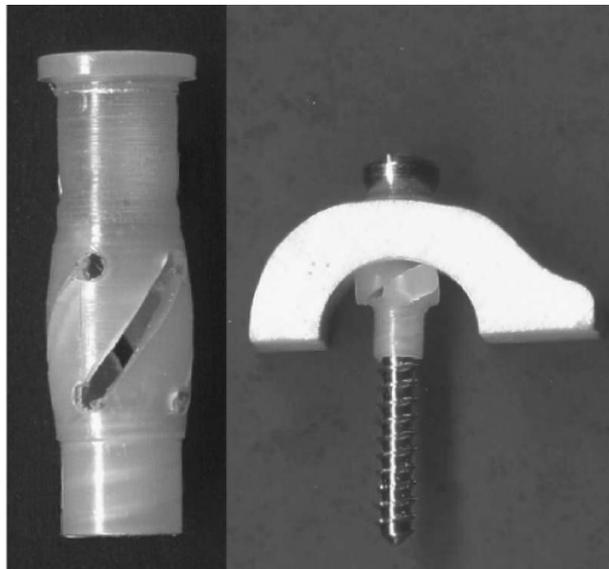


Figure 3-19 An expandable nylon cavity plug tested by Drew and Allcock (2002)

Zeiter, Montavon, Schneider, and Ito (2004) conducted an in-vivo study of expandable rivets for tibial fracture internal fixation in sheep, and demonstrated osseointegration earlier, closer to the bone–implant interface and over a wider area compared to a conventional orthopaedic screw.

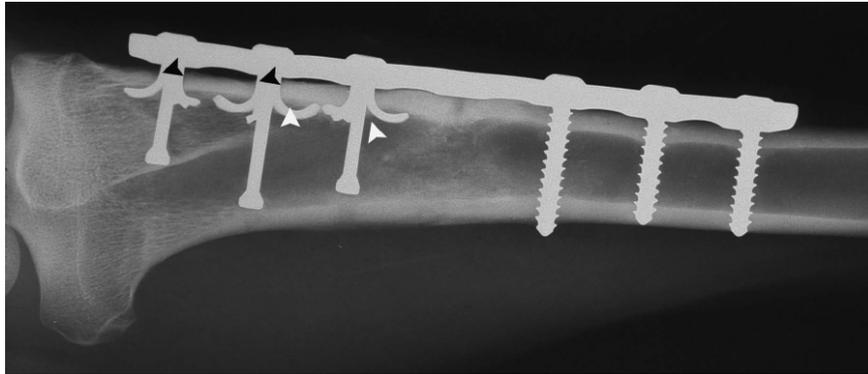


Figure 3-20 An X-ray from an in-vivo sheep study of expandable rivets compared to cortical screws by Zeiter et al. (2004)

X – Bolt

The only commercially expandable fixation devices for use in long bones is the X-Bolt, which is designed for use in the treatment of intertrochanteric hip fractures as shown in Figure 3-21. A study assessing the performance of the X-Bolt compared to the established implant of choice, the dynamic hip screw (DHS) and the DHS blade did not demonstrate a significant increase in push-out energy over 4 mm of displacement in a severely osteoporotic polyurethane foam bone model (sawbone) with density of 0.08 g/cm^3 (O'Neill et al., 2013). However, Gibson et al. (2012) demonstrated a significant increase in the cyclic resistance of X-Bolt compared to the DHS screw in a low density sawbone (0.08 g/cm^3) but did not compare against the DHS blade, the gold standard.

The major drawbacks of the X-Bolt are:

1. it requires an additional major surgical step of reaming out the bone surrounding the pilot hole to allow for the expansion of the wings (X-Bolt Orthopaedics, 2014); and;
2. bone grows into the inside of the expanded mechanism, potentially jamming it open and preventing removal, if a revision surgery is necessary.

Based on discussion with hip surgeons, they prefer to preserve the existing bone volume where possible and are very concerned about implant removability, especially in long bones fracture fixation where removal is not uncommon.

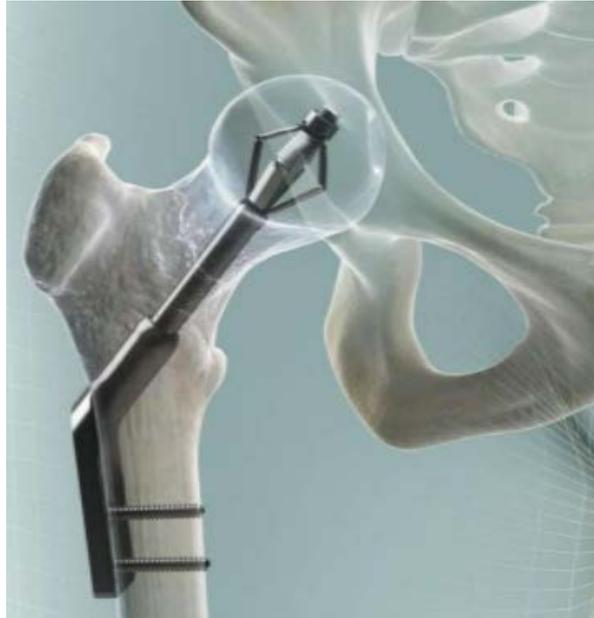


Figure 3-21 The X-Bolt is used for fixation of intertrochanteric hip fractures (X-Bolt Orthopaedics, 2014)

3.7.2 Lumbar spine

An early investigation using a common hollow wall anchors for fixation in cadaveric osteoporotic human lumbar vertebral bodies compared to a standard screw demonstrated a 76% increase in the ultimate holding power (McKoy & An, 2001). A number of expandable fasteners designed specifically for lumbar pedicle fixation have been developed since and are summarised on the following pages.

Omega-21

The Omega-21 Spinal Fixation System was developed in the late 90s specifically for lumbar pedicle fixation. It has a 7 mm outer diameter with an increased screw tip diameter of 2 mm. The Omega 21 has four longitudinal slots creating four expanding fins. Biomechanical testing in cadaveric human lumbar vertebrae demonstrated a statistically significant, 47% increase in fixation strength for Omega-21 expandable screw compared to standard pedicle screws in osteoporotic bone but an insignificant 19% increase in healthy bone (Cook et al., 2000). The clinical outcome of screw loosening and fusion rate when using the Omega-21 expandable pedicle screw in a patient cohort with a large number of osteoporotic and revision cases is comparable to the clinical outcomes of other studies but with less demanding patient cohort (Cook, Barbera, Rubi, Salkeld, & Whitecloud III, 2001). In this study however, in three out of six patients, the expandable screws that had to be removed due to local discomfort broke during removal. In one of these patients the broken part of the expandable screw had to be left inside the bone, which is not ideal as it represents an infection risk among other potential issues.

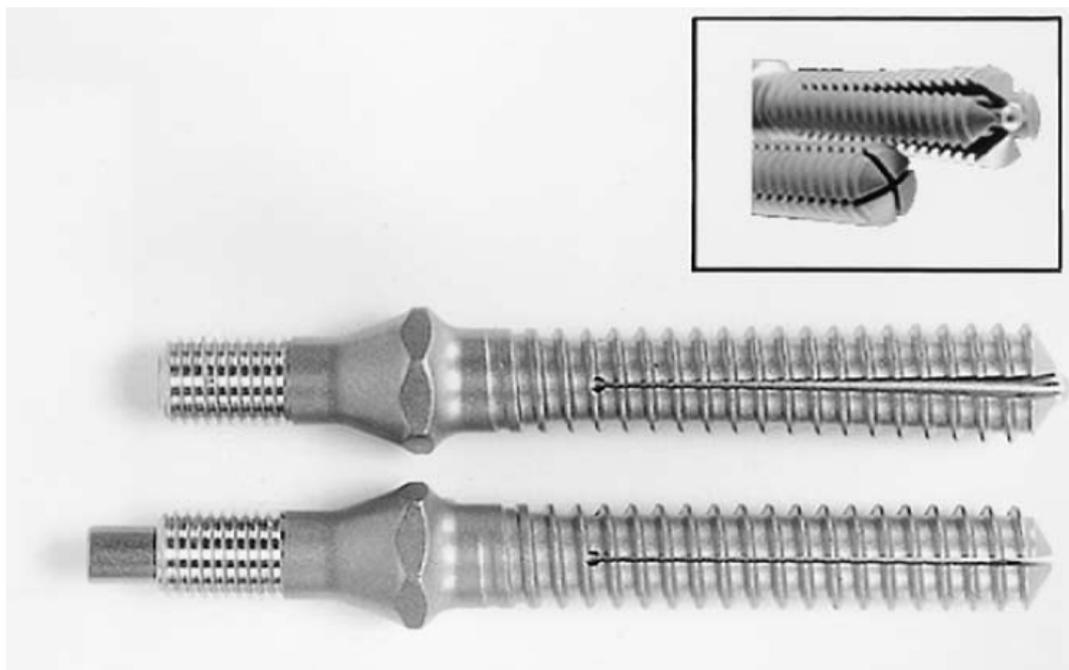


Figure 3-22 The Omega-21 Lumbar Expandable Pedicle Screw (Cook et al., 2001)

Osseoscrew

Osseoscrew is a titanium pedicle screw with an expanded section at the vertebral body-pedicle junction which increases in diameter by approximately 50% as shown in Figure 3-23. Vishnubhotla et al. (2011) conducted axial pull-out testing in human osteoporotic cadaveric vertebrae and reported a 25% increase in yield load of the expandable screw compared to a standard screw, although this increase is not statistically significant. They did however report a statistically significant increase in ultimate load of 30% ($p < 0.5$) and failure energy (area under the load-displacement curve) of 160% ($p < 0.0001$). The study also suggested that future studies on these types of devices should consider evaluating cyclic performance with more representative loading conditions (flexion/extension, lateral bending, and axial torsion).

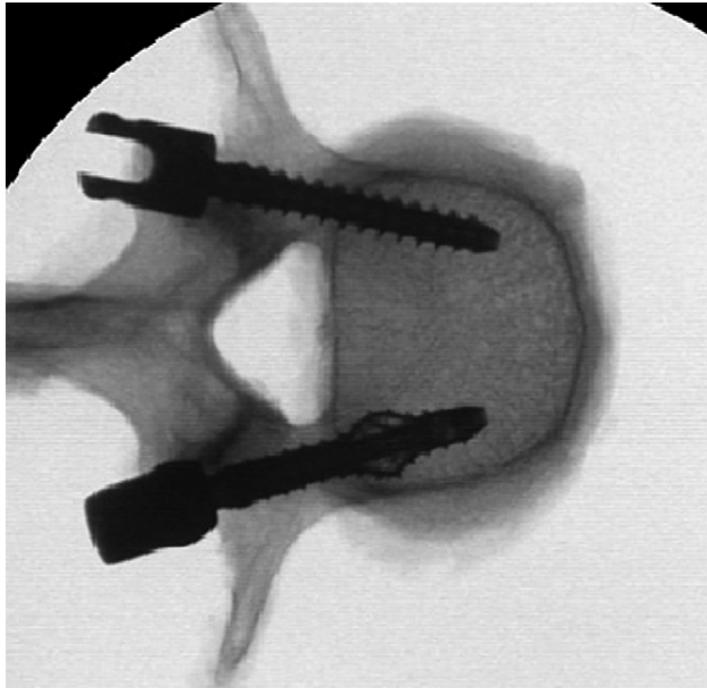


Figure 3-23 The Osseoscrew and a standard 6.5 mm pedicle screw in a lumbar vertebra (Vishnubhotla et al., 2011)

XPed

XPed is another expandable pedicle screw in the market which has four centro-symmetrical fins that expands by advancing an internal gauge screw, as shown in Figure 3-24. Similar to Osseoscrew, the expansion occurs at the vertebral body-pedicle junction but the diameter can increase by slightly more, approximately 60%. Chen et al. (2014) conducted axial pull-out testing of the expandable screw compared to conventional pedicle screws and bone cement augmented pedicle screws in a synthetic bone model with density of 0.09 g/cm^3 . They reported an almost five fold increase in pull-out force of the expandable fastener compared to a conventional pedicle screw from 23N to 110.9N, and a statistically significant 34% increase compared to the pedicle screw with 1 ml of bone cement augmentation, confirming its potential usefulness in patients with osteoporosis without the risks associated with bone cement.



Figure 3-24 The XPed expandable pedicle screw (Hofheinz, 2014)

EPS

The EPS expandable pedicle screw has four longitudinal slots which allow the expansion of four fins by inserting a smaller gauge screw into the threaded interior. The EPS is barrel-shaped with an outer diameter of 6.5 mm or 7.0 mm and a 2.5 mm bore and can be expanded by approximately 2.5 mm in diameter at the tip. This is a 36-38% expansion, slightly less than the Osseoscrew.

Lei and Wu (2006) conducted biomechanical testing of the EPS in calf vertebrae and were able to demonstrate a statistically significant increase in axial pull-out strength over conventional pedicle screws of 43%. They also demonstrated equivalent fatigue strength of the EPS compared to conventional screw at 1.5M cycles. Wan et al. (2010) conducted in-vivo animal study to assess the long term osseointegration and biomechanical characteristic of the EPS with osteoporotic induced sheep.

The design of the EPS in this experiment and subsequent publications only has two rather than four fins. After six months implantation the EPS provided 59.6% increase in pull-out strength over conventional pedicle screw and were able to withstand greater number of cycles before loosening. Furthermore, micro-CT and histology imaging demonstrated denser trabecular architecture and more favourable bone morphological properties around the EPS compared to the conventional screw. However, as was also shown through the histology imaging, newly formed bone tissues have grown into the centre of the EPS which can potentially inhibit its ability to close and be removed in case of a revision surgery.

Wu et al. (2012) conducted a randomised clinical trial with 157 patients with osteoporosis to assess the performance of the EPS compared to conventional pedicle screws (CPS) with a minimum follow-up time of 24 months. They reported a significantly lower rate of screw loosening for the EPS group of 4.1% compared to the CPS group of 12.9%. Furthermore, the fusion rate in the EPS group was significantly higher at 92.5% of patients compared to the CPS group at 80.5% of patients. So the authors concluded that the use expandable pedicle screws in patients with osteoporosis can achieve better outcome than using conventional pedicle screws.

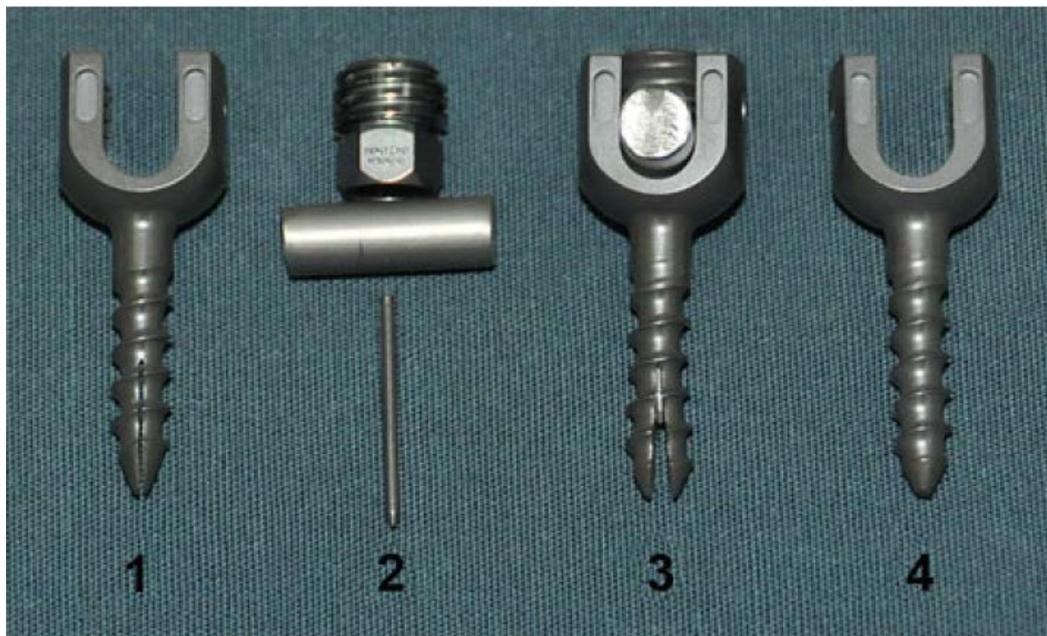


Figure 3-25 The EPS Expandable pedicle screw (Wan et al., 2010)

3.7.3 Cervical spine

There are less expandable screws for the cervical spine compared to the lumbar pedicle application, potentially because of the challenge in making small diameter expandable screws. Zhou, Xu, Zhang, Chen, and Lv (2014) developed a built-in expandable anterior spinal internal fixation system which was biomechanically tested in a porcine model. They demonstrated improvement in axial rotational stability compared to two other commonly used systems and also better pull-out strength than a common fixation screw.

Osmium

The Osmium screw (see Figure 3-26) developed by Ulrich Medical and is commercially available in diameters 4.0, 4.5 and 5.0 mm (Ulrich Medical, n.d.). Similar to the design of the Omega-21 pedicle screw, the Osmium screw has four fins that are expanded by inserting a screw gauge into the internal hole. Rohl et al. (2009) conducted range of movement testing using artificially de-stabilised cadaveric cervical spine which is then stabilised with anterior cervical plating either with bicortical fixation of conventional screws or monocortical fixation of expandable screws. They demonstrated similar stiffness in all three axes of movement which suggests clinically that the expandable fastener can provide equivalent fixation strength and cervical spine stabilisation to bicortical fixation without its associated risk of overpenetration.

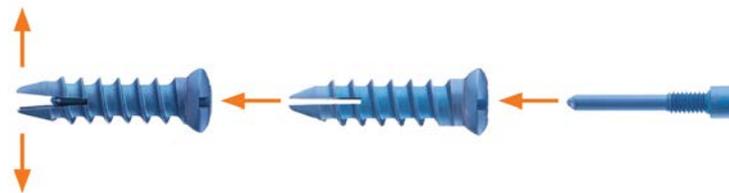


Figure 3-26 The Osmium expandable anterior cervical vertebral body screw (Ulrich Medical, n.d.)

3.7.4 Soft tissue anchors

A number of expandable devices have been developed for the application of soft tissue anchors. Two products that are currently commercially available are the Appian KFx and Medshape Morphix.

KFx

The AppianFx expandable anchor was developed by KFx Medical for fixation of soft tissues to bone in many different areas throughout the body such as shoulder, foot and knee. Ehrensberger, Hohman, Duncan, Howard, and Bisson (2013) conducted a biomechanical testing of the AppianFx compared to a market accepted product AperFix in porcine femurs as a model for anterior cruciate ligament reconstruction and demonstrated a statistically higher yield load for the AppianFx but no difference for the maximum load and stiffness.

Morphix

Morphix was developed by Medshape with the theoretical basis that increase in bearing area increases the fixation strength of tissue anchors. A study by Yakacki, Griffis, Poukalova, and Gall (2009) demonstrated and validated this hypothesis in synthetic bone model with varying sized conical plugs as an expandable fastener model for pull-out testing.

3.7.5 Summary

Previous studies on expandable fasteners have focused on demonstrating proof-of-concept in that expandable fasteners provide increased fixation strength compared to conventional screws, typically for a potential orthopaedic product. This is usually performed using pull-out testing from a synthetic bone sample, an animal bone model or a human cadaveric sample. Additionally, a clinical trial has also demonstrated better clinical outcomes for an expandable screw (Wu et al., 2012).

No previous studies have investigated the effect of bone morphology on expandable fasteners compared to conventional fasteners, however studies have suggested that expandable fasteners may perform better in osteoporotic bone (Cook et al., 2000; McKoy & An, 2001). Furthermore no previous studies have investigated the effect on failure force when varying design parameters such as expansion size or expansion angle, or critical surgical parameters such as pilot hole size. Understanding better the advantages and constraints of expandable fasteners is a critical step for this technology to be widely adopted.

Chapter 4 Design of the EXF Screw

The design process conducted in this thesis follows the Rudimentary Design Process (RDP) (Wright, 2005) a minimalist version of the Pahl and Beitz design process (Pahl & Beitz, 2013). The overall process can be divided into four stages, including design basis development, concept design, design development and detailed design, as shown in Figure 4-1 below. In addition to these stages this chapter also discusses the patentability analyses performed over the project.

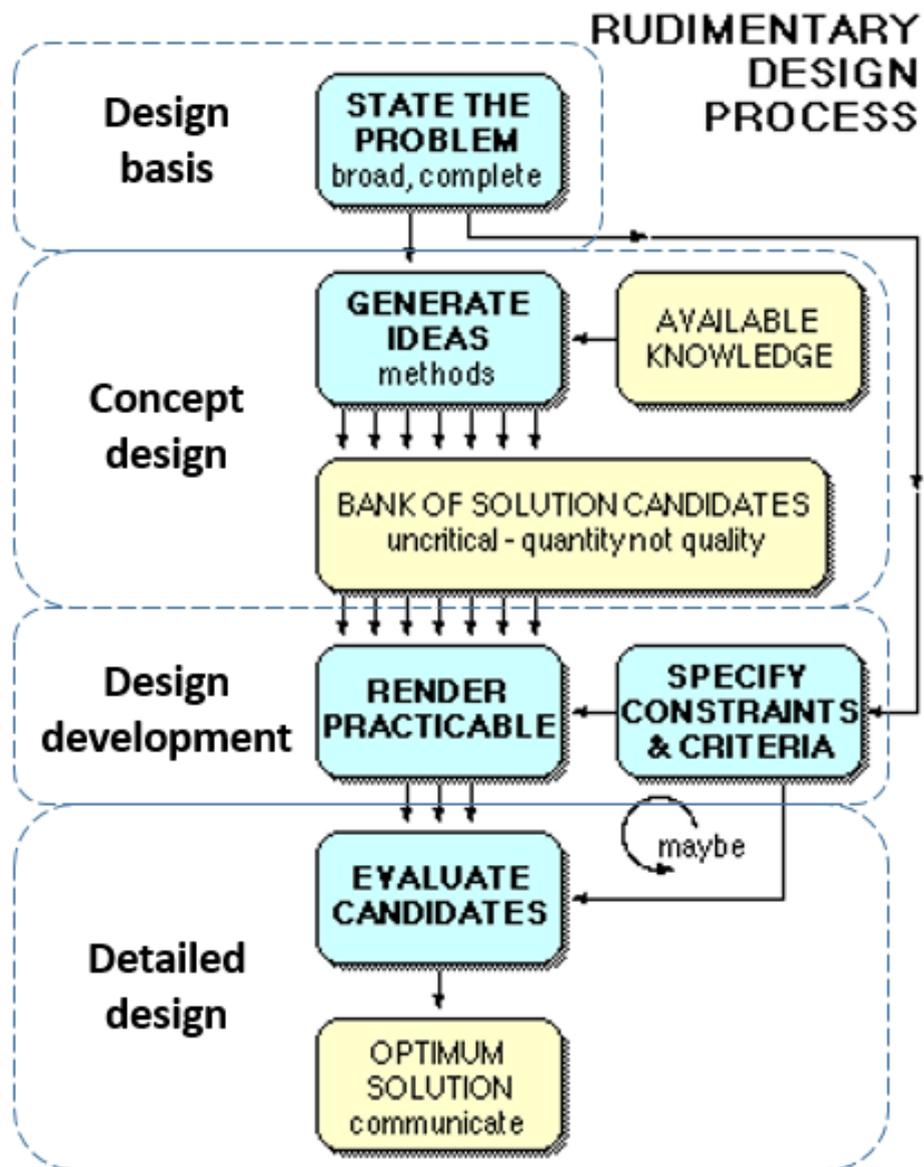


Figure 4-1 The Rudimentary Design Process (Wright, 2005) annotated with the design stages used in this thesis

The initial focus of the thesis to develop an integrated dynamic stabilisation device (SZ) went through concept design, patentability analysis and basic prototypes were manufactured before it was concluded that dynamic stabilisation was not currently commercially feasible. The focus of the project then went to developing a stand-alone unthreaded expandable fastener (UEF), which was initially designed for fixation in the cervical spine. The UEF went through concept design, patentability analysis and design development for prototyping and mechanical testing. However after some feedback on the criticality of removability from surgeons and industry contacts, as well as a number of issues with the prototypes, the design was modified to the EXF (EXpandable Fastener) Screw, a threaded and removable expandable screw. This involved repeating the previous stages before moving to detailed design.

The following chapters will provide details of the different stages of development for the three product iterations, with the EXF Screw proceeding to detailed design for optimisation.

4.1 SZ - Dynamic Stabilisation Device

The design development of the SZ device will not be described in detail as it is no longer the focus of the thesis and is not specifically relevant for the remainder of the thesis document. However a brief description will be provided in this chapter to provide context for subsequent chapters.

4.1.1 Design basis

Problem statement

Decrease the incidence of adjacent segment degeneration associated with cervical spine fusion surgery, without the associated additional risks and complications of a total disc replacement, by providing a posterior cervical dynamic stabilisation device that can be adjusted by the surgeon to provide an appropriate range of motion to suit the patient pathology.

Design constraints

Design constraints are those conditions that must be met for the design to be viable to achieve the intended goal. Many of these design constraints are standard requirements for medical devices, whilst others are necessary to ensure the commercial viability of the product. The list below is the design constraints that were applied in the design generation of the SZ.

The SZ:

1. must provide an adjustable, restricted range of motion for the affected spinal segment;
2. must not fail under typical physiological loading;
3. must be biocompatible;
4. must be manufacturable;
5. must be sterilisable; and
6. must involve commercially protectable IP.

Constraint 1 is required to satisfy the problem statement. Constraints 2-5 are the basic service requirements of any medical implant, without satisfying these constraints the fastener would not be functional. Constraint 6 requires the critical features of the design to be novel and inventive and therefore patentable, which is necessary for viable commercialisation of the project.

4.1.2 Concept design

To generate the initial concept design, a survey of available dynamic stabilisation devices for spinal application was conducted and various designs that can achieve the problem statement as well as satisfy the design constraints were generated. The various designs generated during this design phase can be found in the published patent document (Oldakowski, Oldakowska, et al., 2013).

4.1.3 Patentability analysis

After the concept design phase, a patent landscape search using “Espacenet Worldwide”, a patent database, was conducted to determine whether the concept was sufficiently novel and inventive to be patented. The search was conducted specifically for all patents with the classification code “A61B17: Surgical instruments, devices or methods, e.g. tourniquets” using the search terms “dynamic stabilisation/stabilization”

To determine whether the concept was novel all the distinct design features that comprised the design were listed and all the relevant patents were reviewed to determine which of these design features each patent contained. A table was produced by the author to demonstrate the gap in the IP landscape and can be found in Appendix J.

Two fundamental aspects of the preliminary design were not found anywhere in the patent search:

- the integrated expandable fasteners with a bone stabilising element to form a single part unit; and
- the adjustable, controlled range of motion mechanism as part of a bone stabilising element.

In order to convey the necessary information to the patent attorney, a document was created by the author which contained information required for drafting the patent specification. The full text of the patent is available online (Oldakowski, Oldakowska, et al., 2013).

4.1.4 Design development

Once the provisional patent was submitted, a number of designs were generated and prototype manufactured. A poster that summarises the chosen design was presented at the International Society for Technology in Arthroplasty Annual Congress (Appendix D) and the abstract was published (Oldakowski, Hardcastle, et al., 2013). However during this conference and subsequently through the industry contacts, it became apparent that dynamic stabilisation was not currently commercially attractive. Subsequently the thesis changed focus to develop the expandable fastener aspect of the project as a standalone device, the UEF (Unthreaded Expandable Fastener).

4.2 UEF – Unthreaded Expandable Fastener

4.2.1 Design basis

The UEF was developed on the basis that integrating an expandable fastener with a stabilising element to form a single part fixation unit (as compared to a plate and screws or rod and screws) may simplify surgical procedures involving small screws and plates. For example in some surgeries, such as tarsal fusion or high tibial osteotomies, surgeons may opt to use a staple, rather than a plate and screw, to hold two bones together (see Figure 4-3). However staples provide less fixation strength than screws. Consequently adding an expanding section and increasing the fixation strength of staples may render them feasible in new indications. In these new indications or previous indications, the simplicity of a single part unit compared to a conventional plate and screw system may reduce the difficulty of these procedures by eliminating the need to align the fasteners.

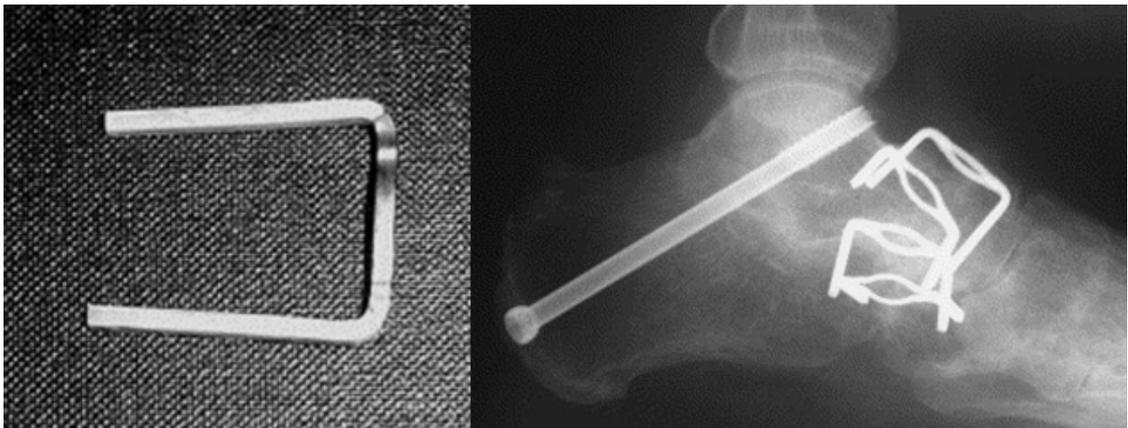


Figure 4-3 A surgical staple (left) used to connect small bones in the foot for fusion (right)
(Malal, Hegde, & Ferdinand, 2006)

Problem statement

Integrate the fasteners and stabilising elements together to form a single part unit and decrease the risk of orthopaedic screw fixation failure.

Design constraints

The following list are the design constraints that were applied in the design generation of the UEF.

The UEF:

1. must be able to be integrated to a stabilisation device;
2. must increase the pull-out force and/or reduce the fastener length;
3. must fit within the bone;
4. must not crack the bone during expansion;
5. must be able to survive physiological loading;
6. must be biocompatible;
7. must be manufacturable;
8. must be sterilisable; and
9. must generate protectable IP.

Constraints 1 and 2 are required to satisfy the problem statement. Constraints 3 and 4 are necessary for successful implantation of the expandable fastener but depend on the screw trajectory and implantation procedure. Constraints 5-9 are basic service and commercial requirements as previously outlined for the SZ device.

4.2.2 Concept design

To generate the initial concept design, a survey of available expandable fasteners in the orthopaedic space as well as in other non-medical application was conducted. Many of the expandable fasteners found in the orthopaedic application have been described in Chapter 3 ('Literature review') in Section 3.7 ('Expandable orthopaedic fasteners'). Three major design types were identified within the literature with minor differences within each type.

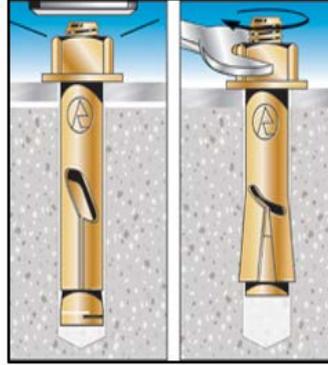
These three types are listed below:

1. 'Molly-bolt' type fasteners (such as X-Bolt or X-Ped) whereby axial compression, causing the fastener to bend open, can be created by turning an expansion bolt or applying compressive pressure;
2. 'Dynabolt' type fasteners (such as Morpheus, KFx) whereby a pulling action on a central pin splays open the fastener; or
3. 'Wall plug' type fasteners (such as Omega-21, EPS, Osmium) which open with an expansion pin pushing open the fastener from above.

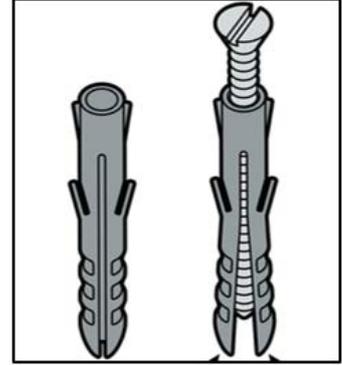
Molly-bolt design



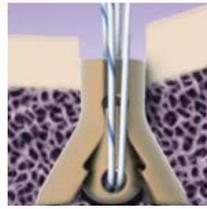
Dyna-bolt design



Wall-plug design



X-bolt



Morphix



Osmium



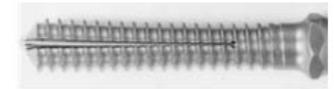
X-Ped



KFx



EPS



Omega-21

Figure 4-4 A molly-bolt (top left) design is used by the X-bolt (centre left) and the X-Ped (bottom left). A dyno-bolt (top middle) design is used by the Morphix (middle middle) and the KFx (Bottom middle). A wall-plug (top right) design is used by the Osmium (middle right) and the Omega-21 and EPS (bottom right)

The Molly-bolt mechanism is the only type that can create a contraction force without a complex mechanism, by turning back the expansion bolt in the reverse direction (this requires the head of the expansion bolt to be restrained in both axial directions, unlike typical hardware molly-bolts). However the strain in the fastener is higher than the other two mechanisms due to the severe bend (twice the expansion angle) required at the junction of the two expandable sections. Furthermore the mechanism, due to limited mechanical advantage can require high axial force to bend open the expansion tabs and the mechanism can twist during expansion or under rotational loading. In preliminary testing it was found that hardware molly-bolts twisted during expansion even in low density, synthetic bone. This issue was also raised by Gibson et al. (2012) who were unable to expand the X-Bolt in low density synthetic bone during their testing, which has subsequently forced the X-Bolt to include a bone reaming procedure in their surgical instructions to allow the expansion. Lastly because the molly-bolt designs have expansion tabs facing different directions (upwards and downwards) this means that approximately half of the expanded section (the bottom half) does not engage the bone during pull-out (and the top half doesn't engage the bone in push in).

The Dyna-bolt mechanism is suited to tension only fasteners (soft tissue anchors) as pulling up the expansion member leaves a void below the fastener which would significantly weaken the fastener in push-in. Furthermore to un-expand the fastener the central member has to be forced downwards to its original position (difficult if bone has grown underneath it) and then contracted (via another mechanism) and removed, which is difficult in practise.

The Wall-plug mechanism is the simplest mechanism to implement and consequently the earliest prototypes found in the literature used this mechanism. The entirety of the expanded area engages the bone in a single direction, pull-out. Furthermore the voids inside the fastener where bone can grow preventing contraction for removal are typically smaller than other expansion mechanisms.

Other, more creative, expansion mechanisms outside of these three 'types' that have been considered previously include:

1. Inflation (See Figure 4-5), whereby hydraulic pressure can be used to expand open a fastener, such as the Expandable Fixation Nails (Steinberg et al., 2006). Although potentially complicated, this provides the potential for an entirely gapless expansion with no potential for bone in-growth. However because of the complex and indeterminate expanded and contracted shape, removal may be difficult.



Figure 4-5 Hydraulic pressure is used to expand the Expandable fixation nails (Steinberg et al., 2006)

2. Shape Memory Alloy actuation, whereby heating of the fastener by placing it in the body would cause an expansion. This method has been successfully used for fracture reduction in surgical staples (Malal et al., 2006) and has been previously used to create prototypes of an expanding pedicle screw (Tabesh, Goel, & Elahinia, 2012). However the force required to expand into bone was too high for the shape memory alloy actuation.

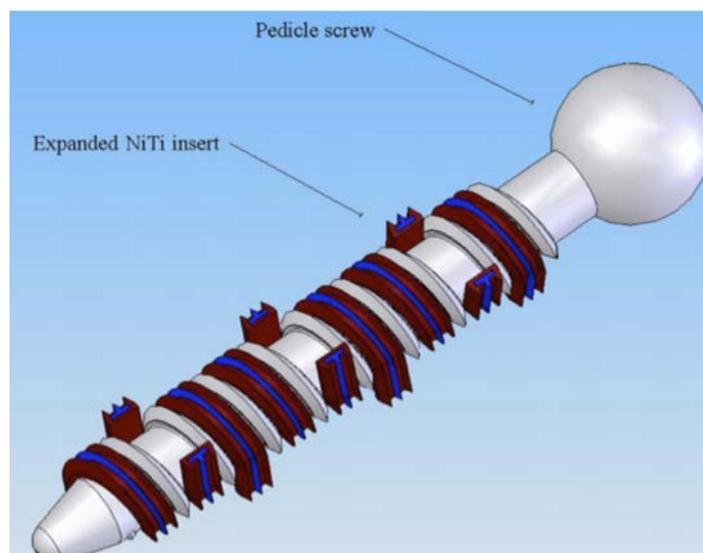


Figure 4-6 Shape Memory Alloy could potentially be used to expand a screw into the bone, similar to the concept of the SMArt Screw (Tabesh et al., 2012)

The various expandable fastener designs generated during the concept design stage can be found in AU2014900596, the published patent (Oldakowski, Oldakowska, et al., 2015).

4.2.3 Patentability analysis

Another patent landscape search was conducted for the specific features of the stand-alone expandable fastener after the concept design phase and a feature table to assess the novelty and inventiveness of the new design was produced by Intan Oldakowska (another PhD student). Although many of the obvious design concepts were found within the patent literature, the specific design feature of ‘largely rectangular expansion tabs’ to allow large expansion whilst still staying within the material’s elastic region was novel and inventive. This formed the main claim within AU2014900596, the second patent (Oldakowski, Oldakowska, et al., 2015).

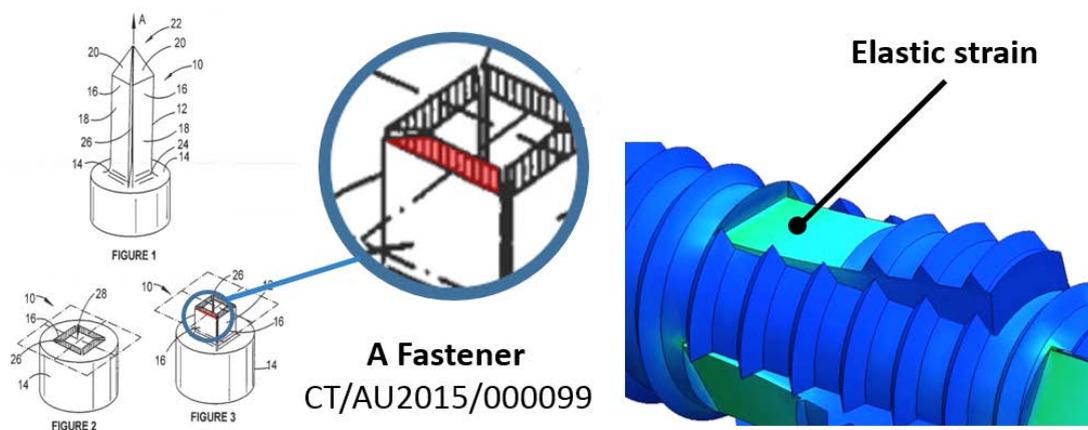


Figure 4-7 The ‘largely rectangular expansion tabs’ (highlighted in red) as described in the patent as filed (Oldakowski, Oldakowska, et al., 2015)

4.2.4 Design development

The first and only design to progress through prototyping and mechanical testing was the square UEF (Unthreaded Expandable Fastener) shown in Figure 4-8 below.

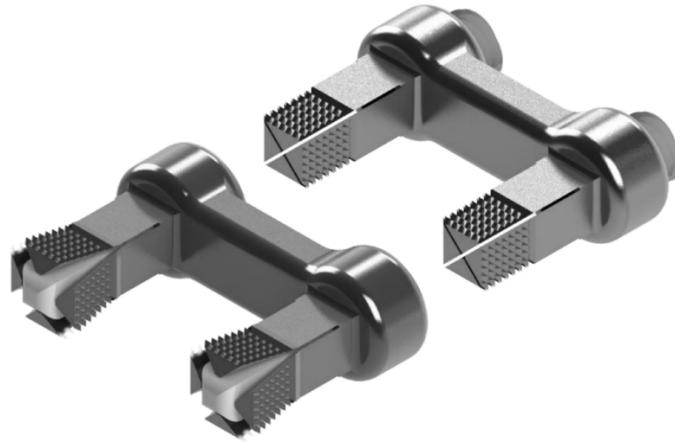


Figure 4-8 An expanded (bottom) and unexpanded (top) UEF design

The UEF design was selected as it satisfies all the design constraints. The unthreaded nature of the fastener allows it to be inserted into the bone linearly, unlike screws (which must be rotated about their axis), so that it can be integrated to the stabilising element. The UEF may have pointed self-awling tips so that hole drilling could be avoided, potentially allowing the implant and all its fasteners to be implanted in a single action (like a staple), reducing the complexity of the procedure.

Prototypes of the UEF were manufactured from a low-modulus pure-beta Titanium alloy (Ti-24Nb-4Zr-8Sn, all in wt%) using Selective Laser Melting, to determine feasibility and in order to mechanically evaluate the design. The detailed methodology and results of the mechanical testing is described in Chapter 5 ('Preliminary UEF pull-out strength testing').

During the mechanical testing phase, a number of design problems were encountered including high expansion force, expansion pin wear down, uneven expansion and difficulty in creating a square bore hole. Furthermore during that period feedback was received from the industry and surgeons that removability was critical and that surgeons had reservations about the square fastener requiring a square bore hole, necessitating a change in the surgical procedure from rotational insertion, as is the case with conventional screws, to linear insertion. These issues are discussed in detail below.

High expansion force

The force required to expand the UEF prototypes in ovine bone was very high. In a pilot study, in one sample the thread of the actuating screw was stripped and in another sample torsional failure occurred in the head of the screw during expansion. After this, care was taken to ensure the axis of the screw and screw driver were perpendicular and the samples

tested in Chapter 5 ('Preliminary UEF pull-out strength testing') did not experience this failure mode.

The expansion force is high because the expanding arms of the fastener are pushing a large volume of cancellous bone outwards during expansion. The expansion force can be reduced by decreasing the amount of bone under compression by reducing the height of the expanded section or the expansion size, removing volume from the expansion arm or potentially by sharpening the edges of the expanding arm to promote penetration of the cancellous bone, as shown in Figure 4-9 below.

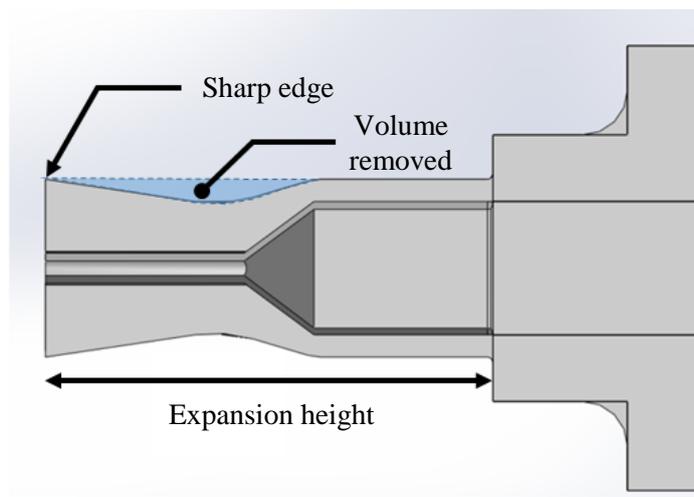


Figure 4-9 The expansion force can be reduced by reducing the expansion height, removing volume from the expansion arm or sharpening the edge of the expanding arm

Expansion pin wear

High Resolution Computed Tomography (HR-CT) scans of the expanded fasteners inside the bone and visual inspection of the samples post failure demonstrated that the thread of the actuating screw was worn down by the relative motion of the thread and the rough expansion surface (surfaces created by SLM, especially those built on an angle have high surface roughness). Consequently the fasteners did not achieve their theoretical, designed expansion size. Furthermore, a fine steel powder was found within the failed bone which created bloom artefacts in the CT images. Clinically this powder could cause osteolysis, an inflammatory response of the bone that may lead to bone density reduction and eventual failure of the fastener.

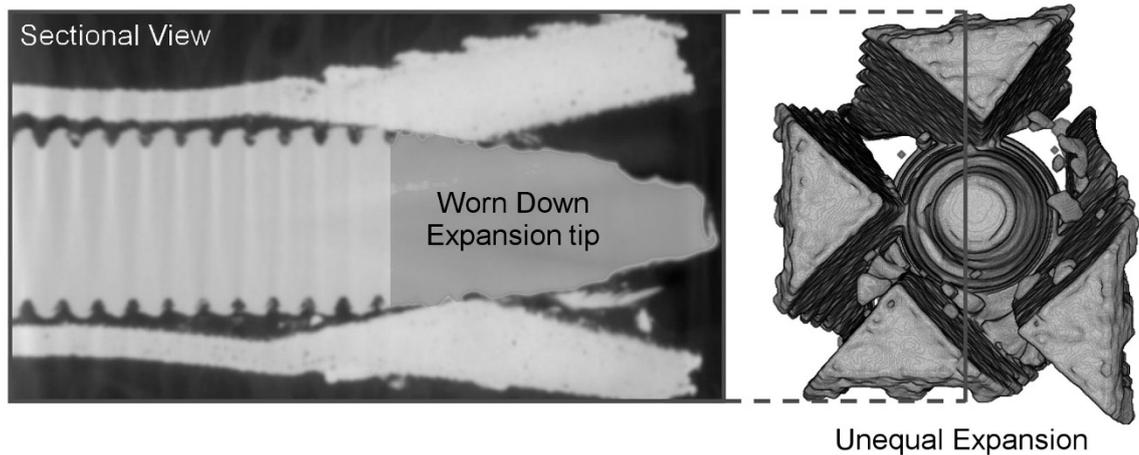


Figure 4-10 CT scanning the expanded samples inside the bone samples demonstrated a worn down expansion tip (left) and uneven expansion (right)

In subsequent designs, to address this, the fasteners were expanded with a square profile pin that was introduced via a linear pushing force. Unfortunately this method also presented some issues because the fidelity of the square SLM hole was low due to the rough surface, meaning that the square expander pin needed to be significantly undersized to be able to be advanced within the hole. This allowed the expansion pin to extend on a non-axial angle, causing uneven expansion (see Figure 4-11 below). A solution to this problem was to use a higher tolerance round expansion pin.

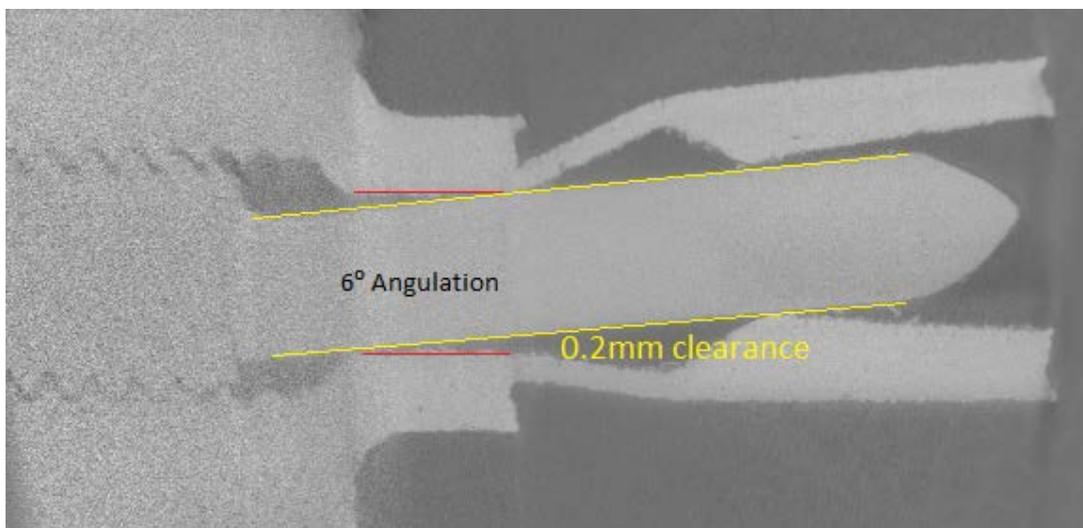


Figure 4-11 High clearance (0.2mm) around the square expansion pin allows significant expansion pin angulation (6°)

Uneven expansion

Another issue with the threaded expansion pin was the tangential force applied to the inner surface of the fastener as the expansion bolt was turning. Under a large expansion force this could twist the fastener, causing uneven expansion (see Figure 4-10 right). Although uneven expansion is a consequence of high expansion force there are methods to deal with this problem, such as increasing the stiffness of the fastener material or the sectional modulus of the expansion tabs. Increasing the modulus of the expansion tabs is not ideal as minimum sectional modulus is preferable to maximise the range of elastic expansion. A guide could be provided to limit the ends of the expansion legs to linear movement. This was achieved in the subsequent EXF Screw design, where the tab sat within a channel in the body of the screw.

Square UEF criticism

Surgeons indicated that creating a square hole in surgery was unattractive. It may require a pre-drilled hole and then an awling step (which was the experimental procedure for the UEF testing) and it may be ambiguous as to how much force needed to be applied to the awl and run the risk of cortical bursting or over-penetration of the awl.

These problems were experienced in the UEF tests. The awl was difficult to insert without using excessive force and was difficult to remove afterwards. Furthermore 1 of the 10 post-awled bone samples had a burst cortex that was identified from the CT scan. This was the sample which required the most force to remove the awl. Furthermore the corners of the square hole may create stress raisers, which could limit the failure force of the fastener. These problems could be addressed by creating a round fastener that still had the planar bending profiles that form the basis of the second patent (Oldakowski, Oldakowska, et al., 2015) and was achieved with the subsequent EXF Screw design.

Removability

Surgeons strongly prefer for implants to be removable (see Appendix A: EXF Screw voice of customer surgeon survey for details) so that if there is a complication during or after surgery they are able to remove the fasteners if required and don't have to damage the bone excessively when removing the fasteners. In previous studies with expandable screws there have been cases of screw breakage (Wu et al., 2012; X-Bolt Orthopaedics, 2014) and of bone fracture during revision surgery after the screw has been in the bone for a period of time. Conventional screws are relatively easy to remove if the implant has just been implanted and no bone in-growth has occurred. Similarly the UEF was designed to be removable by removing the central pin and pulling the fastener out linearly. However, after the implant has osseointegrated removal may be more difficult, especially if bone has grown inside the expanded fastener jamming open the mechanism. Consequently, preventing bone in-growth inside the fastener was the focus of the EXF Screw design.

4.3 EXF Screw

The feedback received from surgeons and implant manufacturers about the UEF was that:

1. A linear push implantation procedure (as required for the square, unthreaded UEF) would require the surgeon to do a non-standard surgical procedure which could hinder surgeon adoption; and
2. Full removability, even after potential bone in-growth into the mechanism over time, is critical for most orthopaedic applications and a major hurdle in adoption for other expandable screws.

Considering the technical issues with the UEF outlined above and the industry feedback, the project pivoted to develop a stand-alone expandable fastener which addresses these issues, the EXF Screw.

4.3.1 Design basis

Problem statement

Decrease the risk of orthopaedic screw fixation failure without increasing difficulty of the initial surgery or the revision surgery.

Design constraints

The list below is the final design constraints that were applied in the design generation of the EXF Screw.

The EXF Screw:

1. must increase the failure force;
2. must be removable, even after being in-vivo for a significant period;
3. must be able to endure physiological loading (fatigue strength);
4. must be biocompatible;
5. must be sterilisable;
6. must generate protectable IP;
7. must not require excessive force to expand; and
8. must not significantly increase manufacturing cost.

Constraints 1-2 are required to satisfy the problem statement. Where the UEF focused on increasing pull-out strength (for spinal applications), the EXF Screw focused on push-in and shear failure, which was the failure mode in the primary indication, proximal humerus fractures. Constraints 3-6 are the basic requirements of an orthopaedic fastener project, as was the case for the UEF design basis, described in detail in that section. Constraint 7 was based on the investigation with the UEF design, whereby a high expansion force caused problems. Lastly, Constraint 8 was modified from the design basis of the UEF based upon feedback from implant manufacturers that any significant increase in manufacturing cost (more than “a couple of dollars” per screw) would make the screws commercially non-viable.

4.3.2 Concept design

The majority of the concept design generation related to achieving removability even after long term implantation, as this was the critical design flaw of previous expandable fasteners based on the industry and surgeon feedback. This requirement can be divided into two sub-requirements: allowing forced removability of the fastener to overcome osseointegration and preventing bone from growing into the mechanism. The EXF Screw designs also involved a shallow conventional thread to allow the screw to be implanted and removed by the conventional means of screwing in and out, based on surgeon preference.

Forced expandable fastener contraction

The simplest method to allow the expandable fastener to be removable is to use the elastic response of the material in the bending sections of the fastener to return the fastener to its contracted state once the pin is removed. However, FEA demonstrated that for the expansion sizes designed for the UEF, this was not possible using the standard medical grade titanium alloy (Ti-6Al-4V), which had a low yield strain of approximately 1%. However, using Shape Memory Alloy (SMA), which has a yield strain of 4-8% this may be possible. SMA has a similar Young's Modulus to titanium and has been used previously in orthopaedic applications (Malal et al., 2006; Van Kampen, Thoreson, Knutson, Hale, & Moran, 2013).

Therefore if the elastic response of the material does not fully close the expandable screw, some radial compression force is required to contract it for removal. This can be achieved by a number of methods detailed below:

1. Filleted edges, where the edges of the expansion tab are filleted (see Figure 4-12) so that the anti-clockwise rotation initiated by the surgeon when they are removing the screw, will preferentially urge the expansion tabs radially inwards to their unexpanded orientation if they become jammed.

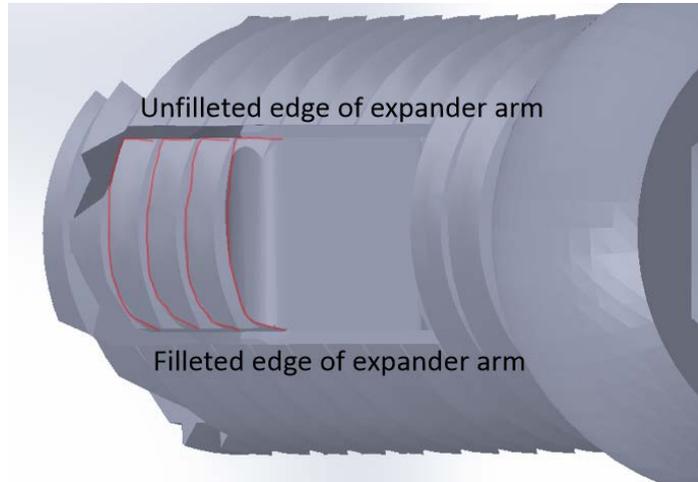


Figure 4-12 Filleting one side of the expander tab and not the other allows the fastener to preferentially close during turning

2. An elastic, spring element could be introduced into the design to allow increased elastic un-expansion force. In the case of additive manufacturing this could be introduced mid-build to allow the element to be entirely encapsulated. The elastic element could be constructed in a number of different ways from an elastic ring (such as an ‘O-ring’) or else an entirely metal, such as nickel titanium ‘C-spring’.

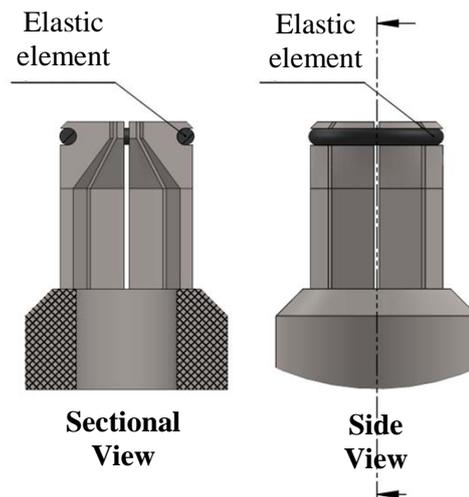


Figure 4-13 An elastic element such as an ‘O-ring’, shown above, could be used to augment the elastic response of the fastener

3. A contraction tool that could be introduced into the fastener that interferes with pre-designed radial slots that taper inwards in order to pull the expansion tabs inwards. As the element advances the slots taper inwards and forward movement of element pulls the arms together.

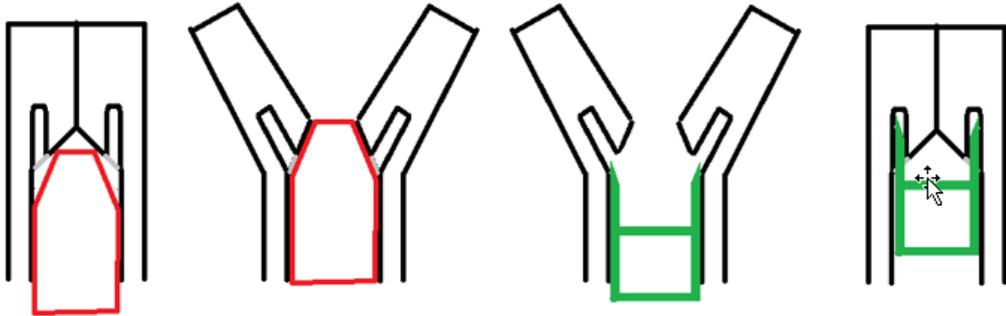


Figure 4-14 The fastener may be expanded using the red expander tool (left) and contracted using the green contraction tool to return to its unexpanded orientation (right)

4. The expansion pin could be designed so that it fits within the dynamic expansion tabs of the fastener so that pulling back on the pin could initiate contraction of the fastener, as shown in Figure 4-15.

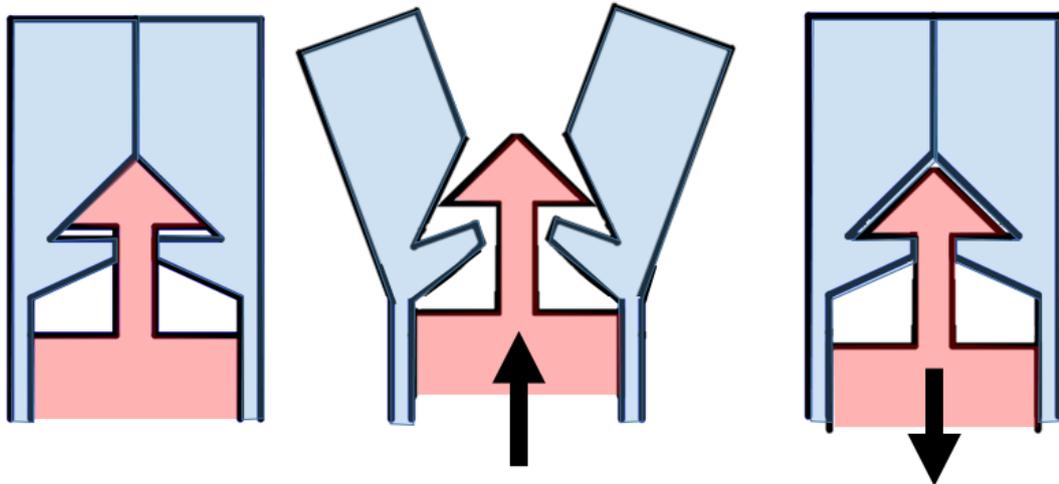


Figure 4-15 A pin (red) could be designed to fit within the dynamic expansion tabs (blue) of the fastener, so that after expansion (centre), under a pulling force on the pin, the expander can be closed (right)

Preventing bone in-growth

The most effective way to prevent bone in-growth is to create a fastener with ‘gap-less expansion’. Gapless expansion is an expandable fastener that, once expanded, doesn’t have any gaps in its exterior surface where bone can grow into. This prevents bone in-growth from jamming the mechanism and allows it to be closed even after being in the body for a significant period of time, allowing easy removal during revision surgery.

Gapless expansion can be achieved by having sections of the fastener that expand (dynamic expansion tabs) and sections that don’t (static columns). This allows the creation of a line of contact that runs down the fastener’s dynamic expansion tabs and encompasses all external junctions between the static columns and the dynamic expansion tabs. In Figure 4-16 below the red line represents the interface between the static column and dynamic arm which prevents bone from growing inside the fastener.

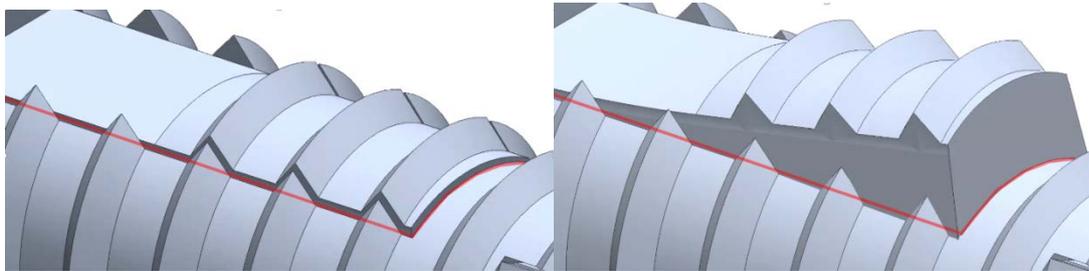


Figure 4-16 The red line denotes the contact between the static columns and dynamic expansion tabs of the screw before (left) and after (right) expansion

A number of methods of achieving gapless expansion were identified including:

1. Effectively ‘zero-thickness’ slots that may be created by the SLM allows parallel expansion tabs to create gaps that are so small bone cannot grow through them;
2. Angulated expansion arm profiles, where the slightly inwardly wedging sides of the expansion tabs interfere with parallel or outwardly wedging static columns, leaving no gaps (as seen in Figure 4-17).

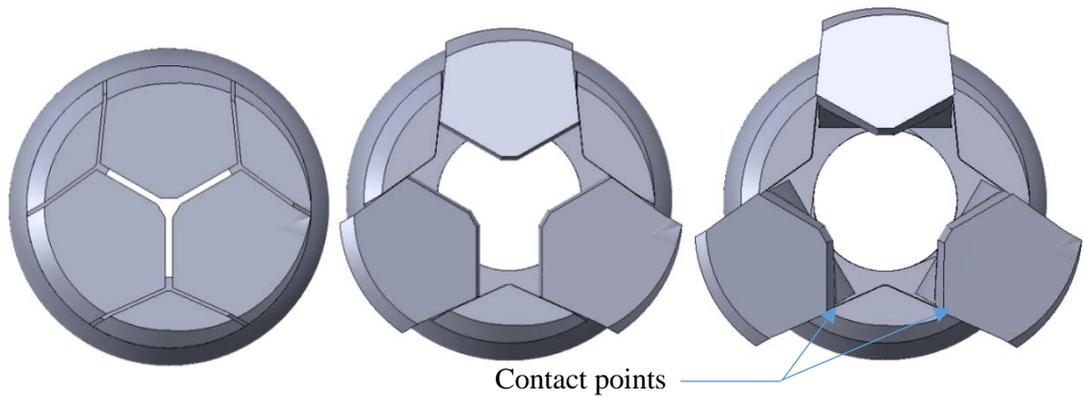


Figure 4-17 The angulation between the static and dynamic sides causes the gap between them to close as the fastener expands

3. A metallic seal may be created by using a very thin section of material at the exterior of the static columns. This section is designed to slide over the expansion tabs creating effectively a metallic seal, preventing bone in-growth (as seen in Figure 4-18). This may only be feasible using selective laser melting or another 3D printing technology.

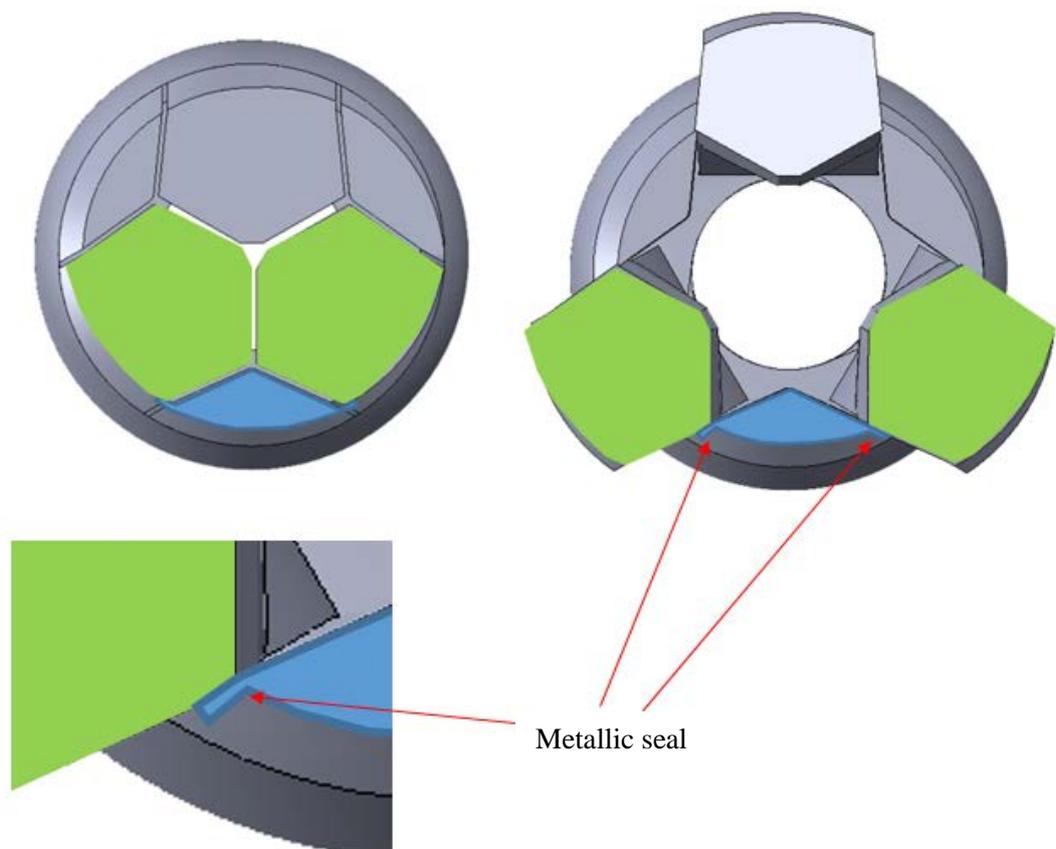


Figure 4-18 A 'metallic seal' could be created between the green dynamic expansion tabs and the blue static columns

Other non-geometric strategies were devised to prevent bone in-growth including:

4. A sealant that could either fill the gaps between the dynamic expansion tabs and static columns (see Figure 4-19), or fill the void that the fastener creates (see Figure 4-20) preventing bone from growing inside the fastener

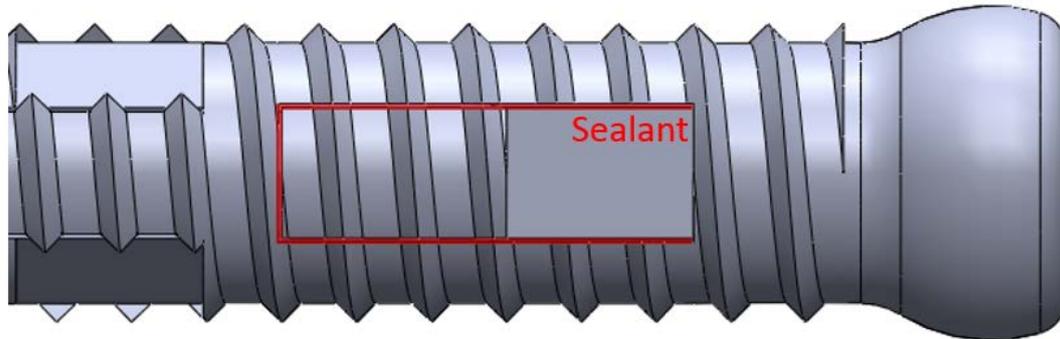


Figure 4-19 A sealant (red line) could be applied to fill the gaps between the dynamic expansion tabs and static columns

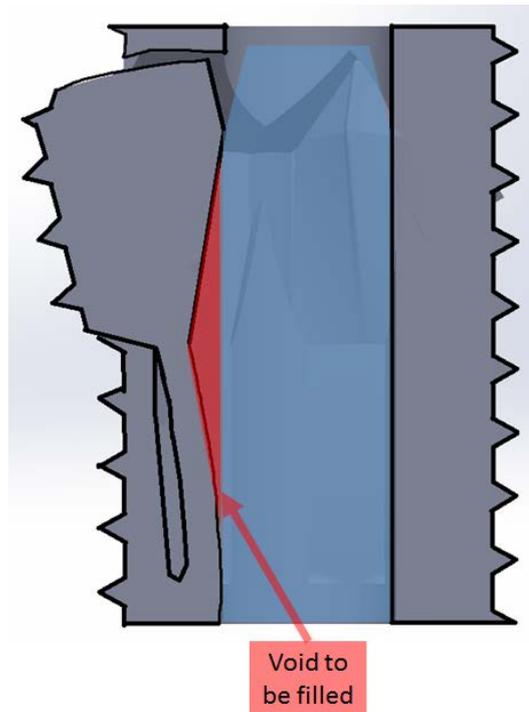


Figure 4-20 After expanding there is a void created within the fastener (red) which could be filled using an elastic material

5. A barrier membrane that is stretched across the gaps preventing bone from growing into the gaps in the fastener. This membrane would have to be sufficiently robust so as to not break during implantation and thin enough to not significantly increase the diameter of the screw.

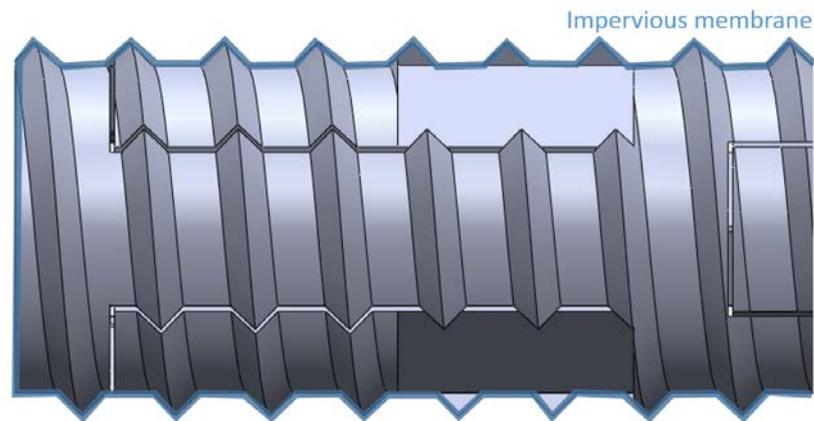


Figure 4-21 A barrier membrane (blue) could be created that would prevent bone from growing inside the screw

4.3.3 Patentability analysis

Based on the design phase as outlined above a provisional patent was filed, which is attached as Appendix G.

4.3.4 Design development

Forced expandable fastener contraction

Although initially it was thought that closing the EXF Screw would be difficult and prone to jamming, it was found empirically that twisting the EXF Screws (turning them out) after the expansion pin was removed closed the expansion tabs, allowing easy removal. This was achieved when the EXF Screw was tested with PMMA bone cement impregnated polyurethane foam to simulate surface osseointegration (but without bone in-growth inside the fastener). 'Turn-closing' is the simplest solution both for manufacturing (no complicated tools or features) and surgical standpoint. For the surgeon, removing the screw involves removing the expansion pin and then removing the screw like any other conventional screw. For these reasons, the design that progressed to detailed design did not involve a forced contraction mechanism.

Preventing bone in-growth

Gapless expansion can be achieved by creating ‘zero-thickness’ slots around the dynamic expansion tabs. Zero-thickness slots are ideal in that they require the least complicated geometry, however using the Realizer SLM100 SLM machine at UWA with conventional ‘optimised’ build parameters it was not possible to build a slot with both zero theoretical potential for bone in-growth without the two sides of the slot partially fusing together to an unacceptable degree.

The most favourable slot widths tested were 80 μm and 90 μm . A 90 μm slot width resulted in 12% erroneous connectivity across the slot and single viable bone in-growth path through the slot which had a throat area of less than 1%. An 80 μm slot width resulted in 35% erroneous connectivity and presented no viable transmission path through the slot (although 8% of the volume of the slot was wide enough for bone to grow). Further details about the investigation into minimum gap size can be found in Chapter 8 (‘Design constraints for selective laser melting manufacture of the EXF Screw’).

Erroneous connectivity (partial fusing of the slot) can be overcome by either pre-expanding the fasteners to break the ‘perforation’ (unfortunately this adds an extra manufacturing cost and can result in plastic deformation of the bending sections) or breaking the slots open in-vivo using the expansion pin (which requires a lot of force and could potentially create metallic particles causing osteolysis (Goodman, 2007)).

A metallic seal (Figure 4-18) can be designed to ‘seal’ the gaps, however there are potential issues with wear particles during expansion (potential for osteolysis), increased expansion force and jamming. Angulated tabs (Figure 4-17) are an alternative design, the degree of angulation required depends on the distance that surface moves during expansion, which increases as the distance from the base of the slot increases. This results in spiral shaped slots, which at the bottom of the slot (where the translation due to expansion is zero) would be horizontal (not possible).

An elastomeric or polymeric seal can be injected into the fastener inner channel during manufacture, to seal the gaps when expanded. Upon expanding the fastener, the seal would remain connected to the static column and interfere with the expandable arm to seal up the gaps and prevent bone in-growth. Both an elastomeric (silicone rubber filler) and a polymeric (polymorph) seal were prototyped. The silicone filler worked better because the polymorph, once solidified jammed the mechanism. Another advantage of this technique was that the void within the fastener could be at least partially filled with a substance that could be doped with antibiotics to prevent infection.

A bone barrier membrane was also prototyped using polyolefin heat shrink and tested in bone cement impregnated synthetic bone. Although it was successful in some tests unfortunately the membrane was prone to getting damaged during insertion or expansion, which on some instances let in a small amount of bone cement, preventing full closure of the device.

The design candidate that moved forwards to the detailed design stage was to minimise the gap size without any additional design features, to minimise manufacturing and regulatory approvals testing complication. Future work will involve in-vivo animal testing to determine whether bone can grow into the EXF Screw with low width slots and jam open the mechanism. More information about this test can be found in Chapter 11 ('Future work') in Section 11.4.2 ('In-vivo animal study').

4.3.5 Detailed design

As discussed in the previous section, the design that was optimised during detailed design had a standard locking screw thread design with at least two expanding dynamic expansion tabs and is expanded by inserting a circular pin into the middle channel by an expansion pin. The design parameters of this design will be optimised considering a number of design criteria outlined in the next section.

Design criteria

Design criteria are those criteria by which the design candidates can be evaluated and by which the design parameters can be optimised. Below are the design criteria for the detailed design phase:

1. Maximise fixation failure force;
2. Minimise fastener diameter increase over conventional screws;
3. Minimise removal torque;
4. Minimise expansion force;
5. Maximise surgical simplicity;
6. Minimise manufacturing cost increase over conventional screws; and
7. Maximise static strength.

Fixation failure force is the primary measure of performance for the EXF Screw to be maximised. Increased fixation strength theoretically decreases the risk of mechanically induced screw fixation failure. An exception to this is in tendon reconstruction application whereby the tendon or the connection between the tendon and the fastener can be the weakest link rather than the bone implant interface. Additionally an increase in fixation strength can also be used to reduce the length or diameter of the screw required for equivalent fixation failure risk.

Increasing screw diameter is disadvantageous in that it makes revision surgery more difficult (surgeons typically use a larger diameter screw for revisions) and it necessitates an increase in the size of the plate and rod holes and consequently increases the size of plates and rods. Additionally, surgeons prefer minimal change to their operating procedure and so common screw sizes should be maintained where possible (between 3.5 mm to 4.5mm for proximal humerus fracture fixation screws).

Removability is a critical characteristic to surgeons, and with the final design, can be quantified as the torque required to remove the fastener after the central pin has been removed, which should be minimised.

Expansion force should be minimised to reduce the stresses on the fastener during expansion, reduce the risk of the fastener opening unevenly and reduce the expansion force/torque required of the surgeon. Both expansion force and removal torque affect the perceived 'difficulty' of the surgery.

The difficulty and amount of additional surgical actions required to be performed by the surgeon should be minimised. Based on discussions with surgeons and other experts, eliminating 'stress-points' during the surgery where the surgeon must perform a technically demanding or an ambiguous action during the procedure is critical to reduce perceived 'difficulty' of the procedure. This is particularly relevant in trauma application where, as emergency procedures, the surgeries are generally done by less experienced surgeons.

Significant increase in manufacturing cost (more than “a couple of dollars” increase, according to discussions with implant manufacturing companies) will make most orthopaedic devices commercially non-viable. If possible the device should only use materials and processes that are commonly used for implants. This eliminates the requirement for costly and onerous testing in the regulatory approvals process and reduces the capital investment required for an implant manufacturing company to commercialise the EXF Screw. This is particularly relevant for products in the trauma setting as most of these surgeries are done in the public hospital setting and are not elective and consequently are more cost sensitive.

Lastly the static strength of the screw should be maximised to minimise the risk of fastener breakage. Although this is a design constraint (must survive physiological loading) because the EXF Screw can be used in a range of different orthopaedic applications (with a range of different loads and screw geometries), its static strength may be suitable for one application but not another. Consequently increased static strength broadens the application of the EXF Screw. Furthermore increased static strength makes demonstrating equivalence with previous devices simpler, easier and consequently with less cost in the regulatory approvals process.

The relationship between these criteria is complex and depends on the patient and the surgery being performed. For example in patients with low quality osteoporotic bone, where screw failure is more likely, a high fixation failure force is paramount to reduce the risk of fixation failure. Whereas for patients with good bone quality, using a shorter fastener may be more advantageous to reduce the difficulty of surgery and the risk of soft-tissue injury at the expense of fixation failure force, which in that circumstance is less critical.

Design optimisation

Table 3 below indicates the effect of modifying the design parameters (rows) on the performance criteria (columns), where green indicates positive influence on the design criteria for an increase in the design parameter (e.g. increased expansion size results in increased failure force, which is positive) and red indicates a negative influence (e.g. increased tab width results in decreased fatigue strength, which is negative). White indicates no influence and orange indicates that it is unclear, or that there is an influence but it is dependent on another design parameter or the testing conditions (e.g. increasing the number of expansion tabs from two to three may increase fixation strength, depending whether the expansions are staggered).

Table 3 The effect of the design parameters on the design criteria

	Failure Force	Diameter	Manufacturing/surgical simplicity	Expansion force	Removal torque	Fatigue strength
Expansion size	Green		Red	Red	Yellow	
Expansion tab height / Expansion angle	Yellow			Yellow	Yellow	Red
Expansion tab width	Green			Red	Yellow	Red
Number of expansion tabs	Yellow		Red	Yellow		Green
Thread depth	Yellow	Red	Green		Yellow	Red
Multiple expansion levels	Green		Red		Red	Red
Expansion pin diameter		Red				Green

Table 3 indicates that most design parameters affect both the failure force and the fatigue strength, usually in opposite directions with the exception of expansion size, which doesn't affect fatigue strength and expansion pin diameter that doesn't affect failure force. Each design parameter is discussed below with reference to the design criteria. General design recommendations for each parameter are underlined at the end of each section.

Expansion size

The mechanical testing in Chapter 6 ('Effect of design parameters on mechanical performance of the EXF Screw') demonstrates that increased expansion increases the pull-out force. The magnitude of the increase depends on the pilot hole size (smaller pilot hole size resulting in less increase due to expansion) and the total expansion arm width (wider expansion tabs resulting in more increase due to expansion). Theoretically, in other modes of failure (push-in, shear failure, torque failure) increased expansion size should also increase performance. However the magnitude of this relationship depends on whether:

1. Increased expansion is able to engage the cortex. If it does, even a moderate expansion can significantly increase the failure force;
2. Increased expansion is able to provide more useful radial compression than is already created by under sizing the pilot hole. This depends on the pilot hole size, the density of the bone and assumes that increasing the fixation strength of the screw can reduce the failure force (true for pull-out and push-in failure, not for torque failure, shear failure or arresting screw migration); and
3. The post-fixation failure migration performance of the screw is critical. For example, in proximal humerus screws, the fixation might fail, but if the migration can be arrested, screw over-penetration can be avoided and the failure will be asymptomatic.

However, higher expansion size may increase the expansion force and may increase the removal torque, both of which may compromise the simplicity of the surgery. For the expansion sizes that were investigated, there is minimal effect on the static strength of the fastener as failure does not occur at the bending section of the expansion tabs (more detail in Chapter 7 ('EXF Screw breakage strength')). Therefore, assuming a mild expansion angle, increased expansion size will not directly affect the static strength of the screw and increased expansion size does not necessarily affect the diameter of the screw.

The expansion size should be maximised whilst ensuring acceptable expansion force and removal torque.

Expansion tab width

There is a direct compromise between wider expansion tabs providing increased fixation strength (in pull-out and push-in, but not in shear or rotation) but higher expansion force, higher removal force (assuming that osseointegration holds the tabs out proportional to the outside area of the tab) and lower fatigue strength due to smaller static columns.

However the investigations in Chapter 6 ('Effect of design parameters on mechanical performance of the EXF Screw') demonstrated that, assuming gapless expansion, the pull-out force is independent of the tab width (because wider tabs can create less expansion without creating gaps).

For a gapless expandable fasteners (like the EXF Screw), thinner tabs are preferable to reduce expansion force and increase fatigue strength whilst allowing equivalent failure force due to increased allowable expansion size.

Expansion angle

Expansion tab height is inversely proportional to expansion angle. Higher expansion tab height decreases static strength but did not demonstrate an increase in fixation strength per unit length for the range of angles tested in Chapter 6 ('Effect of design parameters on mechanical performance of the EXF Screw'). Higher expansion tab height will increase expansion force (more bone needs to be compressed). High expansion angle reduces the elastic response of the material, however if the screw is being contracted via torque applied to the screw then this is not critical so long as the bending section doesn't rupture.

However if the EXF Screw is limited to a single expansion level (to minimise stress) then the longer the expansion tab (and the smaller the expansion angle), the larger the increase in fixation force will be in pull-out. This is because a higher proportion of the length of the screw is expanding and therefore gains the benefit of radial compression. However increasing the height of the expanding sections will not increase push-in migration force.

For single level designs, where pull-out strength is critical, expansion angle should be minimised whilst ensuring sufficient static strength and expansion size. For multiple level designs, expansion angle should be maximised whilst preventing plastic rupture of the bending sections. For single level designs, where push-in failure is critical (proximal humerus fractures) expansion angle should be maximised, whilst ensuring removability and preventing rupture of the bending section.

Number of expansion tabs

In Chapter 6 ('Effect of design parameters on mechanical performance of the EXF Screw') it was demonstrated that a three tab design performed better than a two tab design in pull-out force and Chapter 7 ('EXF Screw breakage strength') demonstrated equivalence in static strength. However a two tab design has increased shear resistance (but only in one plane, at the cost of no increase in shear resistance in the perpendicular plane).

Additionally two tab designs have the ability to provide a staggered expansion (see Figure 4-23) which can provide approximately double the expansion size, but at the cost of reducing fatigue strength and using up more fastener length. Furthermore opening each tab separately halves the maximum expansion force required.

Three tab designs perform better than two tab designs, unless staggered. Staggered expansions should be used if they perform better than multiple level expansions and the fatigue strength and removability are acceptable.

Thread depth

Increased thread depth may make removal easier, by increasing the stripping torque of the thread, allowing more torque to be applied to contract the screw without stripping. However increased thread depth decreases the size of the static columns of the fastener and consequently reduces fatigue strength of an EXF Screw.

Increased thread depth could increase pull-out force but will decrease expansion size, which may decrease pull-out force. The tests in Chapter 6 ('Effect of design parameters on mechanical performance of the EXF Screw') were inconclusive as to whether thread depth affected fixation strength given gapless expansion. However, increased thread depth will not increase push-in screw migration force (critical for primary application), failure in shear or torque.

For proximal humerus screws the thread depth should be small to maximise the advantage that can be provided by the fastener expansion, to increase push-in strength.

Multiple expansion levels

Multiple expansion levels increase fixation strength at the expense of significantly reducing fatigue strength. Closing multiple levels simultaneously via torque may require more torque but this may not significantly increase the difficulty of removal. However in the primary application (proximal humerus fractures), the bone morphology (high density subchondral bone, low density cancellous bone) means that multiple expansion levels will likely not significantly increase fixation strength because the proximal expansion levels will be engaging with low density cancellous bone.

In general multiple expansion levels should be used as long as fatigue strength, expansion force and removability are acceptable but for proximal humerus screws, a single level should be used.

Expansion pin diameter

Increased expansion pin diameter, increased pin material stiffness or decreased screw outer material stiffness increases static strength according to the analysis in Chapter 7 ('EXF Screw breakage strength'). Pin diameter is limited by the geometry of the fastener; as shown in Figure 4-22, the diameter of the screw is affected by the thread depth, the tab width and the bending section thickness.

Pin diameter should be maximised within practical limits.

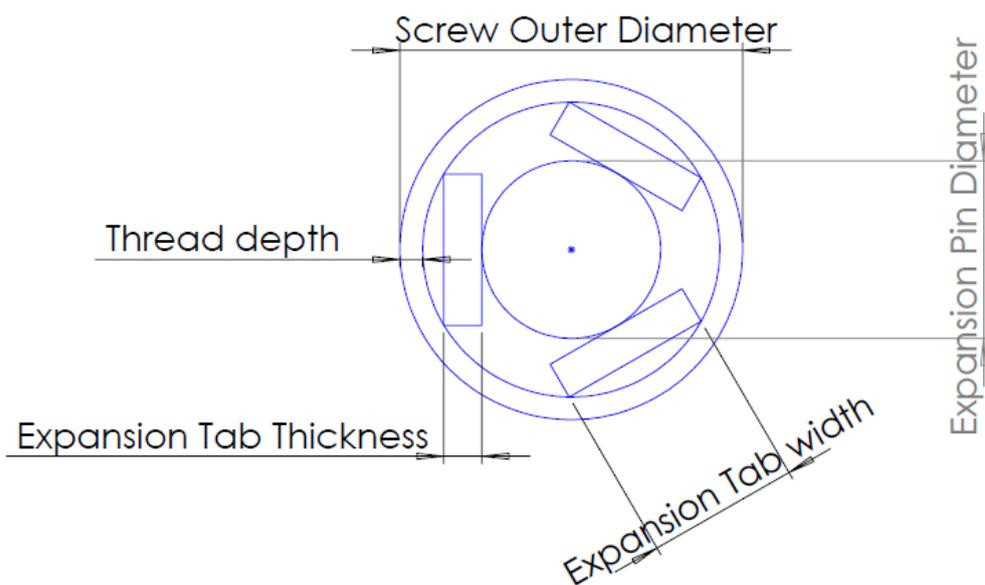


Figure 4-22 The dimensions that affect the expansion pin diameter

4.3.6 Final design

The final design chosen for preclinical testing as per the scope of works of the NHMRC Development grant (see Chapter 11 ('Future work'), Section 11.4 ('EXF Screw project') for details) is shown below in Figure 4-23, with the values for the design parameters in the final design outlined in Table 4 and discussion of each of the design parameters below.

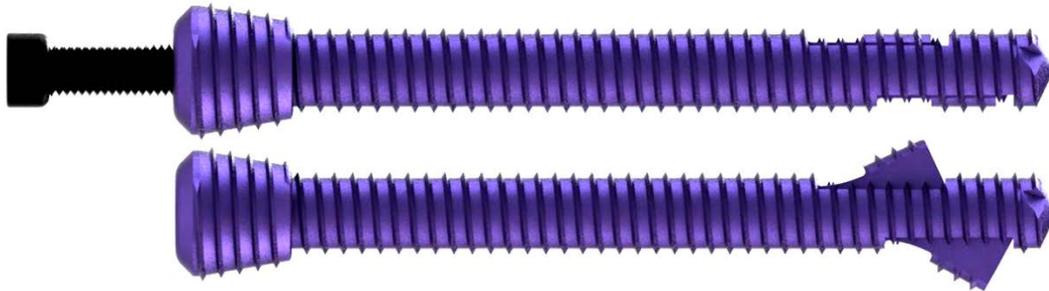


Figure 4-23 The final design of the EXF Screw

In the final design, the expansion size was maximised for a feasible static arm diameter. A two arm, staggered design was chosen to reduce expansion force and maximise expansion size within the subchondral bone at the tip of the screw. Multiple expansions were not utilised due to the importance of the bone right at the tip of the screw. A standard 0.3 mm thread depth was chosen, to minimise variation from existing proximal humerus screws. The largest feasible pin diameter was chosen. Given a 0.3 mm thread depth and two 2.25 mm wide and 0.5 mm thick bending sections, this resulted in a 1.7 mm pin.

Table 4 The chosen design parameters for the final design of the EXF Screw

<u>Design parameter</u>	<u>Value</u>
Screw Diameter	4.5 mm
Expansion size	8.3 mm (85% increase in diameter)
Expansion tab height / Expansion angle	7 mm / 25°
Expansion tab width	2.25 mm
Number of expansion tabs	Two expansion tabs, staggered
Thread depth	0.3 mm
Multiple expansion levels	No
Expansion pin diameter	1.7 mm / Titanium

Chapter 5 Preliminary UEF pull-out strength testing

This chapter describes the mechanical testing of the first expandable fastener design, the Unthreaded Expandable Fastener (UEF), in an ovine spine model. The results of this mechanical testing has been published in the Journal of Medical Engineering and Technology (Oldakowski, Oldakowska, et al., 2016b). The influence of bone morphological properties on the performance of the UEF was also investigated during this experiment and will also be discussed in this chapter. This aspect of the work was published in the Journal of Physics: Conference Series (Oldakowski, Oldakowska, et al., 2016a).

5.1 Method

5.1.1 Sample acquisition

When this study was carried out the proposed primary application was posterior fixation in the cervical spine and consequently the spines of commonly available animals were investigated for similar structures to the human lateral mass. Unfortunately, due to humans bipedal gate, the structure of the lateral mass is absent in quadrupeds (sheep, pigs, dogs etc.). An option that was explored was the kangaroo, which has a similar structure but that is too small to fit a lateral mass screw reproducibly. Consequently ovine vertebral bodies were used because sheep were available free of cost.

Thoracic spines were opportunistically harvested from two sheep cadavers from an unrelated study at the Large Animal Facility (LAF) at the University of Western Australia (UWA). The original study was approved by the UWA Animal Ethics Committee. The project approval number is RA/3/100/1203.

The UEF samples were manufactured using the Realizer SLM100 machine at UWA from a low-modulus pure-beta titanium alloy Ti2448 (Ti-24Nb-4Zr-8Sn, all in wt%), with the assistance of Associate Professor Time Sercombe. The parts were produced using a standard contour and vector fill scanning strategy, with the direction of the fill vectors rotated 90° between layers. The laser power was 120W for the contour and 175W for the fill, while the scan speed, scan spacing, beam compensation and layer thickness were 1000 mm/s, 100 µm, 60 µm and 50 µm, respectively. The particle size of the powder was 45 µm.

The UEF samples were 10 mm long, 4 mm wide and expanded to approximately 6.2 mm. The UEF samples had dedicated bending sections that have a thin rectangular profile providing minimal area moment of inertia. This allows a much larger expansion than currently available expandable fasteners with minimal plastic strain (see Figure 5-1). A “barb” feature was also printed on the distal section of the screw to increase the friction of the expanding tabs and provide a means interlocking with the surrounding trabeculae. More details on the design development can be found in Chapter 4 (‘Design of the EXF Screw’). An ISO 5835 cancellous orthopaedic screw was also tested for comparison purposes (*ISO 5835:1991 Implants for surgery - Metal bone screws with hexagonal drive connection, spherical under-surface of head, asymmetrical thread, Dimensions*, 1991). The screws were self-tapping and had a 4 mm outer diameter, were 40 mm long, had a pitch of 1.9 mm and thread depth of 0.5 mm (see Figure 5-1). Both the fasteners and screws were inserted at 10mm depth and tested in pull-out using an ovine vertebral body.

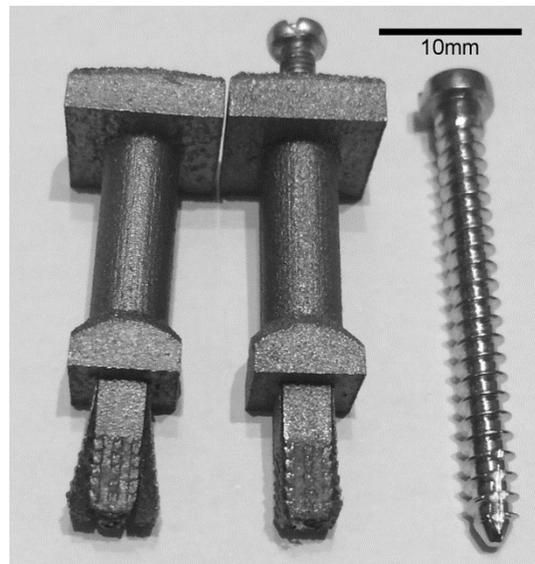


Figure 5-1 Expanded UEF (left), unexpanded UEF (middle) and control screw (right) (Oldakowski, Oldakowska, et al., 2016b)

5.1.2 Mechanical testing methodology

The spines were harvested, disarticulated and frozen to -20°C during storage. The samples were thawed for five hours and cleaned before transported to the Centre for Microscopy, Characterisation and Analysis (CMCA) at UWA for High Resolution Computed Tomography (HR-CT) scanning. The samples were scanned in batches of five with a scanning time of approximately an hour, meaning that they were unfrozen for approximately five hours. The samples were re-frozen after CT-scanning until mechanical testing was conducted.

The samples were again thawed for five hours and a 4 mm square hole was made for the UEF samples using a specially designed square awl. For the screw samples a 2.5 mm pilot hole was drilled, in accordance with the AO/ASIF (Arbeitsgemeinschaft für Osteosynthesefragen/Association for the Study of Internal Fixation) technique manual (Allgöwer, Müller, & für Osteosynthesefragen, 1991). Although the literature has reported higher pull-out strengths for screws with smaller pilot holes (Steeves et al., 2005) these results are not indicative of typical clinical practise. The fasteners were then implanted whilst restrained in a vice. The screws were screwed into the bone samples using a surgical screwdriver and the UEF prototypes were knocked into the bone samples with a hammer and expanded by turning in an M3 expansion bolt.

The samples were mechanically tested using Instron 8874 servo-hydraulic materials testing machine at the Medical Engineering and Physics Department at Royal Perth Hospital (RPH). Samples were mounted in a custom rig, as shown in Figure 5-2, consisted of an upper part which attaches to the top of the mechanical testing machine with a slot to restrain the fastener and a lower section with a plate with a 13 mm wide slot, attached to the base of the mechanical testing machine to restrain the upper section of the bone during pull-out. The custom rig and the aspects of the mechanical testing methodology were designed by another PhD Student, Intan Oldakowska. Poly Methyl MethAcrylate (PMMA) bone cement (Vertex cold-curing acrylic denture repair material) in the doughy state was used to fill any gaps between the bone and the plate. The Instron was manually moved until the bone cement compressed onto the plate forming a flat contact plane to ensure purely axial loading. Care was taken to ensure that excess bone cement inside the 13 mm slot was removed with a tooth-pick and the bone cement was left to set for 15 minutes. Pull-out was performed at a rate of 5 mm/min and measurements were taken at 10 Hz until the screw and UEF had been pulled out by at least 5 mm. Video records of each test were created and photos of the failed samples were taken. After mechanical failure the bones were rescanned to evaluate failure mode.

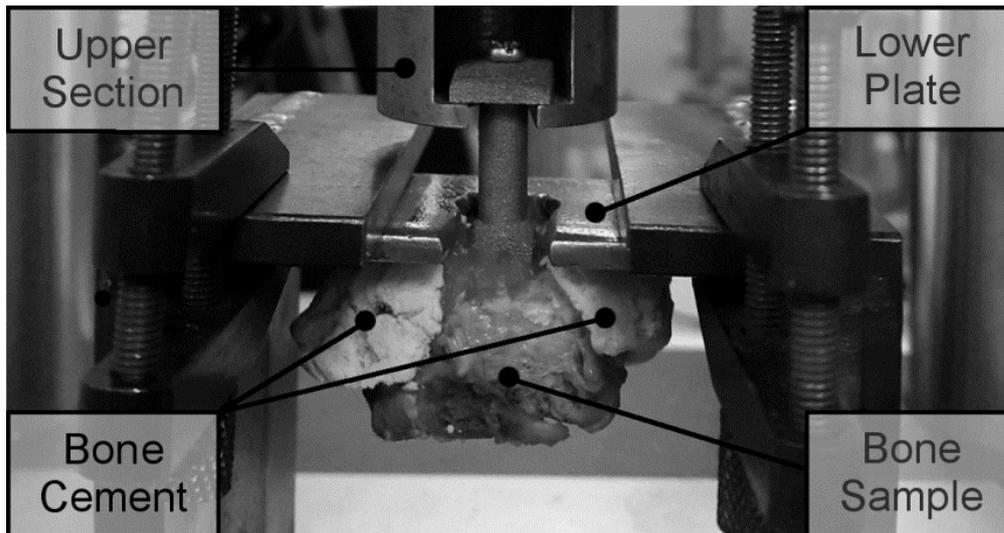


Figure 5-2 Samples mounted in custom designed testing rig (Oldakowski, Oldakowska, et al., 2016b)

5.1.3 Bone morphology characterisation

Bone morphology characterisation conducted during this experiment is aimed at quantifying the effects of bone quality on the pull-out strength of the UEF and compare this to standard orthopaedic screws. Furthermore the study investigated the Volume of Interests (VOI) in which the bone properties are most critical, allowing future studies to use the most appropriate VOI.

The bones were CT scanned using the Skyscan 1176 micro-CT scanner at the CMCA, UWA. Scanning was performed before and after the pilot holes were created at 18 μm resolution, using a rotation step of 0.5°, 2 frame averaging, a source voltage of 80 kV, an exposure time of 285 ms and Cu+Al filter. Using FIJI (Schindelin et al., 2012) a 3D median filter was applied to remove noise and the data was resampled to 35 μm to reduce processing time. Threshold values were calculated using the iterative inter-means histogram method (Ridler & Calvard, 1978) and purified to ensure only a single connected volume. Cortical segmentation was performed using a modified method based on the work of Buie, Campbell, Klinck, MacNeil, and Boyd (2007).

Bone property measurements were calculated from CT scans of the bone samples in the VOI created by centring a cylinder on the fastener location, with varying diameters and heights measured from the bottom of the fastener (Figure 5-3). VOIs were created from 6 mm to 16 mm diameter in 2 mm increments and from 2 mm height to 10 mm height in 2 mm increments.

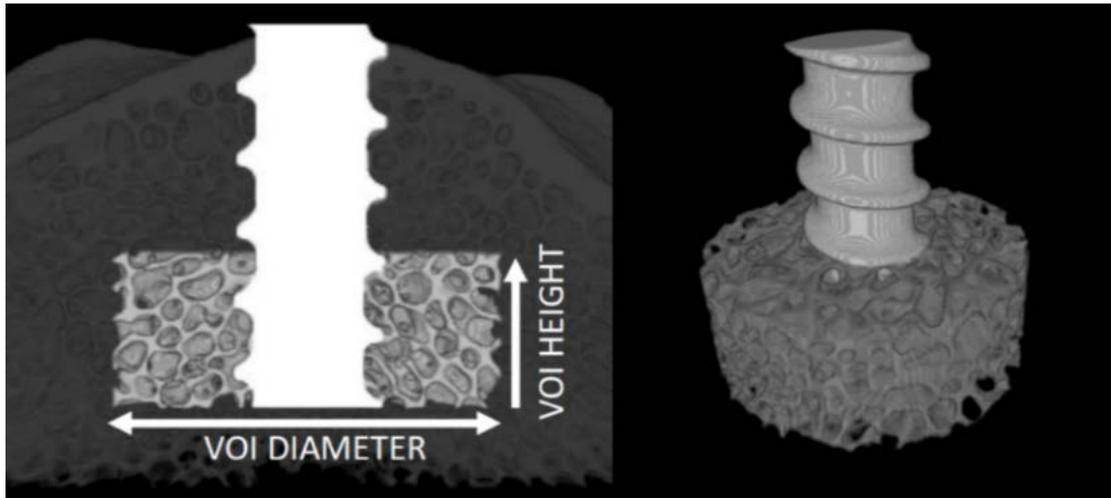


Figure 5-3 A Volume Of Interest (VOI) defined by the VOI diameter and VOI height.(Oldakowski, Oldakowska, et al., 2016b)

Bone property measurements were calculated from CT scans of the bone samples taken before pilot holes were drilled to prevent the inclusion of bone detached during drilling and awling that would erroneously affect the results. Instead, pilot holes were digitally created in the scans made before the pilot hole. It was found that digital pilot holes improved correlation significantly, primarily due to the elimination of some Volkmann's canals that passed through the centre of the VOI. The fastener location and orientation for the pre-pilot hole scans was calculated by aligning the data with post-drilled/awled scans. The data was aligned using the Align3 TP plugin in FIJI (Schindelin et al., 2012).

Bone properties were calculated using FIJI (Schindelin et al., 2012), an open source image analysis program and the BoneJ (Doube et al., 2010) plugins. Trabecular volume (Tb.V) and cortical volume (Cor.V) were calculated by voxel counting. The trabecular bone volume fraction (Tb.V/TV) was calculated as the quotient of the trabecular bone volume and total bone volume, where the total bone volume was calculated by applying a 15 iteration 3D voxel dilation and erosion to create a solid bone volume. Trabecular length (Tb.L) was calculated using a 3D skeletonisation procedure. Trabecular Bone surface area (Tb.SA) was calculated by creating a surface mesh using the marching cubes algorithm and summing the area of the triangles making up the mesh (Lorensen & Cline, 1987). Structural Model Index (SMI) was calculated using the voxel dilation method (Hildebrand & Rüegsegger, 1997). All calculations were performed at 35 μm resolution.

5.1.4 Data analysis

Failure force was defined as the maximum force before significant non-linearity in the force-displacement curve and maximum force was defined as the maximum force anytime during the pull-out test. The failure energy was defined as the area under the curve before the maximum force and pull-out stiffness was calculated by measuring the gradient of the linear portion of the force displacement curve, illustrated in Figure 5-4. The failure mode was determined based on the force-displacement curve and the CT scans of the failed samples.

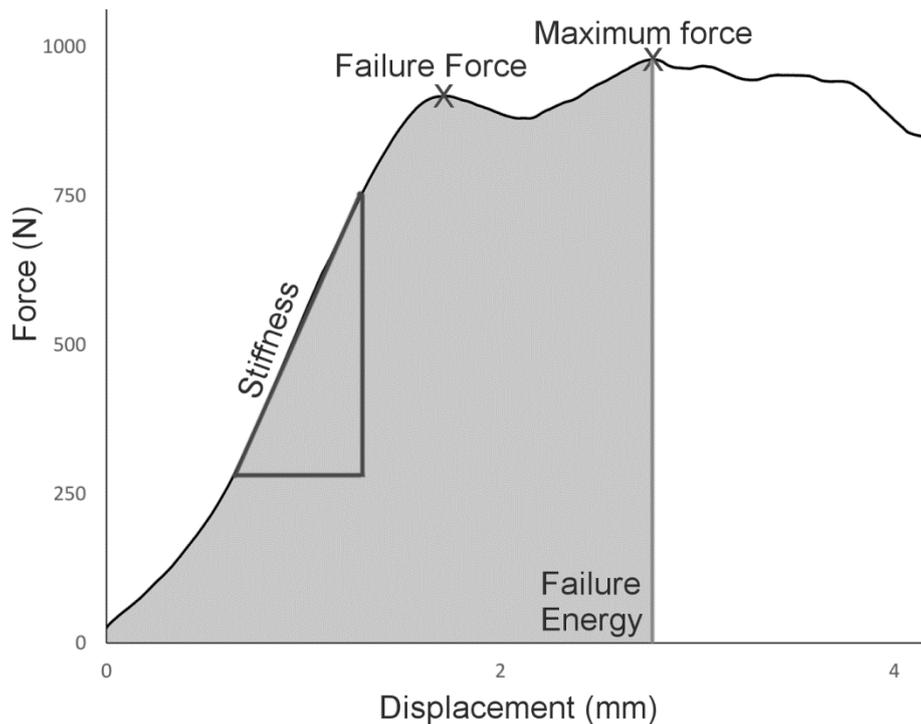


Figure 5-4 A typical force displacement curve (Oldakowski, Oldakowska, et al., 2016b)

Independent, two tailed Student's t-tests were used to determine whether the recorded mechanical performance parameters of two fastener groups were significantly different and whether the bone properties of the two sample groups were the same (if applicable). Levene's tests were used to determine whether the variances were significantly different between fastener groups. Inter-correlation between stiffness, failure force and maximum force was assessed using paired Pearson coefficients and the significance was calculated using a two-tailed test. All tests used a $p < 0.05$ significance threshold.

Correlation analysis of sample bone properties to failure force and maximum force were performed using paired Pearson coefficients with a high degree of correlation defined as $r > 0.6$. The probability of significance of the correlation was calculated using a two-tailed test with a correlation having $p < 0.05$ considered to have a high probability of significance.

5.2 Results

As shown in Table 5, the UEF samples demonstrated a significantly higher failure force ($p < 0.001$) and maximum force ($p < 0.001$) than the screw set. The variance in the UEFs was significantly lower than the screws for both failure force ($p < 0.001$) and maximum force ($p < 0.001$). The UEFs had a 41% higher failure force and 44% higher maximum force than the screws. The stiffness of the UEFs was 17% higher than the screws, but this was not significant ($p = 0.186$). The variance of the stiffness was 70% higher for the UEFs, but this was not significant either ($p = 0.167$). On the other hand, the failure energy of the UEFs was significantly higher than the screws with a 222% increase ($p < 0.001$). One UEF was determined to be an outlier and excluded from analysis. This was caused by cortical cracking during the awling step that was not detected until after mechanical testing. The failure and maximum force for the sample that was removed as an outlier was 614 N, which was 11.7 standard deviations below the mean.

Table 5 Summary of pull-out testing results

	Expandable fastener		Screw		Difference (Significance)	
	Mean	SD	Mean	SD	Mean	SD
Stiffness (N/mm)	720.7	193.8	618.5	114.1	17% (0.186)	70% (0.167)
Failure force (N)	978.5	43.4	695.0	82.4	41% (1.61E-06)	-47% (4.14E-07)
Maximum force (N)	1000.0	32.8	695.0	82.4	44% (1.15E-06)	-60% (8.72E-08)
Failure energy (N.mm)	1834.6	496.5	570.6	88.6	222% (5.01E-05)	461% (7.19E-07)

Statistically significant results in bold.

Figure 5-5 demonstrates a significant correlation between pull-out stiffness and failure force for the screw set ($r=0.833$, $p=0.003$). However, no correlation was demonstrated between the UEF samples pull-out stiffness and failure force ($r=0.316$, $p=0.407$). The mean expansion width, averaged across both directions, was 6.21 mm compared to the expected theoretical expansion size of 7 mm, a 26% reduction in expansion size.

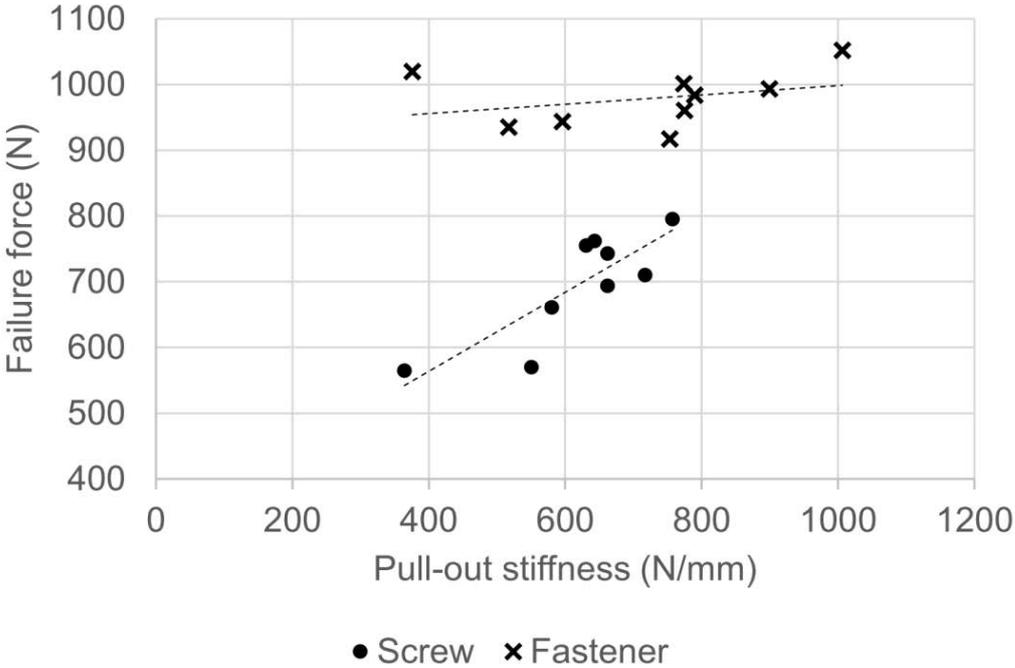


Figure 5-5 Correlation between failure force and pull-out stiffness for the UEF and the control screws (Oldakowski, Oldakowska, et al., 2016b)

As shown in Table 6, the screw and UEF bone sample sets were not significantly different in mean or standard deviation for Bone Volume (BV), Bone Surface area (BS), Trabeculae Thickness (Tb.Th), Structure Model Index (SMI), Trabecular Number (Tb.N) or Cortical Volume (Cort.V) using a 10 mm diameter cylindrical volume of interest around the fastener site.

Table 6 Summary of bone morphology characterisation analysis

		BV/TV (%)	BV (mm ³)	BS (mm ²)	Tb.Th (mm)	SMI	TbN	Cort.V (mm ³)
Mean	Screw	39.1	254	3115	0.236	-0.284	14108	44.0
	UEF	38.5	248	3043	0.235	-0.348	14768	41.8
	%difference	2%	2%	2%	0%	-18%	-4%	5%
	Significance	0.650	0.572	0.429	0.847	0.511	0.702	0.502
Standard deviation	Screw	0.042	38.0	358	0.023	0.308	4608	13.3
	UEF	0.021	20.6	263	0.013	0.217	3862	14.2
	% difference	51%	85%	36%	71%	42%	19%	-6%
	Significance	0.648	0.674	0.632	0.908	0.619	0.746	0.735

Table 7 reports the correlation coefficients (r-values) and the corresponding probability of its significance (p-values) for the relationships between mechanical performance and the bone morphological properties. Only the VOI diameter and height combination with the lowest p-value is reported to highlight the critical VOI for the screws and expandable fasteners. For screws, the maximum force is equal to the failure force.

Table 7 Correlation between mechanical performance and bone morphology characteristics

		Tb.V/TV	Tb.L	SMI	Tb.SA	Cor.V
EF - Failure Force	r-value	0.740	0.870	-0.471	0.769	-0.538
	p-value	0.018	0.002	0.201	0.015	0.135
	VOI Diameter (mm)	8	14	10	14	8
	VOI Height (mm)	2	2	4	2	-
EF - Maximum Force	r-value	0.526	0.765	-0.343	0.838	-0.857
	p-value	0.146	0.016	0.366	0.005	0.003
	VOI Diameter (mm)	8	16	10	16	14
	VOI Height (mm)	2	2	4	2	-
Screw – Failure/Maximum Force	r-value	0.710	0.414	-0.685	0.580	0.222
	p-value	0.032	0.268	0.042	0.102	0.566
	VOI Diameter (mm)	8	6	8	6	16
	VOI Height (mm)	10	10	10	10	-

Trabecular bone volume fraction demonstrated a high degree of positive correlation with failure force for the screw over all full height VOI diameters (Figure 5-6). The highest correlation ($r=0.710$) was demonstrated at full (10mm) height and 8mm diameter ($p=0.032$). For the UEF samples a high degree of positive correlation was only demonstrated for failure force over a small range of VOI diameters (6-8mm) and VOI heights (2-4mm). The highest correlation ($r=0.740$) was found at 2mm height and 8mm diameter ($p=0.018$).

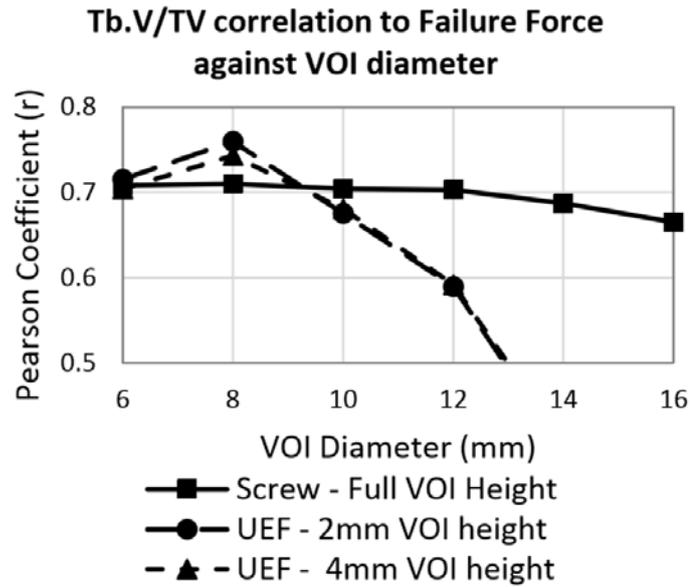


Figure 5-6 Correlation coefficient between Tb.V/TV and failure force against VOI diameter for the UEF and screw samples (Oldakowski, Oldakowska, et al., 2016b)

Cortical volume demonstrated a high degree of negative correlation with maximum force for the UEFs over all VOIs tested. The highest correlation ($r=-0.857$) was found for a 16 mm diameter VOI for cortical volume ($p=0.003$, Figure 5-7). This relationship was negative, indicating a higher pull-out strength for thinner cortices. Only a weak correlation was found between the cortical volume of the screw set and the failure force.

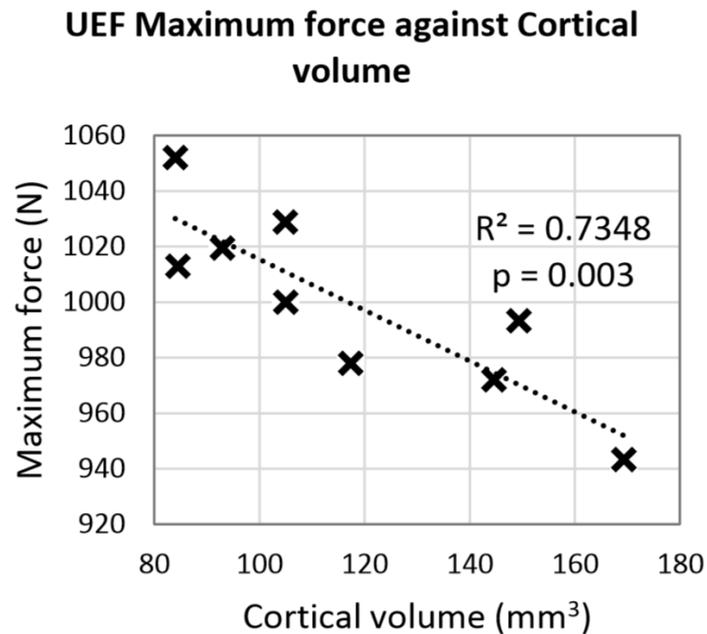


Figure 5-7 Correlation between UEF maximum force and cortical volume for the UEF samples (Oldakowski, Oldakowska, et al., 2016b)

Trabecular length demonstrated a high degree of positive correlation ($r=0.870$) with UEF failure force ($p=0.002$) and trabecular bone surface area also demonstrated a high degree of positive correlation ($r=0.838$) with UEF maximum force ($p=0.005$). A weak correlation was demonstrated between screw failure force and trabecular bone surface area. SMI demonstrated a high degree of negative correlation with screw failure force for VOIs between 6 mm and 10 mm diameter with a full height VOI, however no significant correlation was found for the UEFs.

5.3 Discussion

In this study the UEFs displayed on average a 41% higher pull-out failure force than conventional screws for the same width and length, which exceeds the 28.7% increase in failure force for bicortical compared to unicortical fixation, reported by Heller, Estes, Zaouali, and Diop (1996). This indicates that unicortical fixation with the UEF may exceed the failure force of bicortical screw fixation. Therefore, the UEF could potentially be used for fixation in bone, which would otherwise require bicortical fixation, but without the added risk of critical nerve root injuries, making surgery simpler and safer.

The standard deviation in the failure force of the UEFs was significantly lower than that for the conventional orthopaedic screws. Given that the standard deviation of the bone properties tested was not significantly different between the bone sample groups, this indicates that the UEFs are either less sensitive to variation in the measured bone properties or other uncontrollable parameters such as installation procedure, micro-positioning or fastener rotation angle and are therefore more likely to be clinically robust.

Failure force (Figure 5-4) is the most important property of a fastener, as once the failure force has been exceeded, the fastener would have either been displaced or plastically yielded and, therefore, no longer functions mechanically and would need to be revised. However, increased maximum force would reduce the likelihood of catastrophic failure and increased failure energy would reduce the likelihood of catastrophic failure due to a transient trauma force such as a fall or a traffic accident. Although the maximum force was the same as the failure force for screws, on average the maximum force is 3% higher than the failure force for the UEF and the failure energy of the UEF was 222% higher than for the screws.

For the screws, a similar failure mode to the Seller et al. (2007) study was observed based on the force-displacement curve and post-failure CT analysis. The force displacement curve, as shown in Figure 5-8, demonstrate an initially linear region, maximum force marginally before a single thread pitch of pull-out displacement (1.63 mm on average) and then rapid failure. The CT post-failure analysis demonstrated the cortex had cracked open, but only minimal cancellous bone had been removed. However, the UEF failure mode was less consistent. All fasteners had an initial linear force-displacement curve which corresponded to the initial compression of the trabeculae. After this, there was either cortical failure, indicated by a continuous reduction in force (Figure 5-8: UEF cortical failure), or frictional failure leading to slipping, indicated by an approximately constant force over several millimetres. If slipping occurred, a second loading peak was sometimes observed (Figure 5-8: UEF interlock failure), perhaps corresponding to the fastener barbs reconnecting with some well aligned trabeculae voids, before eventual cortical failure. This indicated that failure force was limited by two different failure modes: cortical cracking or bone-implant interlock failure. Therefore, future optimisation of the UEF design must consider and prevent both of these failure modes.

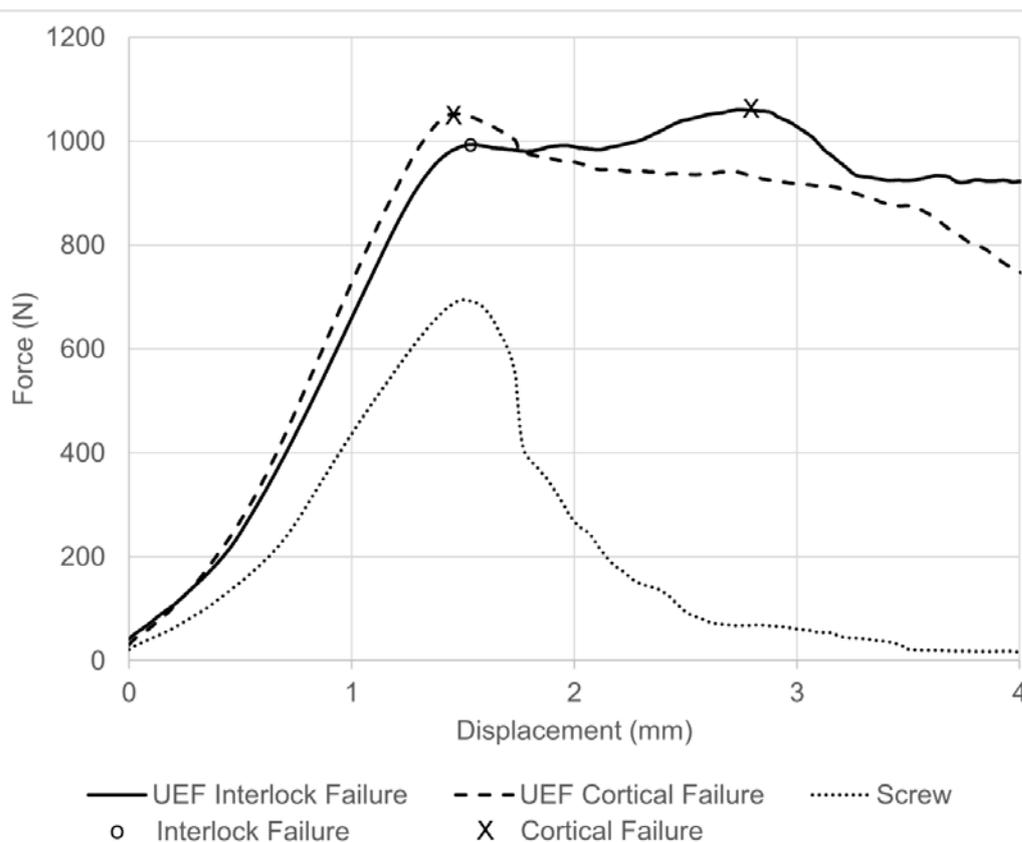


Figure 5-8 A typical force-displacement curves for the UEFs interlock failure and cortical cracking failure modes and the screw failure mode (Oldakowski, Oldakowska, et al., 2016b)

Correlation of fastener performance to bone properties was found to vary with the VOI over which the bone properties are measured. By taking an arbitrary VOI or else by including the entire bone volume a significant relationship can be obscured, which may explain some previous inconclusive attempts to correlate bone properties to pull-out strength.

Previous studies reported on the significance of correlations between pull-out force and up to nine microstructural properties without correcting for multiple comparisons (Ab-Lazid et al., 2014; Poukalova et al., 2010). In this study, not correcting for multiple comparisons would be particularly problematic as multiple comparisons were made across different VOIs to determine the effect of VOI size in addition to multiple microstructural properties. Consequently p-values and r-values were reported without commenting on significance.

It was found that the critical VOI for screws covered the entire length of the screw with the highest correlation at 8 mm diameter, reducing in degree of correlation in both directions (Figure 5-6 Correlation coefficient between $Tb.V/TV$ and failure force against VOI diameter). This relationship (critical VOI twice the diameter of the screw) is similar to the deformed area calculated with FEA by Wirth et al. (2011) and the experimental set up of Ab-Lazid et al. (2014).

Trabecular bone volume fraction, trabecular length and trabecular surface area only demonstrated a high degree of correlation with UEF failure load when only the bone around the bottom of the fastener is considered in isolation. The authors hypothesise that this is because the UEF fails due to slipping and so only the bone that contributes to increased pressure at the expansion zone is critical. This hypothesis would indicate that the expandable fasteners will be less sensitive to fastener length.

Discussion of trabecular architecture often qualitatively describes individual trabeculae as either “plate-like” or “rod-like”. The breakdown of trabecular architecture due to osteoporosis is usually characterised by a conversion of plate-like trabeculae to rod-like trabeculae. The structural model index (SMI) quantifies this by examining the change in surface area due to a surface dilation, assuming that the surface area of an infinite plate will remain constant whereas the surface area of an infinite rod will increase. Unfortunately trabecular bone structure is not ideal and contains many concave surfaces that reduce in volume during dilation, artificially skewing the result towards plate-like in an unpredictable way. However, despite this SMI is a measure that has been reported in previous studies to correlate strongly with pull-out strength of screws. It was found that this relationship only existed for the screw set using the Skyscan software CTAn methodology of voxel dilation, rather than surface dilation methodology outlined by Hildebrand and Rüeggsegger (1997). This is unusual because surface dilation should theoretically provide a more accurate result and indicates that perhaps SMI using the CTAn methodology is measuring some other property of the bone than rodness/plateness, perhaps a correlation with bone volume fraction or some other established correlated parameter.

These results confirm previous studies with trabecular SMI and trabecular bone volume fraction being the most highly correlated parameters for the screws. Some deviation is inevitable, as previous studies use the epiphysis of human long bones where the current study used ovine vertebral bone. Contrary to previous studies in long bones (Ab-Lazid et al., 2014; Poukalova et al., 2010) no correlation between cortical volume and screw failure force was found. The authors hypothesise that this was because, in the vertebral body, the cortex was thinner and the trabecular bone denser than in the epiphysis of the long bones and therefore the influence of the cortical properties was reduced. For the current study the average cortical thickness was 0.59 mm whereas Seebeck et al. (2004) reported an average of 2.83 mm. For the current study the average Bone Volume Fraction was 38.0% whereas Poukalova et al. (2010) reported an average of 14.8%. Therefore the influence of the cortical properties was reduced.

Compared to screws, UEFs demonstrated a similar dependence on trabecular bone volume fraction but no relation to SMI and an inverse relationship with cortical thickness. Considering that osteoporotic bone can be characterised by a reduction in bone volume fraction, cortical thinning, and a deterioration of plate-like trabeculae into rod-like trabeculae (Stauber & Muller, 2006), indicates that the UEFs may be more suited to osteoporotic bone.

The screws and UEFs used in the study were the same width; however, the screws were round and the UEFs were square which made direct comparison of their sizes problematic. The diameter of the round screw could be matched with either the flat-to-flat width of the UEF or the corner-to-corner width. The decision as to which of these was most appropriate depended on whether the surrounding bone was square or round, as in the case of a round bone the corner-to-corner width was the limit and a square bone was limited by flat-to-flat width. The authors chose flat-to-flat width because the UEFs were designed for the cervical lateral mass, which are roughly square. However, ultimately the UEF should be tested against what was used clinically, which in the case of the cervical lateral mass was 3.5 mm screws, and so the authors rationalised that comparing 4 mm flat-to-flat square UEFs with 4 mm diameter screws was sufficiently conservative.

The depth of penetration was set to be 10 mm for comparison. However, clinically there are many variations of screw penetration length depending on the screw insertion method used, which has a significant effect on the pull-out strength (Errico, Uhl, Cooper, Casar, & McHenry, 1992; Heller et al., 1996) . Although a study in polyurethane foam bone replacement has shown a small but significant effect on pull-out strength with different screw designs, notably thread pitch and configuration (DeCoster, Heetderks, Downey, Ferris, & Jones, 1990) however these features had no significant effect when tested in cadaver bone (Seller et al., 2007) and consequently testing multiple screw designs was not undertaken.

Ovine bone was used because it was readily available and has been used previously as a test model for human bone (Liu et al., 2011; Sandén, Olerud, & Larsson, 2001; Shi et al., 2012; Wan et al., 2010). The average Bone Volume Fraction (BV/TV) of the sheep across all the samples in this study is 37.9%, which is comparable to the BV/TV for human cervical lateral mass samples for young bone (43–53 years of age) of 35%, reported in a study by Wilke, Zanker, and Wolfram (2012). Furthermore, a study by Kandziora et al. (2001) comparing sheep and human cervical spines did not find a significant difference in bone mineral density. Although there is no substitute for testing in actual cadaveric bone, the internal morphological properties of the sheep are sufficiently similar to human that it is justifiable to use it for comparative pull-out strength testing as an initial assessment of the UEF design compared to conventional screws. The upper thoracic spine was used because the cervical, lower thoracic and lumbar vertebral bodies were anatomically irregular, making screw and fastener pilot hole preparation and insertion more difficult and inconsistent.

Fresh frozen bone was used rather than formalin fixed to minimise the alteration of the bone properties (Öhman, Dall'Ara, Baleani, Jan, & Viceconti, 2008). Borchers, Gibson, Burchardt, and Hayes (1995) demonstrated that up to eight freeze–thaw cycles at 20°C did not affect the mechanical properties of the bone and so the five freeze–thaw cycles used within this study should not have caused significant changes.

The 4 mm square hole was awled for the UEFs using a bespoke square awl with a 4 mm pilot hole. The UEF sample with a cracked cortex during awling indicated that awling a square hole could be problematic due to the stress concentrations at the corners of the hole. This was exacerbated by the severely curved cortex of the ovine vertebral body, which increased the radial area moment of inertia and reduced the allowable displacement before failure. Pre-failure was also difficult to detect using HR-CT scanning because fracture could occur without significant plastic deformation, which would allow the fractured surfaces to re-contact, obscuring the crack in the HR-CT scan. However, even with a pre-cracked cortex the UEF still performed better than some of the screw test results.

The pull-out testing experimental rig used a plate with a 13 mm hole to restrain the vertebrae on the upper cortical surface during testing (Figure 5-2). This was used instead of potting the vertebrae to ensure that the bone wasn't supported radially to allow the vertebral body to split open if the radial force was too high during expansion or pull-out. Bone cement was applied at the bone–plate interface to ensure that the loading was purely axial. This method of sample restraints has been used before (Seller et al., 2007; Seybold et al., 1999) and often the potted methods extend the surface of the potting very close to the fastener (Harris et al., 2001; Wan et al., 2010), which provides equivalent loading conditions. However, using this arrangement it was possible that the plate may have supported the cortical shell during failure if the cortical failure zone extended to the supported area. To demonstrate that this was not the case, all HR-CT scans of the failed samples were checked to ensure that they failed significantly far from the support. Average failure diameter was 7 mm for the UEFs and 8 mm for the screws, well inside the 13 mm slot.

There were a number of other design problems that were discovered during this experiment, including reduced than theoretical expansion size and uneven expansion that is discussed in more detail in Chapter 4 ('Design of the EXF Screw').

5.4 Conclusions

A novel unthreaded expandable fastener (UEF) designed by the author, in collaboration with Intan Oldakowska, performed significantly better than an orthopaedic screw at 4 mm fastener width and 10 mm depth, demonstrating that unthreaded expandable fasteners can outperform screws in a cadaveric model, especially in terms of failure energy. This increase (41%) is more than the amount previously reported for bicortical fixation (28.7% according to Heller et al. (1996)). Additionally the failure force appeared less sensitive to bone properties, in particular cortical thickness and SMI, parameters associated with osteoporosis. Furthermore the critical bone volume for the expandable fastener samples was substantially smaller than the screws.

Chapter 6 Effect of design parameters on mechanical performance of the EXF Screw

Detailed design of the EXF Screw involves the optimisation of a number of design parameters in order to maximise fixation performance whilst satisfying the design constraints. This chapter describes the mechanical testing that was performed to determine the effect of design variations on fixation performance in order to optimise the EXF Screw design. For more detail on the design process, see Chapter 4 ('Design of the EXF Screw') Section 4.3.5 ('Detailed design').

6.1 Methods

6.1.1 Synthetic bone samples

Evaluating the effect of small changes in expandable screw design on failure force using destructive testing of biological bone samples is infeasible due to the high variance in the results as a consequence of the unique microstructure of each bone sample. Predicting the effect of microstructure and correcting for it may not be accurate enough to investigate small effect sizes and is extremely time consuming due to the sample extraction, preparation, CT-scanning, and bone parameter analysis. Furthermore the use of animal and human material must be justified ethically, which is difficult for preliminary studies and limits the number of samples that can be tested and consequently the statistical power of the experiment. Consequently the testing in this chapter was performed using synthetic bone samples that provide uniform material properties.

Cellular rigid polyurethane foam (Sawbones, Pacific Research Laboratories Inc.) with a density of 0.20 g/cm^3 was used in this study. This foam density has been used in a previous study as an equivalent model of mildly osteoporotic cancellous bone (Milne, Kop, & Kuster, 2014). Although polyurethane foam samples do not have exactly the same failure characteristic as real bone, it is an adequate model and has been used extensively to provide performance comparison between different fastener designs (DiPaola, Jacobson, Awad, Conrad, & Rehtine, 2007; Hickerson, Owen, Wayne, & Tuten, 2013; Palmer et al., 2012; Patel, Shepherd, & Hukins, 2010; Rios et al., 2012).

6.1.2 Prototype manufacture

Prototype designs were created using SolidWorks, a Computer Aided Design (CAD) package and expanded sizes and expansion angles were calculated using COSMOS, a FEA plugin for SolidWorks (Version 19; Dassault systemes, 2011). The designs were converted to .STL surface files for manufacture using SLM. The Realizer SLM100 machine, at UWA was used to 3D print the EXF Screw with a standard medical grade Titanium (Ti6Al4V) material. A standard contour and vector fill scanning strategy was used, with the direction of the fill vectors rotated 90° between layers. The laser power was 120 W for the contour and 175 W for the fill, while the scan speed, scan spacing, beam compensation and layer thickness were 1000 mm s⁻¹, 100 µm, 60 µm and 50 µm respectively and the particle size of the powder was between 45–106 µm.

Samples were manufactured to test effect on pull-out force of the following design parameters:

- Expansion size
- Expansion angle
- Expansion tab width
- Thread depth
- Fastener diameter

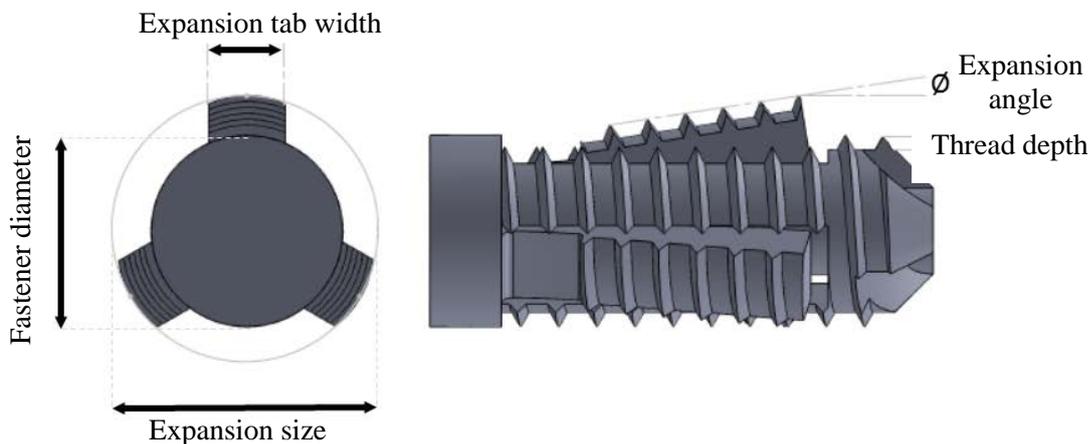


Figure 6-1 The design parameters that were investigated in this study

The EXF Screws were manufactured either have a 5 mm outer diameter with a 4.3 mm core diameter or a 4 mm outer diameter with a 3.3 mm core diameter. The thread on the EXF Screw prototype are manufactured to the same dimensions as an equivalent sized NCB locking screws, which were used as control screws.

6.1.3 Mechanical testing procedure

Polyurethane foam blocks with an approximate dimension 35 (W) x 55 (L) x 30 (D) mm were prepared for each sample. A pilot hole of a specific diameter was then drilled before screwing the sample screws or EXF Screw to the depth appropriate for the particular design. For the EXF Screw, an expansion pin of a specific diameter is inserted to expand the tabs, before mechanical testing was conducted. Axial pull-out testing was conducted at the Medical Engineering and Physics Department at RPH using the Instron 5566 MicroTester materials testing machine using a 10kN load cell. Axial pull-out testing of the screw and EXF Screw were conducted at a displacement rate of 5mm/min with load and displacement value recorded at 10 Hz. The test is stopped when the recorded load falls below 10 N. Maximum force recorded during the test is used for result analysis and the pull-out stiffness is automatically calculated in the INSTRON software based on the gradient of the linear portion of the force-displacement curve (see Figure 5-4). The failure energy is calculated by summing the area under the force displacement curve using various failure criteria.

Only a single EXF Screw of each design was manufactured for testing. This was due to the large number of designs that were tested and the cost of printing and threading them. Consequently the same EXF Screw is tested five times for each test. However, the repeated expansion and unexpansion of the tabs may, in some instances, have plastically deformed the expanding tabs, resulting in the EXF Screw being slightly opened during implantation which may reduce the initial compression around the screw. However analysis of the effect of retesting over 10 tests did not find a significant negative linear trend ($p=0.129$).

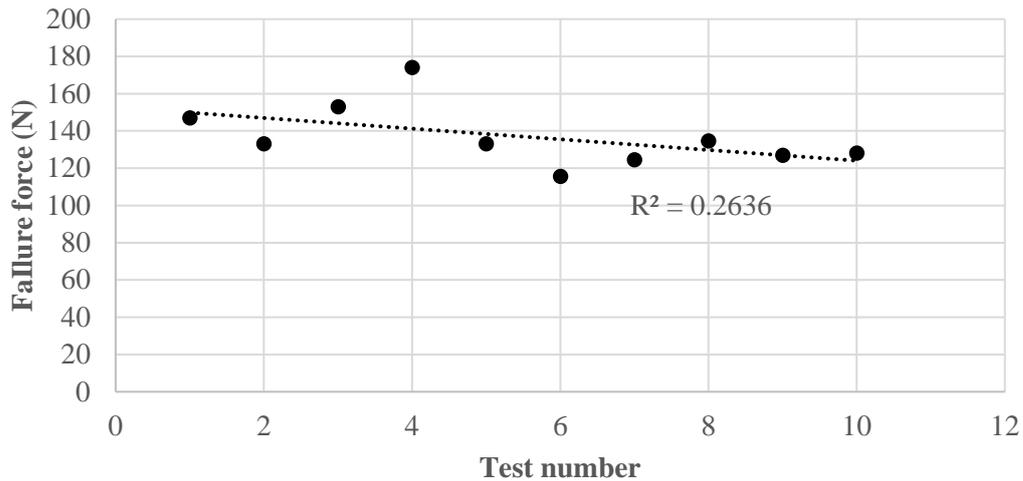


Figure 6-2 Although the line of best fit had a negative gradient indicating that potentially the expandable screw is decreasing in pull-out force the more it is tested, this was not statistically significant

6.1.4 Statistical methods

Independent, two tailed Student's t-tests were used to determine whether the recorded mechanical performance parameters of two fastener groups were significantly different. Correlation between failure force, design and other testing variables was assessed using paired Pearson coefficients and the significance was calculated using a two-tailed test. All tests used a $p < 0.05$ significance threshold.

6.2 Results and discussion

6.2.1 Effect of pilot hole size

NCB locking screws (Zimmer GmbH, 2015) and EXF Screws with a low and high expansion sizes were tested across different pilot hole sizes ranging from 4.4 mm to 3.4 mm. The NCB and EXF Screws used in this test had an equivalent outer diameter (5mm). The low expansion design was expanded using a 1.7 mm pin to increase the outer diameter by 47% and the high expansion design used a 2.5 mm pin to increase the outer diameter by 65% (see Figure 6-3). The core diameter of both the NCB screw and the EXF screws threads were 4.4 mm, which equates to a range from no compression to 1.0 mm of radial compression, where compression describes the diameter of bone that must be compressed to allow the screw to fit into an undersized pilot hole. Unlike other studies in this chapter, only three samples were tested per pilot hole size to increase the number of pilot hole sizes that could be tested.

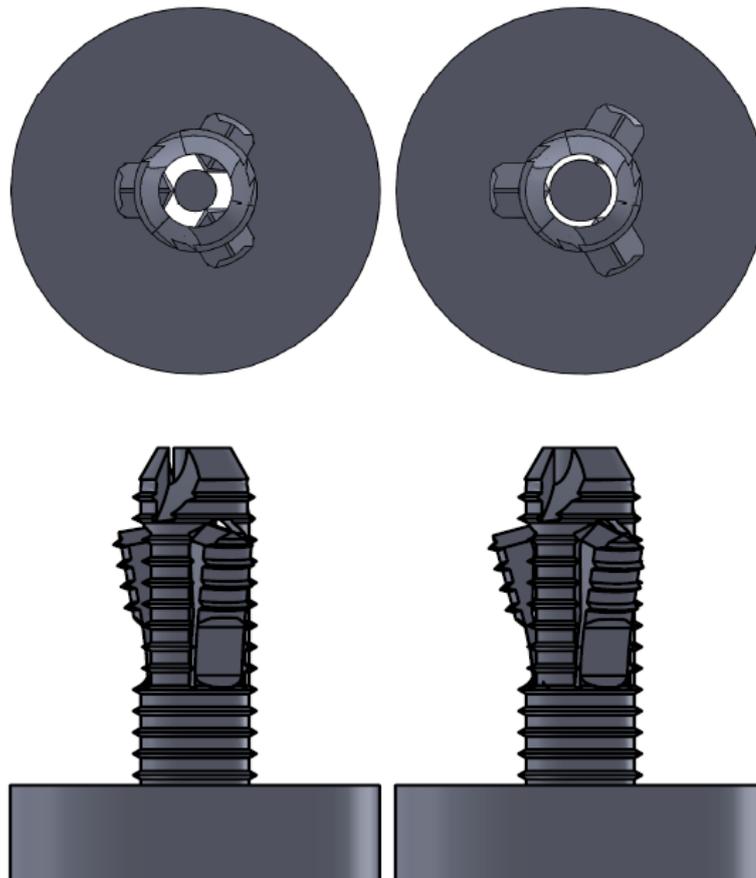


Figure 6-3 The low expansion design (left) expanded using a 1.7 mm pin, increasing the diameter by 47% and the high expansion design (right) expanded using a 2.5 mm pin, increasing the diameter by 67%

As shown in Figure 6-4, all three screws have increased failure force on average with the increased compression caused by decreased pilot hole size. A significant increase in failure force was demonstrated for the NCB Screw and the High and Low expansion EXF Screw from no compression to 1.0 mm compression ($p=0.0276$, $p=0.003$ & $p=0.006$ respectively). However the NCB locking screw was more affected by the higher compression than either of the expandable screws, with a line of best fit gradient of 116 compared to 39 and 44 respectively for the high and low expansion EXF Screw.

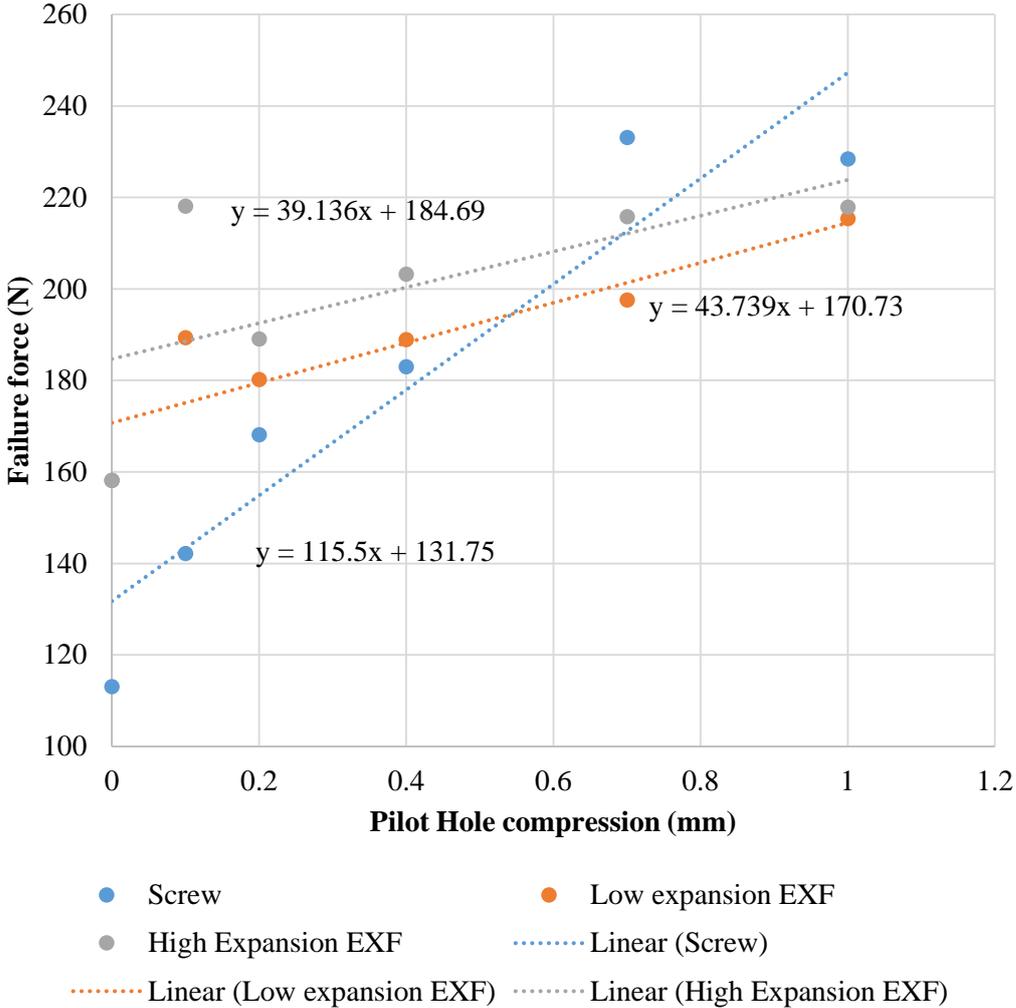


Figure 6-4 A graph of the effect of pilot hole compression on failure force for the EXF Screw compared to a conventional screw

At the pilot hole sizes resulting in no compression and 0.1 mm compression, the high expansion EXF Screw had a significantly higher failure force than the NCB screw ($p=0.005$, $p=0.037$ respectively). However at higher compression and for the low expansion EXF Screw design, there was not a statistically significant difference between the EXF Screw and the NCB Screw.

Previous studies have demonstrated that decreased pilot hole size increases fixation strength. However this has not been previously examined for expandable screws. This phenomenon is critical to studying expandable fasteners because this study has indicated that an increase in fixation strength by expandable screws may be primarily due to compression. This hypothesis is supported by subsequent testing of expansion size and angle detailed below.

6.2.2 Effect of expansion size

In this study, the effect of expansion size was investigated for two different expandable fastener designs with 5mm outer diameter, one with three expandable tabs of 2.1 mm width and the other with only two expandable tabs of 2.1 mm width, compared against a Zimmer NCB locking screw of equivalent diameter (see Figure 6-5).



Figure 6-5 A picture of the three samples tested; an EXF Screw with three expansion tabs (left), an EXF Screw with two expansion tabs (centre) and an NCB locking screw (right)

Expansion pins of diameters 1.25 mm, 1.70 mm, 2.10 mm and 2.50 mm were used to create different expansion sizes ranging from 37% to 65% increase in outer diameter (see Figure 6-6). Both designs were tested five times with each expansion pin and unexpanded. The average failure force was reported graphically in Figure 6-7 below. The recommended pilot hole size for the NCB locking screw (4.3mm) was used for all samples, as the EXF Screw samples were manufactured to have NCB locking screw thread dimensions.

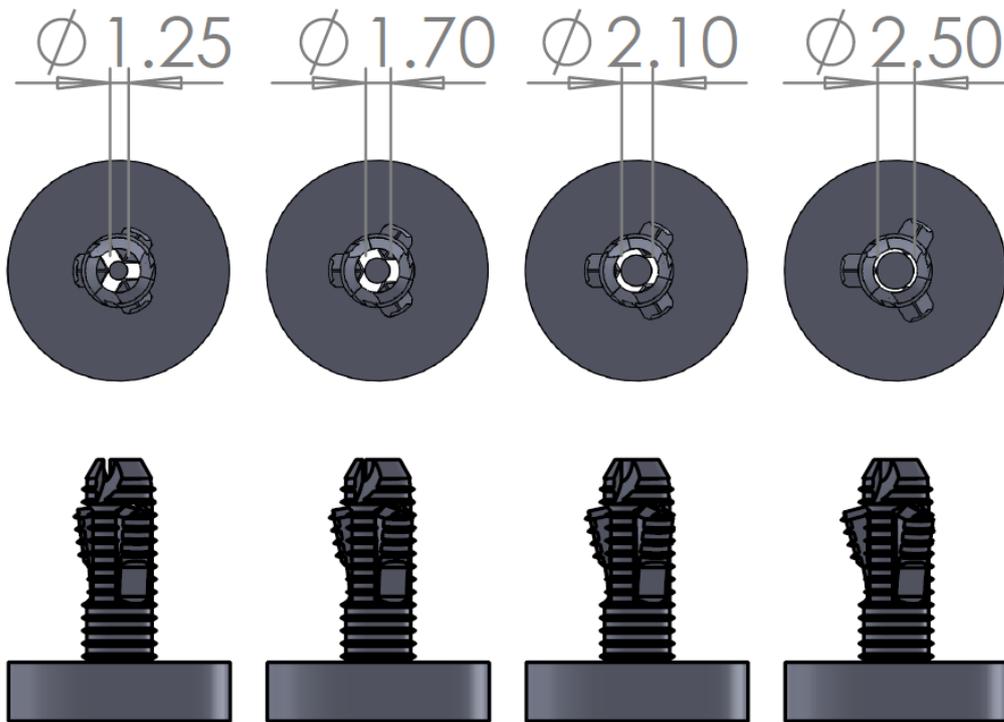


Figure 6-6 A single sample was able to test multiple expansion sizes by using different diameter expansion pins ranging from 1.25 mm to 2.50 mm providing expansion sizes ranging from 37% to 65% increase in outer diameter

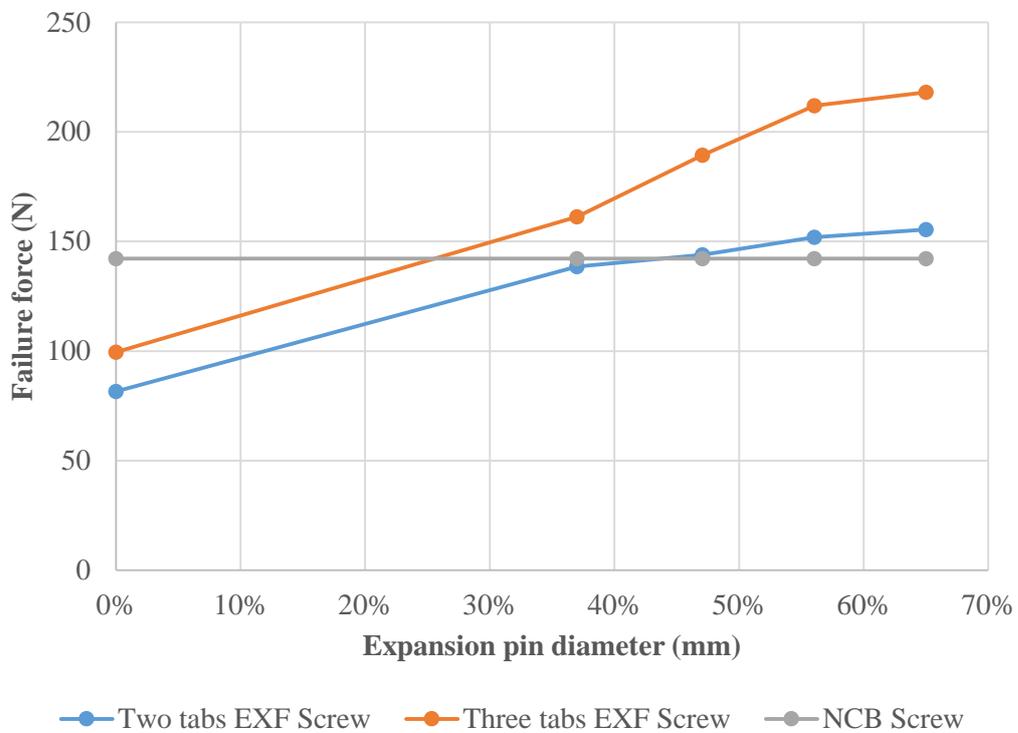


Figure 6-7 The effect of expansion size on the pull-out force of two expandable screw designs with two tabs and three tabs compared to a conventional NCB screw

As shown in Figure 6-7, increased expansion size resulted in increased failure force for both EXF Screw designs, as expected. The three tab design demonstrated statistically significantly increased failure force compared to the NCB screw for expansion sizes 47% and above ($p=0.048$, $p=0.017$, $p=0.003$ for 47%, 58% and 65% expansion size respectively). However the 2-tab design did not demonstrate significantly increased failure force compared to the NCB, even at the maximum expansion size tested ($p=0.382$). The 3-tab design demonstrated a significantly higher failure force than the two tab design at 47% expansion size and above ($p=0.004$, $p=0.024$, $p<0.001$ for 47%, 58% and 65% expansion size respectively). The three tab design was more affected by the amount of expansion than the two tab design with a line of best fit gradient of 190 compared to 117 for the two tab design.

The unexpanded expandable screws provided significantly less force than the NCB locking screws for the two tab design (37.6% reduction, $p=0.025$) but not for the three tab designs (42.6% reduction, $p=0.0707$) due to lower variance in the two tab unexpanded tests.

The author hypothesises that the increased fixation strength with increased expansion size for the EXF Screws is due primarily to increased compression of the synthetic bone foam around the fastener. This compression increases fixation strength in the same manner as conventional screws with smaller pilot holes. Although the statistical power and the range of expansion sizes tested in this study are not sufficient to verify this, the author predicts that diminishing returns will be observed with increased expansion size, due to a critical threshold of compression, after which a significant increase in fixation strength is not observed with an increase in expansion size. This is supported by the investigations reported above into the effect of pilot hole size, where a characteristic asymptotic curve was observed for the NCB Screw (Figure 6-8).

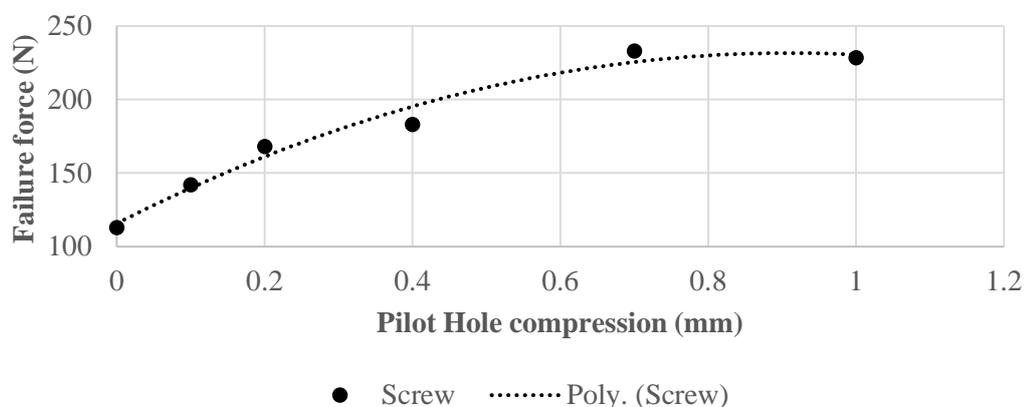


Figure 6-8 The effect of pilot hole size on a non-expanding screw using a polynomial line of best fit

The two tab design performed significantly worse than the three tab design, demonstrating that an increased expanded area increased the fixation strength. This is congruent with the hypothesis that the expansion increases fixation strength by increasing the compression of the bone onto the thread.

The unexpanded, expandable screws have less fixation strength than the locking screw. This is primarily due to the bending sections of the expandable screws being unthreaded and consequently not engaging with the bone. Consequently the thread engages less bone for the expandable fasteners. However, this effect alone cannot account for the difference given that there was 11.3% and 16.9% less threaded area for the two tab and three tab designs respectively, but a 37.6% and 42.6% reduction in fixation strength, respectively. The author hypothesises that, due to repeated expansion, loading and unexpansion cycles, the bending sections of the expandable fasteners were slightly plastically deformed, creating a slightly larger threaded hole during implantation. This larger hole reduces the compression around the rest of the screw in the same way that using a larger pilot hole does, reducing the failure force of the unexpanded EXF Screw.

6.2.3 Effect of expansion angle

EXF Screw prototypes of 4mm outer diameter were manufactured and tested across a range of feasible expansion angles (ranging from 10-16°). The expansion angle was varied by adjusting the height of the bending and transition sections of the fastener whilst keeping the expanded diameter the same (Figure 6-9). Consequently the length of the fasteners varied where more aggressive expansions resulted in shorter screws. Therefore the failure force per unit length was reported to account for disparate lengths. The samples were tested five times each with a pilot hole size of 3.3mm, the recommended size for the 4mm NCB locking screw that the screw thread was based upon.

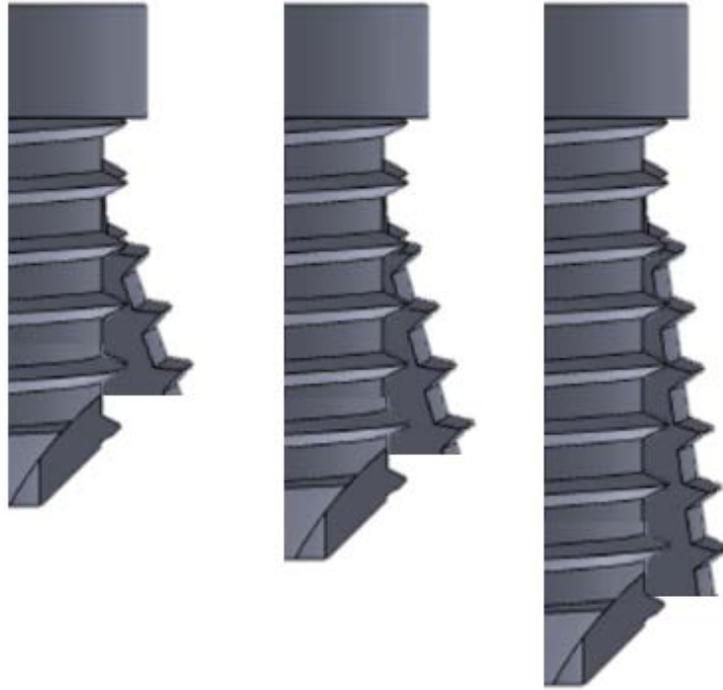


Figure 6-9 Three different samples with different expansion angles (16°, 13°, 10°), but the same expansion size, resulting in different sample lengths

As shown in Figure 6-10, comparing the pull-out force per unit length of the different expansion angle designs using the screw length, resulted in a weak, statistically insignificant negative correlation ($p=0.237$).

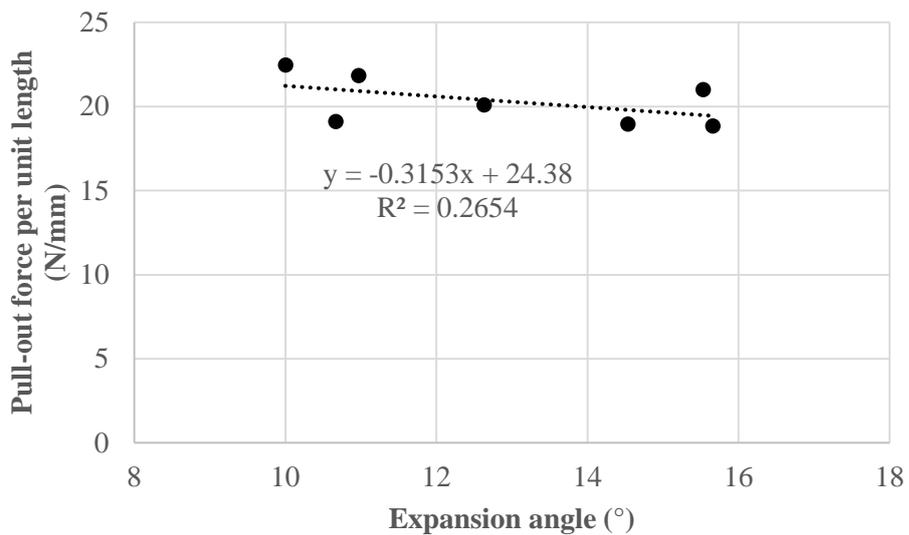


Figure 6-10 A graph of length corrected pull-out force against expansion angle for the expandable screws tested

Prior to this experiment it was hypothesised that increased expansion angle would increase fixation strength per unit length by increasing the proportion of load that is transmitted radially into the walls of the bone hole (see Figure 6-11: Left) and adding this force to the compression around the screw thread. However, the result from previous studies above demonstrated that compression is the most important factor in expandable screws increasing fixation strength. This would suggest that expansion angle would not affect the failure force, given the same overall compression. Furthermore it would indicate that rather than trying to use the angulation of the screw to reduce the load on the expandable screw, a better strategy would be to expand each section of the screw as much as possible by having straight vertical sections and a rectangular expanded profile, as shown in Figure 6-11 (right).

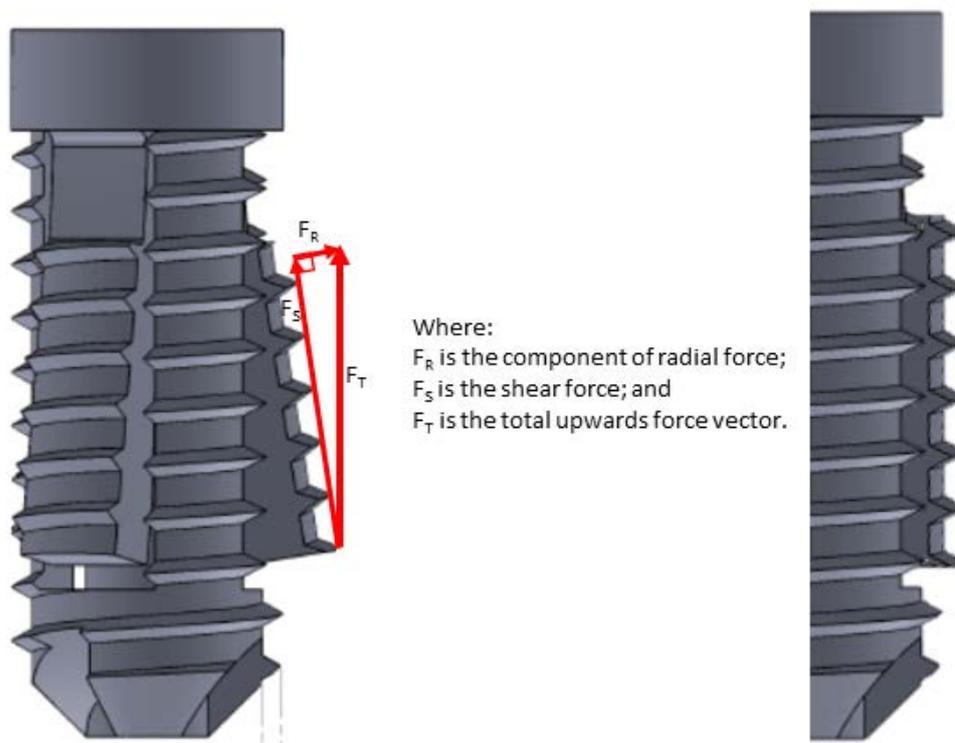


Figure 6-11 A component of the total upwards force is applied radially to the bone surrounding the screw (left). Compression can be maximised by expanding every section of the expandable fastener the same, maximal amount providing a rectangular expanded profile (right), rather than a triangular expanded profile (left)

For the current design of the expandable fastener increasing expansion angle past 16° is infeasible due to the limitation of gapless expansion. This upper limit of expansion angle means that there may be potentially a greater effect on failure force, outside the range tested. Future work should dispense with this requirement and utilise a larger range of different expansion angles to understand the effect of expansion angle more generally.

Future work on expansion angle should use screws of the same insertion length with expanded sections of different length on the bottom of the screw. This is because although the failure force is theoretically directly proportional to the length of engagement (Chapman et al., 1996) this is not true for very short screws (the size tested in this study). If designs of equal length with different expansion angles were tested, the author hypothesises that decreasing the expansion angle may result in increased fixation strength by compressing a larger area.

6.2.4 Effect of expansion tab width

The maximum expansion size for a given screw diameter whilst maintaining a gapless expansion is affected by the width of the expansion tab (see Figure 6-12). Consequently wider expansion tabs results in a smaller allowable expansion size (given the requirement for gapless expansion).

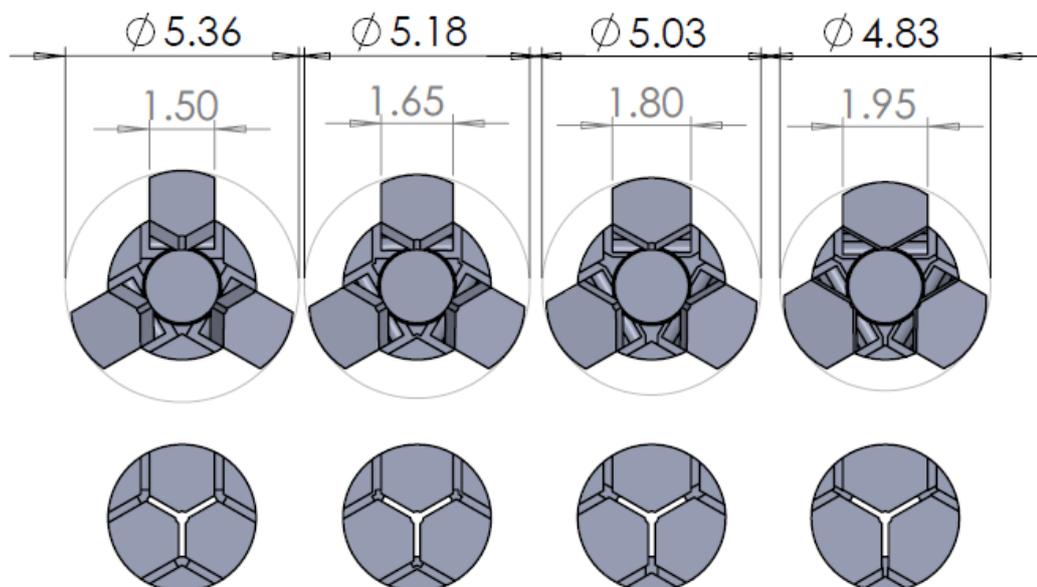


Figure 6-12 The 4mm EXF Screw prototypes had different bending section widths (1.5, 1.65, 1.80 and 1.95 mm) and consequently, maintaining gapless expansion, had different expansion sizes

Consequently the author investigated whether thinner expansion tabs with a larger expansion size or wider expansion tabs with a smaller expansion size resulted in a higher failure force. Four EXF Screw designs with expansion tab widths of 1.50 mm, 1.65 mm, 1.80 mm and 1.95 mm (see Figure 6-12) were manufactured, spanning the feasible range for a 4mm outer diameter fastener with the maximum gapless expansion size. The sample with the largest tab width (1.95mm) was broken (over multiple trials) during the CNC threading process, indicating the infeasibility of smaller static columns (see Figure 6-13).



Figure 6-13 The sample with the thinnest static columns was broken during the process of turning the thread

Comparing the pull-out force of the remaining three expansion tab width designed (Table 8) demonstrated that the bending section width did not significantly affect the failure force with no significant difference between any of the designs.

Table 8 Pull-out forces for each of the five tests for the three different expansion tab width designs evaluated

Expanding tab width (mm)	Test 1 (N)	Test 2 (N)	Test 3 (N)	Test 4 (N)	Test 5 (N)	<u>Average (N)</u>
1.5	173.9	158.6	146.1	155.1	129.6	<u>152.66</u>
1.65	163.1	151.8	151.8	157.5	142.1	<u>153.26</u>
1.8	143.3	133.5	149.5	152	190	<u>153.66</u>

Previous studies in this chapter have demonstrated that increased expansion size and area of expansion both increased fixation strength significantly. However taking into account the relationship between these parameters indicates that failure force is independent of expansion size and expansion tab width, given gapless expansion.

Therefore the decision whether to have a large expansion size or tab width depends on whether having reduced tab width (to increase the size of the static columns on the screw and consequently static strength of the screw) or having a reduced expansion size (to reduce expansion force) is more critical to the clinical performance of the EXF Screw. This is discussed in detail in Chapter 4 ('Design of the EXF Screw').

6.2.5 Effect of thread depth

EXF Screw prototypes of 4 mm outer diameter with four different screw thread depths between 0.2 mm and 0.5 mm, were manufactured to investigate the effect of thread depth on pull-out strength. Due to the different sizes of thread depth, the allowable gapless expansion size was slightly different across the different samples. There are also small length differences across the different samples as the expansion angles were maintained. Consequently failure force was reported per unit length. Testing was performed with a 3.3 mm pilot hole (as per Zimmer recommendation for a 4mm NCB locking screws, which had a 0.3 mm thread depth) and with a 2.5 mm pilot hole (as per Zimmer recommendation 4.5mm cancellous screws, which have a 0.65 mm thread depth).

The 0.5 mm thread depth sample was damaged during removal from the sample after the 2.5 mm pilot hole test and so no pull-out forces were recorded for the 3.3 mm pilot hole for that sample. A 0.65 mm thread depth EXF Screw was manufactured twice but both times was broken during the process of turning the thread on the lathe (Figure 6-13), this is due to the thread depth reducing the area of the static arms and the fact that deeper cuts resulted in higher forces on the arms during the threading operation on the lathe. This indicates that 0.4 mm may be a practical manufacturing limit for thread depth for the design tested.

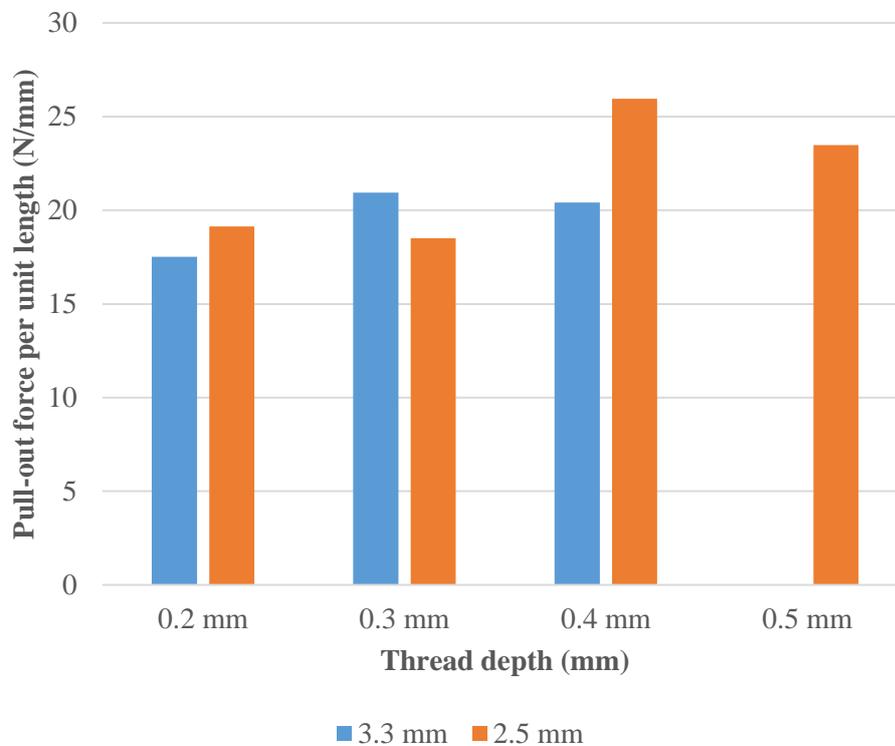


Figure 6-14 The failure force of the EXF Screw prototypes with different thread depths with different pilot hole sizes

Comparing the pull-out force per unit length of the different thread depths demonstrated no significant difference between thread depth groups for the 3.3 mm pilot hole and only a significant difference between the 0.4 mm and both the 0.2 mm and 0.3 mm groups ($p=0.002$ and $p=0.006$ respectively) for the 2.5 mm pilot hole groups.

The data from this study does not demonstrate that thread depth significantly affects pull-out force, given gapless expansion. More variation was observed in the 2.5 mm pilot hole study and a single statistically significant different sample (0.4 mm thread depth), suggesting that increased compression may increase the influence of the thread depth.

However because the designs have different core diameters (due to varying the thread depth) each had a different degree of compression for the same pilot hole size. Consequently the smaller thread depths may have been advantaged by the fact they have more compression for a given pilot hole size.

6.2.6 Effect of fastener diameter

The effect of outer diameter on the performance of gapless expandable screws was investigated to determine whether expandable screws perform better at higher or lower diameters. Three equivalent EXF Screw designs (same designs scaled up) were manufactured at 4.0 mm, 4.5 mm and 5.0 mm outer diameter.

The average failure force per unit length, corrected to 4 mm according to the Chapman equation was 20.3, 20.6 and 18.5 N/mm for the 4.0 mm, 4.5 mm and 5.0 mm designs respectively (Chapman et al., 1996). There were no statistically significant differences between the three groups.

Prior to the experiment it was hypothesised that higher diameter expandable screws may provide higher increase in fixation strength as the expansion sizes would be larger due to non-scaling limitations (minimum gap sizes, minimum bending thicknesses, etc.) but the results did not support this hypothesis. The result indicates that, across the range of diameters tested, EXF Screws were not affected by outer diameter differently than conventional screws.

6.2.7 Failure energy

Failure energy is a measure of the energy required for the screw to fail. Failure energy is calculated as the area under the load-displacement curve up to the displacement at the failure criterion, giving units of Nmm or mJ. The small and large expansion EXF Screws (47% and 65% increase in diameter respectively) and the NCB locking Screw were tested using the recommended pilot hole size (0.1 mm compression) and at a reduced pilot hole size (1.0 mm compression). Averaging all the samples tested provides a ‘typical’ curve for the samples for visualisation purposes (Figure 6-15).

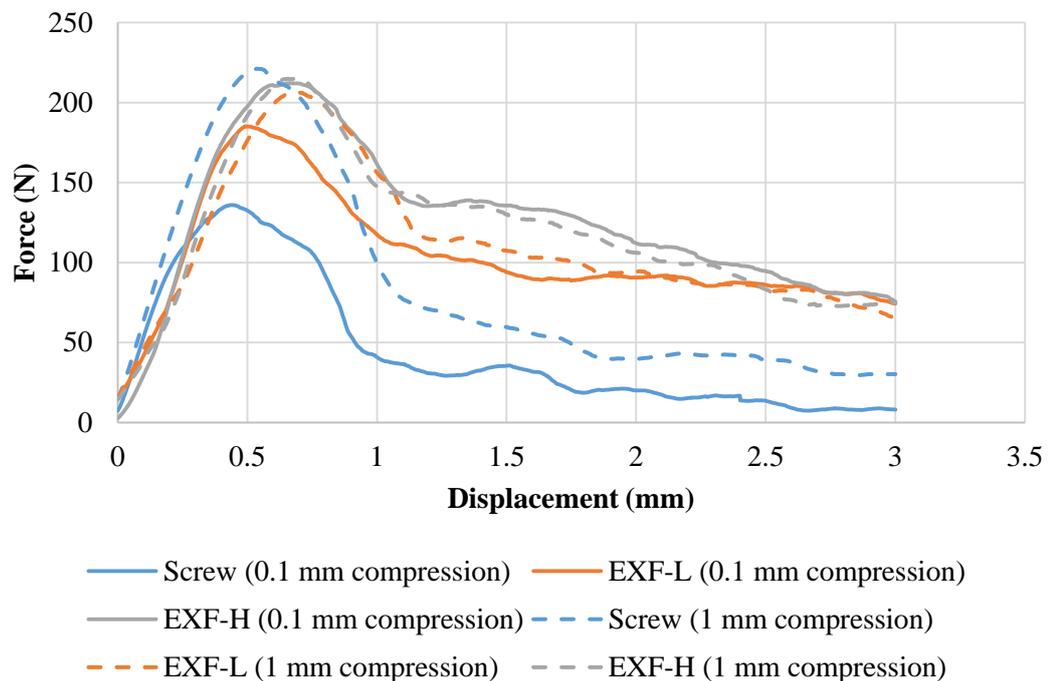


Figure 6-15 An averaged load-displacement curve for the EXF Screw low expansion and high expansion designs and the NCB Screw samples for the recommended pilot hole size (0.1 mm compression) and a reduced pilot hole size (1.0 mm compression)

At the recommended pilot hole size the failure energy of the NCB locking screw was significantly lower compared to both the EXF-H and EXF-L Screw designs at 1 mm ($p=0.002$, $p=0.033$), 2 mm ($p<0.001$, $p=0.003$) and 3 mm ($p<0.001$, $p=0.001$) displacement failure criteria as shown in Figure 6-16. Using the 3 mm failure criterion the EXF-H had 175% higher failure energy compared to the NCB Screw. The only statistically significant difference in failure energy between the high and low expansion EXF Screw designs was with a 2 mm failure criterion ($p=0.047$).

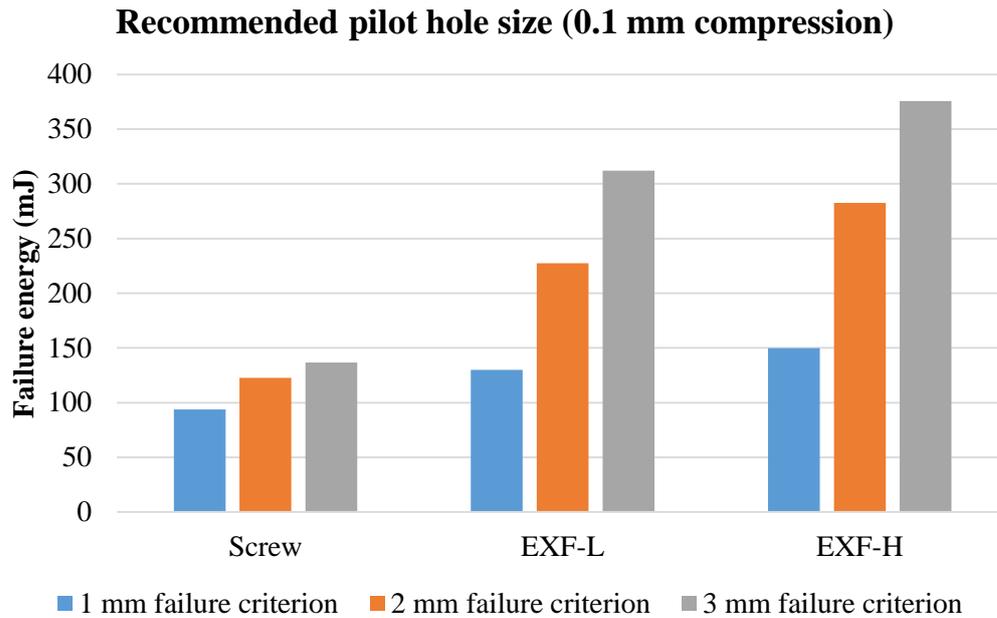


Figure 6-16 The failure energy of the EXF Screw low and high expansion designs and the NCB Screw for the different failure criteria at the recommended pilot hole size

At the reduced pilot hole size, the failure energy of the screw was only significantly less for the high expansion design using a 3 mm failure criterion ($p=0.019$). Using this failure criterion the EXF-H had 41% higher failure energy.

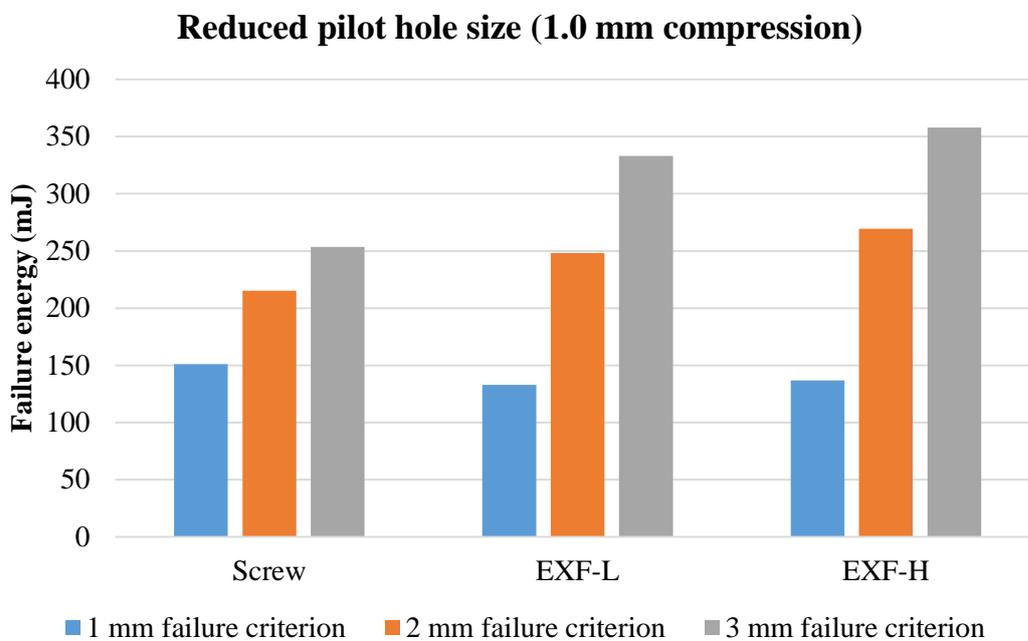


Figure 6-17 The failure energy of the EXF Screw low and high expansion designs and the NCB Screw for the different failure criteria at the reduced pilot hole size

Failure energy is clinically important if significant displacement of the screw doesn't necessarily constitute failure, or when failure with reduced displacement reduces the injury to the patient. For example in proximal humerus fractures (the primary indication for the EXF Screw), bone fragment movement, causing varus malunion are often asymptomatic, so long as the screw tips do not penetrate the shoulder joint. In this case, increased failure energy can potentially prevent or delay the joint penetration failure mode. Consequently other studies, especially those with expandable screws, have reported failure energy as a performance metric (Chen et al., 2014; Vishnubhotla et al., 2011).

However the profile for the EXF Screws was not the same as the UEF tested in Chapter 5 (see Figure 5-8). This is because the UEF relies entirely on the friction generated between the two surfaces and so 'failure' in the sense of movement is ongoing as the fastener is dragged out of the bone.

In the present study failure criteria up to 3 mm were examined. Although this number is arbitrary and increasing the failure criterion advantages the expandable screws, it is not clinically unrealistic. For example in proximal humerus fracture fixation the screws are typically 50 mm long, rather than the 8 mm samples tested in this study and the surgeon aims to provide approximately 5 mm to 10 mm of clearance below the joint surface, providing an average failure criterion of between 5 mm to 10 mm.

Future studies on expandable screws must assess the failure energy in more clinically relevant testing method, such as cyclic testing with a full fracture fixation construct similar to previous studies investigating the failure of conventional screws in cadaveric bone (Erhardt et al., 2012; Sommers et al., 2004).

6.2.8 Failure stiffness

A significant correlation between failure stiffness and force was demonstrated for both the conventional screws ($p < 0.001$) and the expandable screws ($p < 0.001$). The correlation coefficient was marginally higher for the expandable screws ($R^2 = 0.7$) than the conventional screws ($R^2 = 0.6$).

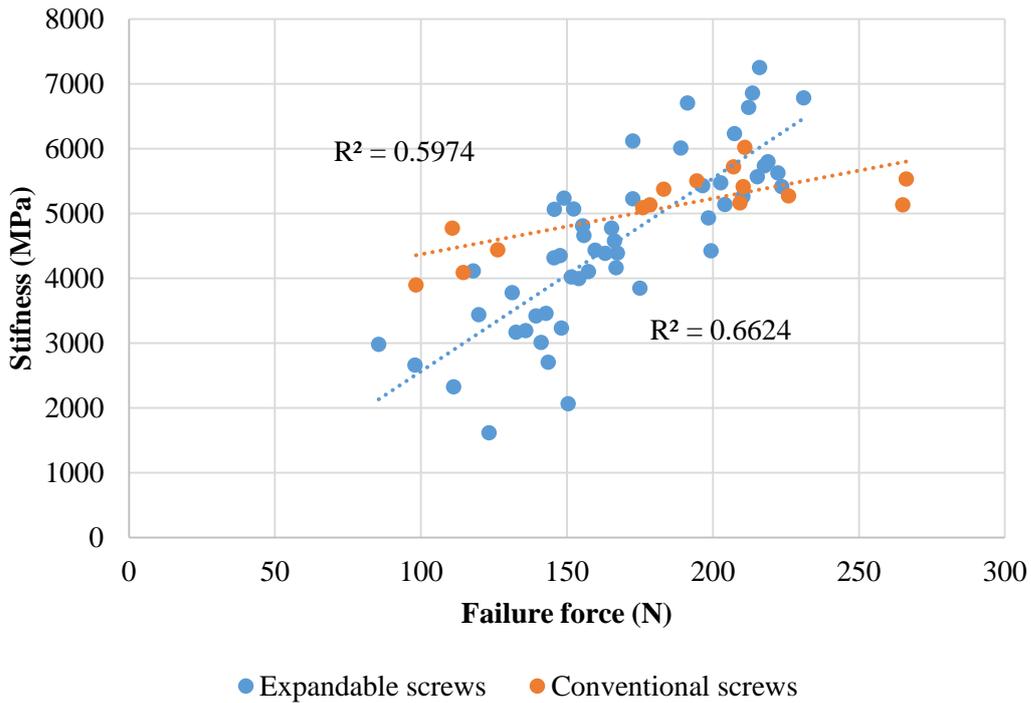


Figure 6-18 The failure stiffness and force for individual tests, divided into expandable screws and conventional screws

A significant relationship was also seen in the average stiffness and average failure force across the multiple tests of each EXF Screw design, as shown in Figure 6-19.

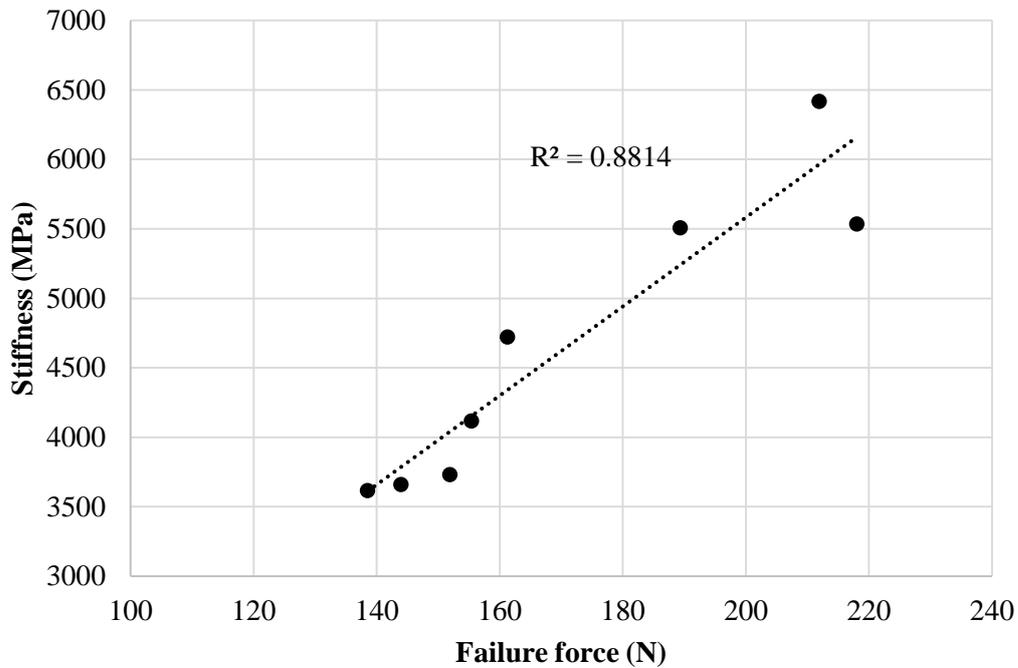


Figure 6-19 The average stiffness and average failure force for individual expandable screw designs, by averaging the tests of each design

Predicting the pull-out failure force of the fasteners allows the design candidates to be evaluated for fixation strength and consequently design parameters optimised to achieve maximum fixation strength. However iterative mechanical testing of different expandable screw designs is costly and time-consuming due to the destruction of the testing media and the manufacturing time and cost for each different design iteration. Furthermore multiple designs in each design parameter must be tested multiple times to provide sufficient statistical power to demonstrate with statistical significance the small differences in the failure force due to small design variations.

For the above reasons Finite Element Analysis (FEA) is an attractive tool for the design of orthopaedic screws and to augment bench-top mechanical testing. However FEA must be based on a thorough and accurate understanding of the fundamental physical processes being modelled. Previous studies with conventional screws have used FEMs to determine fixation stiffness which they use as a predictor for failure force in both cancellous bone structural model (Ruffoni et al., 2012; Wirth et al., 2010; Wirth et al., 2011) and an idealised, homogenous model (Wirth, Müller, & Harry van Lenthe, 2012).

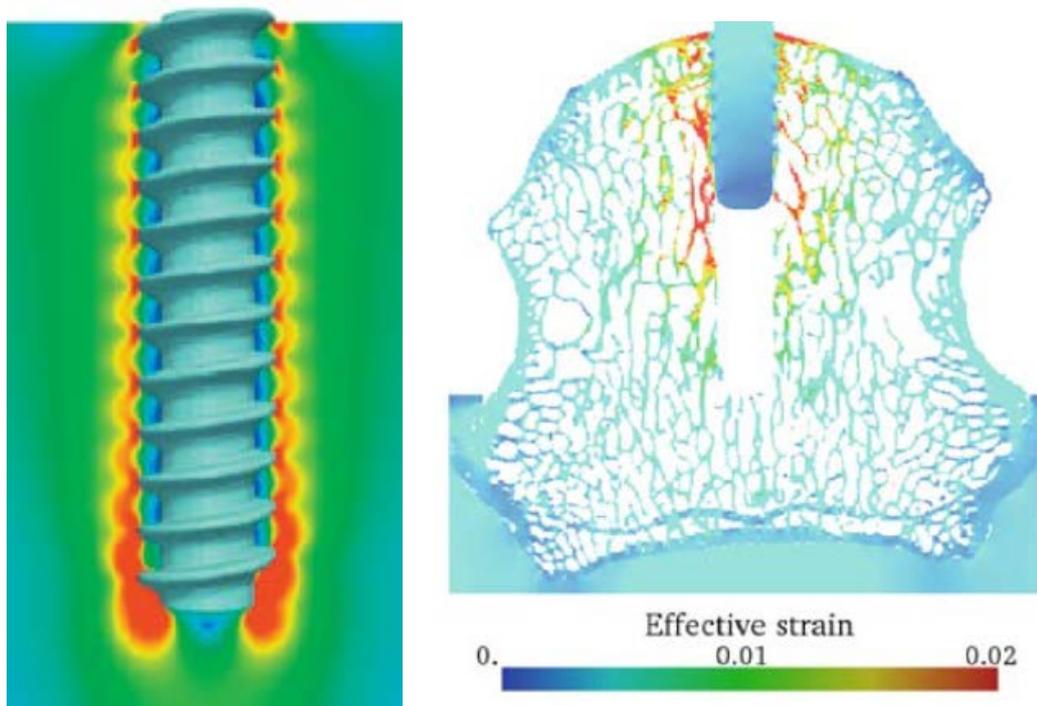


Figure 6-20 Pull-out stiffness has been previously used as a predictor of pull-out force for idealised homogenous models (left: (Wirth et al., 2012)) and cancellous structural models (right: (Wirth et al., 2010))

The results in this section indicate that this relationship is valid for expandable screws and the correlation is not weaker than for conventional screws. This finding is contrary to the findings reported in Chapter 5 ('Preliminary UEF pull-out strength testing') for the UEF where a friction based expandable fastener does not have a correlation between failure force and failure stiffness. The author hypothesises that the difference is in the failure mode of frictional slipping versus screw thread shearing.

However, whether there is a correlation between the two parameters or not, based on the results presented in Chapter 6 ('Effect of design parameters on mechanical performance of the EXF Screw'), Section 6.2.1 ('Effect of pilot hole size') the compression around the screw bone interface is critical to the failure force. Therefore to accurately predict failure force the expansion of the expandable screw must be modelled to determine this compression. Consequently previous linear elastic FEA, which cannot model post-yield strain involved in expanding the screws, is not suitable for predicting the failure force of expandable screws.

6.3 Conclusions

This work demonstrates that compression of the synthetic bone foam around the expanded screw is a significant cause of the increased pull-out strength provided by expandable screws compared to conventional screws, in a cancellous-only bone model.

Additional compression around the screw, provided by under-sizing the pilot hole, increases the pull-out strength of conventional screws to a greater degree than with expandable screws. This is because the foam around the expandable screws is already compressed by the expansion and so additional compression (provided by under-sizing the pilot hole) only increases the fixation strength of the non-expanded sections. Therefore it is imperative that testing of expandable screws against conventional screws is performed using a representative pilot hole size and ideally at multiple, clinically feasible, pilot hole sizes.

Clinically, this indicates that expandable screws would be particularly advantageous as rescue screws in revision cases where the size of the pilot hole is predetermined by the size of the failed screw hole and therefore relatively large (typically approximately the core diameter of the screw providing zero compression), and the risk of fixation failure is known to be high (given the patient just had screw failure).

Consequently the author concludes that the advantage available in terms of pull-out strength for 'gapless' expandable screws in cancellous bone is only moderate and dependant on the pilot hole size. However the advantage in terms of increased failure energy is significant regardless of pilot hole size given a sufficiently high displacement failure criterion.

Failure energy, in pull-out and other failure modes, is critical to performance when failure occurs over significant screw displacement or when fracture settling occurs. A clinical example of this is push-in failure of screw in proximal humerus fractures. In this failure mode there are two distinct failure events: the first when the screw thread fixation fails and the second when the screw pushes through approximately 5-10 mm of subchondral bone before the screw penetrates the joint, necessitating revision surgery. In these cases providing a larger tip area can significantly increase the force required during this second stage failure. Furthermore axial failure is not the only failure mode for screws and so preliminary work has demonstrated the potential for an increase in shear area leading to increased shear failure force.

In addition, expandable screws in biological bone can be placed by the surgeon so that the expansion engages cortical bone rather than cancellous bone, which can potentially greatly increase the fixation strength. For example, in lumbar pedicle fixation, expansion into the vertebral body on the distal side of the pedicle or for screw fixation of acetabular components where the short screws could expand to better engage the proximal cortex (see Figure 3-23).

Additionally it is hypothesised that pull-out force advantage over conventional screws would be improved in a lower density synthetic bone or highly osteoporotic biological bone, as has been suggested previously in the literature (Cook et al., 2000; McKoy & An, 2001).

This study has demonstrated that increasing expansion size and the expansion tab widths significantly increases fixation strength and that, given the relationship between these two parameters that ensures gapless expansion, the failure force is not affected by a reduction in expansion size to allow a wider tab and vice versa.

For the EXF Screw design specifically, with maximum expansion size to maintain gapless expansion, the expansion angle does not affect pull-out force for the range of expansion angles tested. Increased thread depth may increase pull-out strength (maintaining maximum expansion size), especially for small pilot hole sizes (and consequently high compression), but the testing in this thesis did not have sufficient power to demonstrate this statistically.

In terms of increasing the performance of the EXF Screw this could potentially be achieved by increasing expansion size, creating gaps in the outside of the screw which could be filled in with a sealant or by using a staggered expansion. Both of these methods have been prototyped and are described in Chapter 4 ('Design of the EXF Screw').

This study has also demonstrated that there is a statistically significant relationship between pull-out stiffness and pull-out force for expandable screws and so theoretically FEM of fixation stiffness could provide a good prediction of pull-out force. However, simplified FEMs, which model the expanded shape of the expandable screw inside a volume of continuum element representing the trabecular bone, cannot take into account the compression of the trabeculae and consequently is not suitable for predicting failure force. Increasing the complexity of the model to include this affect in a physically accurate model would be difficult and resource intensive due to the non-linear nature of the buckling and partial fracture of the foam 'trabeculae' during implantation of the screw or during expansion of the screw.

Chapter 7 EXF Screw breakage strength

Expandable screws typically have decreased strength compared to equivalent conventional orthopaedic screws due to multi-part construction creating less favourable load sharing, the addition of a stress concentration due to features such as expanding arms and the elimination of material. Predicting stress in expandable screws under simulated physiological loading is critical to understand the effect that design parameters have on the strength of expandable screws. This will allow the EXF Screw and other expandable screws to be designed to have acceptable static strength with minimal compromise on the design parameters that affect other performance criteria.

Ultimately, beyond the scope of this thesis, mechanical testing of the final design of the EXF Screw under fatigue loading will be used to demonstrate equivalence to potential predicate screws for a regulatory approval submission. This is part of the NHMRC Development Grant (Grant ID: 1121702) scope of works, with more details in Chapter 11 ('Future work'), Section 11.4.3 ('ASTM testing'). This FEA study compared potential EXF Screw designs to conventional screws under loading conditions clinically relevant to proximal humerus fracture fixation, the primary indication of the EXF Screw.

Additionally the effect of different loading conditions on the stress in the EXF Screw was also investigated, so that the feasibility of using the EXF Screw for other orthopaedic applications could be evaluated.

Consequently analysis was performed in three stages:

1. Establishing the sensitivity of the Finite Element Model (FEM) to mesh size and fillet radii, the effect of loading conditions and the critical loading direction for each design;
2. Evaluating the effect of design parameters including the number of tabs and whether the tabs are staggered, number of expansion levels, fillet radii, expansion tab height and width and the diameter and material properties of the expansion pin and screw; and
3. Comparing a range of feasible EXF Screw design candidates against a series of conventional screws under clinically relevant loading conditions.

Note that after these three stages, a fourth stage of validating the model physically will be performed. This work will be undertaken by another PhD student, Intan Oldakowska.

7.1 Method

In this FEA study, stress in the EXF Screw model was evaluated as a measure of resistance to screw failure under a static, cantilever bending load. Screw design forces are not available for most orthopaedic applications (including the primary application) and so the EXF Screw was designed and evaluated under an arbitrary set load of 1N using a linear, elastic model.

This study was based on the methodology described in the American Society for Testing and Materials (ASTM) Standard for bending tests of spinal screws ASTM F2193 (*ASTM F2193 - 14 - Standard Specifications and Test Methods for Components Used in the Surgical Fixation of the Spinal Skeletal System*, 2014). The methodology from a spinal screw standard was used because the general bone screw standard ASTM F543 (*ASTM F543 - 17 - Standard Specification and Test Methods for Metallic Medical Bone Screws*, 2017) did not have any bending failure test methodology. In this standard (ASTM F2193) the fastener is embedded in a block of synthetic bone (or other material) and loaded as shown in Figure 7-1 below, creating a distributed load.

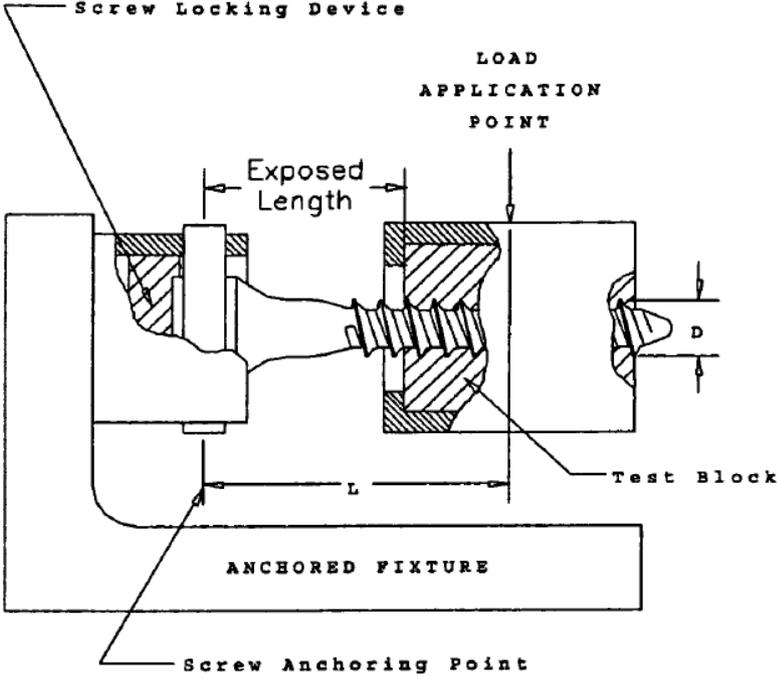


Figure 7-1 The testing methodology described in ASTM F2193 (*ASTM F2193 - 14 - Standard Specifications and Test Methods for Components Used in the Surgical Fixation of the Spinal Skeletal System*, 2014) whereby a distributed load is applied over the length of the testing block

For the purposes of this study this methodology simulates loading on the tip of the screw from the far fracture fragment whilst the head of the screw is fixed, simulating a rigid connection to a locking plate for proximal humerus fracture fixation, as illustrated in Figure 7-2.

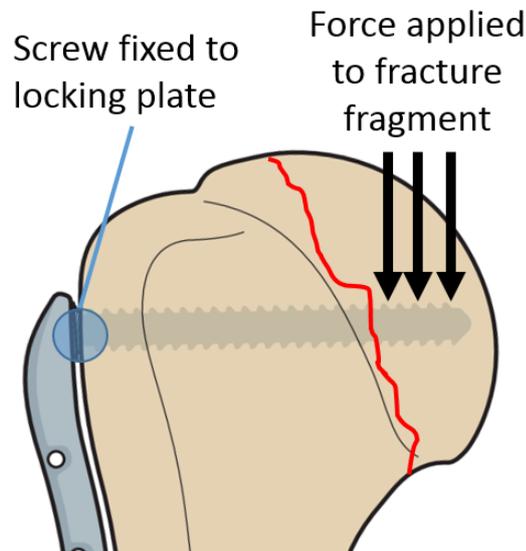


Figure 7-2 The clinical boundary conditions for the screw with fixation to the locking plate and a distributed cantilever bending applied to the furthest portion of the screw, where the length over which the load is applied is determined by the fracture geometry

The contact relationship between the expansion pin and the fastener was defined as ‘no-separation’ to prevent unrealistic axial stress whilst ensuring contact stability. The expanded tabs were not modelled because they do not provide resistance to bending and instead transfer their load directly to the pin, as illustrated in Figure 7-3 below, where the distributed force (red arrows) results in a point load, which was applied to the pin (yellow arrow) assuming that the bending section of the expansion tab were infinitely elastic. The FEM did not include the thread of the screw to reduce the complexity of the model. Elimination of the thread did not affect the maximum stress results as the three potential points of maximum stress were unthreaded.

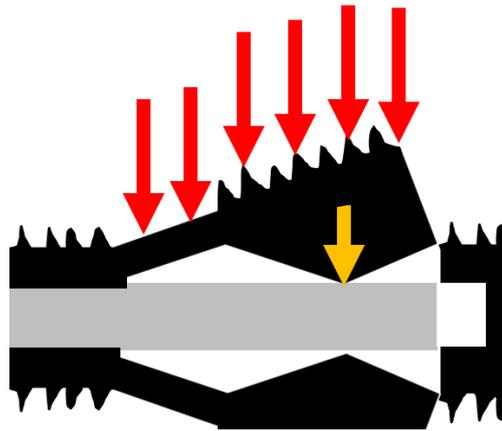


Figure 7-3 The loading on the screw (shown in red) is transferred to the pin via the contact point between the bending arm and the pin (shown in yellow)

Under all loading conditions in the FEM, conventional screws have the maximum stress at the base of the screw, the point of failure most often seen clinically. In the EXF Screw FEM, maximum force was encountered at a number of different locations in the model depending on the loading conditions and design parameters. These include; the base of the screw (junction between screw and plate), the base of the expansion tab and the pin at the base of the tab (see Figure 7-4).

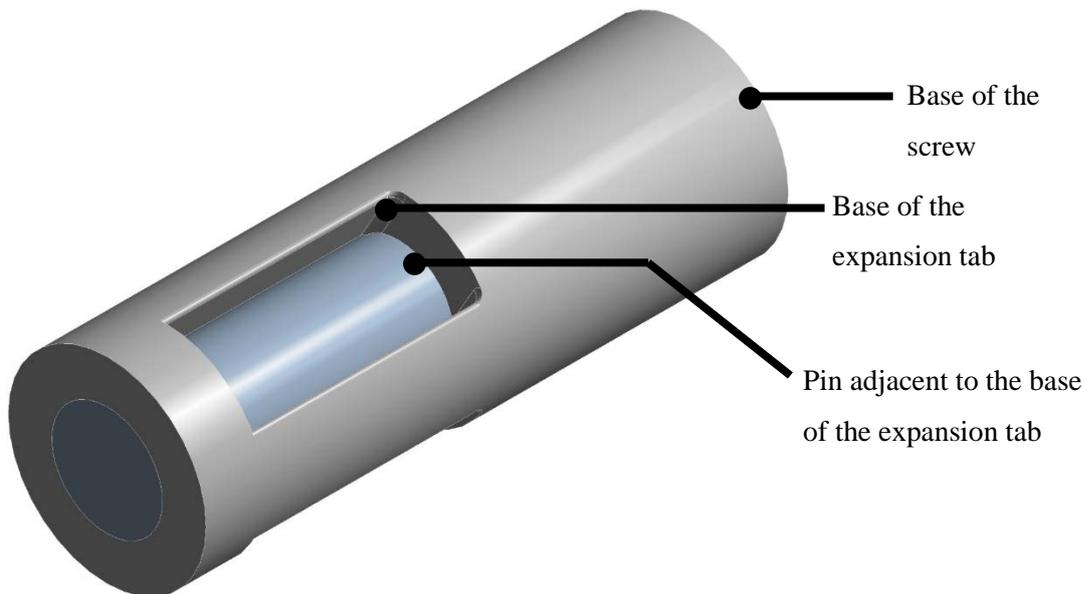


Figure 7-4 The critical points of maximum stress in the EXF Screw FEM

7.1.1 Model sensitivity

Due to the discontinuous connection at the base of the expansion tab, a stress singularity was encountered. A fillet was created at this location as well as along the edge of the static arm to modify the stress singularity into a stress raiser (Figure 7-5).

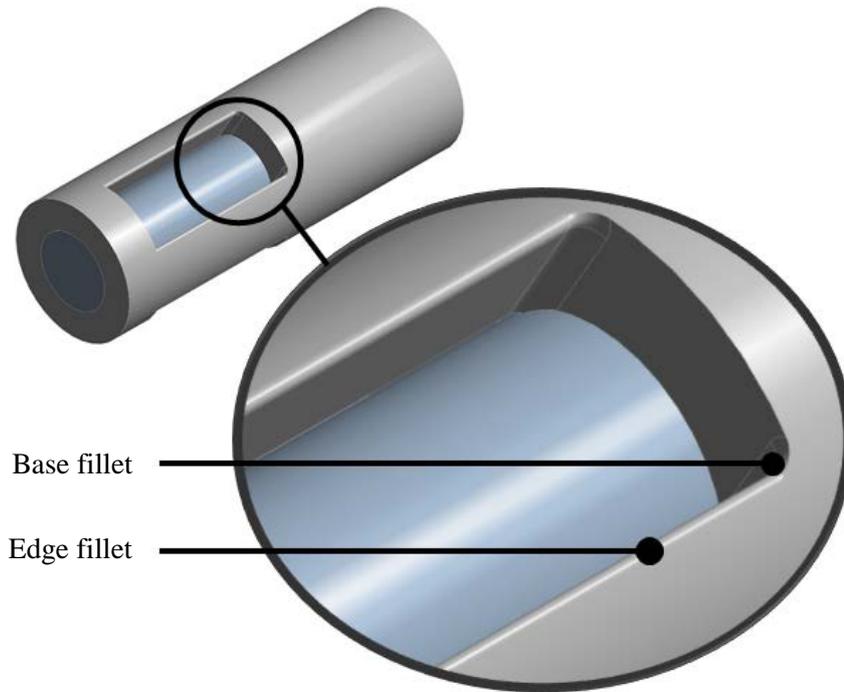


Figure 7-5 Fillets were added at the base of the expansion tab and along the edge of the static section

Mesh sensitivity analysis was performed for various ‘edge’ and ‘base’ fillet radii to determine the critical mesh size on the fillet face for convergence of the stress at this location, as shown in Figure 7-6. For a base fillet radius of 0.1 mm and above less than 1% deviation was observed from the highest resolution stress result at mesh size 0.03 mm and below whereas for a base radius of 0.05 mm the critical mesh size was 0.009 mm. All subsequent analysis was performed at a mesh size of 0.01 mm with a base radius of 0.1 mm.

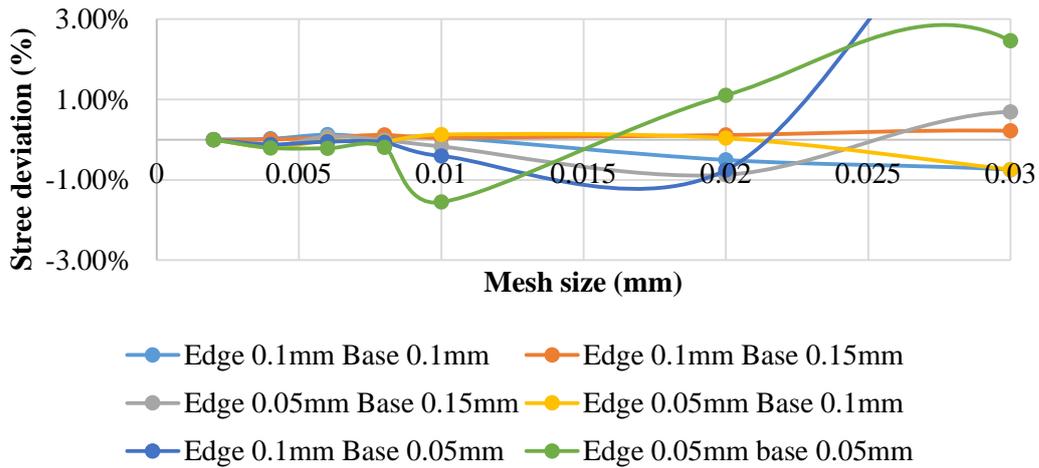


Figure 7-6 The sensitivity of the FEM to mesh size

A stress singularity was also encountered at the base of the screw if a fixed boundary condition was applied (Figure 7-7). To address this, the head of the screw was modelled with a fillet at the junction between the screw and the screw thread and the fixed boundary condition attached to the head of the screw. A point of maximum stress was located on the fillet and also at the end of the fixed boundary condition face (which was ignored, due to St Venant’s principle). St Venant’s principle states that ‘the difference between the effects of two different but statistically equivalent loads becomes very small at sufficiently large distances from the load’ (Richards, 2000).

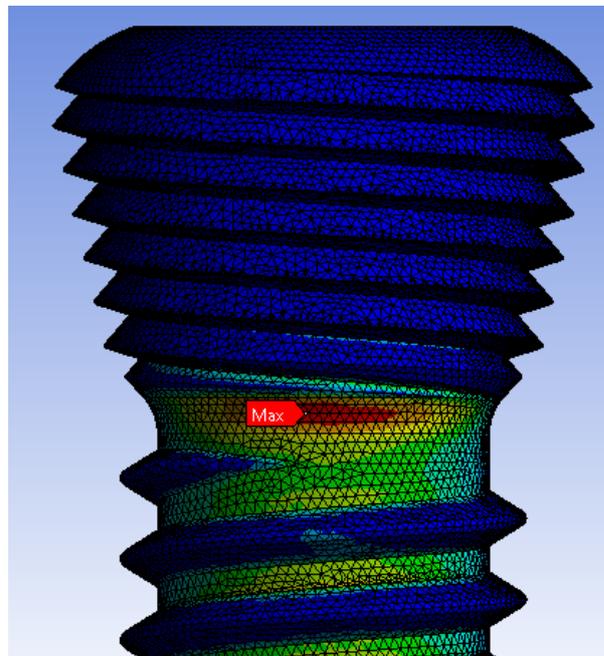


Figure 7-7 A filleted connection to a locking head that was restrained at the base was modelled to accurately predict fatigue and avoid a stress singularity

Mesh sensitivity analysis was performed on the screw model to determine the critical mesh size on the fillet face for convergence. For a fillet of 1 mm and above, less than a 1% deviation was observed from the highest resolution stress result at mesh size 0.2 mm and below. All subsequent analysis was performed at the mesh size of 0.1 mm. The effect of fillet radius was also examined and reported in Figure 7-8. Based on the design of the Depuy Synthes Philos locking screw for proximal humerus fracture fixation and the observation that increasing radius beyond 3 mm would not significantly reduce the maximum stress, all subsequent analysis was done at a screw base fillet radius of 3 mm.

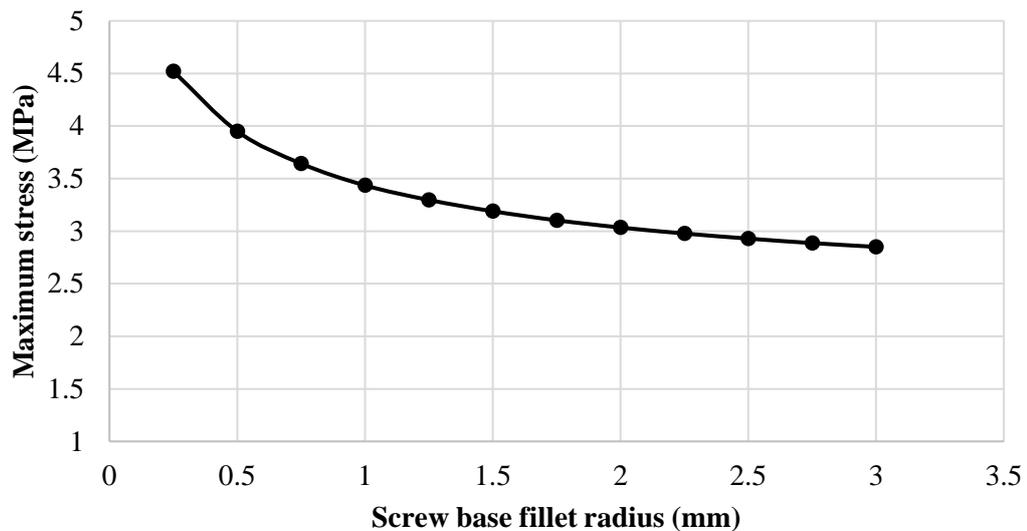


Figure 7-8 The effect of fillet size on the stress in the control screw model

7.1.2 Loading conditions

For all designs end point loads were modelled in all directions to determine the critical loading direction, which generated the highest stress (Figure 7-9). The critical loading direction for all designs was found to be when the load was applied to the centre of an expansion tab (0° in Figure 7-9). Consequently this loading direction was used for all subsequent analysis.

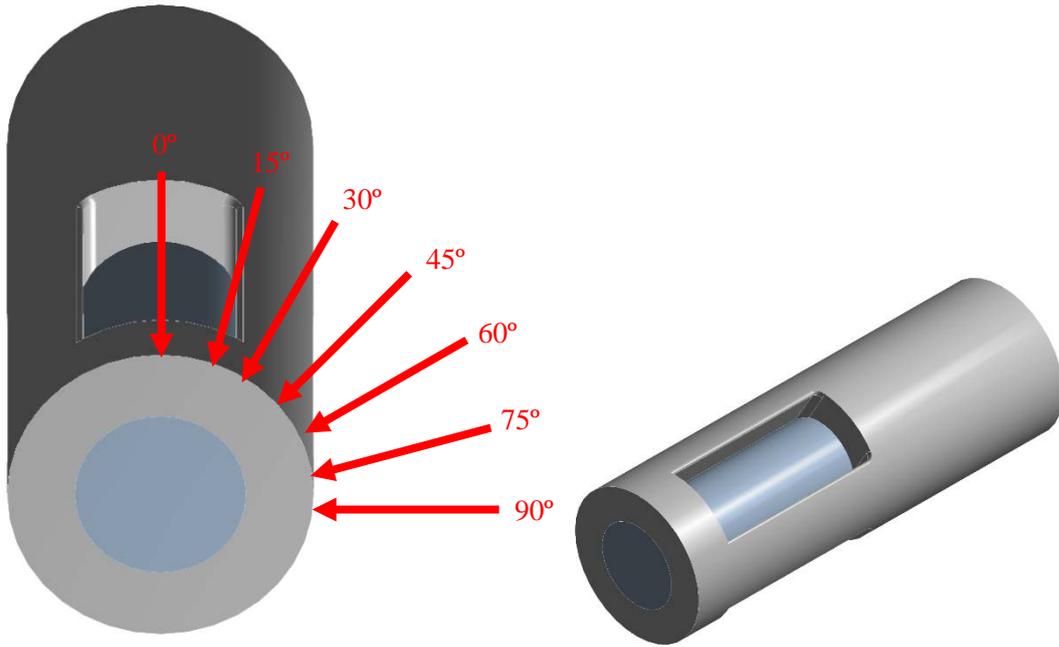


Figure 7-9 The effect of loading direction was examined for both two tab and three tab designs

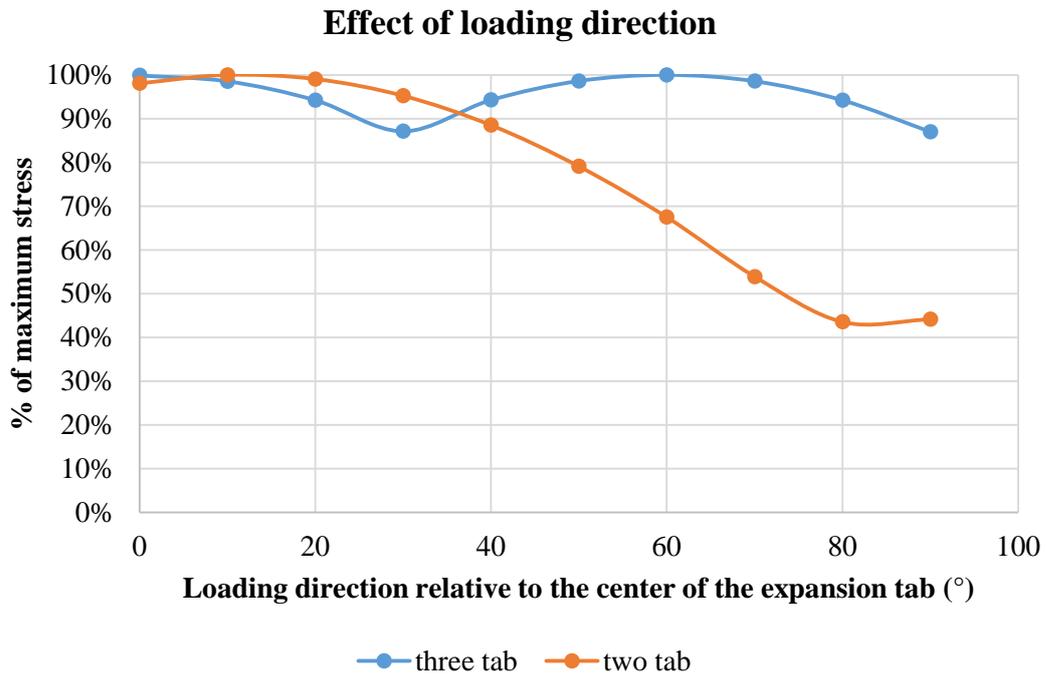


Figure 7-10 The effect of the loading direction on the maximum stress in the model

The two tab designs demonstrated a pronounced difference between two orthogonal loading directions whereas the three tab design only demonstrated a relatively minor reduction in stress which alternated every 60° due to the 120 degree radial offset between expansion tabs and static arms. For all designs, the critical loading direction was directly onto the centre of the expansion tab. These loading conditions can be approximated by three discrete loading locations in the FEM including:

1. Load onto the tip of the screw;
2. Load onto the expansion tab, which is transferred directly to the pin at the point of interference; and
3. Load directly onto the static columns.

The FEM assumed an equally distributed pressure across these locations, creating the forces that were proportional to the area that was loaded. The effect of the length over which the load was distributed was investigated for the three different designs with equivalent total tab width (4.2 mm total tab width).

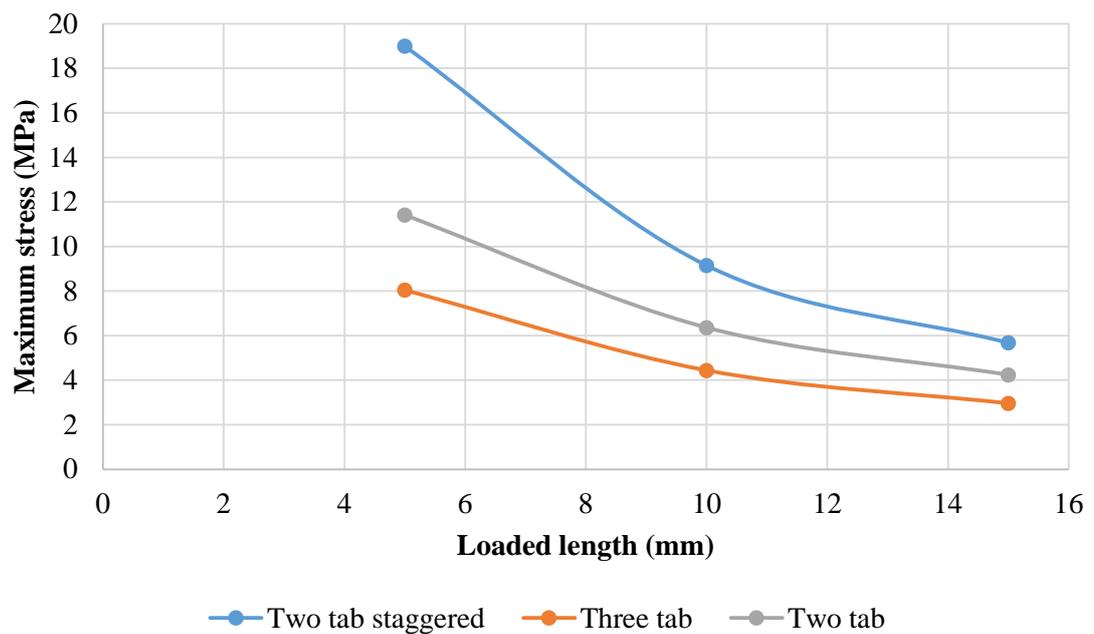


Figure 7-11 Increasing the loaded length significantly reduced the stress at the base of the expansion tabs for all three designs

Distributing the loads over a longer distance significantly decreased the maximum stress in all the EXF Screw designs (see Figure 7-11) by reducing the moment arm on the base of the tabs and by eliminating a portion of the load because it is applied below the base of the tab (for the 10 mm and 15 mm cases). Therefore, as an absolute worst case clinically relevant scenario, the 5 mm long distributed loading conditions were used for all subsequent design tests.

The EXF Screw was compared to four other proximal humerus screws that are identified as suitable predicates and based on the dimensions provided by Zimmer for the NCB locking screw (Figure 7-12):

1. a 4.0 mm non-cannulated screw;
2. a 4.0 mm cannulated screw;
3. a 3.5 mm non-cannulated screw; and
4. a 3.5 mm cannulated screw.

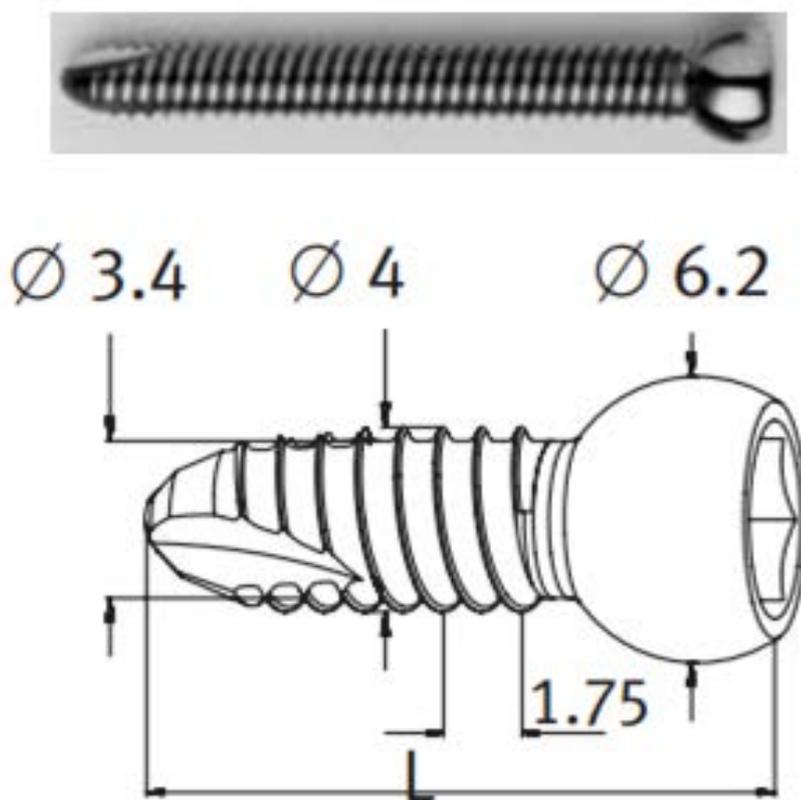


Figure 7-12 The dimensions of the Ø4.0 mm NCB locking screw for proximal humerus fracture fixation which was used as a control (Zimmer GmbH, 2015)

7.1.3 Design optimisation parameters

The design parameters that can be manipulated to minimise breakage stress in the EXF Screw include the following:

- Base fillet radius;
- Number of tabs;
- Tab width;
- Tab height;
- Pin diameter;
- Pin material;
- Multiple levels; and
- Staggered expansions.

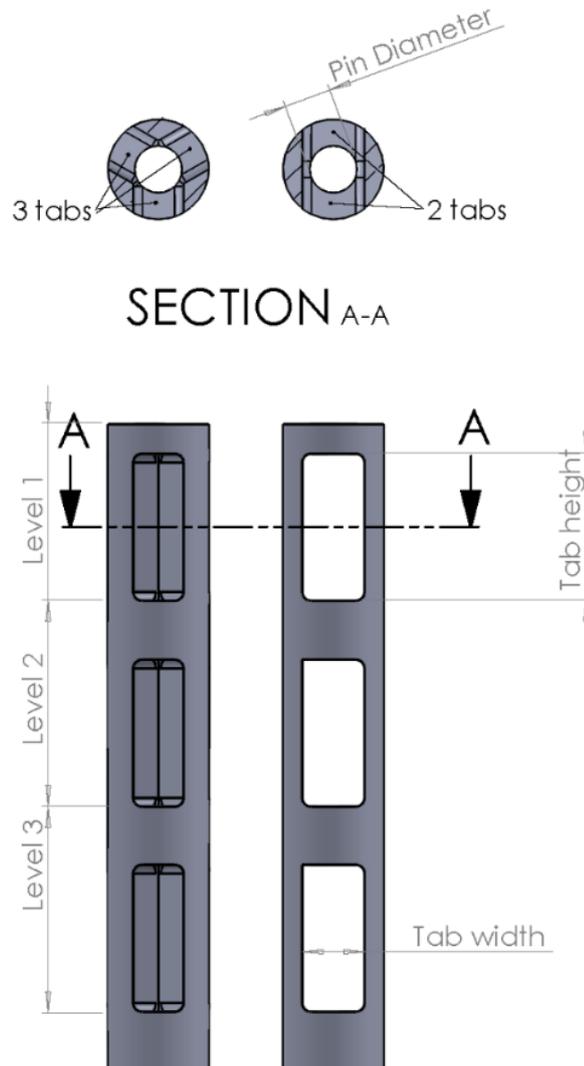


Figure 7-13 An illustration of the design parameters studied in the Finite Element Model

7.2 Results

7.2.1 Effect of fillet radius

The radius of the fillet on the edge of the static arm ('edge fillet' in Figure 7-5) had negligible effect on the maximum stress at the base of the tab. However the base fillet radius had a strong relationship to maximum stress (Figure 7-14). The maximum feasible value for this parameter was approximately 0.15 mm, as dictated by the gap size between the static arm and the bending tab, and this value was used for all the design studies below.

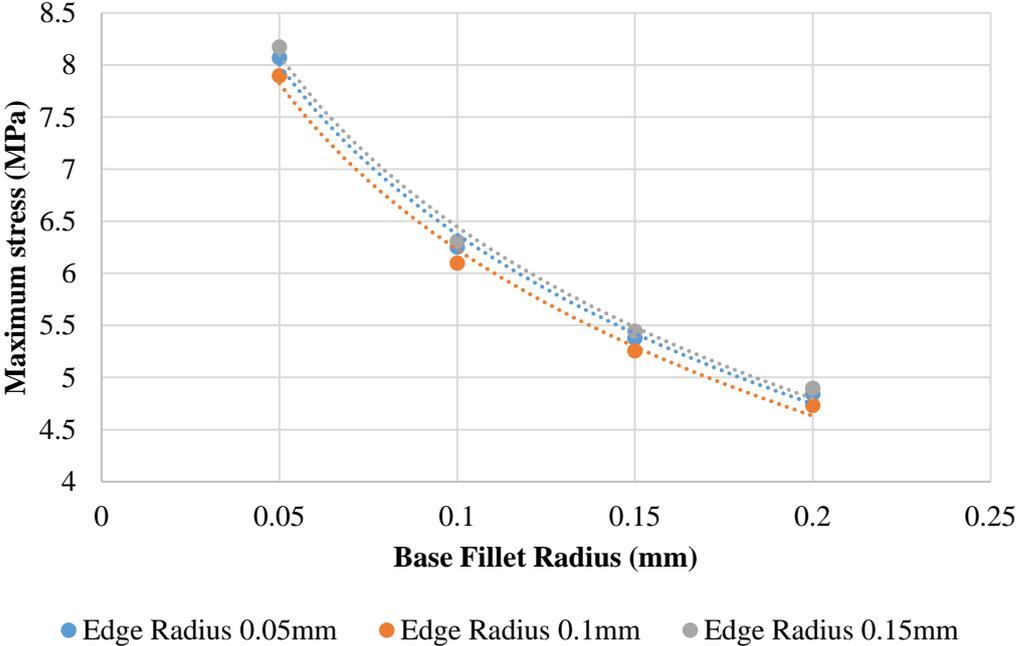


Figure 7-14 The effect of the fillet radius at the base of the expansion tab on maximum stress

7.2.2 Effect of tab width

For all designs there was a positive relationship between tab width and maximum stress with narrower tabs reducing stress because the static columns were thicker. Under equivalent loading conditions and with equivalent design parameters (tab height 5 mm), the two tab (non-staggered) design demonstrated lower maximum stress than the three tab design over all expansion tab widths (Figure 7-15) however the three tab design demonstrated marginally lower maximum stress when considering the total expansion tab width (Figure 7-16). The staggered design had higher maximum stress than the in-line design. For all subsequent studies a total tab width of 4.2 mm was used (two tab: 2.1 mm wide tabs, three tab: 1.4 mm wide tabs) to allow the two tab and three tab designs to be compared directly.

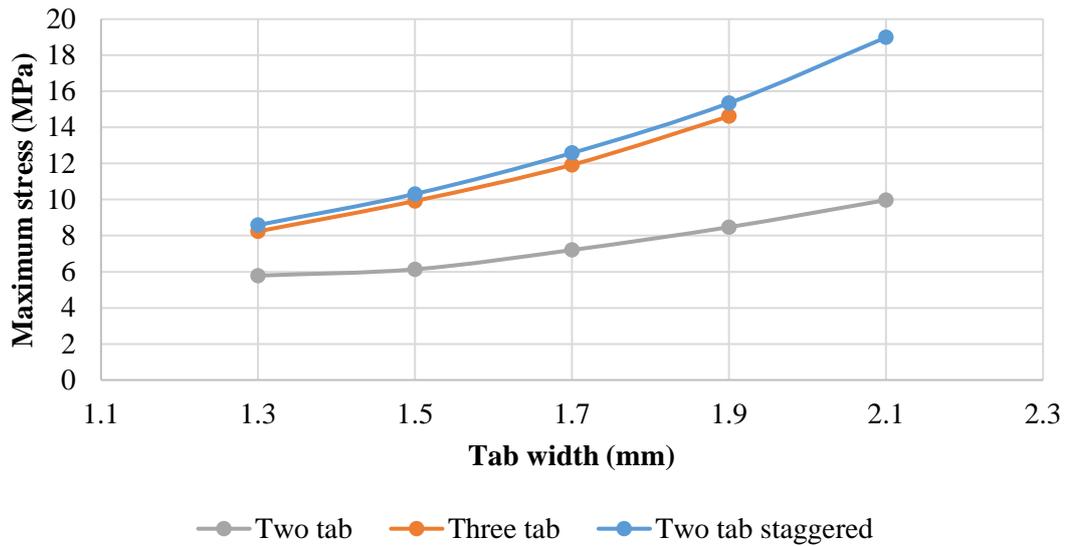


Figure 7-15 The maximum stress in the screw for the two tab, two tab staggered and three tab designs, compared to the expansion tab width

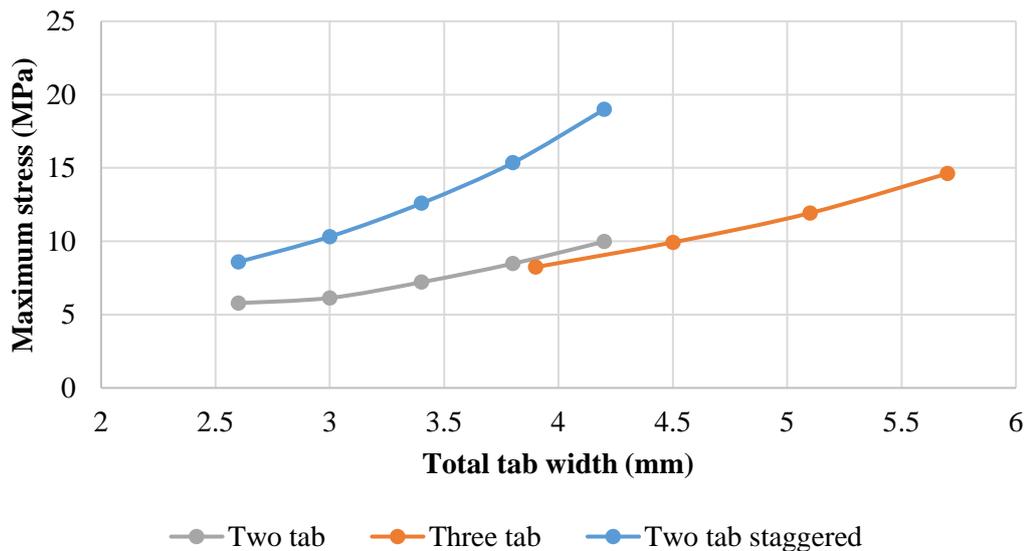


Figure 7-16 The maximum stress in the screw for the two tab, two tab staggered and three tab designs, compared to the total (summated) expanding tab width, correcting for the fact the three tab design has more of it's perimeter expanding

7.2.3 Effect of expansion tab height

For both two tab and three tab designs with 5 mm distributed loading length, there was a positive relationship between expansion tab height and maximum stress (Figure 7-17). The gradient of the line is steeper when the tab height is below 4 mm because the loading length is 5 mm and at 3 mm tab height (including the 1 mm end height) 20% of the load is applied below the tab base and consequently doesn't affect the critical stress.

For the 10 mm loading length, significantly less stress was observed for both designs. This is due to the combined effect of simultaneously eliminating some load (applied below the base of the expansion tab) and decreasing the average distance this load is applied from the tab base and consequently the moment arm.

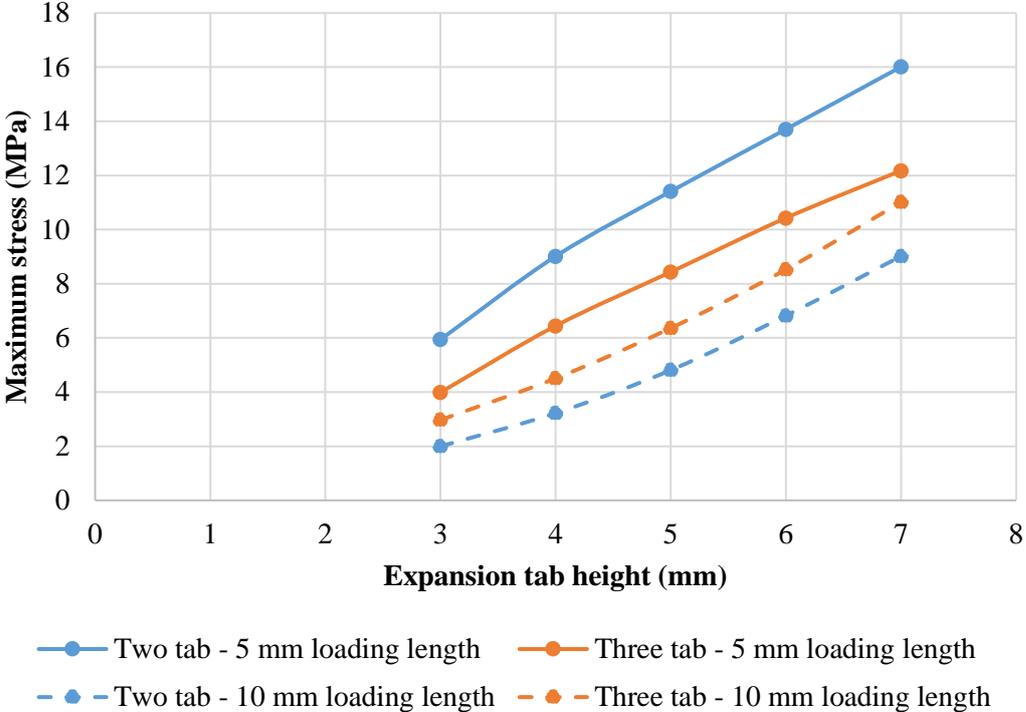


Figure 7-17 The maximum stress in the screw for the two tab, two tab staggered and three tab designs, compared to expansion height for both 5 mm and 10 mm loading length cases

7.2.4 Effect of pin diameter and material properties

The load sharing between the pin and the screw was investigated for three tab designs for different pin diameters and screw outer and pin material combinations including standard medical grade titanium (Ti64), medical grade steel and an experimental Low Beta Modulus Titanium (low-modulus pure-beta titanium alloy Ti2448 (Ti-24Nb-4Zr-8Sn, all in wt%)). Higher young’s modulus variation between the pin and the expanding screw body (stiffer pin, less stiff screw outer) resulted in more favourable load sharing, decreasing the critical stress in the base of the tab at the expense of the stress in the pin. Increased pin diameter reduces the stress in the screw by increasing load sharing, whilst decreasing the stress in the pin due to the increased diameter. However the stress in the screw was always higher than the stress in the pin with the exception the TiLBM screw and steel pin combination with pin diameters less than 1.6 mm.

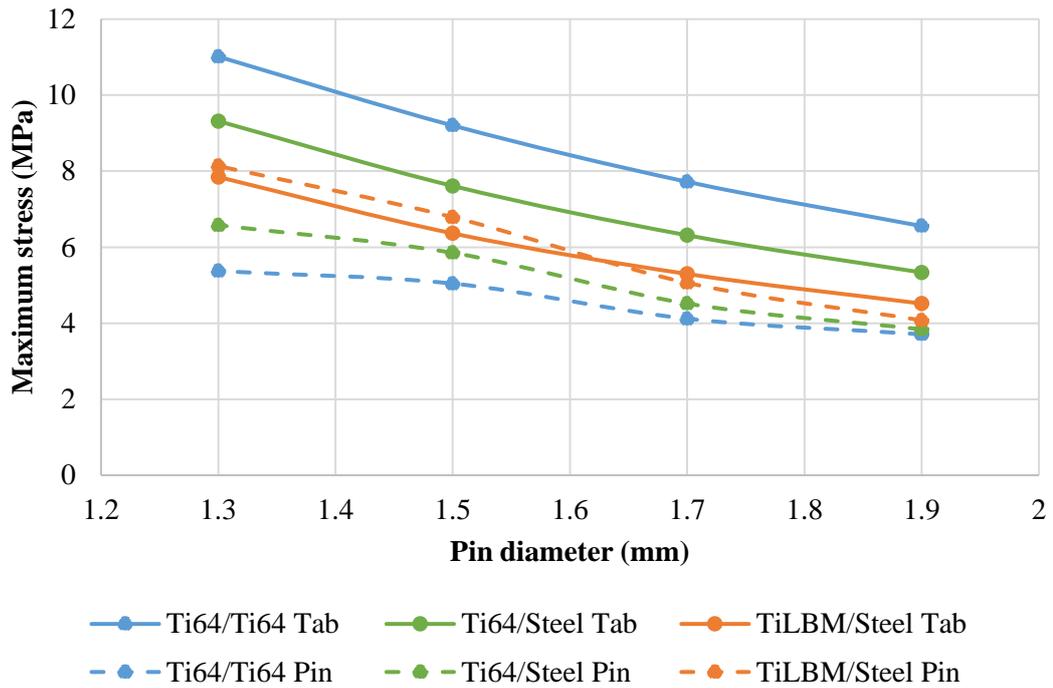


Figure 7-18 The maximum stress in the screw for the two tab, two tab staggered and three tab designs, compared to the pin diameter and the construction of the pin and body of the expandable screw

7.2.5 Effect of multiple expansion levels

For all designs evaluated, having more than one expansion level substantially increases the stress in the fasteners (see Figure 7-19) by a factor of approximately the number of levels (e.g. two levels, about twice the stress). This is because adding an extra level of the same height, doubles the moment arm at the base of the bottom tab (the point of highest stress).

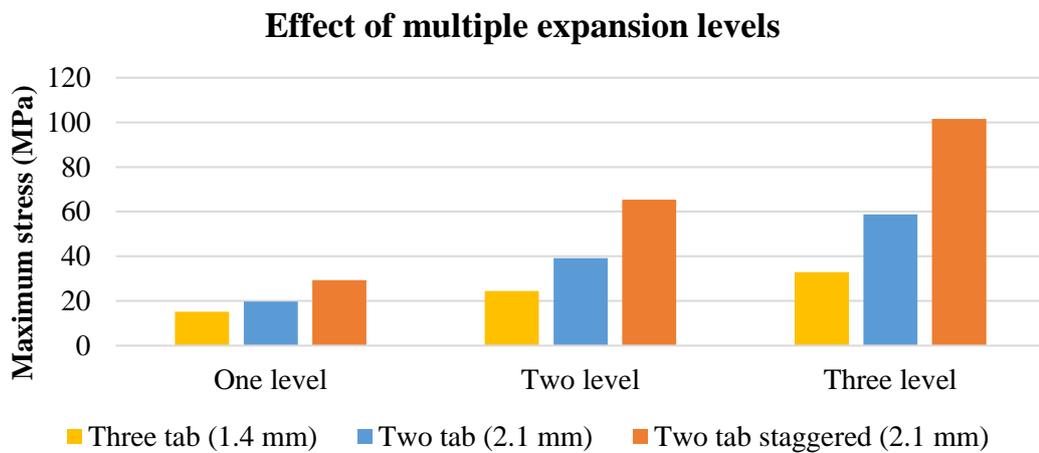


Figure 7-19 For the three tab, two tab and two tab staggered designs adding multiple levels increased the stress significantly

7.2.6 Comparison against predicates

Based on the analysis above the following designs were chosen to be evaluated against the predicates at the worst case loading length (5 mm) and at clinically feasible screw length (50 mm).

Table 9 The design candidates with various design parameters evaluated for maximum stress under a distributed cantilever bending load of 1 N with a 5 mm loading length

#	<u>Tab number</u>	<u>Staggered (Y/N)</u>	<u>Tab width (mm)</u>	<u>Tab Height (mm)</u>	<u>Number of levels</u>	<u>Pin Diameter (mm)</u>	<u>Screw/Pin Material</u>	<u>Max stress (MPa)</u>
1	2	N	2.1	5	1	1.6	Ti64/Ti64	10.9
2	2	Y	2.1	5	1	1.6	Ti64/Ti64	19.0
3	2	Y	2.1	5	1	1.9	TiLBM/Steel	12.9
4	3	N	1.7	5	1	1.6	Ti64/Ti64	10.7
5	3	N	1.4	5	1	1.6	Ti64/Ti64	8.6
6	3	N	1.4	4	2	1.9	TiLBM/Steel	20.3
7	3	N	1.4	4	1	1.9	TiLBM/Steel	5.3

Table 10 The conventional screw predicates evaluated for maximum stress under a distributed cantilever bending loading of 1 N with a 5 mm loading length

<u>Screw name</u>	<u>Max stress (MPa)</u>
4.0 mm non-cannulated locking screw	14.5
4.0 mm cannulated locking screw	15.9
3.5 mm non-cannulated locking screw	22.8
3.5 mm cannulated locking screw	26.7

Under an equivalent load, all the designs have less stress at the base of the expansion tab than a 50 mm long, 4.0 mm diameter screw at the base of the screw at 5 mm loading length with the exceptions of design 2 (non-optimised staggered two tab design) and design 6 (optimised two level, three tab design). However both of these designs had less stress than the 3.5 mm diameter locking screw. The cannulated screws has marginally higher stresses than the non-cannulated screws, indicating that removing material from the centre of the screw only marginally decreases fatigue strength.

7.3 Conclusions

Screw breakage is not a failure mode that has been previously described in the indexed literature for proximal humerus fracture plate screws. In systematic review only plate breakage was described and then only in cases of fracture non-union and resulted in fatigue failure of the plate, rather than the screws (Sproul et al., 2011). Consequently improved screw fatigue strength over and above the predicates is not necessary or advantageous in that indication. It is possible that even a significant reduction in fatigue strength of the screw may be acceptable given that for proximal humerus fracture fixation the screw is not the weakest link in fatigue. However, the minimum acceptable fatigue strength for the screws is difficult to determine without being excessively conservative given the complex load sharing that occurs over five or more different screws with multiple possible fracture types and the unknown intensity and duration of physiological loading.

However the FEA in this thesis has determined that, for the EXF Screw designs examined, the base of the expanding tab is not the point of highest stress under clinically relevant loading conditions, instead it is at the screw head junction as is the case for conventional screws. Therefore these EXF Screw designs may have equivalent fatigue performance to the predicate conventional screws, as long as the EXF Screw is designed to have equivalent fatigue strength as a conventional cannulated screw at the screw head junction.

Note that, as with all FEA, this conclusion is entirely geometric and reflects only that the effect of the increased moment arm at the screw head outweighs the effect of the reduction in material and the stress concentrations, at the base of the expanding section. Future work will be undertaken by another PhD student, Intan Oldakowska, to validate these findings using benchtop testing and ensure that the final chosen EXF Screw design has acceptable fatigue strength compared to a conventional screw. This testing is included within the NHMRC Development Grant (Grant ID: 1121702) scope of works. See Chapter 11 ('Future work') for more details.

However, in other orthopaedic surgeries that use shorter screws, failure at the base of the tab in the expanding section of the EXF Screw may be clinically possible. Methods of decreasing stress at this location, across all the designs investigated, include:

1. Not using multiple expansion levels;
2. Not staggering the expansions;
3. Reducing the height of the tabs;
4. Reducing the tab width;

5. Using a higher diameter expansion pin; and
6. Using a steel expansion pin or a low modulus titanium alloy for the screw body.

Detailed discussion of the effect of the above design parameters on the design criteria and the final design decisions can be found in Chapter 4 ('Design of the EXF Screw').

Chapter 8 Design constraints for selective laser melting manufacture of the EXF Screw

The final design of the EXF Screw has demanding manufacturing requirements. In particular, the rectangular profile of the bending arms which require an internal flat surface that cannot be machined and the requirement for negligible clearance between the expanding arms and the static columns, to prevent bone in-growth. Additionally the small size of proximal humerus fracture fixation screws ($\text{Ø}3.5\text{-}5.5$ mm) significantly increases the difficulty of conventional manufacturing. Consequently it is possible that the current EXF Screw design may only be cost effectively manufactured using an additive manufacturing process, such as Selective Laser Melting (SLM).

Design is often constrained by manufacturing limitations, especially during the prototyping stage when the cost of creating complex parts can be prohibitively high. SLM is an additive manufacturing process (3D printing), whereby a laser scans across a bed of metal powder melting together the particles to form an intricate and nearly fully dense part layer by layer (Figure 8-1).

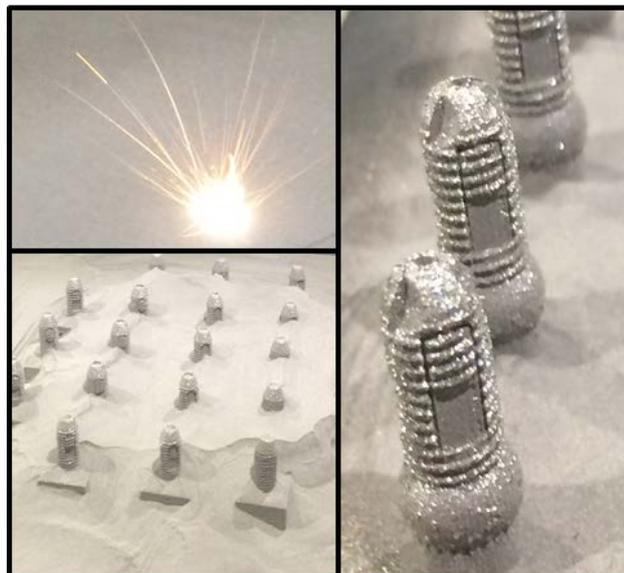


Figure 8-1 Test samples are manufactured by a laser (top left) that scans over a bed of titanium powder (bottom left) to create a high density metallic part, in this case the EXF Screw (right)

SLM can allow the manufacture of parts that cannot be manufactured in any other way. However, as an additive process, SLM has unique manufacturing limitations which need to be considered during design, including:

1. High clearances must be observed due to high surface roughness (due to part construction from fused, discrete powder particles and the effect of uneven heat dissipation, see Figure 8-2: Right). Previous studies have recommended clearances between 200-400 μm depending on geometric, orientation and manufacturing variables (Adam & Zimmer, 2014; Thomas, 2009; Yadroitsev, Shishkovsky, Bertrand, & Smurov, 2009);
2. Build angle must be selected to minimise printing with high overhang angle, which can cause erroneous particle attachment (known as z-growth, Figure 8-2: Left) and reduced part fidelity (Yang, Lu, Luo, & Wang, 2012). Previous studies have recommended limits between 27-45° (Thomas, 2009; Wang, Yang, Liu, Xiao, & Sun, 2013; Wang, Yang, Yi, & Su, 2013).
3. Minimal design thicknesses must be observed in each dimension theoretically due to finite laser point size and layer thickness. The laser point size and the layer thickness for the SLM100 Realizer are both reportedly 20 μm (Realizer GmbH, n.d.), however studies have reported a minimum wall thickness of between 120-400 μm (Thomas, 2009; Wang, Yang, Liu, et al., 2013; Yadroitsev et al., 2009).

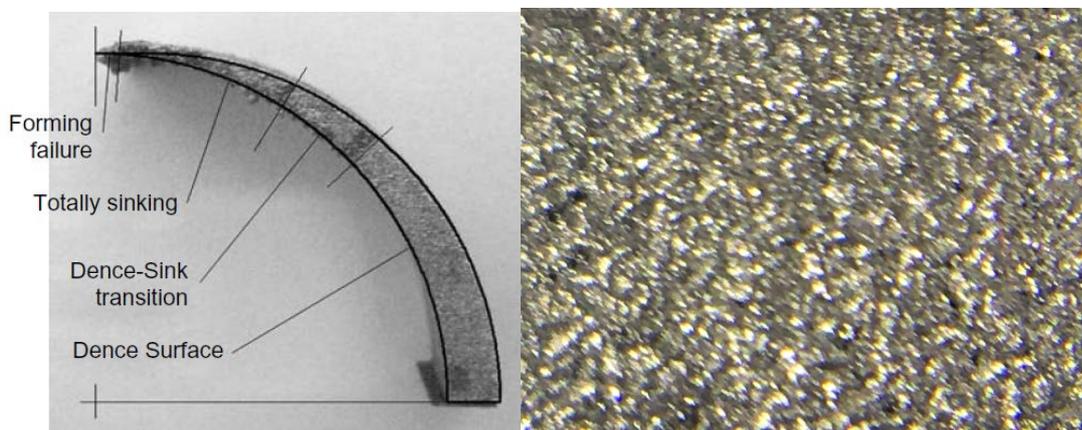


Figure 8-2 A progressively overhanging structure demonstrating that for low overhang angles the absence of z-growth and the progressively increasing z-growth as the overhang angle increases (left(Yang et al., 2012)) A micrograph of the surface roughness of one of the samples manufactured using SLM for this study (right)

In this study, the limitations of the SLM process to manufacture geometries required for the EXF Screw were investigated by creating test samples with reproducible standardised geometry. These standard geometries were slots with varying width and build angles and the clearance required around holes with mating pins that are printed in the build plane. These specific geometries were investigated because they are relevant to the EXF Screw design (Figure 8-3).

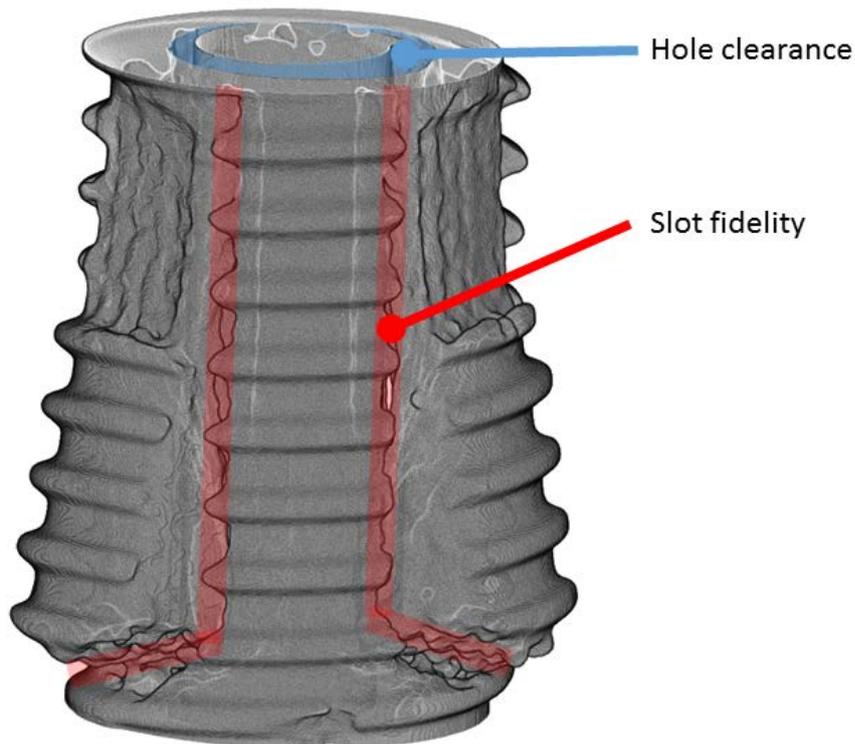


Figure 8-3 The locations on the EXF Screw where slot fidelity and hole clearance are critical

Manufacturing functional slots is essential to realise the design concept of the EXF Screw. These slots must allow the expansion tabs of the EXF Screw to move relative to the static columns of the screw during expansion, but the slots must be thin enough to prevent bone from growing through them into the screw when the arms are expanded. Otherwise the bone inside the EXF Screw may jam it open and prevent the screw from being closed. In the EXF Screw design, the slots vary from vertical orientation along the side of the expansion tab to either horizontal or inclined at the tip of the expansion tab (at the bottom of Figure 8-3).

The tolerances required around holes with mating pins are also important for the EXF Screw because the pin which expands the fastener must maintain a straight trajectory during expansion to prevent uneven expansion. Early prototypes had uneven expansion which were a result of excessive clearance between the pin and the hole (see Figure 4-11). Additionally excessive force required to insert the pin into the hole with insufficient clearance, should also be avoided.

Although many previous studies have investigated the geometric limitations of additive manufacturing and created design rules (Adam & Zimmer, 2014; Kruth, Vandenbroucke, Vaerenbergh, & Mercelis, 2005; Thomas, 2009) there is ‘insufficient availability of comprehensive design rules for additiv manufacturing’ (Gausemeier & Echterhoff, 2011) and the design rules reported in the literature are often technology specific (Adam & Zimmer, 2014). Additionally technology is rapidly improving, which may invalidate early studies as limitations are reduced. Furthermore, to maximise relevance, these studies use basic, generalised geometries and non-performance-specific success criteria. For example, Figure 8-4 illustrates the pass/fail criteria used in one study which determined the minimum manufacturable hole size for ‘acceptable’ fidelity (Govett, Kim, Lundin, & Pinero, 2012). Furthermore previous studies used a range of different manufacturing equipment and process parameters, most of which are unavailable to the author. Consequently samples were manufactured with the Realizer SLM100 at UWA, with the specific geometries required for the EXF Screw design and evaluated against specific performance-based failure criteria for the EXF Screw, to investigate the feasibilities of the EXF Screw designs.

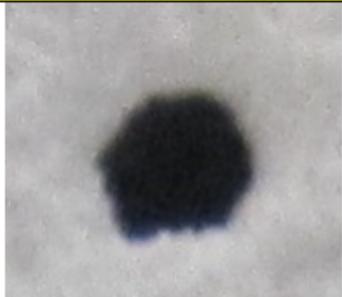
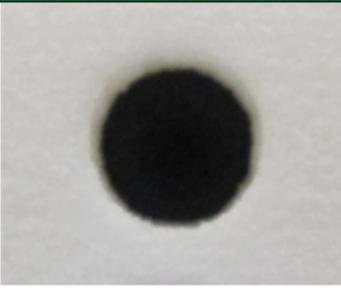
Circular Hole Pass/Fail Criteria		
Fail	Neutral	Pass
		
Hole is completely closed	Hole is formed, but shape is irregular	Hole is formed with no irregularities

Figure 8-4 A typical fidelity based pass/fail criteria for minimum hole size (Govett et al., 2012)

Slot Fidelity

Although previous studies have investigated the slot width fidelity (Adam & Zimmer, 2014; Kruth et al., 2005; Thomas, 2009) these studies have only investigated the vertical orientation (plane of the slot perpendicular to the build plane). However, this is not always the case for designs of the EXF Screw, which require a horizontal or overhung slot at the tip of the expansion tabs (see Figure 8-3). Furthermore, so as to generalise their findings, previous studies typically focussed on strict fidelity or buildability, rather than function. For example, for the EXF Screw the slot must not only be buildable, but must also function as a slot (allows relative movement between two sections without providing an in-growth passage for bone) and the actual fidelity between the as-designed and as-built part is of only secondary importance.

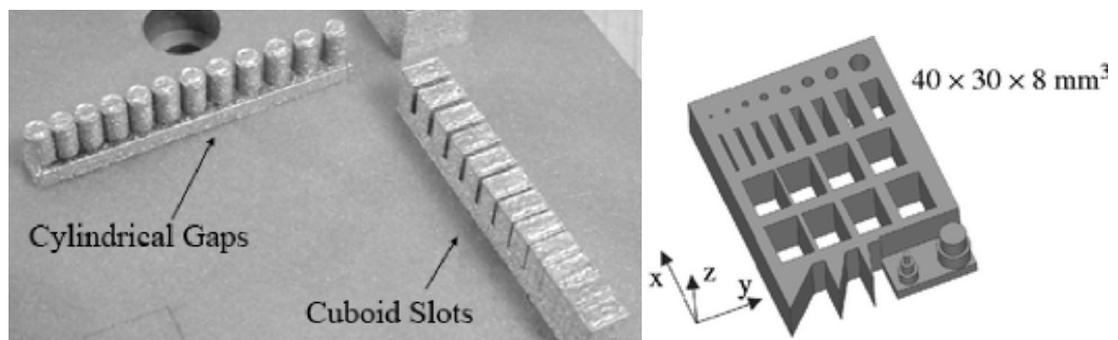


Figure 8-5 Previous studies have investigated the minimum buildable slot width, including Thomas (2009) (left) and Kruth et al. (2005) (right)

Minimising potential bone transmission paths through narrow slots manufactured by SLM has not been previously investigated. Previous work in this field focused on investigating the potential for bone in-growth into a porous surface (Karageorgiou & Kaplan, 2005). Typically studies aimed to determine either the optimal pore size (Chang et al., 2016; Taniguchi et al., 2016) or the minimum required pore size for in-growth (Hulbert et al., 1970; Itälä, Ylänen, Ekholm, Karlsson, & Aro, 2001; Li, Liao, Fartash, Hermansson, & Johnsson, 1997). These studies involve a porous sample, such as a laser perforated plate, a sintered bead mesh or a scaffold manufactured using additive manufacturing. This sample is implanted into an animal model (such as a rabbit, goat or rat) and then bone in-growth is analysed using various imaging techniques. For example one study implanted a laser perforated triangular plate into the distal rabbit femur and used histology to investigate bone after 12 weeks (Itälä et al., 2001).

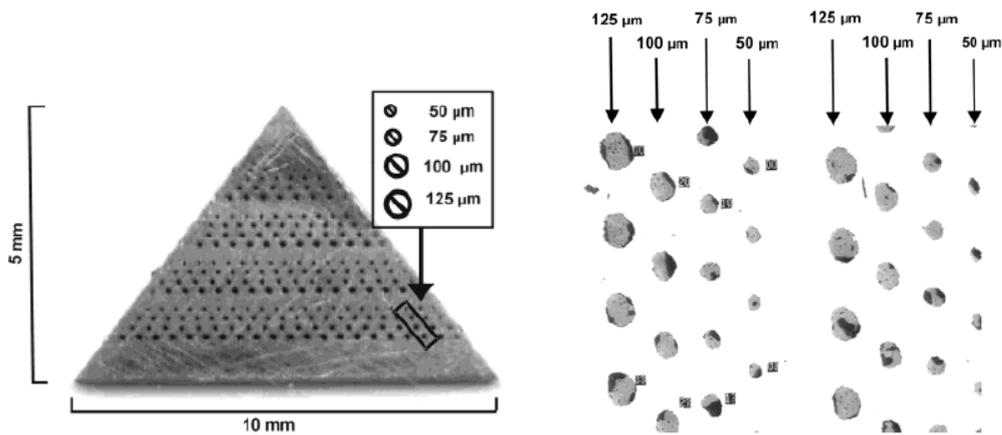


Figure 8-6 A typical sample implanted (Left) and the bone in-growth results (Right) (Itälä et al., 2001)

Although early studies (Hulbert et al., 1970; Li et al., 1997) determined that a pore size of between 100-140 μm was the minimum pore size required for bone in-growth, subsequent studies demonstrated that bone in-growth was possible with smaller pore sizes. Itälä et al. (2001) reported that the smallest pore size tested (50 μm as designed, 67 μm as measured) allowed bone in-growth (Itälä et al., 2001). These conclusions are in accordance with previous studies (Bobyln, Pilliar, Cameron, & Weatherly, 1980; Pilliar, 1987).

However studies have demonstrated that loaded implants, due to the relative motion between the implant and the bone, have a higher minimum pore size for bone in-growth (Harris & Jasty, 1984; Harris, White Jr, McCarthy, Walker, & Weinberg, 1983). These studies reported a minimum pore size of 140 μm for bone in-growth into acetabular cups in an in-vivo canine model (Harris & Jasty, 1984; Harris et al., 1983). Consequently, given that the EXF Screw will be a loaded implant, for this study 140 μm was used as the theoretical critical threshold for bone in-growth.

However pore size also affects in-growth rate (Götz et al., 2004), which may be the reason why earlier studies failed to demonstrate bone in-growth with smaller pore sizes (Hulbert et al., 1970; Li et al., 1997). Furthermore other studies indicate that osseointegration of human cancellous bone may progress even slower than the animal models previously studied (Hofmann, Bloebaum, & Bachus, 1997). Therefore it is possible that mechanical damage to the bone-implant interface during relative movement between the implant and the bone prevents bone in-growth with sub-140 μm pore sizes in loaded implants.

Previous studies have also demonstrated that pore throat size (defined as the diameter of the largest sphere capable of reaching the pore from the outer surface) was a significant factor in determining the amount of bone in-growth, determining that pores with narrow throats are disadvantageous for bone formation (Otsuki et al., 2006; Taniguchi et al., 2016). This may indicate that for transmission of bone through a sample the pore throat size may be a more suitable parameter than maximum or average pore size and so this parameter was also reported in this study.

Pin Hole Clearance

Previous studies have investigated hole size to determine the smallest hole manufacturable in the build plane (Kruth et al., 2005), the largest hole that can be manufactured perpendicular to the build plane (Govett et al., 2012; Thomas, 2009; Vandenbroucke & Kruth, 2007), the size of the hole required to allow post-machining to create a full sized hole (Thomas, 2009) and the clearance required for a pin-hole couple to be printed (Govett et al., 2012). However in this study the clearance required to insert a pin into a hole without post-processing of the hole was investigated. This was because there are sections of the EXF Screw design that cannot be post-processed because of internal features behind other features.

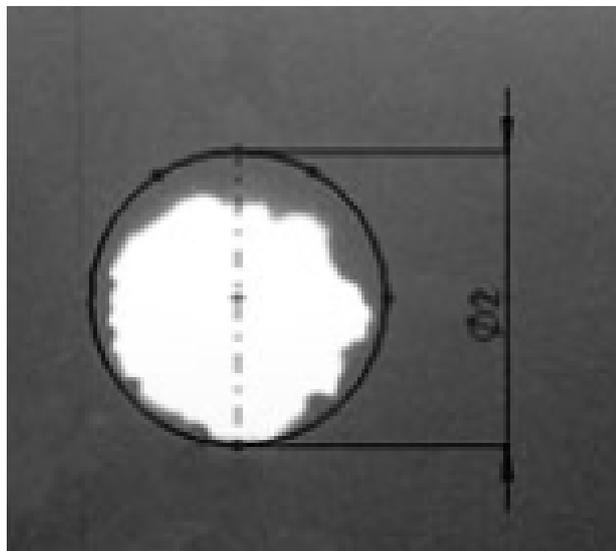


Figure 8-7 A hole manufactured perpendicular to the plane of build typically has significant infidelity, particularly on the top of hole where there is maximum overhang angle (Thomas, 2009)

Design Thickness

Minimum design thicknesses for SLM manufactured parts has been reported previously in the literature (Adam & Zimmer, 2014; Vandenbroucke & Kruth, 2007). Additionally requirements for the EXF Screw (minimum thickness of 400 μm in the bending section of the EXF Screw) was achieved without complication when manufacturing early prototypes. Consequently further investigation of this limitation was not performed in this thesis.

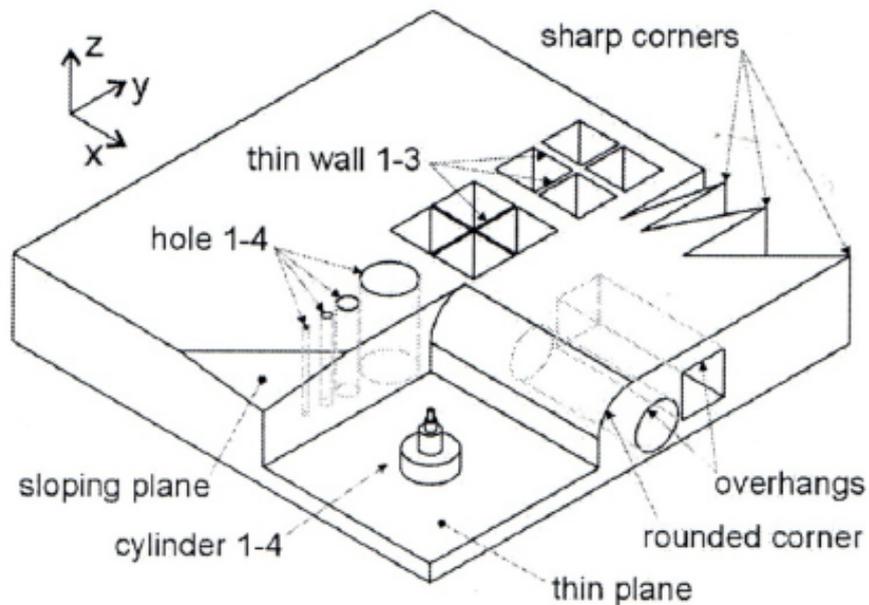


Figure 8-8 A sample designed for investigation of thin planes and thin walls as well as other variables (Vandenbroucke & Kruth, 2007)

8.1 Method

8.1.1 Part manufacture

Prototypes and test parts were manufactured using SLM in collaboration with Associate Professor Sercombe (Oldakowski, Oldakowska, et al., 2016b) at UWA using the Realizer SLM100 machine. Preliminary parts for the cadaveric sheep study were manufactured by Associate Professor Sercombe (Oldakowski, Oldakowska, et al., 2016b) using Ti2448 (Ti-24Nb-4Zr-8Sn, all in wt%), an experimental low modulus beta titanium alloy. Subsequently, all parts analysed in this chapter were manufactured by the author from standard medical grade titanium alloy Ti6Al4V for mechanical testing and fidelity testing.

The process for manufacturing a part using SLM involves the following steps:

1. Geometry is created using Solidworks (software) and exported as a .STL file;
2. STL file is oriented and repaired, support structures are designed and the geometry is sliced to form contours using Magics (software);
3. Printing parameters, including contour and fill laser power, scan speed, scan spacing, beam compensation, layer thickness and contour and vector fill scanning strategy, are defined using REditor (software);
4. Contours are converted to laser paths using Realizer (software);
5. Parts are then oriented within the build platform and manufactured by the SLM under the control of the Realizer Operator (software);
6. When the build is completed, powder is removed and parts are removed from the build plate using a chisel;
7. Parts are sandblasted to detach any loosely connected particles and compressed air is used to blow out any remaining powder or sandblasting grit.

If a part is overhung by more than 45°, supports can be created to prevent curling or drooping and reduce infidelity (Thomas, 2009), as shown in Figure 8-9. Support structures are built from a thin cross hatch and are designed to be detachable.



Figure 8-9 A screw printed at a 45° angle with supports to minimise z-growth and curling

The parts were produced using a standard contour and vector fill scanning strategy, with the direction of the fill vectors rotated 90° between layers. The laser power was 120 W for the contour and 175 W for the fill, while the scan speed, scan spacing, beam compensation and layer thickness were 1000 mm s⁻¹, 100 µm, 60 µm and 50 µm, respectively. The particle size of the powder was 45–106 µm.

8.1.2 CT scanning and image analysis

In order to analyse the SLM samples, they were scanned using the Skyscan 1176 micro-CT scanner at the CMCA at UWA with 18 µm resolution using a rotation step of 0.5°, a source voltage of 80 kV and an exposure time of 285 ms. The raw radial scans were reconstructed using the Nrecon software with a modified Feldkamp cone-beam algorithm using a 30% beam hardening correction coefficient and an 8-ring artefact correction coefficient.

The image stack was filtered with a median filter with a 3x3x3 kernel size to eliminate noise and thresholded using IsoData method (Ridler & Calvard, 1978). The image stack was aligned, using the interactive stack rotation plugin, so that the plane of the image was parallel with the build plane (Figure 8-10).

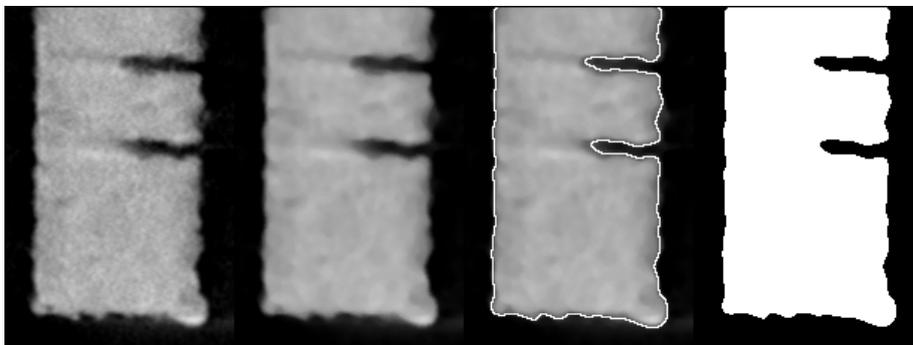


Figure 8-10 Image analysis steps for a single slice of a slot sample with the raw reconstructed image (far left), the filtered image (middle left) and the thresholded image (far right)

8.1.3 Slot fidelity

Slot fidelity was investigated for slots of different width and build orientation (see Figure 8-11). The slots were rotated so that they were aligned horizontally and a volume of interest was created around the slot that excluded the top 0.25 mm, the bottom 0.25 mm and 1.0 mm from either side to eliminate possible influence of the ends and sides of the slot, simulating a continuous slot. Two possible problems were investigated: erroneous connectivity across the slot fusing the slot; and allowable in-growth, where there was sufficient space for the bone to grow into the slot, which can jam open the expansion tabs.

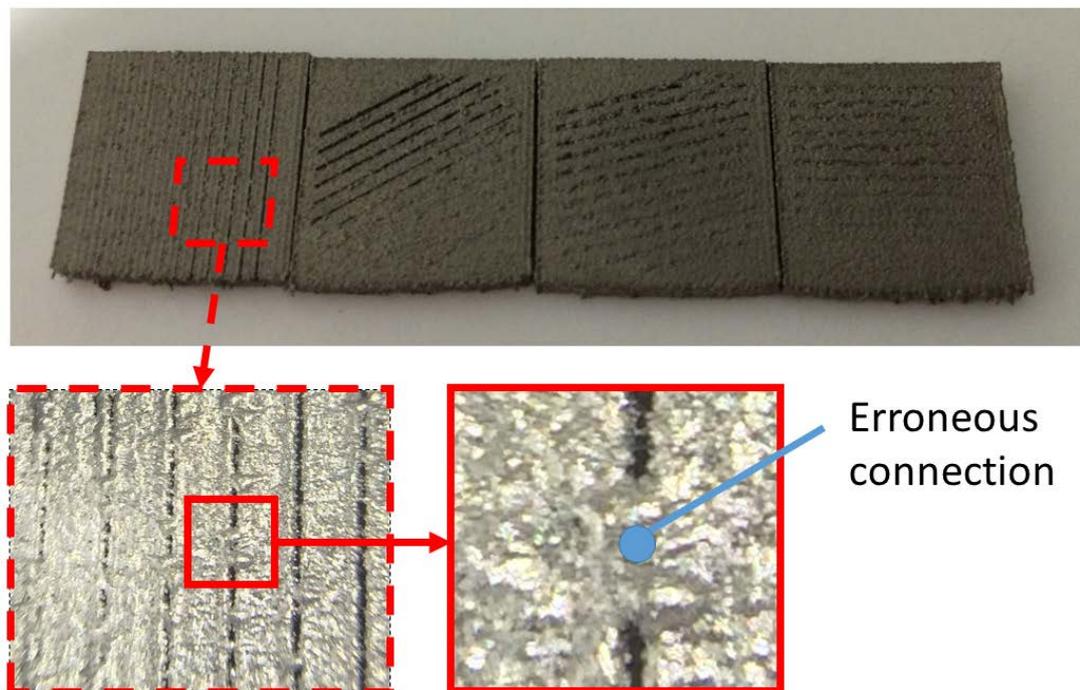
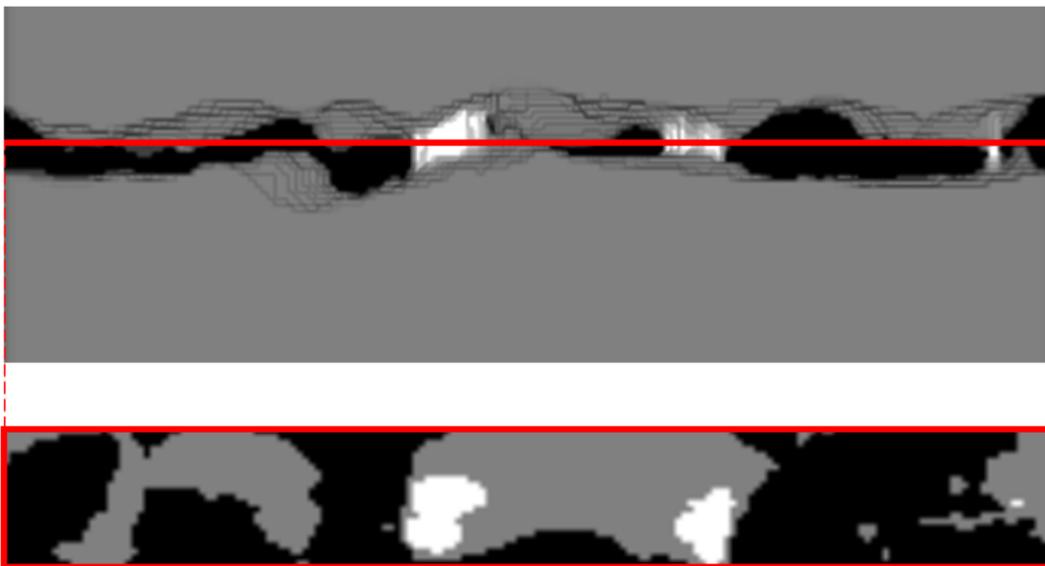


Figure 8-11 The slot samples with build angles 90° or vertical (far left), 30 degree (center left), 15° (center right) and 0° or horizontal (far right). The slots get wider across the sample to the right as seen in the inset

Erroneous Connectivity

Due to uneven heat distribution and finite particle size, sometimes a bridge of material is erroneously created across the slot (Figure 8-11). Erroneous connectivity across the slot was investigated by taking an image stack with slices that were parallel to the plane of the slot and summing together the slices. The resultant image was then thresholded for the maximum value, which identifies any material that is present all the way across the slot (shown in white in Figure 8-12 below). From this image a percentage of erroneous connected area across the slot can be calculated. For example in Figure 8-12 there are three 'bridges' across the slot, two large and one small. Evaluating the percentage cross sectional area through the centre of the slot of the image that is white, demonstrated that 5% of the slot is erroneously connected together.



Cross sectional view through the 'centre' of the gap

Figure 8-12 A bridge of material across the gap erroneously connects the gap together, where the gap is shown in black, the grey is the material and the white is the erroneous connection

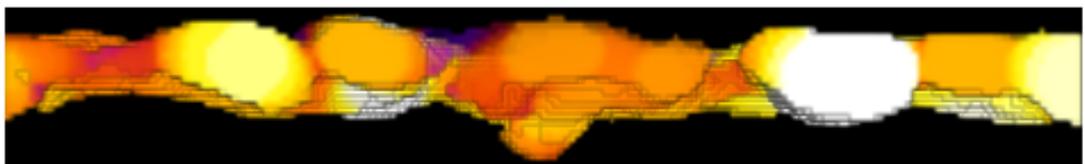
Allowable In-growth

Due to the variation of the slot width, the slot can be wide enough to allow bone to grow into the slot, even if the slot is designed to be thinner than the threshold for bone in-growth. This can be evaluated by inverting the scanned data to create a volume of interest that represents the gap (shown in white in Figure 8-13).

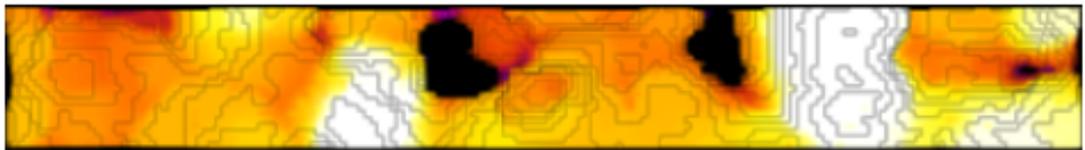


Figure 8-13 Inverting the scanned data isolates the gap (in white) as the VOI

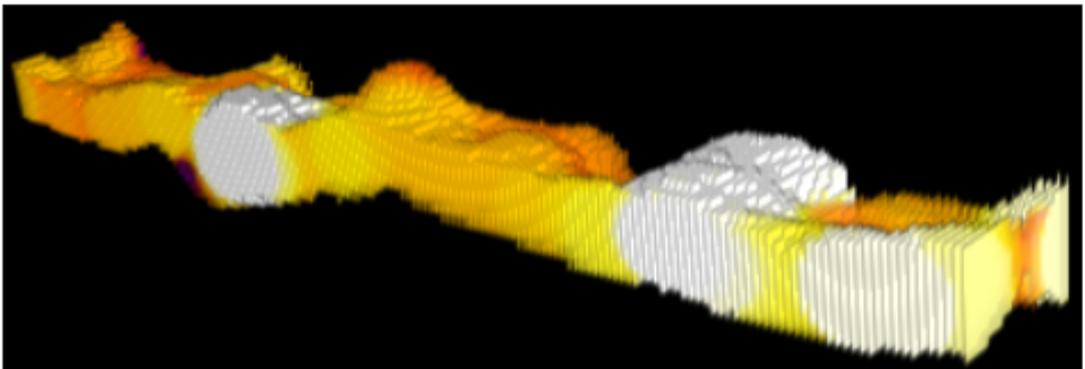
The local thickness at each voxel of the gap volume was evaluated using BoneJ's (Doube et al., 2010) thickness plugin (Dougherty & Kunzelmann, 2007; Hildebrand & Rüeggsegger, 1997) (see Figure 8-14).



Top view



Side view



Isometric view

Figure 8-14 The above gap VOI is processed to display the local thickness in a heat map.

The local thickness data is then thresholded for the critical gap size of 140 μm for bone in-growth into a loaded implant (Harris & Jasty, 1984; Harris et al., 1983). This creates the output shown in Figure 8-15, whereby the thresholded volume represents a viable ingrowth volumes. Functionally, a chain of these viable growth volumes from the top to the bottom of the gap creates a potential path of bone ingress through the slot and is shown in Figure 8-15 using red arrows going through the slot. Finally the percentage of the slot volume that is viable for bone in-growth is reported as a measure of the risk of bone in-growth. Note that the presence of viable bone in-growth volume does not necessarily create an in-growth path, but provides a slot depth independent measure of the risk of bone in-growth.

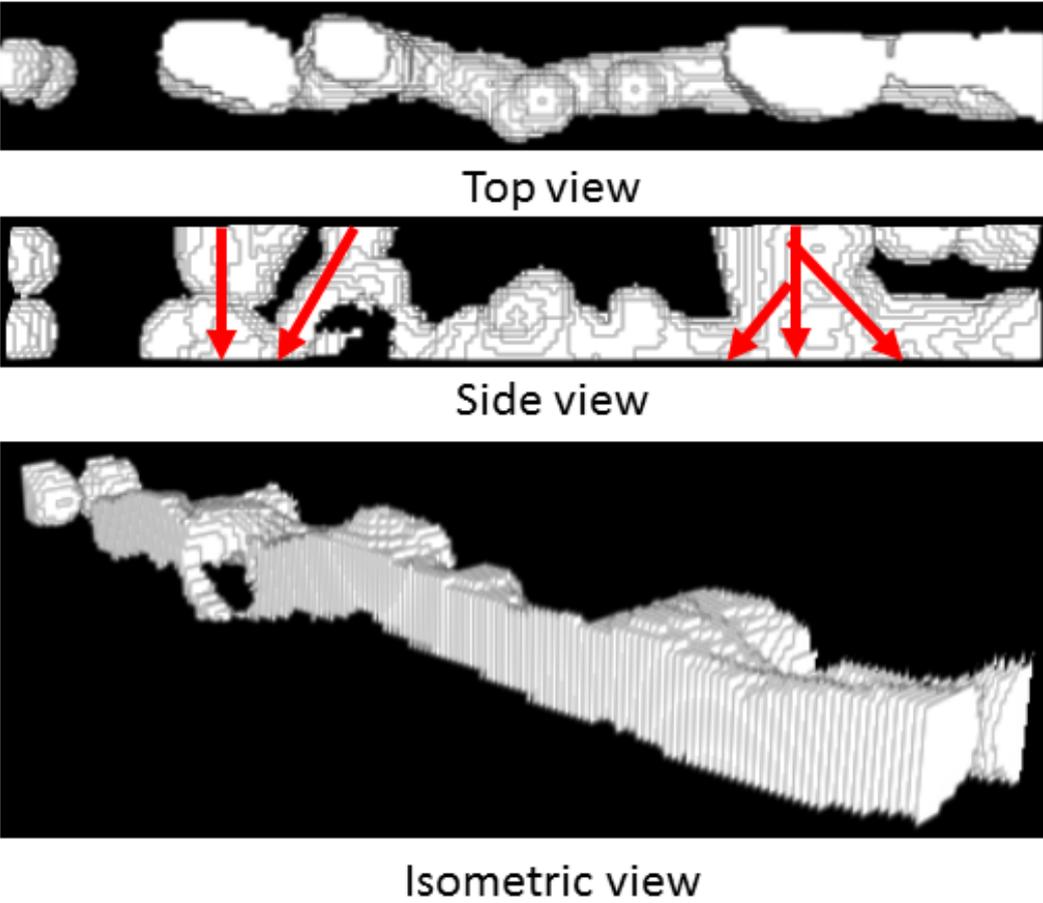


Figure 8-15 The above image is Figure 8-14 thresholded for 140 μm , so that only the viable in-growth points remain. The red arrows represent possible transmission paths of bone across the slot

8.1.4 Hole clearance

Samples with holes ranging from 2.125 mm to 2.3 mm in increments of 0.025 mm were manufactured to determine the design clearance necessary for a hole manufacturing using SLM to accept a 2.1 mm nail (Figure 8-16). The samples were square in cross-section (5 mm by 5 mm) to allow them to be clamped in a vice and 10 mm long. These samples were CT-scanned and the image stacks processed as described in Section 8.1.2 above.

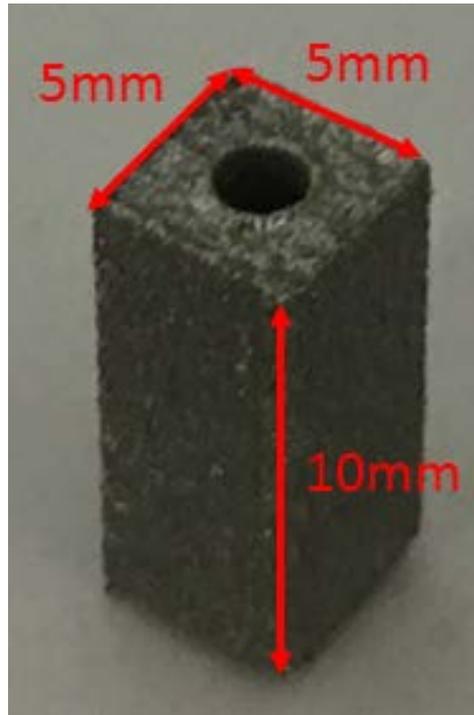


Figure 8-16 The SLM hole sample construction and dimensions

The slices in the image stack were inverted to create a VOI that represented the hole in the sample (Figure 8-17, top left in white). These slices were then summed together and thresholded to the maximum value. This VOI of the maximum value represented a continuous vertical void in the sample (Figure 8-17, top right in red). Visually this can be understood by imagining the sample sitting on a red surface and an observer looking down the hole and seeing only the red surface that is not obscured by any part of the sample.

The thickness of the continuous vertical void was then calculated using BoneJ's (Doube et al., 2010) thickness plugin (Dougherty & Kunzelmann, 2007; Hildebrand & Rüegsegger, 1997) which provides the largest circle that can fit entirely within the 2D area of interest. The maximum value of the thickness map (blue in Figure 8-17: Bottom left) was recorded as the largest pin that could theoretically fit all the way along the hole, without deforming either the hole or the pin (Figure 8-17: Bottom right).

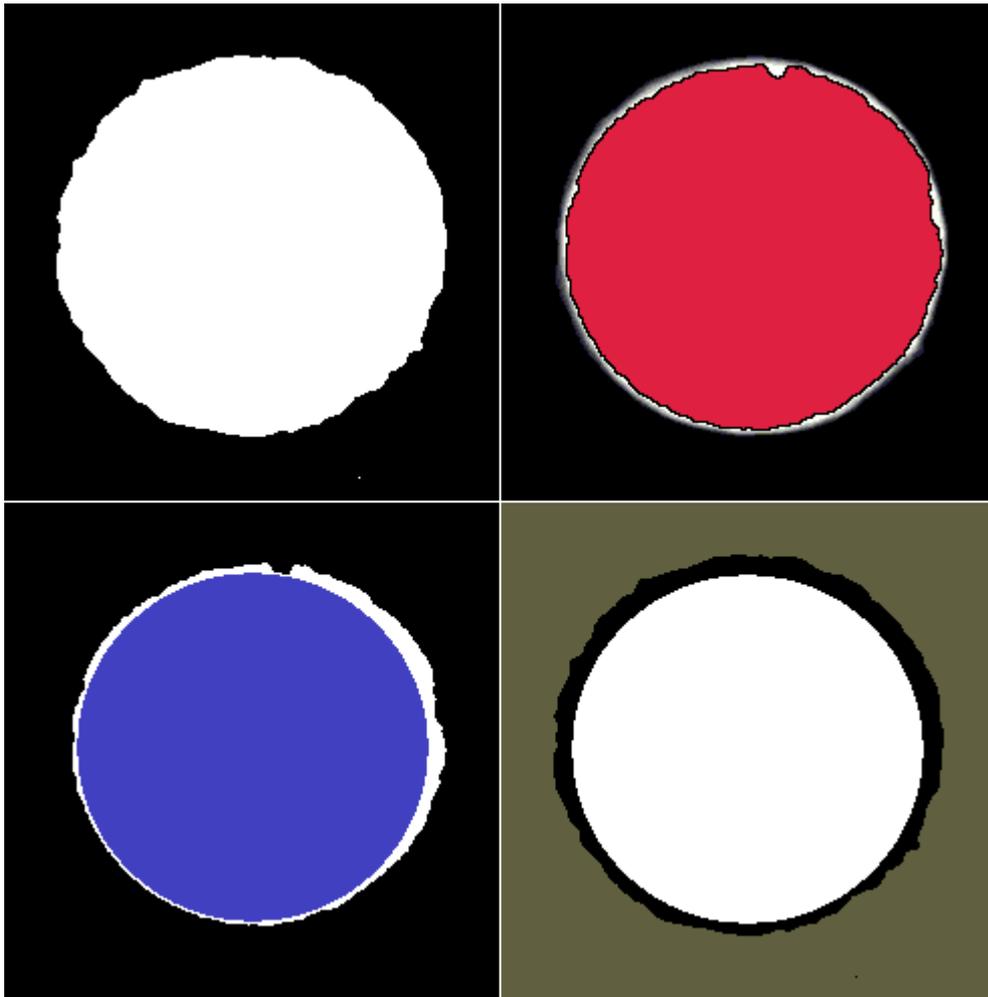


Figure 8-17 Top Left: A single image from the image stack. Top Right: The image stack is summed together and thresholded for the maximum value, resulting in the red shape, which represents the shape of the continuous void through the material. Bottom Left: The blue shape is the largest 2D circle that can fit within the red shape. Bottom Right: This image demonstrates the clearance required for the theoretical pin

After the samples were CT-scanned, 2.1 mm bright steel nails were inserted into the hole samples to determine empirically the smallest hole that could accept the pin and to validate the image analysis (see Figure 8-18).



Figure 8-18 Bright steel nails were inserted into the hole under finger force or impacted with a hammer

8.2 Results and discussion

8.2.1 Slot fidelity

Erroneous Connectivity

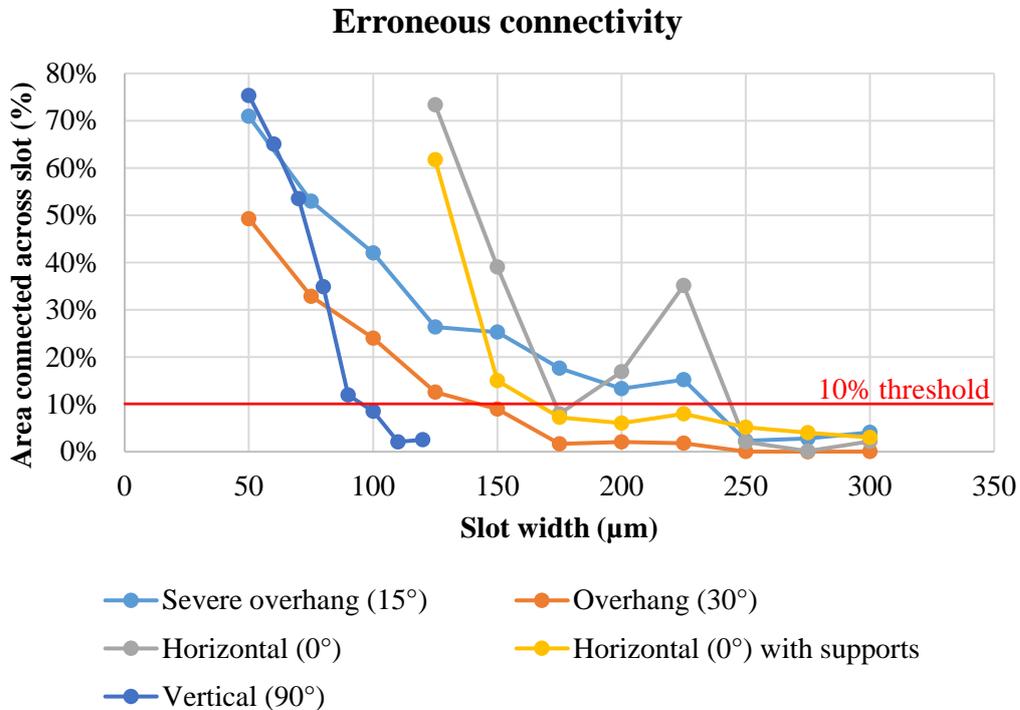


Figure 8-19 A graph of the percentage area connected across the slot for the slots of different width and build orientation

The erroneous connectivity for all samples is shown in Figure 8-19 above. As expected, all the samples typically have more erroneous connectivity with a smaller slot width. All samples have a slot width threshold over which there is negligible connectivity (<10% area connected) ranging from 100 µm for the vertical sample to 250 µm for the severely overhung (15°) sample.

More severe overhang angles have increased erroneous connectivity and a higher slot width threshold. This is due to increased surface roughness at increasingly severe overhang angles (see Figure 8-20) as described previously in the literature (Thomas, 2009).

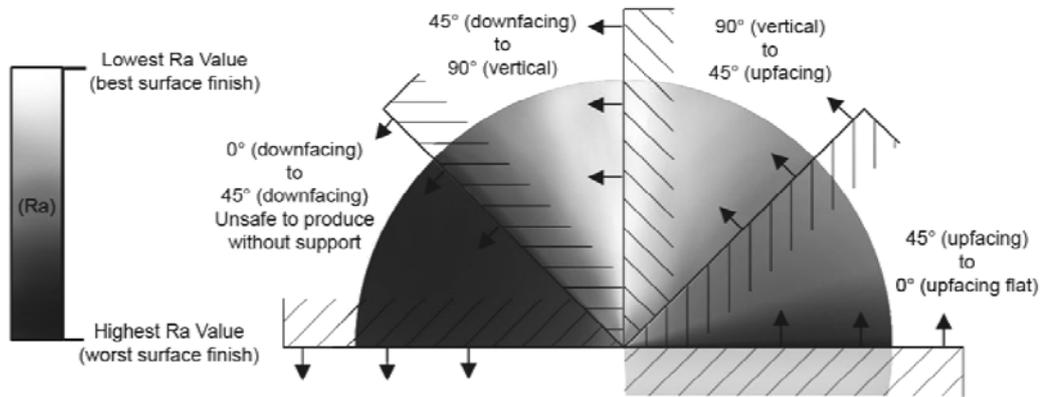


Figure 8-20 A figure demonstrating the effect of build angle on surface roughness (Thomas, 2009)

The exception to this is the unsupported horizontal samples, which have similar erroneous connectivity as the severely overhung samples (15°). This may be because of the additional error generated in creating an angulated slot from layers of a finite thickness (see Figure 8-22). This phenomena has been described previously as the ‘Stair-case effect’ (Vandenbroucke & Kruth, 2007).

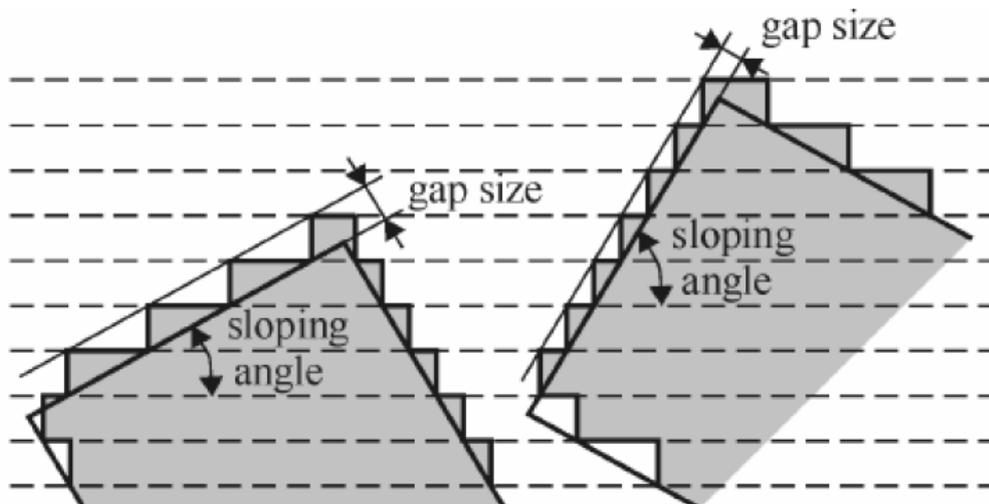


Figure 8-21 An illustration of the 'stair-case effect' whereby building on an angle increases the surface roughness of the part (Thomas, 2009)

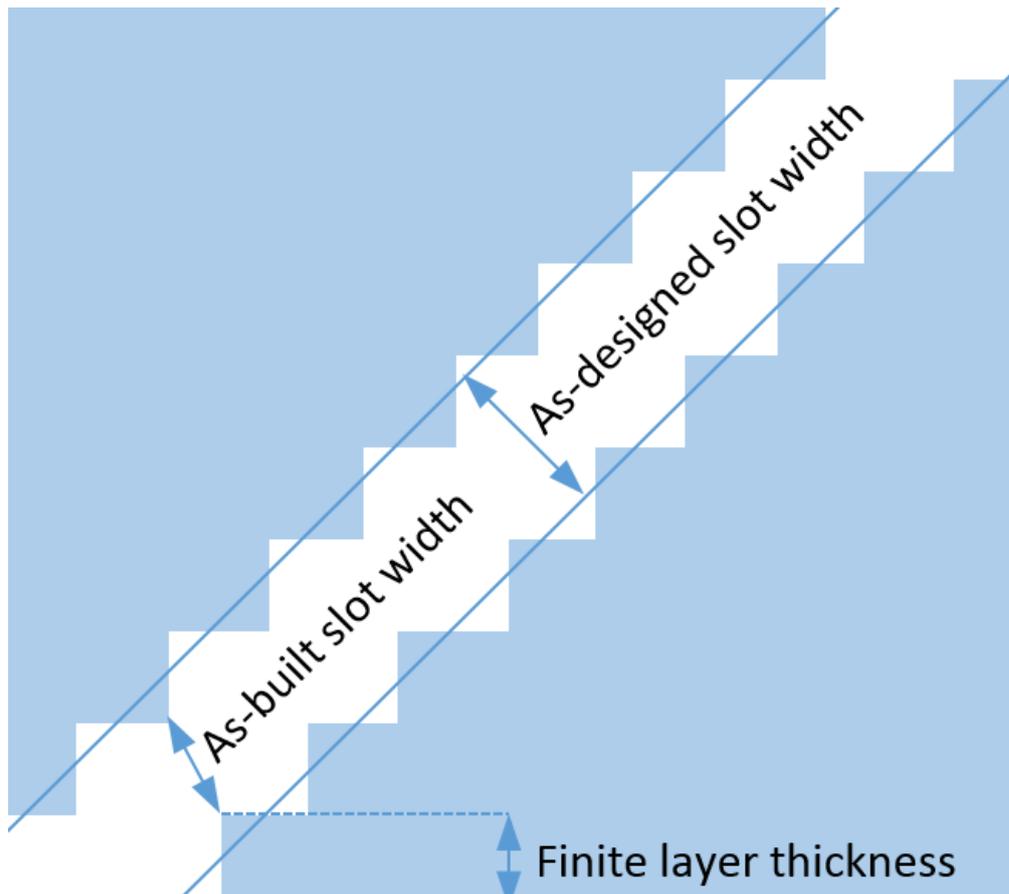


Figure 8-22 The finite layer thickness of a 3D printed part creates a jagged angulated slot due to the stair-case effect, meaning that the ‘as-built’ slot width (closest distance across the jagged slot) is less than the ‘as-designed’ slot width, increasing erroneous connectivity

In general the horizontal slot with built supports had less erroneous connectivity, especially for smaller slot width. However for larger slot widths it had marginally higher minimum connectivity than the unsupported horizontal slots due to the supports, which aim to reduce the amount of z-growth that occurs, at the expense of adding additional erroneous connectivity in the form of the supports themselves. Consequently supports should only be used for horizontal slots where the slot is smaller than the minimum slot width for an unsupported slot (250 μm in this case).

The vertical slot width threshold (100 μm) is similar to the maximum particle size (45-106 μm). As a consequence, the author hypothesises that for the vertical slots, the surface roughness, caused by both the finite size of the powder particles and the uneven heat dissipation across the powder from the laser is responsible for limiting slot width. Consequently decreasing surface roughness (potentially by using smaller particle sizes or further optimisation of the process) may allow a reduction in erroneous connectivity.

Comparing the results from this study to previous studies, Thomas (2009) reported a minimum slot width for a vertical orientation of 300 μm , whereas Adam and Zimmer (2014) recommend a minimum gap size of 200 μm in order to account for ‘small dimensional deviations and to ensure the removal of powder’. Adam and Zimmer (2014) suggesting a higher ‘recommended’ gap size than the minimum gap size observed in this study is not surprising, given that significant ‘dimensional deviations’ were observed in the ‘successful slots’ in this study which was a failure criterion in that study. However minimum gap size reported by Thomas (2009) is significantly higher than the findings reported in this thesis. The author hypothesises that this was due to the way the slot was measured. In the study by Thomas (2009), using a shadowgraph, a continuous void would have to be present through the cross section of the sample to create a ‘gap’ and consequently any deviation of slot path through the sample, even if the slot was still present would register as connected and therefore failed.

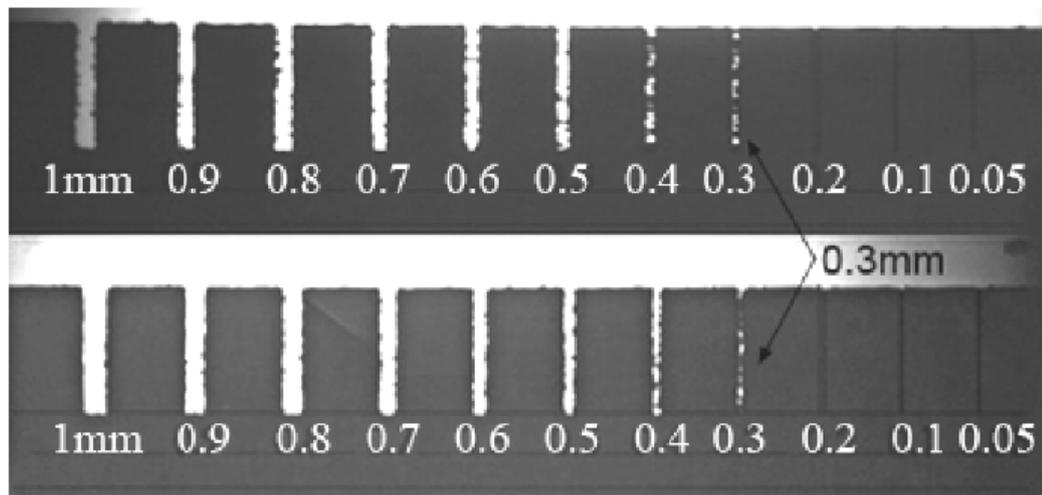


Figure 8-23 A shadowgraph output indicating a 0.3 mm slot width threshold (Thomas, 2009)

Allowable In-growth

The percentage volume of allowable in-growth for all samples is shown in Figure 8-24 below. The graph plots represent the series of samples with slots manufactured at a particular build angle 15° (D15), 30° (D30), vertical (V), horizontal (H), and horizontal with support (HS). All the samples have an increased volume of allowable in-growth for wider slot widths. The only samples to have negligible allowable in-growth (assuming a 140 μm threshold for a loaded implant) are the vertical build samples with as-designed slot widths below 70 μm . This demonstrates that the slots that are built are actually significantly wider than designed.

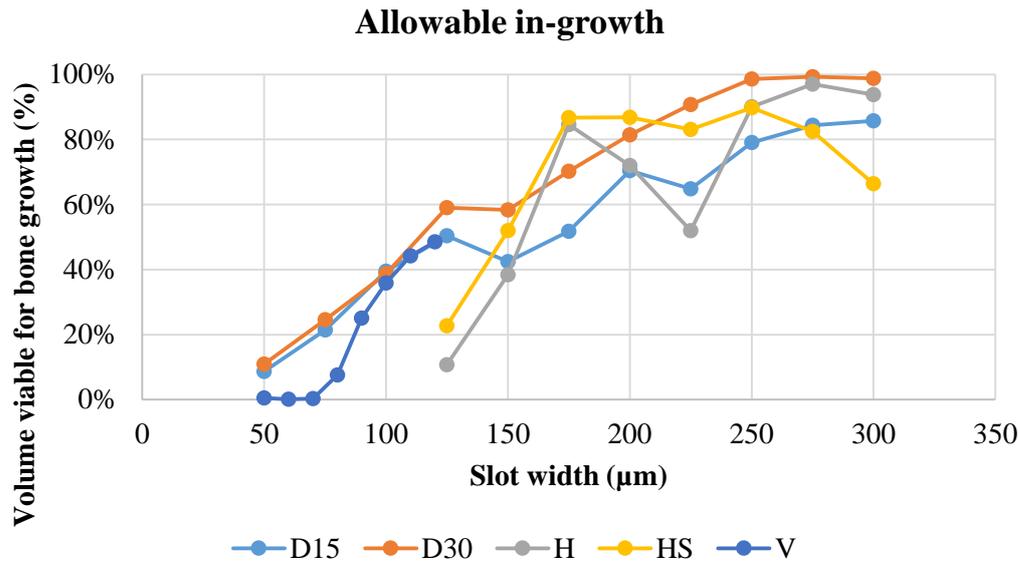


Figure 8-24 A graph of the percentage slot volume that is viable for bone in-growth for the slots of different width for each build orientation

The most viable slot orientation to minimise erroneous connectivity and allowable in-growth is vertical. However, as can be seen in Figure 8-25 below, there is no as-designed slot width where there is both no allowable bone in-growth volume and no erroneous connectivity.

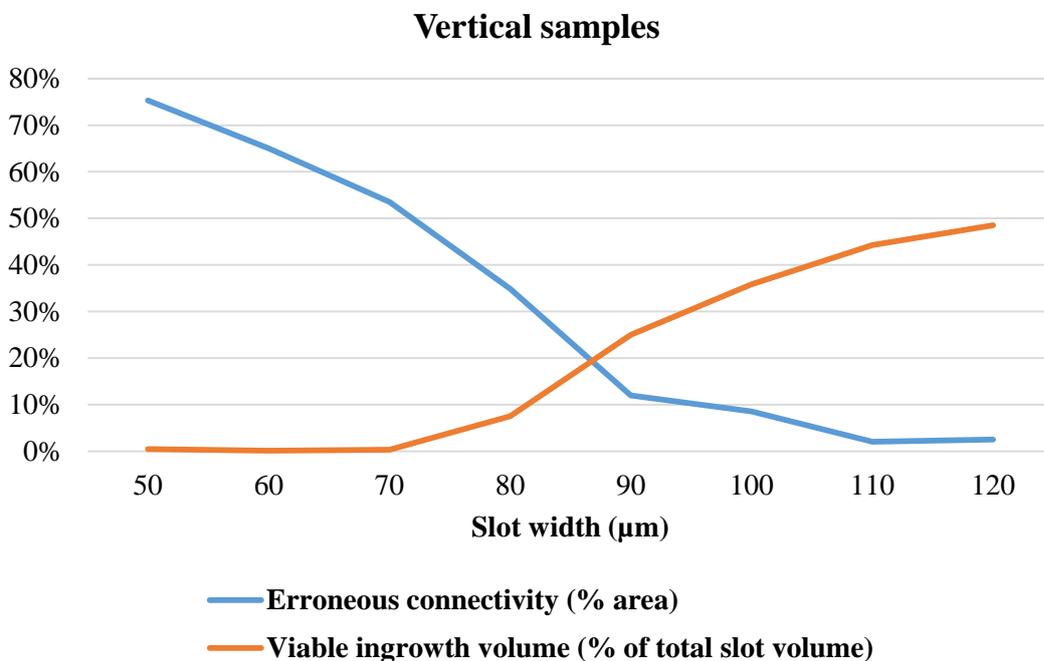


Figure 8-25 Erroneous connectivity and allowable in-growth for the vertical samples at different slot widths

Further analysis of the most favourable slot widths in Figure 8-26 indicates that although the 80 μm sample has 8% viable in-growth volume there is not a continuous in-growth path across the slot. Furthermore the 90 μm sample has 25% viable in-growth volume but only a single in-growth passage. This in-growth passage, at its narrowest (pore throat size) represents 0.8% of the area of the slot. Lastly although the 100 μm sample has many viable bone in-growth passages, summing the narrowest parts of the viable bone in-growth passages (pore throat sizes) for each, provides a total of only 5.8% of the slot area.

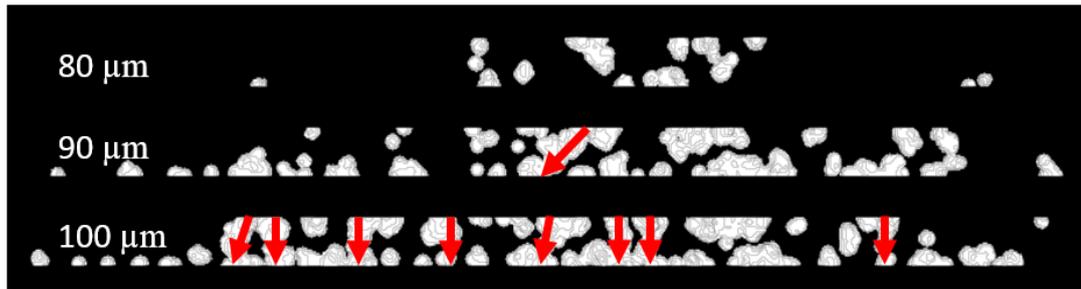


Figure 8-26 The viable bone growth paths (indicated with red arrows) in the vertical samples with slot width 80 μm , 90 μm and 100 μm

Therefore with the SLM technology available to the author, slots either have some erroneous connectivity or the possibility of theoretical allowable bone in-growth. However, future advancements in SLM may allow smaller powder particles to be used or other improvements, which may reduce the surface roughness and as a consequence allow smaller slots to be manufactured.

It is unclear how much erroneous connectivity is acceptable given that if the connection is relatively small, it may be broken during expansion. However excessive connectivity may prevent expansion, increase expansion force excessively or create conditions for a partial expansion where the top of the slot breaks but the bottom doesn't, causing the sample to bend higher up on the bending section than designed, increasing bending strain. Breaking erroneous connectivity during expansion may also increase the risk of osteolysis.

The likelihood of in-growth given its theoretical possibility and its effect on expandable fastener removability after long term implantation is unknown and therefore must be tested empirically. More details of the proposed in-vivo study can be found in Chapter 11 ('Future work'), Section 11.4 ('EXF Screw project'). Furthermore it is possible that other biological growth, such as soft tissue is also able to jam open the fastener.

The current study investigated the ability to create a slot of constant width with low erroneous connectivity and low potential in-growth. However it is not necessary that the potential for bone in-growth is low across the entire depth of the slot. Another strategy that may achieve better results would be to have a variable slot width (Figure 8-27) where the lower thickness slot section (D_1) blocks bone in-growth, but because it only constitutes a fraction of the volume of the slot, the increase in erroneous connectivity would be less than for a constant slot width.

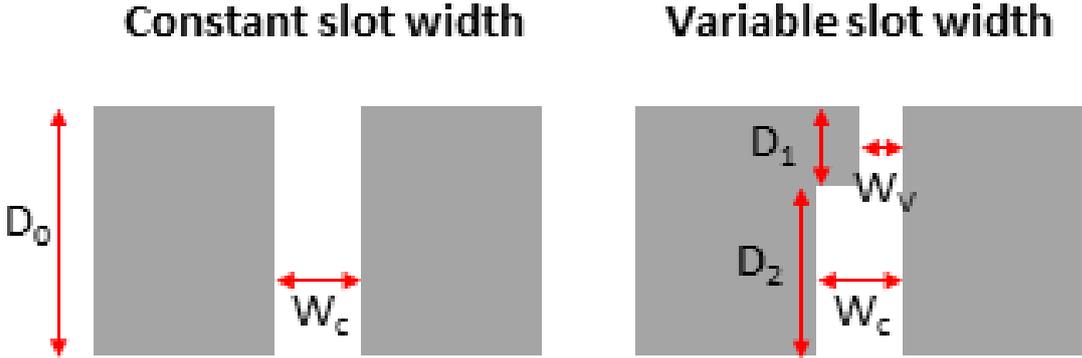


Figure 8-27 Definitions for a constant and variable slot

For example, using the minimum thickness achievable by the SLM machine (Realizer GmbH, n.d.) at UWA ($60\ \mu\text{m}$) for the variable slot depth (D_1) and the typical minimum slot depth for the EXF Screw design ($500\ \mu\text{m}$, limited by the thickness of the bending section of the fastener) the fraction of the D_1 slot would be 12%. Consequently even if the slot width was zero, allowing no potential for bone in-growth, it would only be 12% erroneously connected.

Lastly there are other strategies outlined in Chapter 4 (‘Design of the EXF Screw’) for preventing bone in-growth. These include the creation of a metallic ‘seal’ along the slot or using a polymeric ‘sealant’ that would be deformed into the slot, filling it up and preventing bone in-growth.

Lastly if the slot width becomes too small then removal of the powder from inside that slot may become difficult. This represents a risk of osteolysis if a particle was to detach inside the body. Hot Isostatic Pressing may be able to prevent particle detachment, but may cause increased erroneous connection across the slot.

8.2.2 Hole clearance

The holes as-built were lower diameter than designed as shown in Figure 8-28 possibly due to a combination of surface roughness on the inside of the hole and shrinkage of the parts. A high level of linear correlation ($R^2=0.967$) was demonstrated between the As-Built and As-Designed hole diameter (see Figure 8-28). The gradient of the line of best fit was not 1 (0.6), which indicated that the clearance required was not a fixed value which could be applied independent of hole diameter.

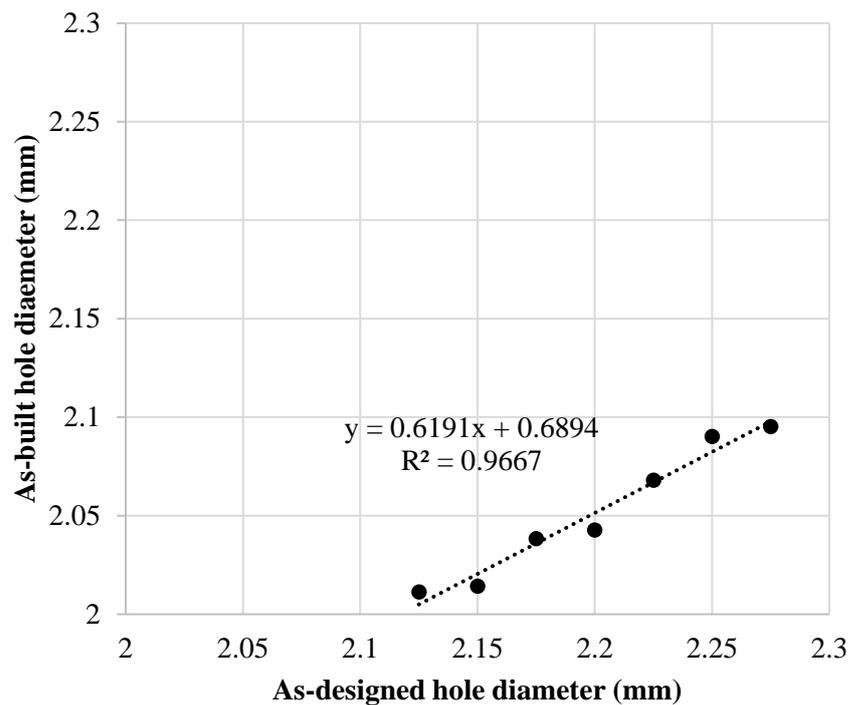


Figure 8-28 Comparison of the As-built hole diameters compared to the As-designed hole diameters

As shown in Figure 8-29, the clearance required was significantly correlated with the diameter of the hole ($p=0.917$), with larger holes requiring increased clearance. This indicates that surface roughness is not the only cause of the clearance required. It is hypothesised that shrinkage, which would scale for larger diameters, could be the cause of the dimensionally dependant clearance.

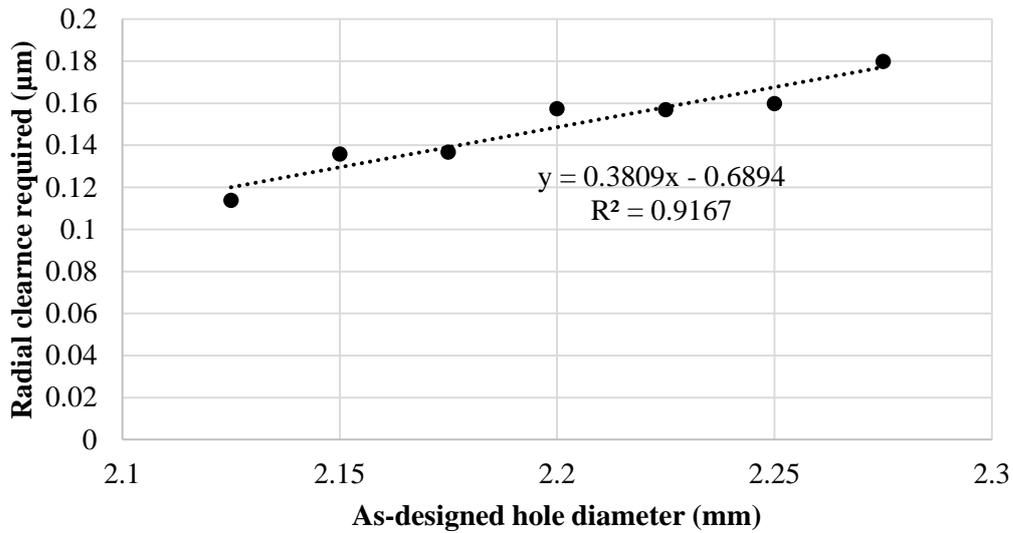


Figure 8-29 Clearance required for the various as-designed hole diameters

After scanning and analysing the samples, a lubricated 2.1 mm bright steel nail was able to be inserted into the 2.3 mm as-designed hole (2.102 mm as-built) using finger force and into the as-designed 2.275 mm hole (2.095 mm as-built) under impaction with a hammer. The nail that was inserted into the 2.275 mm as designed hole was inspected after removal and found to be severely scratched. This supports the accuracy of the image analysis study for pin clearance.

This clearance could be reduced by machining high tolerance holes with a drill, however this is additional cost and not always possible. For example the expansion pin hole at the tip of the EXF Screw design (allowing the pin to load share, reducing fatigue stress), cannot be machined because the expansion tabs are in the way of the drill in a contracted orientation.

8.3 Conclusions

8.3.1 Slot fidelity

There is a minimum slot width that SLM can manufacture without the slot fusing together and failing to function as a slot. This minimum slot width is smallest for vertical slots and increases in width with increasingly severe overhang angles due to increased z-growth. Another factor is the 'stair-case' effect resulting from the layered structure of the parts (Figure 8-22), which results in severe overhangs, such as the 30° overhang tested in this study, having a larger minimum slot size than horizontal slots. For horizontal slots, supports can reduce the erroneous connectivity when it would otherwise be high (greater than approximately 10%).

There also exists a maximum slot size before bone can theoretically grow within the slot and has the possibility to grow into the centre of the expandable fastener, jamming it open and preventing removal. Only the vertical samples were able to reach this theoretical threshold at any of the slot widths tested (50 µm and above). However reducing the as-designed slot width below 50 µm for other build orientations would eventually result in no potential for bone in-growth at the expense of unrealistic erroneous connectivity.

However, even the vertical slots do not have both negligible erroneous connectivity and no theoretical potential for bone in-growth at any one slot width. However the most favourable slot width, with the current manufacturing process is 90 µm. This slot width has 12% erroneous connectivity and only a single viable bone in-growth path which, at its narrowest (pore throat size), is less than a percent of the total slot area.

Consequently future work is required determine the allowable limit for erroneous connectivity before the slot cannot open under reasonable force, the empirical limit for bone in-growth and to determine whether altering the manufacturing process, manufacturing process parameters or the design geometry can allow a smaller slot width to achieve both no erroneous connection and no potential for bone in-growth.

8.3.2 Hole clearance

Significant clearance is required in order to ensure that a pin can fit within a hole that is manufactured using SLM. This clearance varies depending on the diameter of the as-designed hole from 114 μm at 2.125 mm diameter to 198 μm at 2.3 mm. As predicted by the image analysis study, a 2.3 mm as-designed hole is appropriate for a 2.1 mm pin, providing minimum clearance with negligible insertion force. Consequently future EXF Screws manufactured with SLM will be designed using this hole and pin size.

The author hypothesises that the diameter dependant component of the clearance is a result of shrinkage of the SLM part due to low wall thickness around the hole with the remaining clearance due to surface roughness of the material. Additional work will be required to determine whether shrinkage can be reduced by increasing the wall thickness around the sample and to generalise a formulae for all hole diameters.

Chapter 9 Feasible expansion size for expandable screws in the posterior cervical spine

Previous studies have reported the potential for expandable screws to increase fixation strength in the lumbar spine from a posterior approach, for example X-Ped (Vishnubhotla et al., 2011) and Omega-21 (Wu et al., 2012). In the cervical spine from an anterior approach, studies have reported the use of expandable screws (Rohl et al., 2009; Zhou et al., 2014) and there are commercial products available such as Osmium (Ulrich Medical, n.d.). However the potential for an expandable screw in the lateral mass of the cervical spine from a posterior approach has not been studied. Previous work in this thesis has demonstrated that expansion size significantly affects the performance of expandable screws (see Chapter 6 ('Effect of design parameters on mechanical performance of the EXF Screw') Section 6.2.2 ('Effect of expansion size')) and so this study aimed to explore the feasible expansion size in the cervical spine and the effect of the trajectory of the screw on the potential expansion size.

This work was conducted early in the project while the project was still focussed on developing the expandable screw for a spinal application. Although this study is no longer specifically relevant for the current application of proximal humerus fracture fixation, the result can potentially be useful for the project if the EXF Screw as a platform technology is developed for this application in the future and for other researchers investigating expandable screws.

In order to provide a range of design data that is valid across different screw diameters and depths, this study reported the maximum allowable expanded size by determining the largest screw diameter that could fit within the cancellous bone at various depths without penetrating the cortex of the vertebrae.

The experimental aspect of this work has been presented as a poster at the 2015 Australia and New Zealand Orthopaedic Research Society Conference in Auckland, New Zealand (Oldakowski, Oldakowski, et al., 2015) and is reproduced in Appendix H. The novel cortical segmentation methodology developed for, and used in, this work has been presented as a poster at the 2016 Australian Conference on Microscopy and Microanalysis in Melbourne, Australia (Oldakowski, Oldakowska, Ford, et al., 2016) and is reproduced in Appendix I.

9.1 Method

9.1.1 Sample acquisition

This study examined human cervical vertebrae that had been obtained under ethics approval number SMEC-51-13 from Curtin University Human Research Ethics Committee. Samples that had been cleaned by dermestid beetles were used (Figure 9-1) for convenience, cost and quality of imaging. Eight human C5 vertebrae from both genders and ages ranging from 29 to 92 and a single cervical spine of a 42 year old male (C3-C7) (n=13) were examined.



Figure 9-1 A Cervical vertebrae that has been cleaned by dermestid beetles

9.1.2 Sample imaging and processing

The samples were scanned using the Skyscan 1176 micro-CT scanner at the CMCA at UWA with 18 microns resolution using a rotation step of 0.5°, a source voltage of 80 kV and an exposure time of 285 ms. The raw radial scans were reconstructed using the Nrecon software with a modified Feldkamp cone-beam algorithm using a 30% beam hardening correction coefficient and an 8-ring artefact correction coefficient. These parameters were chosen based on previous studies (Oldakowski, Oldakowska, et al., 2016a; Oldakowski, Oldakowska, et al., 2016b) and visual confirmation that the cortex was being appropriately segmented (Figure 9-2). See section 5.1.3 ('Bone morphology characterisation') for more detail.

As shown in Figure 9-2, using FIJI (Schindelin et al., 2012), an open source image analysis program, the scans were rotated to align with conventional anatomical planes, filtered with a 3x3x3 median filter to remove noise and thresholded using the Otsu algorithm (Otsu, 1979). The cortices of the samples were segmented using a modified Buie method (Buie et al., 2007; Oldakowski, Oldakowska, Ford, et al., 2016) developed by the author, which is described in a poster presented at the Australian Conference on Microscopy and Microanalysis (Appendix I). The improvement between the conventional and modified Buie method can be seen qualitatively in Figure 9-3 on the following page.

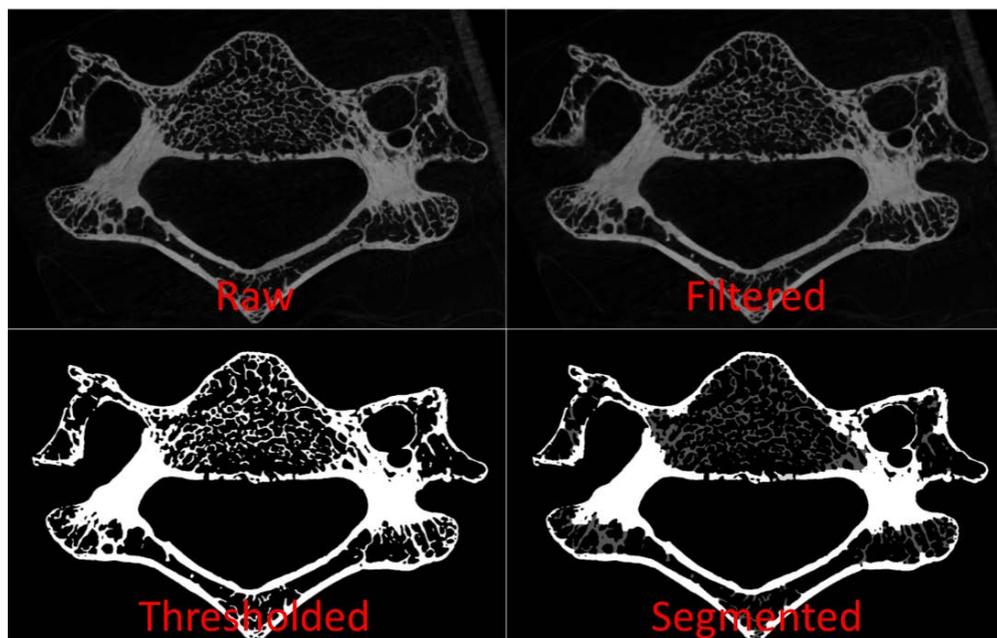


Figure 9-2 The raw data set (top left) is filtered (top right), thresholded (bottom left) and then cortically segmented (bottom right)

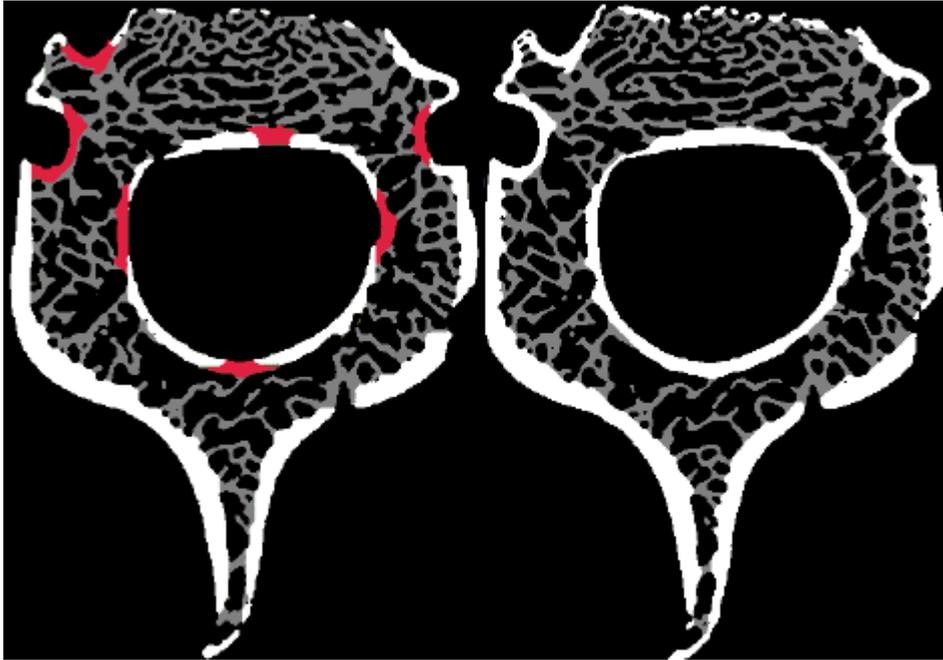


Figure 9-3 The conventional Buie method (left) erroneously excluded some cortical volume (shown in red) that the modified Buie method correctly included (right)

9.1.3 Entry point and trajectory

Cervical lateral mass fixation from posterior approach

Professor Gabriel Lee, an experienced neurosurgeon, denoted the centre point of the lateral mass, from which all the trajectories were based upon. Professor Lee drew the centre point on paper using a printed posterior view with access to each human vertebrae for 3-dimensional comparison. The paper was then scanned and the entry points transcribed digitally. Using FIJI (Schindelin et al., 2012), a volume of interest (VOI) was created for each of the clinically described screw trajectories that were investigated. Based on the entry point provided by Professor Lee and any medial/lateral or superior/inferior offset described by the technique the scan was rotated with the data centred on the entry point to account for varying lateral and cephalad angulation.

The initial conventional techniques examined included those described by Roy-Camille (Roy-Camille, Saillant, & Mazel, 1989), Magerl (Jeanneret, Magerl, Ward, & Ward, 1991), and Anderson (Anderson, Henley, Grady, Montesano, & Winn, 1991) and are shown in Figure 9-4. However, these conventional clinical trajectories did not enter any feasible volume of cancellous bone to expand into, instead staying close or within the cortical bone to maximise cortical engagement. Although this is advantageous to maximise pull-out strength it is not suitable for expandable screws due to the risk of cortical cracking.

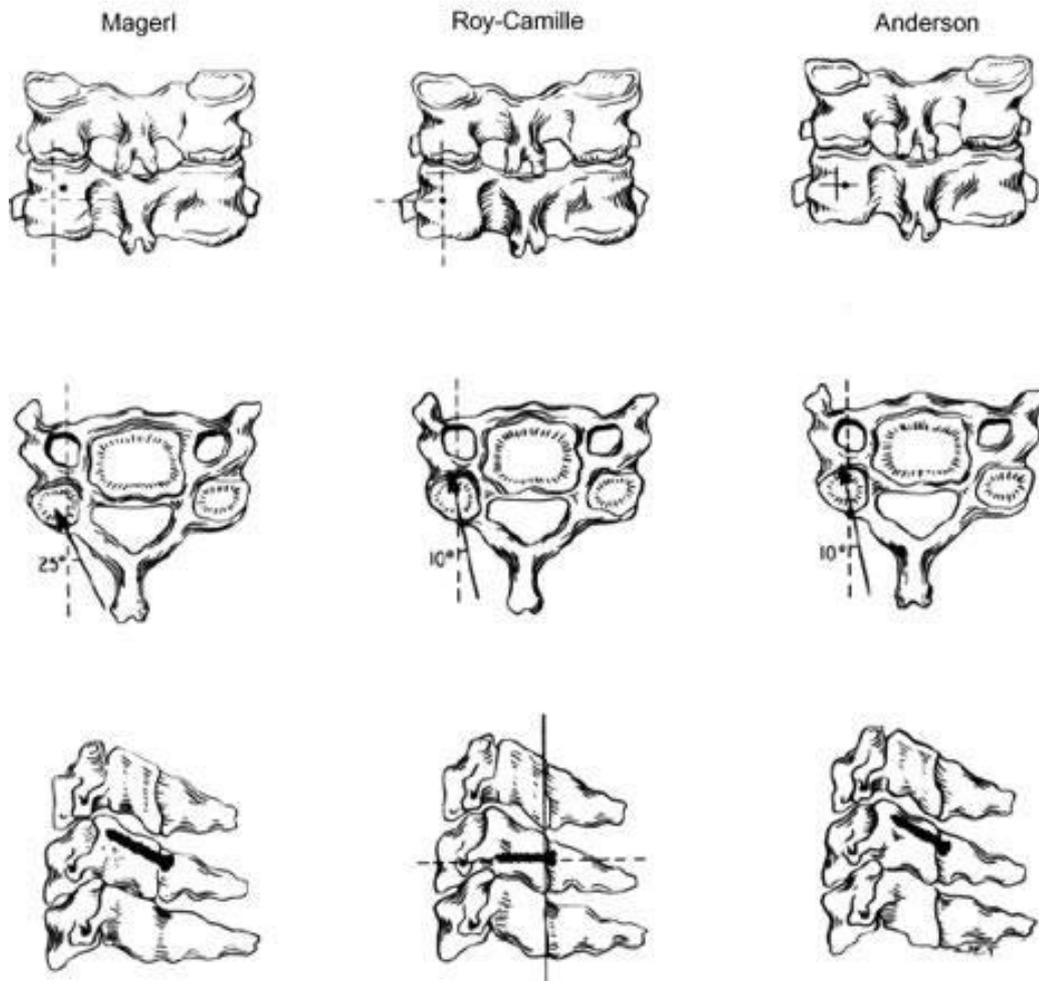


Figure 9-4 The trajectories investigated for expandable screws, defined by an entry point in the posterior view (top) a lateral angulation (centre) and a cephalad angulation (bottom) (Abdu & Bohlman, 1992)

Consequently the Roy-Camille and Magerl trajectories were modified to direct them through the centre of the lateral mass, allowing for a higher maximum expansion size. The Roy-Camille method was modified by moving the entry point to the top of the lateral mass, just below the joint margin, keeping the angulation the same. The modified Magerl method involves an entry point that is 1 mm medial of the centre (the same as the Magerl method) but is 1 mm inferior, rather than 1 mm superior. The angulation for the modified Magerl method is the same as the Magerl method with 25° lateral angulation and angulated cephaladly to match the angulation of the facet joint surface.

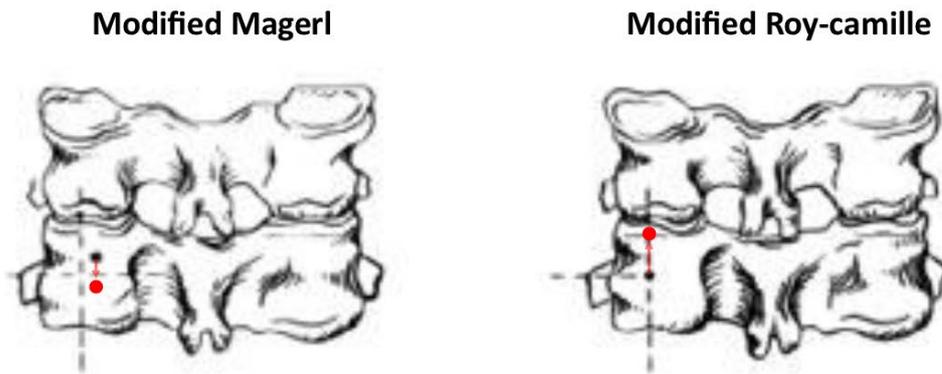


Figure 9-5 The two lateral mass trajectories investigated, the modified Magerl method (left) and the modified Roy-Camille method (right) (Abdu & Bohlman, 1992)

Cervical vertebral body fixation from an anterior approach

The allowable expansion size was also investigated for an anterior approach for both a single and a double screw trajectory. A midline entry point was used without mediolateral or inferior-superior angulation for both a single screw and double screw plate. For the double screw plate the screws were offset by 9 mm which was based on the DePuy Synthes CSLP plate (DePuy Synthes, 2016).

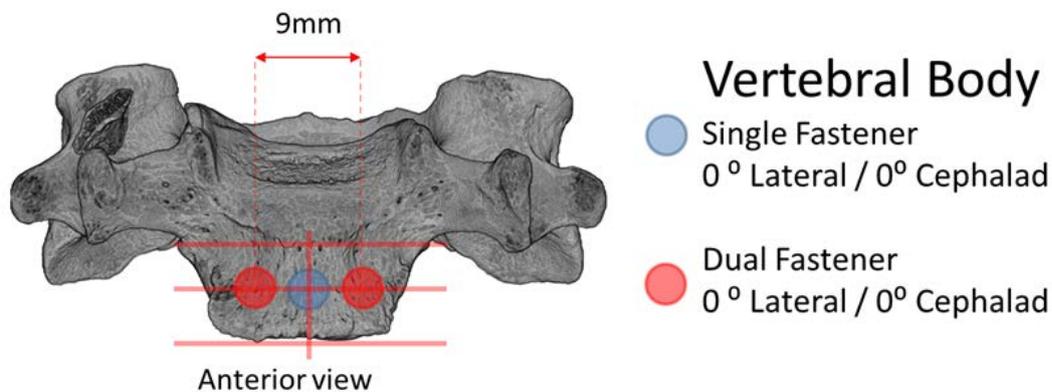


Figure 9-6 Anterior trajectories investigated used a midline entry point without mediolateral or inferior-superior angulation

9.1.4 Maximum expansion size calculation

The maximum expansion diameter at a given screw depth was defined as the largest diameter circle that could fit along the screw trajectory without including any cortical bone (see Figure 9-7). This methodology assumes that the fastener can expand right to the cortex, providing an upper limit to expansion size. A FIJI macro, written by the author, automatically created iteratively larger diameter circles from the centre point of the trajectory until that circle contained cortical bone. The largest circle without containing cortical bone was reported as the maximum allowable expansion size at that depth. This calculation was conducted for each trajectory, in depth increments of 0.5 mm until the far cortex was reached.

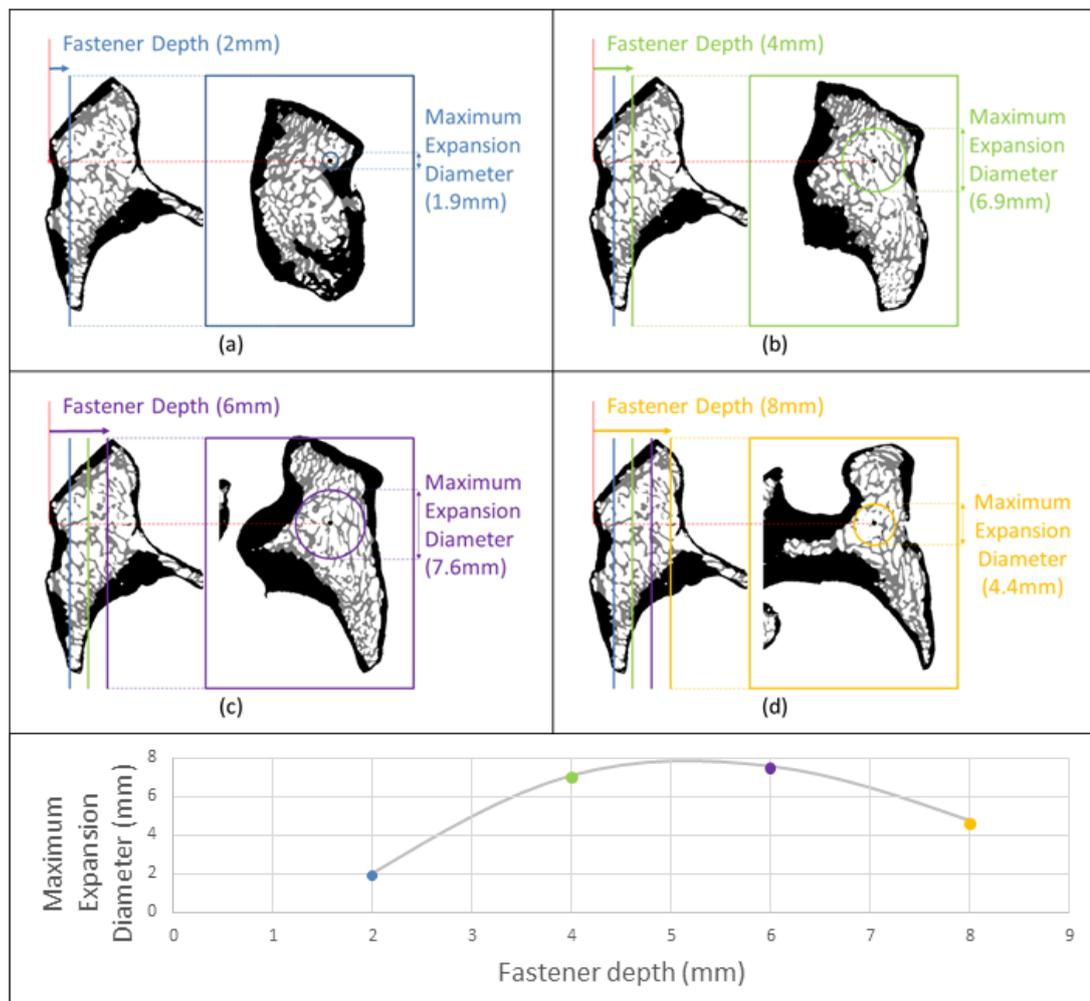


Figure 9-7 Indicative diagram of the process of determining the maximum expansion diameter at each depth. At each depth (2 mm, 4 mm, 6 mm & 8 mm in the diagram), the largest circle that doesn't contain cortical bone is defined as the maximum expansion diameter at that depth

9.2 Results

The maximum expanded diameter of the various trajectories over the allowable range of fastener depth is summarised in Table 11 and presented graphically for a typical case in Figure 9-8. In the vertebral body, significant expansion size is available close to the maximum fastener depth for a significant range of fastener depths for both the single and double screw trajectory. The single screw trajectory does not significantly increase expansion size compared to the double screw approach ($p=0.762$) but increases fastener depth by 2.2 mm on average ($p<0.001$) and has less variation in the maximum expanded diameter ($p<0.001$) but not in the depth of the maximum expansion.

In the lateral mass, the modified Roy-Camille technique allows high expansion only for a very limited fastener depth whereas the modified Magerl method provides less allowable expansion diameter for expansion at a deeper and higher range of fastener depth. Furthermore the depth of the maximum expansion, especially for the Lee method, is highly variable.

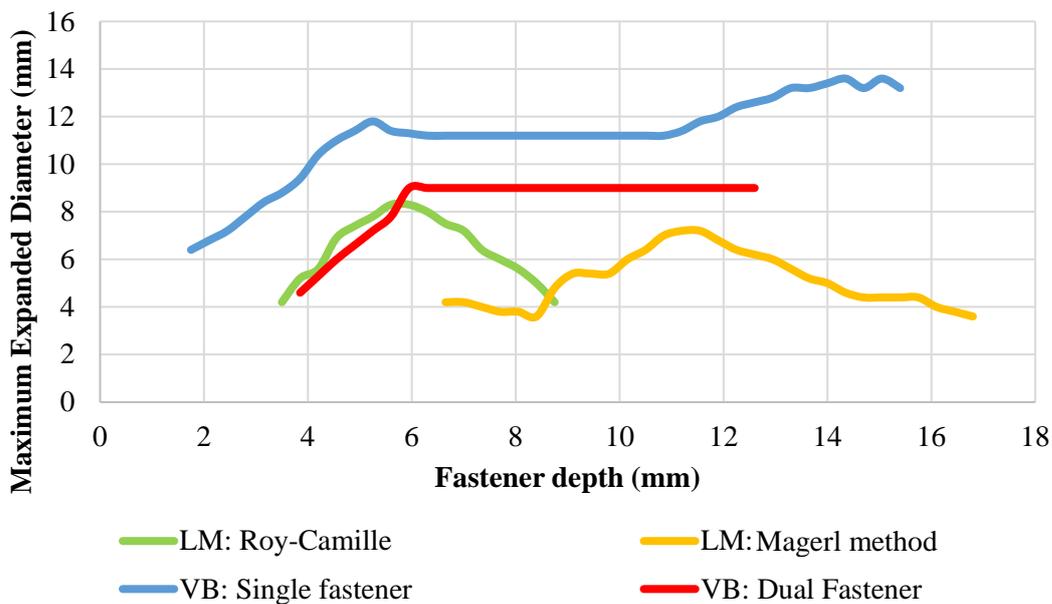


Figure 9-8 Graph of typical, indicative expansion diameter vs fastener depth curves for the trajectories investigated

Table 11 Maximum expanded diameter and the fastener depth this diameter occurs for each of the trajectories investigated

	Lateral mass – Posterior Approach		Vertebral Body – Anterior Approach	
	Modified Roy-Camille	Modified Magerl	Single screw midline	Double screw midline
Maximum expanded diameter (mm)	7.52±2.43	5.85±1.57	8.94±2.84	8.85±1.10
Depth of maximum expansion (mm)	5.41±1.89	14.1±5.46	14.5±2.26	12.3±2.47

9.3 Discussion

Early in the project, trabeculae-level FEA was explored to predict the amount of expansion in cancellous bone that was possible before the reaction force transmitted through the trabecular bone would fracture the cortical shell. However due to the high strain and the complexity of the localised fracture and buckling of trabeculae during expansion, modelling this accurately was not feasible within the timeframe of the thesis. Mechanical testing was also explored to determine how much expansion could occur before the samples cracked open. However destructive mechanical testing of human material would be difficult to justify ethically and the results would be dependent on the diameter and length of the fastener, the specific anatomical dimension of the sample used and the trajectory used. Furthermore other limitations may apply, such as inability to applying sufficient expansion force for cracking.

The high variance of the allowable fastener depth and expansion diameter reported in this study is potentially due to the osteoporotic samples used in this study, where there is anatomical distortion and also consequently ambiguity in terms of the anatomical landmarks which the surgeon uses to determine the entry point (see Figure 9-9). This is especially problematic because osteoporotic patients are the patients that would benefit most from the increased fixation strength provided by expandable screws, due to the increase risk of screw failure, and so they are the patients expandable fasteners would target.

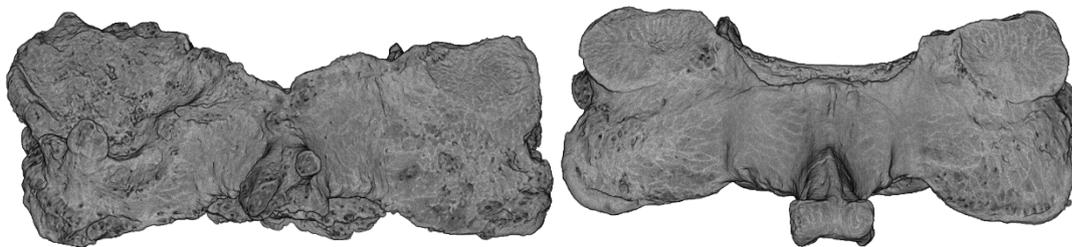


Figure 9-9 Posterior views of two cervical vertebrae demonstrating the anatomical distortion in an osteoporotic sample (left) compared to a young, healthy sample (right)

High variance in the size of the expansion and the depth of the expansion is problematic because the surgeon needs to be able to select the correct screw length to ensure that the expanded screw will fit within the bone. Detailed pre-operative planning based on pre-operative CT or Intra-operative CT navigation could facilitate this, but is costly, time consuming, and adds potentially unnecessary radiation exposure to the patient. Cracking the cortex or being unable to expand the screw during surgery would be catastrophic. Prevention of cortical cracking may be possible by creating an expandable screw that has a load limited expansion.

In this study only a single entry point was marked by a single surgeon for each of the samples. It is possible that the inter-surgeon variance of this entry point across multiple samples could be responsible for the high variance of allowable fastener depths and expansion sizes. The inter-surgeon and intra-surgeon variance of entry points could be evaluated in future work. Quantifying this variability is critical to confirming the feasibility of expandable screws in the lateral mass of the cervical spine.

For the modified Roy-Camille method, the length of screw would have to be extremely low, based on 95% confidence intervals down to 3.5 mm. In this case an expandable screw in this trajectory would have to increase in fixation strength dramatically, compared to a conventional screw to overcome a four fold disadvantage in length. Based on the work presented in Chapter 6 ('Effect of design parameters on mechanical performance of the EXF Screw'), it is unlikely that this is possible without engaging with the cortex.

Although this work was performed to determine how much expansion was allowable without getting too close to the cortex it also approximates how much expansion would be required to engage the cortex at the expanded section of the screw. This value can be potentially useful for future EXF Screw designs where the expansion is intended to reach the cortex.

For the modified Magerl method, based on 95% confidence intervals, the maximum expansion depth can occur anywhere between 8.6 mm and 19.6 mm and that this maximum expansion size varies from 4.3 mm to 7.4 mm. However the Lee method total screw length is similar to conventional screws and so the expansion may only need to increase fixation strength moderately to be clinically advantageous, which is feasible based on the results in Chapter 6 ('Effect of design parameters on mechanical performance of the EXF Screw').

The reason why the double screw method for the anterior cervical trajectory doesn't decrease allowable expanded diameter compared to the single screw method is because the interference with the cortical shell is on the inferior and superior endplates, which is similar for both trajectories.

It is unclear how optimistic these results are in reporting the maximum allowable expansion size, without doing destructive testing of fresh frozen human tissue, as it is possible for load to be transferred through the cancellous bone to crack open the cortical shell even without the expanded screw contacting with the cortex directly. However, inversely it is possible that the expansion could go beyond the maximum described in this study by cutting into the cortical bone or by expanding the bone slightly. In the lumbar spine, pedicle enlargement has been described with expandable screws (Wu et al., 2010) which indicates that the latter may be possible in the cervical spine also.

9.4 Conclusions

Expandable screws with a large expansion diameter are not feasible in the lateral mass of the cervical spine due to the large variation in anatomy. However expandable screws with a relatively small expansion size may be able to engage the cortical shell and significantly increase the fixation strength. This study suggests that, for expandable screws, the modified Magerl method provides more opportunity for expansion compared to the modified Roy-Camille trajectory described or any of the clinical trajectories investigated.

Expandable screws with a large expansion diameter are feasible for the anterior vertebral body. In the vertebral body a single screw approach does not allow significantly more expansion and only marginally more length compared to a double screw approach. Therefore a double screw approach is recommended for expandable screws to maximise the fixation strength.

However future work is required to determine empirically a safe expansion size, for a particular expandable screw design, that will not crack open the cortical shell, given the inter-surgeon and intra-surgeon variation in entry point, angulation and length and the variation in anatomy due to severe osteoporosis. This could be performed by increasing the sample size. Subsequent to this, future work may also demonstrate that with a safe expansion size the expandable screw can engage with the cortical shell to increase fixation strength significantly compared to current methods.

Chapter 10 Conclusions

This chapter focusses on project level outcomes and conclusions. The experimental chapters should be consulted for technical conclusions and outcomes from particular experiments.

This thesis indicates that the increased compression of the bone around expanded screw threads rather than an increase in the area of bone loaded may be the primary mechanism by which expandable screws have improved pull-out strength compared to conventional screws. This hypothesis has not been explicitly published previously in the indexed literature (to the knowledge of the author) and has significant consequences for the design and application of expandable screws. This hypothesis indicates that:

- expandable screws are particularly suited as rescue screws used in revision surgeries, where the initial compression around the screw is low due to the void created by the previous screw;
- the amount of expansion significantly affects the pull-out strength of expandable screws (as confirmed by the testing in this thesis), however there is potentially a non-linear relationship between expansion size and pull-out strength, providing diminishing returns as the expansion size increases. Consequently even a relatively small expansion, especially if the screw is in a dense, stiff medium (such as the cancellous bone immediately adjacent to the cortical shell) can create a significant increase in pull-out strength;
- the angle of expansion should not significantly affect the pull-out strength per unit length of expandable screws;
- the percentage of the perimeter of the screw that expands (expansion arm width) significantly affects the pull-out strength of expandable screws; and
- the pilot hole size that is used to test expandable screws is critical and must be representative of the clinical scenario, otherwise expandable screws are either inappropriately advantaged or disadvantaged.

This thesis has also demonstrated that equivalently sized unthreaded expandable fasteners can outperform conventional threaded screws in an animal bone model, they rely on a different critical bone volume, they may be less sensitive to a reduction in cancellous bone quality and cortical thickness and they can significantly increase failure energy. These advantages indicate that for applications requiring increased pull-out strength unthreaded fasteners are a feasible technology especially in anatomical locations where the structural quality of the bone is low and the cortex is relatively thin, such as the conditions caused by osteoporosis. Also unthreaded expandable fasteners and expandable screws are both suited to cases where failure energy is important (i.e. where there is significant screw migration before patient complications). This part of the thesis has been published as referenced (Oldakowski, Oldakowska, et al., 2016a; Oldakowski, Oldakowska, et al., 2016b).

Although this thesis has demonstrated for the first time (to the knowledge of the author, based on the indexed literature) that expandable screws pull-out stiffness is significantly correlated to pull-out force, the simplified linear elastic FEA (that has been used previously to assess screw design) is not suitable for predicting the performance of expandable screw designs. This is because the compression of the bone around the screw thread, which cannot be accurately modelled without using non-linear models, is critical to the performance of expandable screws.

The work in this thesis has demonstrated that proximal humerus fracture fixation is a clinically unmet need that can potentially be addressed by a removable, expandable screw such as the EXF Screw. This thesis has demonstrated that the EXF Screw has potential to be a superior technique to treat proximal humerus fractures through a technical proof-of-concept demonstrating:

- significantly increased fixation strength compared to conventional screws;
- functional removal in synthetic bone under simulated osseointegration;
- potentially no decrease in fatigue strength compared to conventional screws under typical proximal humerus fracture fixation loading conditions;
- protectable Intellectual Property; and
- practicality, by manufacturing a functioning EXF Screw prototype.

The EXF Screw can potentially satisfy all the stakeholders of proximal humerus fracture fixation surgery providing:

- for the patient, reduced risk of complications and a second revision surgery;

- for the surgeon, better outcomes for their patients and reduced risk of needing to perform a revision surgery (which is significantly more difficult than the original surgery), without increasing the difficulty of screw removal; and
- for the payers (National Health Service or insurance companies), reduced risk of a costly revision surgery or additional ancillary treatment to manage complications (such as physiotherapy, increased hospital stay etc.).

The EXF Screw is anticipated to be a commercially attractive solution, which provides a strong pathway to impact and public benefit (see Appendix B ('Support letters for the project')). Implant manufacturing companies can charge a premium compared to conventional screws and increase their market share if the product is sufficiently beneficial and they have an exclusive license. However implant manufacturing companies rarely invest in technology prior to animal studies and more likely after first in human clinical testing. Consequently, investment will be required to conduct the testing required to achieve these milestones. Investment from venture capitalists or granting bodies is contingent on demonstrating technical proof-of-concept.

The results obtained within this thesis supported a successful proposal to the National Health and Medical Research Council (NHMRC) Development Grant scheme (ID: 1121702). This grant will undertake all the benchtop and animal studies required prior to a first in human clinical test and regulatory approval submission. Details of the NHMRC Grant scope of works can be found in Chapter 11 ('Future work'), Section 11.4 ('EXF Screw project').

During the thesis three related patents have been submitted with two in the national phase (Oldakowski, Oldakowska, et al., 2015; Oldakowski, Oldakowska, et al., 2013) with another still in the PCT stage (Appendix G). These patents cover the critical design features of the EXF Screw, specifically the integration of the fasteners into the stabilising element to form a single part unit (Oldakowski, Oldakowska, et al., 2013), the planar profile expansion wings which allow an even, controlled and optimally elastic expansion (Oldakowski, Oldakowska, et al., 2015) and the ability for the fastener to expand whilst leaving no gaps in the fastener where bone can grow into, allowing the fastener to be unconditionally removable in revision surgery (Appendix G). The EXF Screw project has received resources from DePuy Synthes in the form of testing materials (orthopaedic screws). DePuy Synthes is an international implant manufacturing company and globally the largest provider of trauma implants. This demonstrates the novelty and potential impact of the research.

The EXF Screw concept is a platform technology that can be applied over a large variety of orthopaedic procedures with only minor design variation. Although this is potentially very attractive to an implant manufacturing company, it is imperative that the final design and testing are aligned to a particular use which will form the thrust of the investment proposal. The broad potential application of the technology highlights the fundamental advances made within this thesis. Discussion of the potential applications of the EXF Screw can be found in Chapter 11 ('Future work'), Section 11.4.4 ('Future potential indications').

Chapter 11 Future work

11.1 Design of expandable screws

This thesis has demonstrated that expandable screws achieve increased fixation under axial, pull-out loading primarily due to the compression created at the screw thread and bone interface by expanding the screw. Previous work has demonstrated that compression created by reduced pilot hole size, can significantly increase fixation under pull-out loading for conventional screws (Chapman et al., 1996; Steeves et al., 2005).

Consequently the Chapman equation (Chapman et al., 1996), which is shown below and has been previously modified to account for conical screws (Wu et al., 2009), may also be modified to account for compression, either from a reduced pilot hole size (compression applied to the screw interface equally across the threaded area) or by expansion (compression applied to the expanding areas proportional to the amount they expand).

$$F_{pull\ out} = S_{shear} \times \pi L D_0 \times \left(\frac{1}{2} + \frac{1}{\sqrt{3}} d/p \right)$$

Empirical data for this modification could be gained by testing pilot hole sizes incrementally, as was done in Chapter 6 ('Effect of design parameters on mechanical performance of the EXF Screw'), to determine a suitable empirical correction factor to account for the compression. This testing would need to be performed for a number of synthetic bone densities to account for the different compression pressure achieved with each density for the same expansion size. Also a sufficient number of pilot hole sizes across a clinically feasible range need to be tested to accurately understand the relationship between compression and increased pull-out force. Based on the results from Chapter 6 (Figure 6-4) this relationship is potentially non-linear and could be logarithmic (Figure 11-1). This would result in a correction factor for compression that either has a complex form (logarithmic, quadratic etc.) or else is read from a chart.

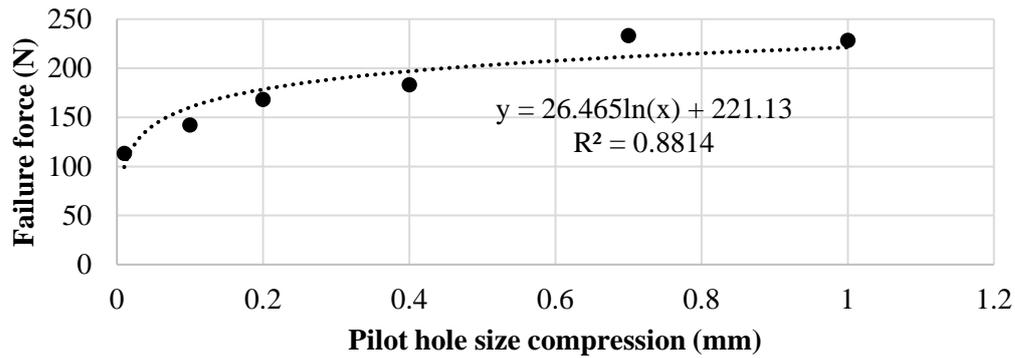


Figure 11-1 The relationship between pilot hole size and failure force, for conventional screws, is non-linear and potentially logarithmic

Correcting for compression of expandable screws is more complex in that the compression is applied unevenly across the outside of the screw, depending on how much expansion occurred at each location. This could theoretically be calculated through a series of integrals based on the expansion profiles for different sections of the screw. However, more feasibly, a less complicated equation could be created based on standard expandable screw geometries.

In addition this work could be performed in bone samples where the expansion would not only increase compression around the screw, but also engage a stronger material, the cortical bone (e.g. in the lateral mass).

Further work may also involve analysing the effect of design variables for other loading modes, including shear, rotation push-in and the effect of synthetic bone density. This work is currently being undertaken by another PhD student, Intan Oldakowska.

11.2 Selective laser melting slots

This thesis was unable to create slots using Selective Laser Melting (SLM) with no erroneous connectivity and no theoretical bone in-growth potential. Future work involving analysing the effect of SLM manufacturing parameters on the ability to create thin, high fidelity gaps, or future advances in SLM manufacturing equipment, may make this possible. In particular it is hypothesised that optimising laser scan speed and powder particle size could potentially increase slot fidelity. Furthermore, evaluating the slot width that allows functional bone in-growth by in-vivo testing, is part of the NHMRC Development grant scope of work. This work may indicate that relatively large slots (~110 μm with no erroneous connectivity) although have the theoretical potential for bone in-growth, will not allow sufficient bone to grow inside the mechanism to jam it open.

11.3 Potential expansion size in the spine

This thesis investigated the viable expansion size for an expanding screw within the cervical spine, by determining the amount of expansion that could be achieved without interfering with the cortex of the vertebrae. This work could be extended to include a larger number of spinal samples to increase the statistical significance and confirm that a surgeon could use a particular geometry of expandable screw safely, along the tested screw trajectory. This work could also be extended to other areas of irregular anatomy where expandable screws are used, such as the lumbar pedicle.

Additionally these maximum expansion size predictions could be compared to empirical testing of maximum expansion size. This would indicate where the limiting factors were (e.g. is the force too high to expand or does the bone burst open?) and allow a correction factor to HR-CT measurements so the feasibility of expandable screws in other applications could be more efficiently explored.

11.4 EXF Screw project

The primary future work from this thesis project will be carried out within the NHMRC Development grant (Grant ID: 1121702) scope of works, which is summarised in the following sub-chapters. The chosen primary indication is proximal humerus fracture fixation.

11.4.1 Cadaveric ex-vivo mechanical testing

In this study, based on the methodology of Erhardt et al. (2012), cadaveric proximal humerus samples will be tested in a construct, with a plate and an osteotomy fracture model (Figure 11-2) to determine the increase in cut-out resistance for the EXF Screw, compared to conventional proximal humerus locking screws. These tests will demonstrate the ex-vivo performance of the EXF Screw compared to screws under simulated physiological conditions in human proximal humeral bone samples. This is critically important to demonstrate that in the unique bone geometry and structure (i.e. osteoporotic) the EXF Screw significantly increases fixation strength and arrest screw cut-out.



Figure 11-2 Cadaveric proximal humerus samples will be tested as a construct for cut-out as part of the NHMRC grant scope of works (Erhardt et al., 2012)

11.4.2 In-vivo animal study

In this study, the EXF Screws and equivalent control screws will be implanted into the vertebrae of living sheep based on the procedure described by Wan et al. (2010). These samples will be harvested at five different time points and used to:

- mechanically compare the stability and pull-out strength after osseointegration;
- qualitatively compare the osseointegration of the expandable fasteners against screws after osseointegration by micro-CT (using a methodology based on the work by Wan et al. (2010) illustrated in Figure 11-3); and
- demonstrate removability with minimal bone destruction and removal torque of the EXF Screw after six months in-vivo.

These studies are graphically illustrated in Figure 11-4.

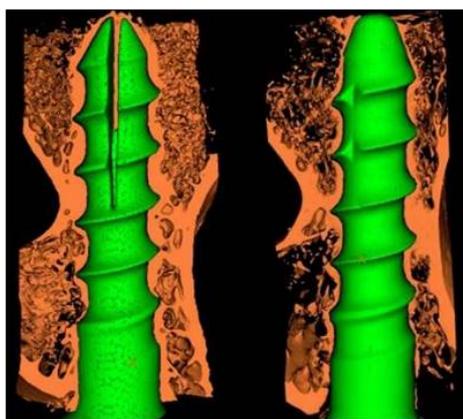


Figure 11-3 A study by Wan et al. (2010) demonstrated increased bone density around expandable screws after a period of time in-vivo

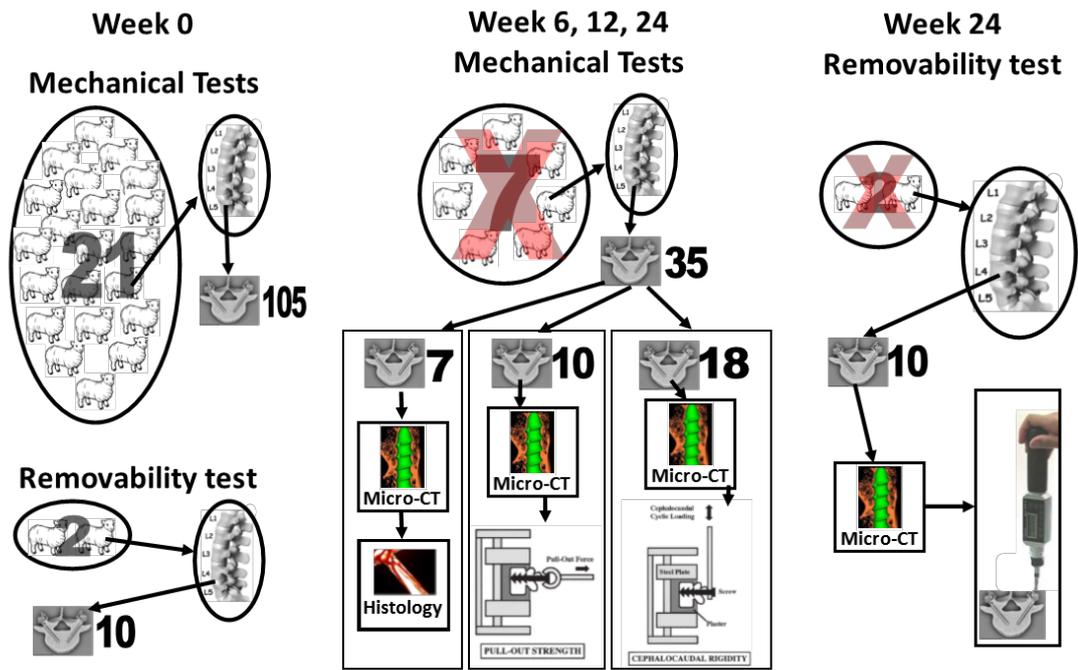


Figure 11-4 A graphical representation of the sheep samples over the four time periods

11.4.3 ASTM testing

Finally the EXF Screw and plate construct will be tested for static and fatigue strength. An industry standard screw and plate system for proximal humerus fixation from Zimmer Biomet or DePuy Synthes will be used as controls. Each test will be conducted using three sample fasteners. Listed below are all the testing required to satisfy the ASTM International standards to prove device safety for the regulatory approval process and a first in human clinical trial:

- Fastener Static and cyclic axial/bend testing (ASTM F543)
- Fastener Static and cyclic torsional testing (ASTM F543)
- Fastener pull-out testing (ASTM F543)
- ASTM F382 – metallic bone plates – 4 point bending test to check load to permanent deformation, stiffness, and fatigue strength (load based or number of cycle based)

If the expandable fastener and plate system satisfies all required standards testing, it can be approved for first-in-human clinical testing and potentially by medical device regulatory bodies.

11.4.4 Future potential indications

Proximal humerus fracture fixation has been chosen as the most suitable indication for the introduction of the EXF Screw due to:

1. Very high complication and revision rates (14% revision and 45% complication rates on average (Sproul et al., 2011)), which lead surgeons to either conservatively manage a patient that would benefit from surgical intervention (with a higher success rate) or to a more costly and complicated alternative surgical procedure (e.g. shoulder arthroplasty);
2. Based on literature, the majority of revisions are caused by screw related complications that can be addressed by increasing fixation strength, including screw push-in leading to joint perforation, shear failure leading to varus malunion and potentially screw loosening leading to fracture non-union (Sproul et al., 2011);
3. Fatigue failure of the screws is not a previously encountered failure mode due to the low force on each screw within the construct, making it a less critical design constraint;
4. Proximal humerus fracture fixation surgeries are ideal for a clinical trial as the follow-up time frame to observe the majority of complications is relatively short (1 year) and the surgery is unlikely to cause mortality or severe complications such as neural damage; and
5. There are no expandable screw competitors currently.

However, the variance introduced by fracture type may make demonstrating a reduction in revision rate of the EXF Screw construct potentially difficult, depending on the effect size achieved. Furthermore the loading on the screws depend on the angulation of the screws and so increasing fixation strength might be less critical for appropriately angulated screws. This means that the improvement in performance of the EXF Screws compared to conventional screws are more difficult to detect in a clinical setting.

We believe that focusing primarily on increasing the push-in strength, to prevent screw cut-out and a secondary focus on increasing shear strength to prevent varus malunion is the optimal strategy for significantly reducing revision rate. This will involve either a two tab staggered single level expansion or a three tab double level expansion, depending on the relative performance of the two and whether they can each satisfy the fatigue, expansion force and removability criteria. Mechanical testing to assess the performance of EXF Screw in these failure modes will be conducted in collaboration with the author by Intan Oldakowska, another PhD student.

As a secondary indication, it is believed that the EXF Screw is well suited to posterior lumbar and thoracic pedicle fixation, with a very large market and a significant unmet clinical need, however there are significant competitor technologies in this application including XPed (Chen et al., 2014) and Osseoscrew (Vishnubhotla et al., 2011), which is an established technology, EPS (Lei & Wu, 2006), and Omega-21 (Cook et al., 2000) which is no longer on the market. This is thought to be commercially less attractive for investors, which would impede the pathway to impact for this application of the EXF screw.

Anterior Cervical Discectomy/Corpectomy and Fusion (ACDF/ACCF) appears well suited to expandable fasteners and it has been demonstrated that there is ample trabecular volume for significant expansion. However, outside of three and above level discectomies and corpectomies (which are both relatively uncommon), the clinical need for increased fixation strength is debatable and therefore may be perceived as a secondary usage by surgeons and implant manufacturers compared to proximal humerus fractures.

Posterior cervical fixation is a possible application for the EXF Screw. There is a concern that this application may lack an overwhelming clinical need to justify investment to develop the technology, a complicated insertion technique and the potential for cortical bursting. However, given the anatomy, even a very small expansion may significantly increase the fixation strength. The design of the EXF Screw for posterior cervical fixation will involve only a single expansion in the centre of the device, as this is the area of maximum expansion potential from the study on the lateral mass in Chapter 9 ('Feasible expansion size for expandable screws in the posterior cervical spine').

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Every reasonable effort has been made to acknowledge the owners of copyright material. I would be pleased to hear from any copyright owner who has been omitted or incorrectly acknowledged

Appendix A EXF Screw voice of customer surgeon survey

Surgeon Questionnaire – Open Reduction Internal Fixation (ORIF) Surgery for Proximal Humerus Fractures

Please complete all questions below and return the completed survey either via:

Email: Russell.Nicholls@curtin.edu.au; or

Post: Russell Nicholls, IP Commercialisation, Office of Research & Development, Curtin University, Kent St, Bentley, WA 6102.

Name (optional): _____

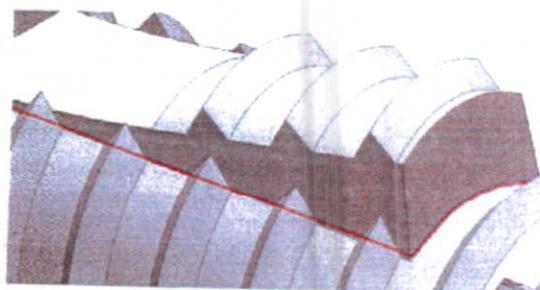
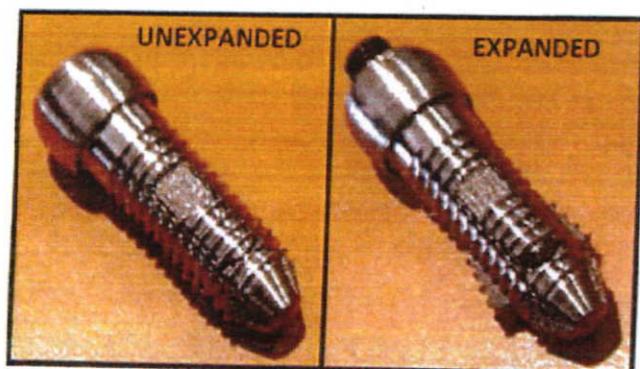
Approximate number of Proximal Humerus Fracture patients treated by Open Reduction Internal Fixation (ORIF) per year: 10

Years of trauma experience: 5 as consultant

A published literature review of locking plate fixation for proximal humerus fractures¹ reported a 49% overall rate of complications, with patients over 60 years of age having the highest complication rate. The most common complications are varus malunion (16%), avascular necrosis (10%), and screw perforation of the humeral head (primary and secondary; 8%). Consequently 14% of patients overall have revision surgery, with the most common cause being screw perforation. We believe that the risk of these complications can be reduced by providing increased fixation strength or using shorter screws with equivalent strength.

Researchers at Curtin University in conjunction with surgeons at St John of God and Royal Perth Hospital are developing a new expandable orthopaedic screw, the EXF (see images below), which provides increased fixation strength but unlike all other expandable screws provides a 'gapless' expansion (the red line represents a sealed interface between the expanding tab and the static screw). This prevents bone growing into the fastener and jamming it open (as is prone to happen for other expandable fasteners) which can lead to significant bone damage or fastener breakage during removal.

The EXF is designed to be simple to expand (turning in a threaded expansion pin) and as removable as a conventional screw, even after spending significant time in the bone. The EXF can be designed to any diameter from 4mm and varying length from 10mm with possibility for multi-level expansion in longer screw design.



¹ Sproul et al. (2011), 'A systematic review of locking plate fixation of proximal humeral fractures', Int J Care Injured, 42:408-13



The aim of this questionnaire is to gain feedback on the potential significance of the technology for ORIF surgery in the treatment of proximal humerus fractures.

Please circle the answer you most agree with.

1. Do you believe that increased screw fixation strength in ORIF surgery for proximal humerus fractures would:

a. improve the surgical outcomes?

Yes Likely Maybe Unlikely No

b. reduce the rate of revision?

Yes Likely Maybe Unlikely No

c. reduce the risk of screw penetration into the glenohumeral joint?

Yes Likely Maybe Unlikely No

2. If you answered no or unlikely to any part of question 1, what do you think are the more critical treatment aspects for improved surgical outcome? _____

3. Would you consider using an expandable screw in ORIF surgery for proximal humerus fracture cases if it was proven to:

a. have significantly increased fixation strength in clinically relevant proximal humerus cadaveric testing (axial pull-out test, resistance to cut-out test, resistance to fracture shear forces),

b. have superior osseointegration earlier and increased bone density surrounding the fastener over time (in an animal study), and

c. be as removable as a standard screw (demonstrated in an in-vivo animal study).

Yes Likely Maybe Unlikely No

4. How many of your patients would benefit from expandable screws in the treatment of their proximal humerus fractures? All

5. If you answered no or unlikely to question 3, would you consider using an expandable screw in proximal humerus fractures if it was proven in clinical studies to reduce screw related complications?

Yes Likely Maybe Unlikely No

If not, why not _____

6. Would the use of expandable screws in ORIF surgery for proximal humerus fracture patients positively affect your rehabilitation procedure for these patients? (e.g. earlier mobilisation, return to work)

Yes Likely Maybe Unlikely No



7. Do you think that using expandable screws with increased fixation strength would enable internal fixation of proximal humerus fractures in patients with lower bone quality (i.e. older, more osteoporotic patients) that would otherwise be managed nonoperatively or offered arthroplasty?

Yes Likely Maybe Unlikely No

8. Approximately how many additional proximal humerus fracture patients per year would you treat by internal fixation using the expandable screws? 1 - 2

9. If you could achieve equivalent or increased fixation strength with a shorter expandable screw, would you choose to use a shorter screw to reduce or eliminate the risk of primary joint penetration?

Yes Likely Maybe Unlikely No

10. How important is it that proximal humerus fracture fixation screws are able to be removed?

Critical Important Neutral Unimportant Irrelevant

11. Do you remove the internal fixation for proximal humerus fracture treatment as a standard procedure after fracture healing is achieved? Yes/No

12. Are there any other areas in the body where you think a removable expandable screw with increased fixation strength can be useful? _____

Other Comments: _____

For further information, additional comments or to organise a demonstration of the technology please contact Russell Nicholls (email: Russell.Nicholls@curtin.edu.au)

EXF Screw – Voice of Customer Survey

		% yes/likely	% maybe	% unlikely/no
Q1a.	Do you believe that increased fixation strength in ORIF surgery for proximal humerus fractures would improve surgical outcomes?	66.7%	14.3%	28.6%
Q1b.	Do you believe that increased fixation strength in ORIF surgery for proximal humerus fractures would reduce the rate of revision?	50.0%	42.9%	14.3%
Q1c.	Do you believe that increased fixation strength in ORIF surgery for proximal humerus fractures would reduce screw overpenetration risk?	33.3%	57.1%	14.3%
Q3.	Would you consider using an expandable screw with positive pre-clinical data?	83.3%	0.0%	14.3%
Q6.	Would the use of expandable screws in ORIF surgery for proximal humerus fracture patients positively effect the rehabilitation procedure for these patients?	33.3%	42.9%	28.6%
Q7.	Do you think that using expandable screws with increased fixation strength would enable internal fixation of proximal humerus fractures in patients with lower bone quality (i.e. older, more osteoporotic patients) that would otherwise be managed nonoperatively or offered arthroplasty?	33.3%	57.1%	14.3%
Q10.	How important is it that proximal humerus fracture fixation screws are able to be removed?	66.7%	28.6%	0.0%

Appendix B Support letters for the project

July 12, 2016

Dear Mr. Nicholls,

I am happy to provide a letter of support for a proposal entitled, "Expandable Fastener for Treating Proximal Humerus Fracture Fixation", being submitted to the Medical Research Commercialization Fund (MRCF) by Curtin University.

We are interested in new technology that reduces revision rates, improves clinical outcomes and ultimately reduces the cost burden of orthopaedic injury on society. Your Expandable Fastener product has the potential to improve fixation and consequently reduce post-operative clinical complications associated with screw fixation failure without increasing the difficulty of revision surgeries, which we believe is critical for surgical adoption.

As I understand it, a major theme in the proposal will be to use the novel expandable fastener to better treat 2- and 3-part and osteoporotic proximal humerus fractures that are likely to have screw fixation failure leading to revision. The basic idea is to replace the conventional screw fasteners with their undesirable properties to reduce clinical failure rates. The clinical problem of fixation failure and revision surgery, particularly in osteoporotic bone, has a significantly negative impact on the orthopaedic surgical market worldwide. There is a compelling need to find better solutions that aligns the interests of the patient, surgeon, payer (health service/insurance companies) and implant manufacturers.

We support the selection of Proximal Humerus Fracture Fixation as a good first indication for development (strategically and commercially). We would consider proximal femur fractures and posterior lumbar fusions as two good secondary indications. However as a platform technology we also see long-term potential for application across our product range, including knee and foot fractures, joint replacements, tendon anchors and neck fusions (cervical anterior).

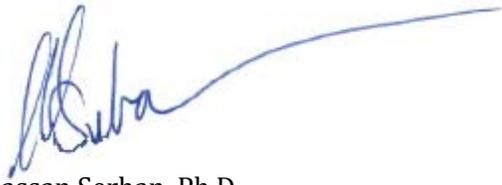
Our companies, DePuy Synthes: Spine, Orthopedics and Trauma (Johnson & Johnson companies), are respectively the largest orthopedic company in the world with a very comprehensive portfolio of orthopedic, spinal and trauma care solutions. The companies' leading solutions align well with the proposed project.

We are interested in evaluating this concept further once the preclinical data is available whilst acknowledging that the expandable fixation device value proposition is not yet fully realized, and the potential is yet to be fully tested, at this stage, which is the purpose of the proposal. Testing may include fatigue testing, in-vivo removal and cadaveric human performance testing.

Mr. Nicholls
July 12, 2016
Page 2

Our collaborations with the group will be in the form of providing data, implants to establish baseline performance, sharing knowledge base and evaluation. If the pre-clinical testing is successful, our company will be willing to take these devices to the next level of testing for potential commercialization.

Sincerely,

A handwritten signature in blue ink, appearing to read 'H. Serhan', with a long horizontal flourish extending to the right.

Hassan Serhan, Ph.D.

Distinguished Engineering Fellow
DePuy Synthes, a Johnson & Johnson Company

Prestige Adjunct Professor
Bioengineering Dept. University of Toledo

HS:jh



October 12, 2016

Mr. Russell Nicholls
Deputy Director IP Commercialisation
Curtin University
Kent St, Bentley, Perth,
Western Australia 6102
Australia

Letter of Support for the Curtin University - Orthopaedic "Expandable Fastener for Treating Proximal Humerus Fracture Fixation" Project.

Dear Mr. Nicholls,

I am happy to provide a letter of support for a proposal entitled, "Expandable Fastener for Treating Proximal Humerus Fracture Fixation", being submitted to the Medical Research Commercialisation Fund (MRCF) by Curtin University. I am the VP of Business Development at Zimmer Biomet. As VP of Business Development of a key industry participant, I routinely evaluate new innovative technologies that are being developed and provide feedback on planned development activities and potential market applications.

While the Expandable Fastener product that was shared with us remains a fairly early stage technology. We are very interested in receiving future updates as you continue to progress development. We support the selection of Proximal Humerus Fracture Fixation as a good first indication for development (strategically and commercially). We would consider hand, wrist, hip, knee, foot, tendon anchor, back fusions (lumbar pedicle) and neck fusions (cervical anterior) as potential secondary and subsequent indications that should be considered for development (strategically and commercially).

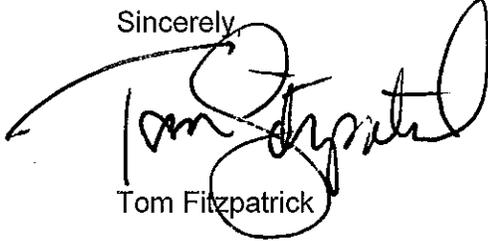
Our company, Zimmer Biomet, is one of the largest orthopaedic companies in the world with a very comprehensive portfolios of orthopaedic care solutions. The company's leading solutions align very well with the proposed project.

As I understand it, a major theme in the proposal will be to use the novel expandable fastener to treat proximal humerus fractures. The basic idea is to replace the conventional screw fasteners with their undesirable properties and failure rates. I feel that there is a need to develop alternate fixation devices. Whilst acknowledging that the expandable fixation device value proposition is not yet fully realized, and the potential is yet to be fully tested, at this stage, which is the purpose of the proposal. The clinical problem of screw pullout and screw loosening and the subsequent risks and costs

associated with fixation failure and revision surgery, particularly in osteoporotic bone, has a significantly negative impact on the orthopaedic surgical market worldwide. There is a compelling need to find better solutions.

We look forward to continuing our ongoing discussions.

Sincerely,

A handwritten signature in black ink, appearing to read "Tom Fitzpatrick". The signature is stylized with a large, sweeping initial "T" and a cursive "F".

Tom Fitzpatrick

VP of Business Development

Zimmer Biomet

17 August 2016

Russell Nicholls
Deputy Director IP Commercialisation
Curtin University

Dear Russell,

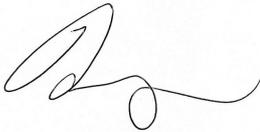
It is my pleasure to provide this letter of support for the Expandable Orthopaedic Screw proposal to the Medical Research Commercialisation Fund (MRCF) by Curtin University.

As you know, I am an experienced and successful entrepreneur in orthopaedic medical devices. In the last 30 years I have developed several innovative technologies and successfully commercialised them. Notably, I founded Advanced Surgical Design & Manufacture Ltd (ASDM) which I listed on the ASX and also have commercialised a number of orthopaedic innovations through deals with large multinational orthopaedic companies.

I am currently CEO of Vestech (www.vestech.com.au), which is an ISO13485 and FDA cleared developer and manufacturer of medical devices and we are ready, willing and able to actively assist with the project. We have an extensive and active network in the sector and specifically in trauma orthopaedic devices.

There is clear potential for the Expandable Orthopaedic Screw to address the large clinical problem of fracture fixation failure, especially in osteoporotic patients. The removability aspect of the Expandable Orthopaedic Screw technology is critical for adoption in the trauma setting and is currently not met by other expandable fasteners on the market. I believe that Proximal Humerus Fracture Fixation is a very good first indication for development and Proximal Femur Fracture Fixation is a very good secondary indication for development. Then, as a platform technology, many other indications can be developed and a whole product range can be commercialised.

We look forward to engaging and supporting the project when you are ready.



Sincerely,

Greg Roger

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E. info@vestech.com.au
Suite 106
275 Alfred Street,
North Sydney, NSW 2060

Regarding 'Orthopaedic Expandable Fastener' NHMRC Development Grant Application from Curtin University and WA Department of Health

To whom it may concern,

The 'Orthopaedic Expandable Fastener' project from the WA Department of Health and Curtin University falls within the scope, interests and eligibility requirements of the MRCF Collaboration. We have been following the development of this project with interest since 2012 and have been delighted to see its evolution based on market feedback. There is a clear need for orthopaedic fixation devices with increased pull out strength, particularly in osteoporotic patients. This clinical need is affirmed by the interest from DePuy and the engagement of Mr Gabriel Lee, a leading local neurosurgeon. Encouragingly, the research program is overseen by an experienced multidisciplinary team of clinicians and engineers with the guidance of the Curtin Commercialisation Office, who have an excellent commercial track record.

The MRCF's investment approach is different from that of many traditional venture capital investors in that we invest in technologies at a very early stage in the development process. Although we require outstanding scientific merit, we do invest once proof-of-concept data is generated, whereas many investors require additional progress along the commercial development path. Further development through the NHMRC Development Grant Scheme, as outlined in this proposal, would bring the technology to a stage where evaluation and potential investment from the MRCF would be considered.

The MRCF was established in late 2007 and has become a successful national initiative that is filling a crucial funding gap and providing 'hands-on' support and expertise for early-stage biomedical opportunities. The MRCF has invested in over 20 early-stage technologies. Ten of these newly created start-up companies have now progressed their technology from the laboratory to human clinical trials, two have launched products around the world and two have been sold to major pharmaceutical companies. To date the MRCF has invested over \$30M into these technologies, with this funding being substantially leveraged through further funding from co-investors, pharmaceutical partners and local and international granting bodies, resulting in a total cash investment into these projects of over \$285M; a significant proportion of which is spent back within the institutes, hospitals and local Australian industry.

Earlier this year the MRCF raised a new \$200M fund, the MRCF3, from local Australian superannuation funds. This fund is now available to take new investments. The MRCF3 has also strengthened our national footprint through increasing our state based capacity. The Western Australian based MRCF Investment Manager, Dr Kath Giles, has a strong background in orthopaedics, having assisted in orthopaedic surgery for the last 12 years. Dr Giles will be managing this project if it makes it into our investment pipeline.

Yours faithfully,



Dr Stephen Thompson
Director, Brandon Capital
Manager of the MRCF Collaboration

Appendix C SZ Device voice of customer surgeon survey

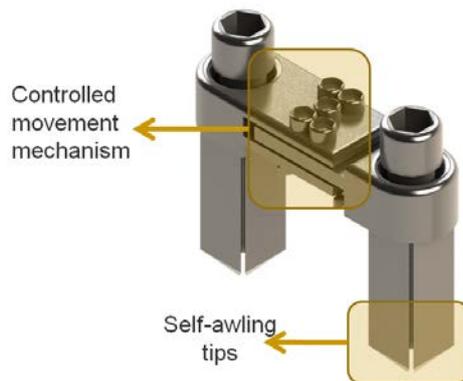
NOVEL SPINE STABILISATION DEVICE

Summary of technology

Researchers at Curtin University have developed a new concept in spinal implants– The SZ Device. It is a single unit allowing an adjustable range of movement for the spine after surgical decompression. It can be inserted into the cervical, lumbar or thoracic spine. It is initially aimed at treating radiculopathy and spinal stenosis.

Key features of the device

1. It is a single integrated device , quick and simple to set up and handle



2. Insertion is simple, the unit is punched into place and the tips are expanded with a simple twist mechanism



3. The range of movement of the device is “set” by removing appropriate pins, allowing up to 6 degrees of flexion and 6 degrees of extension

		Flexion		
		0°	3°	6°
Extension	0°			
	3°			
	6°			

4. If revision is necessary for further pain management, minimally invasive surgery allows the pins to be reconfigured to reduce or increase the range of movement, or if necessary allow no movement

Surgical procedure

The main steps in the surgical procedure to fit the device are :

1. Incision and exposure of the spine
2. Selection of the appropriate sized fastener and associated double-tipped punch
3. Alignment of the spine in the desired position
4. Placing punch on spine surface in correct position and taking initial X ray to check positioning
5. Punching the locating holes and taking second confirmatory X ray (punch is 2 mm x 2 mm and can be removed and repositioned in case of error)
6. Removing the punch and pushing the (larger) fastener into the locating holes
7. Expanding the fastener to lock into position
8. Removing appropriate pins from the fastener to set desired range of movement
9. Closure of incision

Advantages of the device (could leave this as a followup with interested parties to bring down overall size of document)

The advantages of the SZ Device include:

- posterior approach
- single-unit device, quicker and simpler to set up than existing alternatives such as the DePuy AcroMed PEAK system
- safe and technically simple insertion technique, with a number of associated advantages over a more traditional screw mechanism
 - Higher pull-out strength (especially in osteoporotic bone)
 - More flexible placement and less depth, reducing risk of nerve injury.
 - Eliminates risk of back-out or rotation.
 - Passive radial stress may trigger bone regrowth
- controllable range of intervertebral movement via a novel set of removable pins in the centre of the device
- lower cost than traditional fusion and competing surgeries, namely fusion plates, fusion rods or disk replacement implants
- less likelihood of post-operative issues and remedial surgery
- Less likelihood of problems in adjacent vertebrae

Stage of development

The device is currently at the proof of concept stage, with laboratory testing underway and clinical testing planned.

Key questions for medical practitioners

- Is dynamic stabilisation advantageous for the cervical spine?

MM: It's essential.

- Is it an advantage to allow a dynamic intervertebral device to be converted to a fixed device by simple means?

MM: Definitely.

- What procedures do you think would be best served by this device?

MM: Dynamic stabilization of the lumbar spine.

- What characteristics are important in the device :

	Essential	Highly desirable	Desirable	Unimportant
Ease of insertion		X		
Ease of removal		X		
Adjustment at time	X			
Adjustment post-op		X		

- Can you envisage any problems with the device and its intended use?

MM: Resorption at device-bone interface.

- Can you see the device used in other anatomical (non-spinal) procedures?

MM: None at the moment.

SZ Device Surgeon Survey Feedback: Summary of multiple choice responses

	Essential	Highly desirable	Desirable	Unimportant
Ease of insertion	3/9	6/9		
Ease of removal	2/9	5/9	2/9	
Adjustment during surgery	4/9	4/9		1/9
Adjustment post-op	1/9	4/9	3/9	1/9

SZ Device Surgeon Survey Feedback: Summary of written responses

Response #	Is dynamic stabilisation advantageous for the cervical spine?	Is it an advantage to allow a dynamic intervertebral device to be converted to a fixed device by simple means?	What procedures do you think would be best served by this device?	Can you envisage any problems with the device and its intended use?	Can you see the device used in other anatomical (non-spinal) procedures?
1	Essential	Definitely	Dynamic stabilization of the lumbar spine	Resorption at the device-bone interface	None at the moment
2	Possibly	Yes	Lamino-foraminotomy/Laminectomy	Unknown	Unknown
3	Yes	Yes	Foraminectomy	safety	Elbow
4	(No answer)	(No answer)	(No answer)	Failure of the device with lifetime of movement	(No answer)
5	Not always/often not	Simple is always good; not sure stabilising hyper mobile joint	Top-off at end of fusion	Loosening, failure, 'new problems'	No
6	It can be	Yes, if easy to perform	Partial fusions, stabilizations	Failure	Yes, wrist, foot, ankle and hand.

7	No	No	None	Corrosion, fatigue failure and bone resorption	No
8	yes	Yes, in the event of persisting axial pain	Cervical laminectomy, particularly multi-level	Loosening	No
9	It may be	Yes	Spine, foot and ankle, wrist, partial stabilisations and fusions	Difficult insertion, breakage, difficult adjustment, difficulty removing, general operative risks	Spine, foot and ankle, wrist, partial stabilisations and fusions

Appendix D SZ Device poster presented
at the International Society
for Technology in
Arthroplasty Conference
2012

A Novel Implant for Partial Dynamic Stabilisation of the Cervical Spine from a Posterior Approach

INTRODUCTION

Joint instability can be caused by many injuries such as fracture, degeneration, or soft tissue injury. Unstable joints must be stabilised to prevent abnormal or excessive motion which can cause pain and damage to the articulating surfaces, neural system and surrounding soft tissues. Although the concept may be applicable to other joints our preliminary focus is on the Cervical spine in treating neck pain.

BACKGROUND

Neck pain can be caused by pressure on the spinal cord or nerve roots from bone or disc impingement. This can be treated by surgically decompressing the cervical spine, which involves excising the bone or disc that is impinging on the nerves or widening the spinal canal or neural foramen.

Conventional practise is to fuse the adjacent intervertebral joint after surgery to prevent intervertebral motion and subsequent recompression of the spinal cord or nerve root. However this requires either an autograft to be harvested from the patient in a separate procedure or an allograft or synthetic graft to be purchased. Further more fusion procedures cause increased stress on adjacent segments which may lead to Adjacent Segment Degeneration (ASD), a rapid degeneration of the adjacent discs due to the increased stress.

Partial dynamic stabilisation devices (figure 1 below) allow a controlled amount of intervertebral motion (less than physiological, but more than fusion) to reduce the stress on the adjacent segments (potentially preventing ASD) whilst still stabilising the joint, without using a fusion mass. Partial dynamic stabilisation is suitable for treating spinal instability after decompression as well as certain degenerative instabilities and chronic pain syndromes.

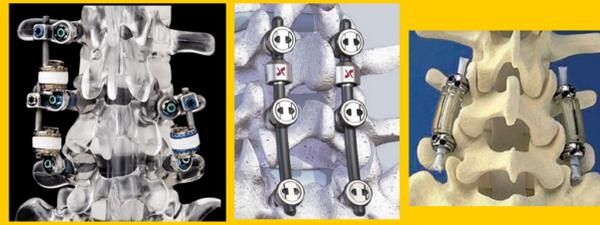


Figure 1: Dynamic stabilisation devices available for the lumbar spine

Posterior dynamic stabilisation systems for the lumbar spine often use the pedicle as an anchor point. However using the pedicle of the cervical spine as an anchor point in the cervical spine is technically difficult because of its small size, angulation and extremely close proximity to neurovascular structures. Consequently the SZ device uses the lateral mass for fixation. However, design of lateral mass fixation systems in the cervical spine is complicated due to the small size of the osseous material available for fixation and the close proximity of neural structures and the vertebral artery. We hope that the design of SZ device will overcome these problems using an integrated one part unit with a simple and safe mono-cortical expanding fastener.

Another potential issue with partial dynamic stabilisation surgery for pain treatment is in ensuring that the restricted range of motion provided by the device does not cause neural impingement and subsequent recurrence of pain. Recurrence of pain is usually treated with a revision fusion. However we hope that the adjustable range of motion feature of the SZ device will solve this problem by allowing more control over the range of motion of the device in vivo and by allowing a simple revision fusion option (reintroduction of a movement pin.)

CERVICAL SPINE DESIGN

In the cervical spine the devices will be implanted on either side of the neck using a posterior approach into the lateral masses to provide either variable mobility dynamic stabilisation or fusion as illustrated in figure 2 below.

INDICATIONS

- Adjunct to laminectomy/ discectomy or central/foraminal decompression
- Mechanical pain (discogenic/ posterior element)
- Inflammatory degenerative arthritis

CONTRAINDICATIONS

- Anatomical variation that affects lateral mass bone stock such as severe osteoporosis
- Other (medical, psychiatric, etc.)

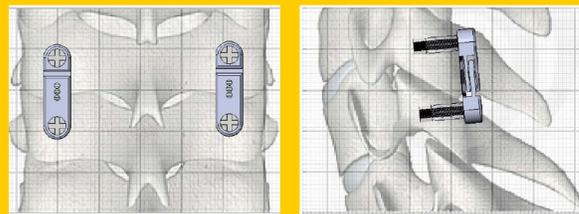


Figure 2: A diagram of the SZ device implanted into the cervical spine before expansion in posterior view (left) and sagittal view (right).

PROCEDURE

1. The specially designed double awl is aligned with the lateral masses (a)
2. The awl is struck with a surgical mallet (b) to penetrate the lateral masses, leaving a hole (c)
3. The SZ device is introduced into the pre-hole (d)
4. The SZ device is expanded by rotating the expansion screw (e)
5. If required, pins are removed from the device (f) to control the range of motion returned.

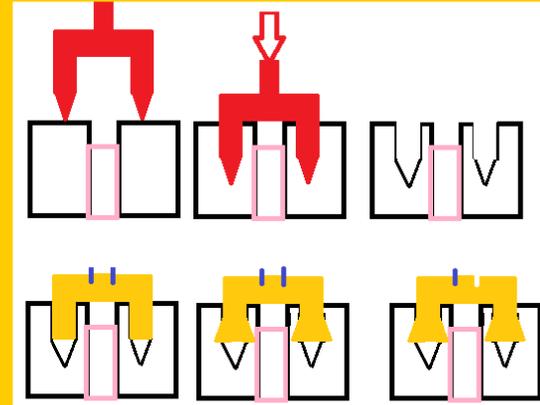


Figure 3: The procedure of implanting the SZ device

ONE PART DEVICE

The SZ device is designed as a single-unit device with fasteners integrated into the stabilising element. This simplifies the surgical procedure as it obviates the need to align the fasteners and stabilising element and allows both holes to be created at the same time using an awl. Consequently the implant procedure is compatible with a minimally invasive approach. A single part device with a simple implantation procedure also reduces the tools and implant stock required. Figure 3 below shows the device with the instrumentation required to install it.



Figure 4: The SZ device kit comprises only the SZ device itself and a custom two pronged awl.

EXPANDABLE FASTENERS

Expanding fasteners are necessary in order to integrate the fastener into the stabilising element however expanding fasteners have several distinct advantages over screws. Firstly they provide higher rotational stability preventing back-out, a typical screw failure mechanism. Secondly expanding fasteners have the potential for superior performance in terms of pull-out strength and implant rigidity (demonstrated in bench-top laboratory testing). This superior performance may allow shorter implants increasing the safety of the procedure by avoiding damage to the intervertebral artery or nerve root. Lastly expanding fasteners also have the benefit of providing passive radial stress around the fastener encouraging faster and more effective bone remodelling. The remodelling process in screws is hindered by bone necrosis caused by thread friction (reference) and limited radial stress. This may be especially important in osteoporotic cases where increased bone density around the fastener may be critical to prevent fastener failure.



Figure 5: Preliminary design of an expanding fastener

ADJUSTABLE RANGE OF MOTION

By removing and inserting pins into the device during surgery the surgeon can control the range of motion of the device and therefore the spine. In this manner the surgeon is able to decide during surgery to perform either a fusion or dynamic stabilisation. If dynamic stabilisation is chosen the surgeon can control the magnitude of the range of motion and the direction of that range of motion (flexion or extension or a combination of both). Additionally, this allows easier revision surgery if pain reoccurs as the range of motion of the dynamic construct can be reduced or eliminated by reintroducing pins. Figure 6 to the left demonstrates the nine different configurations and consequent range of motion options available to the surgeon. The range of motion is between 6 degrees of flexion and 6 degrees of extension.

		Flexion		
		0°	3°	6°
Extension	0°			
	3°			
	6°			

Figure 6: The nine different configurations of the SZ device provide a choice of static or dynamic stabilisation with variable mobility

FUTURE WORK

1. Computer Tomography based Finite Element Modelling investigation to determine the allowable radial loading of the lateral masses in the cervical spine before lateral mass bursting
2. Optimising the design of the expanding fasteners using Finite Element Analysis and the predetermined safe expansion distance
3. Validating the performance of the optimised expandable fasteners against screws in pull-out testing in sawbones
4. Optimising the design of the adjustable range of motion mechanism using finite element analysis
5. Validating fatigue performance of the adjustable range of motion mechanism
6. Validating the performance of the entire device in cadaveric bone against competing systems
7. Investigation into other applications of the concepts such as in the lumbar spine, mid foot and fracture fixation in long bones.

LUMBAR SPINE STABILISATION SYSTEM

The concept of providing an adjustable range of motion can also be applied to dynamic stabilisation and fusion in the lumbar spine by altering the form of the device to a rod and using a conventional pedicle screw fixation system. A preliminary design is shown in figure X below. The next stage of this project will be to manufacture some prototypes and test the fatigue resistance of this system.



Figure 7: A preliminary design of the SZ-Lumbar device

MID-FOOT FRACTURE FIXATION SYSTEM

The concept of a one-part unit with integrated expandable fasteners can also be applied to fracture fixation in the mid-foot. In this case the device can be either static or partially dynamic to prevent stress shielding and implanted in a minimally invasive procedure.

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CONTACT

- For more information about the device, please feel free to contact Matthew Oldakowski on mobile (0431 939 585) or email (matthew.oldakowski@postgrad.edu.au).
- For information about investing in the project, please contact Russell Nicholls at the Curtin Office of IP Commercialisation on mobile 0410 285554 or email (russell.nicholls@curtin.edu.au)

Appendix E National Health and Medical
Research Council
Development grant scope of
works

A. Research Proposal

A1. Aims

The investigators have developed an internationally novel and commercially innovative expandable fastener (EXF), for use in orthopaedic surgery to attach implants to bone (Fig. 1). The EXF can provide **significantly increased fixation strength** compared to conventional screws with minimal change to the surgeon's operating procedure and **without compromising removability** during revision surgery. Superior mechanical performance can reduce the risk of clinical failure, allow a reduction in implant length and allow earlier rehabilitation resulting in improved patient outcome.



Figure 1: The EXF prototype, manufactured through 3D printing, is expanding by advancing a grub screw.

The proposed research will address the commercial barriers to the use of the EXF and will conduct all the testing required to initiate a first-in-human clinical trial for the first target application, proximal humerus fracture fixation. It is expected that within a five-year time frame, the project will have regulatory approvals based on the testing conducted in this grant and a two-year first-in-human clinical trial that will have been performed immediately after the grant. After this point the project will seek a licensing deal with a large implant manufacturing company.

The aims of this research proposal are as follows:

- 1. To develop an expandable fastener platform technology with superior fixation strength and stability to significantly reduce the risk of clinical failure and subsequently reduce the financial impact of revision surgery and improve patient outcome.**
- 2. To establish the value of the developed technologies for the target applications. i.e. increase in performance and expected reduction in clinical complication.**
- 3. To develop the fastener ready for commercialisation.**

The first specifically targeted application for the EXF is proximal humeral fractures (fractures of the shoulder). These surgeries have significant revision rates documented to be related to poor fastener fixation and fastener malplacement (Sproul et al. 2011, Owsley & Gorczya 2008, Sudkamp et al. 2009) and follow-up times are relatively short and so this is therefore a commercially attractive market entry. The second targeted indication is Anterior Cervical Corpectomy/Discectomy and Fusion surgery (fusion of the front of the neck). This surgery also has a significant failure rate, especially for multi-level fusions and a significantly larger commercial market size (Sasso et al. 2003). However there is more competition and regulatory approvals are more onerous than for the primary application.

As a platform technology, the EXF can be adapted to suit many different applications throughout the body including lumbar pedicle fixation for lower back fusion, fracture reduction in fractures of the foot and hand and fracture fixation in the epiphysis of long bones.

A2. Background

Orthopaedic screws are widely used to affix orthopaedic implants to bone in order to stabilise fractures and fuse joints. However screw loosening, back-out, pull-out, stripping and misplacement, causing over-penetration that can damage joints or nerves, are significant problems, especially in older patients with osteoporosis (Owsley & Gorczya 2008, Sasso et al. 2003). These complications can result in serious clinical consequences which creates a significant burden for the individual and the health care system.

The revision rate of proximal humerus fracture fixation, our primary indication is reportedly 14% for the general population in a systematic review by Sproul et al. (2011). The most common complication is varus malunion (16% of patients) which can be caused by insufficient screw

fixation strength. Another complication is damage to the shoulder joint due to over-penetration by the screw. Sudkamp et al. (2009) reported intraoperative screw perforation of the humeral head to be the most common complication in their study (14% of patients). Complication rate in older patients with osteoporosis are also higher due to loss of fastener fixation in low quality bone. Owsley & Gorczyca (2008), observed a much higher percentage of complications in the group of patients older than 60 years, 57% compared to 22%. Proximal humerus fracture fixation surgery is very expensive (approximately AUS\$22,000) and consequently revision surgeries cost the Australian health care system at least \$24m per year, without considering the loss of time and trauma to the patient related to revision surgery or if revision to a total joint replacement is required (Kim et al. 2012, Handschin et al. 2008). Improved fixation strength can also potentially allow earlier rehabilitation which can be critical for athletes and patients with work-related injuries.

In multi-level Anterior Cervical Corpectomy and Fusion (ACCF) of the cervical spine, significant revision rates have been reported in the literature, from 6.8 to 100% for 3 level corpectomy (Yu et al. 2014, Daubs 2005). Several authors and clinicians have recommended that an additional posterior fusion be performed in these cases to address this unacceptable revision rate (Yu et al. 2014, Daubs 2005). This indicates that increased fixation strength and stability could eliminate a second surgery, significantly reducing the risk and cost to the patient, surgeon and payer (government and/or insurance company). This application was the focus of our preliminary study. However, based on our market analysis and conversations with established implant manufacturers, the focus has now shifted to the proximal humerus market as an entry point and the spine market as a secondary market. The proposed research plan will address the primary and secondary markets.

Commercial Advantage: Superior and more reliable performance allow a reduction in length (penetration depth) which corresponds to an inherent reduction in surgical risk associated with over penetration.

The fixation strength of a fastener can be objectively assessed by well-defined experimental protocols that test screw failure under various loading conditions. Preliminary testing of the prototype EXF that was designed for spine applications, compared to conventional screws in sheep vertebral body, demonstrated a 41% ($p < 0.001$) increase in failure force (see Fig. 2) (Oldakowski et al. 2016^{CIE,F,G,I,AI}). Further analysis demonstrated that the EXF was also affected less than conventional screws by lower bone quality such as thinner cortices and deterioration of bone quality (Structural Model Index). This is reflected in the 47% reduction in standard deviation for the EXF which demonstrates greater reliability of performance across a variable bone quality (Oldakowski et al. in press^{CIE,F,G,I,AI}). These results, consistent with those of King & Cebon (1993) are clinically important as systemic and localised loss of bone density is related to ageing and pathological study cohorts.

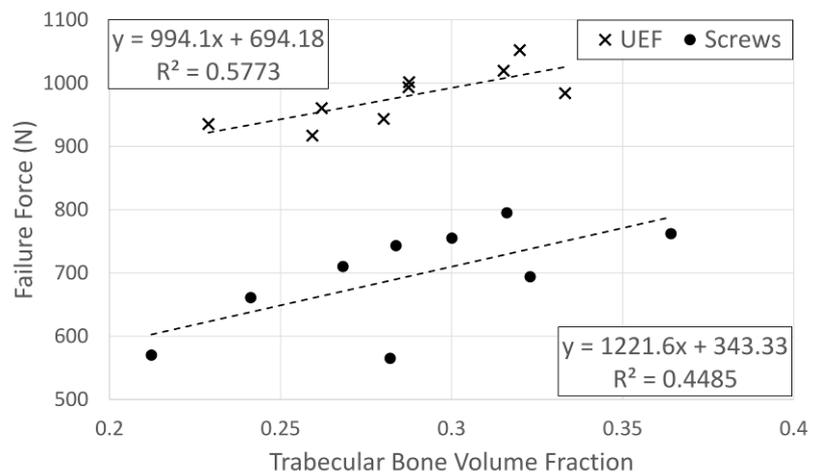


Fig. 2. Linear regression comparing the correlation of failure force and bone density. (Oldakowski et al. 2016)

The EXF has the potential to improve the reliability of fixation in a high risk group and consequently greatly reduce revision rate and the subsequent healthcare burden to society.

Expansion stress can also improve osseointegration and thus further improve fastener fixation strength over time. An in-vivo study in ovine long bones with expandable rivets by Zeiter et al.

(2004) demonstrated osseointegration earlier, closer to the bone-implant interface and over a wider area compared to a conventional orthopaedic screw.

Although other expandable screws have demonstrated increased fixation strength (Chen et al. 2014) they are not desirable to surgeons because they are difficult to remove immediately after the operation and impossible to remove after the implant has been in the patient for a period of a few months and the bone has grown into the space inside the fastener. This is not acceptable as fastener removal is frequently required in cases of infection, nerve impingement or soft tissue irritation and when implanting other devices such as joint prostheses near the fastener. Based on a study by Hanson, Werken and Stengel (2008), 37% of orthopaedic surgeons believe that removal of orthopaedic implants should be routine. Removing an embedded expandable fastener would require extensive bone destruction which represents a very major and invasive surgery for the patient, typically associated with significant blood loss and prolonged recovery periods, and also very stressful and potentially litigious for the surgeon.

Our market research suggests that if surgeons can improve fixation strength without compromising on removability or changing their surgical procedures significantly then they are likely to adopt the EXF.

The EXF addresses this problem by expanding in a way that the deformation is both entirely elastic and occurs without leaving any ‘gaps’ within the mechanism for the bone to grow into (see Fig. 3). This means that, unlike other expandable fasteners where bone growing into the mechanism can prevent contraction, even after significant period of time in the body, the EXF can be unexpanded by simply removing the expander pin. The expansion arms will return to the original contracted orientation ready for simple, reliable removal like a conventional screw.

This functionality is achieved by two key propriety design features. First of all, the expansion arms are designed to remain within the elastic limit of the material at full expansion (see Fig. 3.). This allows the fastener to open without permanently deforming the fastener. These features, among others, are included within the investigators’ first patent (WO 2014/028981 A1) and second patent (WO 2015/123726 A1). Secondly, the profile of the gaps between the expansion wings to prevent bone ingrowth will be protected by the investigators third patent that is currently in preparation.

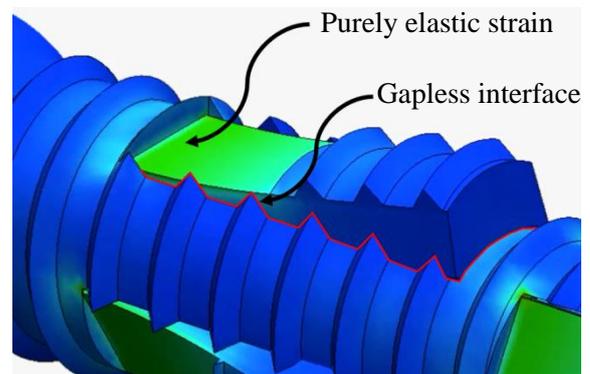


Fig. 3. Key design features of the EXF

A3. Research Plan

The research plan outlines the technical barriers to commercialisation that the investigators will address using a robust scientific approach. The first stage establishes the mechanical performance of the EXF compared to conventional screws by mechanical tests on human cadaveric bone and an in-vivo animal study to determine the biocompatibility, the removability after a significant period in the body and the effect of passive radial stress on osseointegration and subsequently on the failure forces. The second stage will include design refinement of the product ready for manufacturing at a Good Manufacturing Practice (GMP) accredited facility and a series of mechanical tests based on ISO standards to establish the mechanical risk safety margin for the product. The research plan is designed to gather all information required for the first-in-human clinical trial phase following conclusion of the grant period.

Stage 1 – Establishing the Mechanical Performance of the Expandable Fastener

A3.0 Common methodologies

For brevity this section describes the methodologies that are common to all of the experiments.

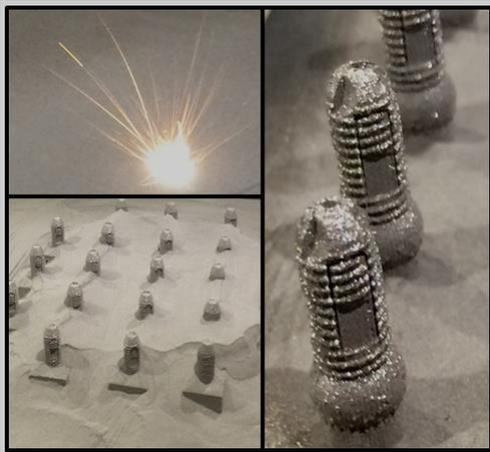


Fig. 4. SLM manufactured prototypes

A3.0.1 Implant acquisition: The EXF prototypes will be manufactured from Ti6Al4V using Selective Laser Melting (SLM), on the Realizer SLM100 machine by Professor Tim Sercombe^{CIG} at the University of Western Australia (UWA) (see Fig. 4). Control screws (industry standard) with a matched diameter to the tested fastener will be obtained from the collection of commercial sample orthopaedic screws at Medical Engineering and Physics at Royal Perth Hospital (RPH) under the guidance of Rob Day^{CII}. Alternatively, orthopaedic screws can be obtained from an implant company (Depuy Synthes) who have previously provided screws to the investigators for a related project.

A3.0.2 Bone imaging: All bone samples will be characterised using Micro-CT by Mr M Oldakowski^{CIE} at the Centre for Microscopy, Characterisation and Analysis (CMCA), UWA using the Xradia Versa XRM before insertion of the fasteners and after mechanical testing (see Fig. 5). The initial scans ensure that there is no significant difference between the bone morphological properties for each sample set and allow analysis of the relationship between bone morphological properties and mechanical performance results. Post-test scans will also allow analysis of the failure mode. Bone morphological properties that have demonstrated significant correlation with fastener pull-out strength in previous studies include Bone Volume Fraction, Cortical Thickness and Structure Model Index (Poukalova et al. 2010, Ab-Lazid et al. 2014, Oldakowski et al. 2016)



Fig. 5. Geometry generated from high resolution CT data

A3.0.3 Ethics approval: Ethics approvals will be sought from the Curtin Human Research Ethics Committee for the studies involving human material (A3.1) and from the Curtin University and Murdoch University Animal Ethics Committee for the studies involving live animals conducted at Murdoch University School of Veterinary and Life Sciences (A3.2). The investigators have had approval for a similar study using human cadaveric bone and similar animal studies have been conducted in many other centres previously, and so the investigators are confident that with appropriate experimental design, ethics approval will be granted for the proposed experiments.

A3.1 Comparison of the expandable fastener against orthopaedic screws in human cadaveric bone

A3.1.1 Purpose: To determine the axial pull-out strength, stability to transverse loads (simulating plate loading on fasteners) and resistance to shear loading (susceptibility to penetrate joint) of the EXF compared to conventional screws in human cadaveric proximal humerus bone.

A3.1.2 Description of experiment design: Fresh-frozen human cadaveric proximal humeri will be obtained from Clinical Training & Evaluation Centre (CTEC) at UWA. Each proximal humerus will be excised, all soft tissues will be removed and the sample will be Micro-CT scanned at CMCA as described in section A3.0.2. The bone morphology of the samples will be analysed to categorise the bone as normal or osteoporotic and covariant analysis will be conducted to determine the influence of bone morphological properties on the biomechanical performance of the fasteners. Samples with severe

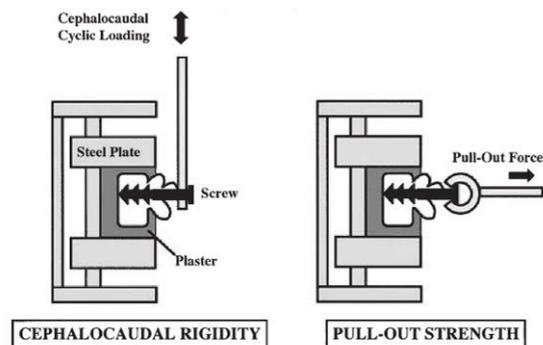


Fig. 6. Cyclic (left) and pull-out (right) testing (Taniwaki et al. 2003)

bone pathology will be excluded. Sample screws and expandable fasteners will be obtained as described in section A3.0.1. All screws and fasteners will be inserted by an experienced orthopaedic surgeon (Prof M Kuster)^{CIA} using established techniques. All mechanical testing will be conducted on the Instron 5566 MicroTester located at Medical Engineering and Physics at RPH with the Assistance of Ms I Oldakowska^{AI} under the supervision of Mr R Day^{CIH}. The specimens will be randomly assigned to groups a, b and c and subjected to the mechanical tests described below. Each group will have equal number of right and left humeri.

- a) Axial Pull-Out – A screw and an expandable fastener will be inserted into either the anterior or posterior half of each proximal humerus bone. The pairs will be block balanced randomised to the anterior or posterior portion, allowing the specimen to serve as its own control group. The proximal humerus will be CT scanned after screw and fastener insertion to ensure both trajectories do not pass the anterior/posterior midline. The specimens will be mounted and secured onto the Instron mechanical tester as shown schematically in Fig. 6 (right) and subjected to axial pull-out until failure. Pull-out force will be evaluated and correlated to bone morphological parameters. The order of testing will be alternated between screws and the EXF to reduce the potential influence of test order in the statistical analysis.
- b) Stability (toggling) testing – The experimental design will be based on a study by Brasilience et al. (2013). The samples will be prepared as described above (A3.1.2(a)). Transverse loads (see schematic in Fig. 6 – left) will then be applied cyclically between tension and compression at a rate of 2.5 Hz for 2500 cycles per round (the order of testing will be alternated). The load will be incrementally increased every round until the fixation is considered “failed”. A pilot study will be conducted prior to the full study to determine for the particular experimental methodology a suitable initial peak compressive and tensile load (25% of the transverse failure load), incremental load increase and failure criteria. Load/displacement data for each cycle will be recorded continuously until failure and initial transverse stiffness, changes in transverse stiffness over time and the number of cycles to failure will be calculated. The failure mode of both constructs will be analysed using Micro CT as described in section A3.0.2.
- c) Cut out testing – The testing methodology will be based on a study by Erhardt et al. (2012)^{CIA}. An unstable intra-articular OTA type C fracture at the anatomic neck will be created. The proximal humerus will then be reassembled and fixated by either the EXF or screw and plate system according to established techniques. The specimen is then mounted on a customised jig to allow a predetermined amount of flexion/abduction, as shown in Fig. 7. The axial loading on the joint will be provided by an anatomically shaped Plexiglass glenoid as shown in Fig. 7. The sample will be tested with cyclical sinusoidal compressive loading at a pre-determined frequency and number of cycles per round, based on the study by Erhardt et al. (2012). The load will be incrementally increased every round until visible perforation of at least 1 screw occurs. Load, displacement and cycle count will be continuously recorded until screw perforation occurs. Correlation analysis between the load and cycle count and bone morphological parameters will be conducted.



Fig. 7. Cut-out testing experimental set-up (Erhardt et al. 2012)^{CIA}

A3.1.3 Test subject and control: The proximal humerus EXF and control screws will have 4mm outer diameter, a common size in this type of surgery. The EXF and industry standard screws will be obtained as outlined in A3.0.1.

A3.1.4 Sample-size: A total of 48 proximal humeri will be harvested from 24 fresh frozen cadavers. The sample sizes

group	sample size	# of humeri
a	8	8
b	16	16
c	12	24
Total		48

Table 1. Experimental sample sizes

shown on Table 1 is calculated based on the results from previous study (Erhardt et al. 2012, Wan et al. 2010, Oldakowski et al. 2016) to achieve p-value of 0.05 and power level of 90% using a 2 sample, 2 sided equality test.

A3.1.5 Statistical methods: Accounting for distribution assumptions, an independent, two tailed Student's t-test is most likely to be used to determine the significance of differences in mechanical performance. Similarly bone properties of the two sample groups will be assessed for systematic differences. Levene's test (or other similar statistical test) will be used to determine whether the variances of two fastener groups are significantly different. Inter-correlation between bone morphology parameters and recorded mechanical parameters will be assessed based on paired Pearson coefficients and the significance will be calculated using a two-tailed test. All tests will use a $p < 0.05$ significance threshold and a Holm-Bonferroni correction for multiple comparisons if appropriate.

A3.1.6 Expected outcomes: Demonstrate superior biomechanical performance in axial pull-out, immediate stability and susceptibility to cut-out of the EXF compared to screws in cadaveric bone. This will demonstrate the ex-vivo performance of the EXF compared to screws under simulated physiological conditions in human proximal humeral bone. CT scanning of the bones will also allow analysis of possible wear debris during expansion and under simulated physiological loading for further development of a clinical safety case.

A3.2 Animal in-vivo study

A3.2.1 Purpose: To mechanically compare the stability and pull-out strength, and qualitatively compare the osseointegration of the expandable fasteners against screws after osseointegration in ovine spine over three time periods. Furthermore, to demonstrate removability with minimal bone destruction of the EXF after 6 months *in-vivo*.

A3.2.2 Description of experiment design: The experimental design will be similar to a study by Wan et al. (2010) and will be conducted at Murdoch University School of Veterinary and Life Sciences. Animal in-vivo study using sheep is conducted for the spinal application as there is already an established protocol and there is no animal model for the proximal humerus application. Furthermore, the mechanical testing result from this study is transferrable to other applications. Surgery will be performed by Prof Lee^{CIH}, with the assistance of Assoc Prof Martin Cake^{AI} from Murdoch University College of Veterinary Science, to implant 4.5 mm EXF and screws (control) in the lumbar pedicles (L1-L5) of 21 sheep. The screws and EXF will be randomly assigned to either the left or right pedicle in each vertebra, allowing each specimen to serve as its own control. After a period of recovery, the sheep will return to normal activity before 7 sheep being sacrificed at 6, 12 and 24 weeks. Post sacrifice, the vertebrae will be harvested, cleaned of all soft tissues and Micro-CT scanned at CMCA as described in section A3.0.2.

Axial pull-out and stability testing will be performed as per section A3.1.2 above. Image analysis using a Micro-CT and transmitted light microscopy will compare osseointegration between the EXF and screws (control) over time. This will involve comparison of the density and bone distribution around the EXF and screws using a similar methodology to Wan et al. (2010) (see Fig. 8). Histology analysis will be conducted by Dr Jian-Ping Wu^{AI}. The statistical methodology will be the same as described in section A3.1.5 above.

EXF removability test will be conducted on two additional sheep with the same implantation configuration as described above, implanted at the same time and the sheep sacrificed at 24 weeks to allow sufficient time for significant osseointegration to occur. Post sacrifice, harvesting and imaging using Micro-CT, the screws will be removed using a torque screwdriver so that the

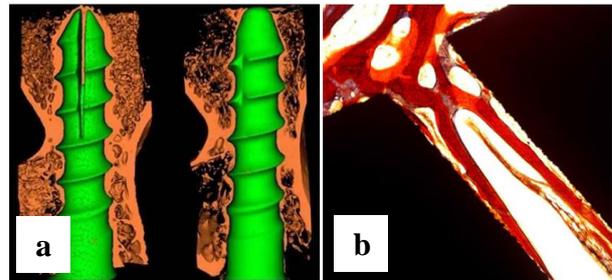


Fig.8. Images from an in-vivo animal study by Wan et al. (2010) (a) Three-dimensional reconstructed micro-CT of bone remodelling with expandable screws. (b) Histology image of the screw and bone interface.

maximum torque applied while removing the screws and EXF can be recorded and the result quantitatively analysed (n=10). It is expected that the torque required to remove the EXF from the sheep bone will not be significantly higher than the torque required to remove the screw. Image analysis of the bone and EXF using a Micro-CT will also confirm if the EXF has elastically returned to its original state and therefore have comparable affect to screw to the surrounding bone after removal.

A3.2.3 Sample Size: The flowchart illustrates the stages of the experiment and the number of samples required for each stage. The sample size is calculated based on the result from previous studies (Oldakowski et al. 2016, Wan et al. 2010) to achieve p-value of 0.05 and power level of 90% using a 2 sample, 2 sided equality test. It is estimated that a 40% increase in axial pull-out force and a 20% increase in number of cycles until failure during the stability test will be detected which will demonstrate performance superiority of the EXF compared to conventional screws.

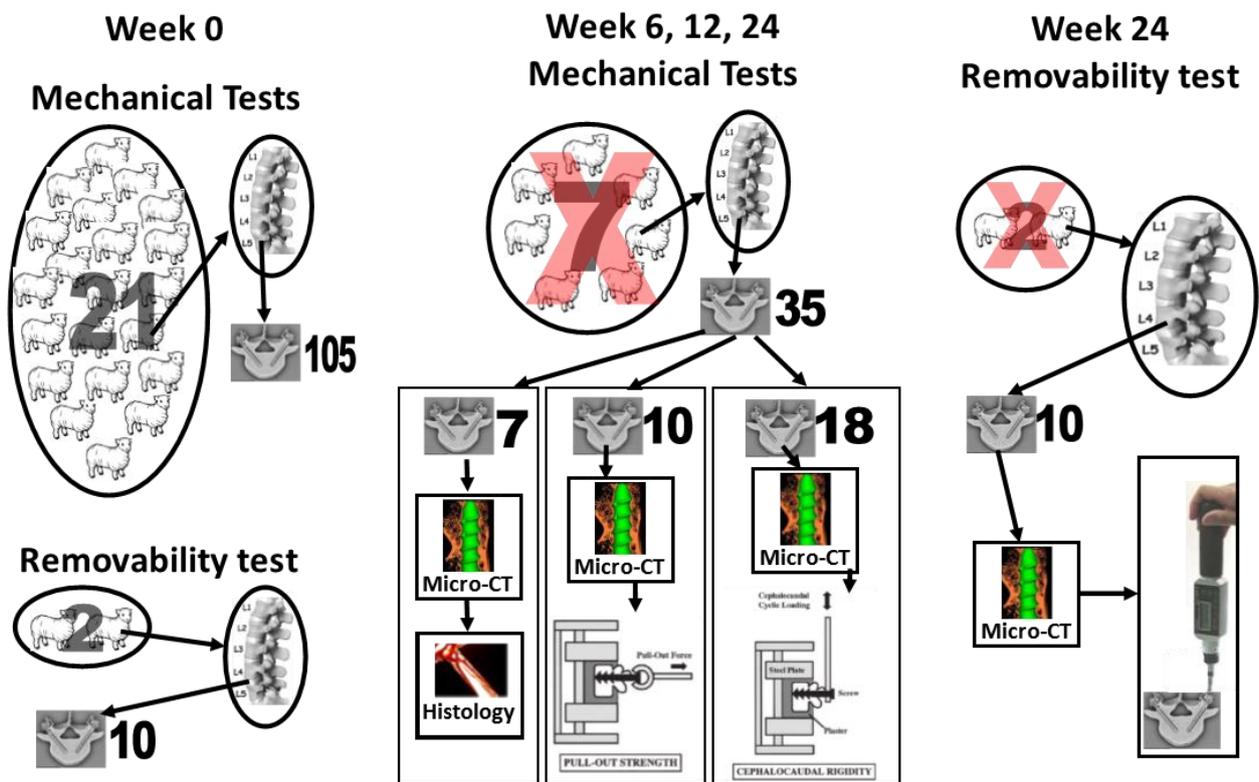


Fig. 9. Animal in-vivo experimental plan schematic

A3.2.4 Expected outcomes: Compare quantitatively the osseointegration between the expandable fasteners and the screws over several time steps to demonstrate the effect of passive radial stress and the effect of increased osseointegration on the pull-out strength. Demonstrates the biocompatibility in-vivo of the expandable fasteners made out titanium alloy Ti6Al4V manufactured using SLM and ensure there are no wear debris after implant removal. Demonstrate removability of the fastener after long term implantation.

Stage 2 – Final Product Design and Manufacturing

A3.3 Final Product Design

A3.3.1 Purpose: To finalise the design of the EXF and plate system for the primary indication of fracture fixation of proximal humerus

A3.3.2 Description: Using computer aided drafting (CAD) software, the design of the EXF will be finalised based on the data gathered during stage 1 of the experimental plan.

A3.3.3 Expected outcomes: A manufacturing data package for the EXF and plate system.

A3.4 Manufacturing

A3.4.1 Purpose: Manufacture final product design at a facility with Good Manufacturing Practice (GMP) accreditation

A3.4.2 Description: Work with a suitable manufacturer to ensure the design can be manufactured. Manufacture 15 fasteners and 3 bone plates for final product testing as per ASTM standards. Several manufacturers with GMP accreditation and ISO 13485 certification have been contacted and preliminary quotes for current design has been obtained to form the basis of approximate cost. One of the manufacturers that have been contacted is Austofix, which has a proven track record in manufacturing orthopaedic trauma devices such as the Austofix VRP Volar Radius Plate.

A3.4.3 Expected Outcomes: Final product of expandable fastener and plate system for proximal humerus fracture fixation manufactured under ISO13485 standard.

A3.5 Establish Mechanical Risk Safety Margin of Final Product

A3.5.1 Purpose: To establish the mechanical risk safety margin of the expandable fastener and plate system by conducting biomechanical testing to satisfy the relevant ASTM International standards outlined below.

A3.5.2 Description of experiment design: The EXF and plate construct will be tested at RPH. An industry standard screw and plate system for proximal humerus fixation from Zimmer or DePuy Synthes will be used as a control. Each test will be conducted using 3 sample fasteners. Listed below are all the testing required to satisfy the ASTM International standards to prove device safety for the regulatory approval process:

- Fastener Static and cyclic axial/bend testing (ASTM F543)
- Fastener Static and cyclic torsional testing (ASTM F543)
- Fastener pull-out testing (ASTM F543)
- ASTM F382 – metallic bone plates – 4 point bending test to check load to permanent deformation, stiffness, and fatigue strength (load based or number of cycle based)

A3.5.3 Expected outcomes: The expandable fastener and plate system satisfies all required standard testing to be approved for first-in-human clinical testing.

A4. Timeline

STUDY	Year 1	Year 2	Year 3
A3.1 Biomechanical testing on cadaveric human bone			
A3.2 Animal In-vivo study			
A3.3 Final product design			
A3.4 Manufacturing of final product			
A3.5 Mechanical testing of final product			

The timeline includes a buffer period to take into account potential delays in conducting the outlined study, especially the animal in-vivo study given the nature of dealing with live animals. However the risk of the animal in-vivo study extending beyond the scheduled period is low as the study is a variant on a published protocol and the team are very experienced with studies involving sheep. Furthermore, the final design phase can be started with preliminary data from the animal in-vivo study (after 6 weeks of implantation) and subsequently run in parallel.

A5. Outcomes and significance

The anticipated outcome of this research project is for the EXF technology to demonstrate the following commercial advantages over conventional screws:

1. Superior immediate biomechanical performance in terms of fixation strength and stability allowing a reduction in screw length to reduce the risk of overpenetration;
2. Superior long-term biomechanical performance through enhanced osseointegration induced by the therapeutic benefit of the expansion stress;
3. Biomechanical performance that is more reliable across a wide range of bone quality, especially in osteoporotic bone; and
4. Ease of removability by ensuring the device can be unexpanded and inhibiting bone in-growth.

After successful completion of the research plan, all the required benchtop testing will have been performed, ready for a first-in-human clinical trial. Clinical trial will be facilitated by the partner institutions, St John of God Hospital Subiaco and Royal Perth Hospital. Following successful clinical trials the project would seek a license, for the primary application (shoulder fractures), with an implant manufacturing company. The project is attractive to a potential partner because we would have demonstrated a clear competitive advantage over screws, in a large and commercially attractive market, in an indication with a strong unmet clinical need. The project will have eliminated all the major technical risks and mitigated many of the commercial risks prior to a clinical trial. Estimated deal size, based on previous acquisitions and mergers is \$100-300m.

The Australian population is aging and this is increasing the average age of patients and consequently the likelihood of osteoporosis. Utilisation of the EXF in these patients would improve surgical outcome by reducing the incidence of screw loosening and over-penetration and the subsequent complications for the patient such as mal-union of the fracture and penetration of the shoulder joint. It would also allow surgeons to treat patients who, due to low quality bone, are untreatable with conventional screws. Reducing complications, allowing earlier mobility and allowing older patients to be treated will support the increasing expectations that Australians have of the ability to enjoy an active and typically Australian lifestyle, even during old age and injury. Furthermore revision currently costs the Australian healthcare system at least \$24m each year and this can be significantly reduced by minimising screw related complications.

Successful execution of this project will build Australia's future capability for research and translation by fostering multidisciplinary and international collaboration between St John of God and Royal Perth Hospitals, Curtin University, the University of Western Australia and the world leading orthopaedic implant development team at University College London^{CIC.D}. After licensing the technology for our primary indication, proximal humerus fractures, we will begin clinical testing of the EXF for our secondary application, neck fusions, which has a larger market size. After this multiple opportunities for further extension of the technology exist. A spin-out company, given the funds obtained from a successful licensing deal, will then be able to support the development of multitude of innovative ideas that clinicians all over Australia have to improve their patient's outcomes. The scientific significance of this research is in understanding the effect of expansion on the mechanical performance of expandable fasteners before and after osseointegration. As far as the team is aware, the EXF will be the first orthopaedic fastener made through an additive manufacturing process, which could be cost effectively manufactured in Australia.

Peter Woodland, an orthopaedic surgeon and President of the Spine Society of Australia *“strongly recommends funding support for the ... expandable fastener project”* and that *“initial results have indicated significantly higher failure force on pullout strength compared to conventional bone screws”* and that consequently the project is *“extremely worthwhile, which has significant potential for the advancement of spine fixation techniques around the world”*. Full text of the support letter can be obtained on request.

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C. Commercial Potential

Competitive edge: The EXF can provide increased fixation strength, especially in osteoporotic bone with reduced length to comparable conventional screws. Consequently the EXF can reduce the incidence of screw loosening **and** primary and secondary overpenetration of the shoulder joint, either of which would necessitate a revision surgery. This can be achieved **without** compromising on removability, which surgeons view as **critical**, or modifying their surgical procedure. We believe that this represents a **very compelling proposition for surgeons**, by providing their patients better outcomes and increasing the age of patients that they can treat **and payers** (insurance companies, health systems), by reducing the revision rate, which is currently very high (14% for general population) and significant waste of resources (~\$25M in Australia each year). This is an internationally competitive edge over all other expandable fasteners which are **not** removable after bone has grown into the expanded fastener, which **severely** limits their applicability and adoption.

Market analysis: Orthopaedic devices is a multi-billion dollar market dominated by large implant companies such as DePuy Synthes and Zimmer. Each of these companies creates independent platforms with limited commercial design redundancies that allow each platform to interchange instrumentation. The global orthopaedic trauma devices market was valued at US\$5.7 billion in 2013 and is expected to grow at a CAGR of 7.2% from 2014 to 2020, to reach an estimated value of US\$9.4B in 2020¹). It is estimated by that US\$6B in screws are sold

annually in the orthopaedic device market². We estimate that our EXF, could ultimately capture an extremely large market, **US\$300M to US\$600M** (or 5% to 10%) of this market and potentially much more as a platform technology in the hands of one of the large players in the market if utilised over their entire trauma range.

Our primary indication, proximal humeral fractures, has an incidence of 61 per 100,000 of population per year and an estimated global market size of **US\$122.7M** for proximal humerus hardware alone. Average cost per surgery is US\$16,300 including US\$830 for the hardware. Fig. 10 illustrates the relative market sizes for the various indications that the EXF may be developed for, with market penetration strategy and relevant commercial hurdles.

Commercial development pathway: The major milestones of the commercialisation strategy for the EXF project are outlined in Fig. 11 below, with an indication of the potential deal flow, based on our commercial experience, where each point represents a possible deal that could be made with a commercial partner. Clearly, as more technical, commercial and regulatory hurdles are eliminated the potential size of a deal becomes high, as indicated by the increased dot size. However it is our understanding, based on extensive commercial consultation that implant manufactures prefer to make deals at a later stage, preferably after first in human clinical testing has been performed.

The medical implant industry is highly regulated by regulatory bodies such as the FDA in the US, the European Commission to obtain the CE Mark in Europe and the TGA in Australia. The EXF is classified as class II medical device under the FDA classification, and class IIb based on the European Commission Directive 93/42/EEC and the TGA classification. Global harmonisation ensures that approval within Australia (TGA) is directly transferrable to the European Commission, thus giving access to the larger European market immediately. The USA is not part of this

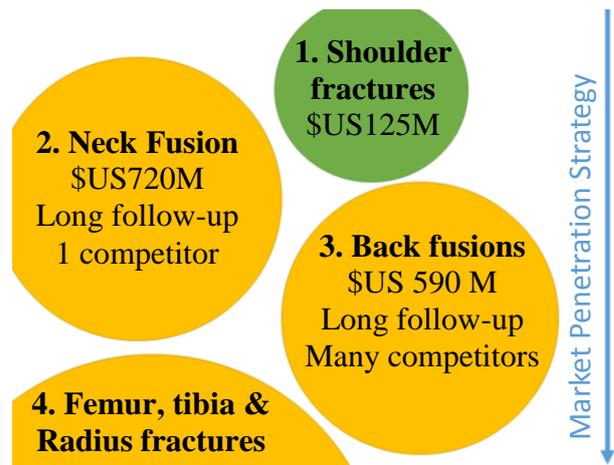


Fig. 10. Relative market sizes and acquisition order for potential EXF applications

¹ Persistence Market Research “Global Market Study on Orthopedic Trauma Devices: External Fixator to Witness Highest Growth by 2020” (US\$4,600).

² <http://www.courant.com/health/hc-woven-orthopedic-mainstreet-20150306-story.html>

agreement and FDA approval would be a separate requirement. In this region, the EXF will need to make a 510(k) pre-market clearance submission for a specific indication and identifying a predicate device that is substantially similar to the EXF.

The experiments planned in this grant application are in line with the requirements of these regulatory bodies and can contribute to the Technical File that will be required to demonstrate compliance and allow registration of the device. The clinical requirements for regulatory approvals are not explicitly defined and depend on the outcomes of the preliminary clinical testing. The requirement is that the new device *performs just as well clinically as all its predicates*. Given the similarity between the EXF and previous conventional and expanding screws and based on the assessment of a regulatory approvals specialist, we estimate that a first in human clinical test with 10-20 patients should be sufficient to satisfy the requirements for regulatory approval. This test is to be performed immediately after the scope of works of this grant have been completed.

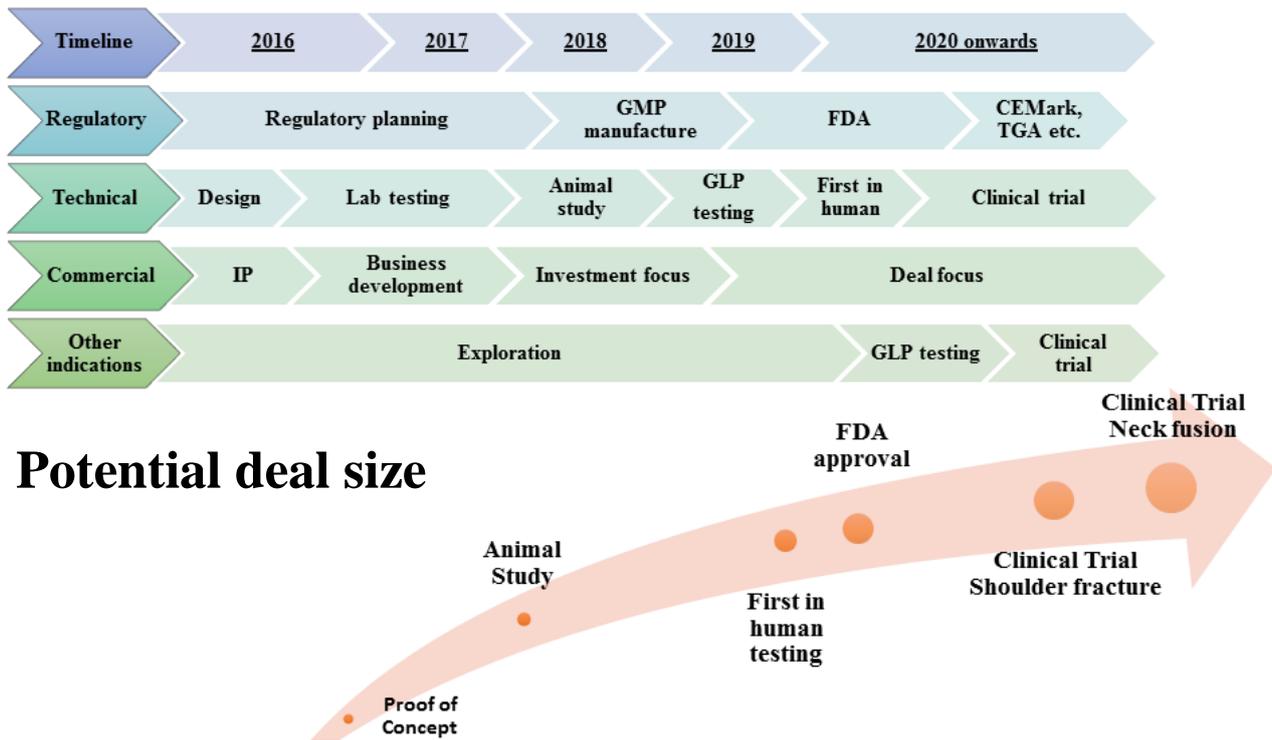


Fig. 11. Project timeline

Technical and Commercial Risks: Due to the size of the market and the cost of a clinical trial and onerous nature of regulatory approvals, the development of a medical device is inherently a high risk and high reward proposition. The most serious technical risk is that, although the EXF is designed to be easily removable (and may be more removable than other expandable fasteners) it may still be difficult to remove after implantation for a long period of time due to osseointegration. If the elastic response of the material was not sufficiently strong to overcome the osseointegration, then various methods of forced unexpansion are being developed and covered by the third patent in preparation. Another risk is that long term problems that were not identified in the animal study surface after a human trial. The investigators believe that the rigorous testing protocol outlined in the research plan that has been conceived by a team of experienced engineers, biomedical researchers and surgeons, based on the requirements for regulatory approval, minimises this risk.

The most serious commercial risk is companies infringing the project's intellectual property without obtaining a licence. To mitigate this risk we are working closely with potential commercial partners early in order to respond to their expectations and requirements to create an attractive licensing proposition. Furthermore we are filing multiple patents to ensure that every aspect of our intellectual property is as robust as possible. Additionally Curtin IP Commercialisation Office (CIPCO) provides excellent institutional commercial advice and support by managing the commercialisation of the project and contribute with experience in all aspects of the

commercialisation process, including engaging experienced life science executives as commercialisation consultant to the project. CIPCO has established 15 companies based on IP developed by Curtin researchers. These companies currently employ over 100 people in new economy jobs and generate revenues in excess of \$15 million p.a. Biomedical projects Neuromonics and Glycan Biosciences Inc, have secured \$26m and \$3.4m of funding to date.

Intellectual property management: Our intellectual property is protected by two patents with a third patent managed by CIPCO. A PCT application to protect the design features of the EXF was filed on the 24th February 2015 (WO 2015/123726 A1). Positive experimental outcomes has warranted the progression of the patent to the national phase, in the United States (US), Australia and Europe, with the financial support of CIPCO. The investigators initially identified potential for the development of an integrated one part unit using a novel expandable fastener with a controlled range of motion designed for posterior stabilisation of the cervical spine and submitted a provisional patent in August 2012. PCT was filed on the 23rd August 2013 (WO 2014/028981 A1) and the patent has now entered the national phase and filed in the US and Australia. The investigators are in the process of preparing a third patent application to protect the removability feature of the EXF, which is expected to be filed by April 2016. These patent applications together with strategic Non-Disclosure Agreements form a very strong IP position and significantly increase the value of the project to potential investors.

Industry/commercial partner involvement: The CIPCO Team has guided the commercialisation of the EXF project by engaging partner organisations and funding bodies. This includes the Curtin Commercialisation Advisory Board (CAB) which has provided \$53,000 of funding for the project based on the project's commercial potential, excluding patent and staffing costs. The EXF project has drawn funding interest from and met with several parties including the DePuy Synthes, the Medical Research Commercialisation Fund (MRCF), Yuuwa Capital, Orthotech and LifeHealthcare. DePuy Synthes has also agreed to supply 20 spinal screws with an approximate commercial value of \$4000 for our preliminary research work. However, based on the discussions with these groups in particular DePuy Synthes and the MRCF, additional testing, as described in this grant, is required before funding can be secured. Consequently funding this grant would significantly increase the likelihood of partnering with a large implant manufacturing company by allowing critical proof of concept work to be carried out.

The investigators have discussed the project with Dr Hassan Serhan from DePuy Synthes, and the feedback we received is as follows:

the EXF "... meets an unmet need in cervical spine by achieving better fixation with reduced dimensions and can improve clinical outcomes and reduce complications of screw mal-placement" and "DePuy Synthes would be interested in continuing an ongoing relationship or possible research collaboration" Dr Hassan Serhan, Distinguished Engineering Fellow DePuy Synthes Spine, July 2015.

Furthermore the project has cleared the Preliminary Investment Proposal (PIP) stage with the MRCF and has been invited to submit an Investment Application Form. Based on the PIP, the feedback that we received from the MRCF is as follows:

"...there is a clear need for orthopaedic fixation devices with increased pull out strength, particularly in osteoporotic patients and the program is overseen by an experienced multidisciplinary team of clinicians and engineers with the guidance of the Curtin Commercialisation Office, who have an excellent commercial track record. Further development as outlined in this proposal, would bring the technology to a stage where evaluation and potential investment from the MRCF would be considered." Dr Chris Nave, Principle Executive of the MRCF, July 2015. Full letters of support can be provided.

Appendix F MRCF investment application form

MEDICAL RESEARCH COMMERCIALISATION FUND INVESTMENT APPLICATION

This form is to be submitted to Brandon Capital in application for investment funding from the Medical Research Commercialisation Fund (MRCF). This form should be submitted after a Preliminary Investment Proposal has been successfully reviewed by the MRCF Investment Review Committee. The applicant should also prepare a detailed presentation. **Do not exceed fifteen A4 pages in a minimum of 10 point font.**

PROJECT NAME (working title)

Expandable Orthopaedic Screw

Originating Institute / Inventor(s) / Applicant(s) Name(s)

WA Department of Health
Curtin University
Matthew Oldakowski, Intan Oldakowska, Ian Brown and Russell Nicholls

If business or company, name of company/ABN

Key contact person and details

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We, the undersigned, hereby certify that to the best of our knowledge and ability, at the time of making this report it is a true and honest representation of the project/technology/venture for which funding has been provided.

Print Name of Researcher/Inventor/Applicant:

**MRCF Project
Manager:**

Signature:

Date:

EXECUTIVE SUMMARY

Curtin University, in conjunction with the Western Australia Department of Health (DoH) is developing an innovative expandable orthopaedic screw (called the EXF Screw) specifically designed to improve performance and reduce the risk of complications in a wide range of orthopaedic applications. We plan to spin out this platform technology in order to partner with a major implant manufacturer to market products incorporating the EXF Screw for multiple indications.

Screws are used in orthopaedic surgeries to attach implants to bone, however often over screws can loosen or the bone around the screw can fail requiring revision surgery. The EXF Screw is being developed to be compatible with existing implants, therefore with our platform technology we could address, if utilised over the entire orthopaedic product range, a large portion of the orthopaedic market. Given the innovative design, application and suitability of the EXF Screw our estimate is that we can target up to 50% of the US\$6B global orthopaedic screws market. Our primary indication is proximal humeral (shoulder) fracture fixation with plate and screw system which has an estimated global market size of US\$123M (excluding surgery costs etc.). Our secondary indication is proximal femur (hip) fracture fixation with a global market size of US\$610M. We have selected shoulder fractures as our first indication as it has a strong unmet clinical need with low clinical risk and short follow-up time.

Unlike other expandable screws, the EXF Screw can provide significantly increased fixation strength compared to conventional screws without compromising removability and with minimal change to the surgeon's operating procedure. We plan to test the EXF Screw with an existing plate system in Open Reduction Internal Fixation (ORIF) surgery for proximal humerus fractures. ORIF is the surgical treatment of choice for patients who cannot be non-surgically managed. The superior mechanical performance of the EXF Screw can reduce the risk of long-term clinical failure, allow patients with lower quality bone to be treated with ORIF surgery (that would otherwise have a more costly and more invasive joint replacement) and allow earlier rehabilitation resulting in improved patient outcomes and reduced revision rates, culminating in reduced cost to the payer (healthcare funders or insurers). The EXF Screw design can be adapted to be compatible with virtually any existing orthopaedic product.

We have demonstrated preliminary proof-of-concept with a functional EXF Screw prototype. Preliminary testing in universally recognised bone models has shown significant increase in fixation strength when compared to standard orthopaedic screws in all bone failure modes (pull-out, push-in and shear). Further testing, including bench-top testing, animal studies and first-in-human clinical testing (Phase I trial) is required to achieve regulatory clearance and de-risk the technology for implant manufacturers.

The most significant technical risks are; a failure to translate increased fixation strength into significant clinical outcomes and the possibility that the EXF Screw cannot be easily removed after a long period of implantation if required. The key business risks are; difficulty in securing a licensee and having companies infringe our Intellectual Property.

We are seeking AU\$2.5M funding to support the formation of a start-up company that will conduct preclinical (2 years) and clinical (2 years) development of the EXF Screw technology. The new company will seek an exclusive partnership with a top 5 medical device company to manufacture and sell the EXF Screws globally. We already have strong interest from potential partners who have provided input to our development plan and have expressed a willingness to participate in clinical development and commercialisation.

We expect to transact the technology within 4 years, once we have phase 1 clinical data, allowing our partner to drive the remaining clinical development and incorporate the technology into their product portfolio and develop a full range of indications. The deal will include an upfront fee and payments for reaching key milestones (market launch in 1st indication, market launch in 2nd indication, reaching US\$1M sales, etc). The deal size is anticipated to be in the range of 5-10 times the initial investment, based upon comparable deals in the sector (listed in Appendix D).

THE INVENTION - SCIENCE AND TECHNOLOGY

Screws are used in orthopaedic surgeries to attach implants such as plates, rods or prostheses to bone in order to repair fractures, fuse or replace joints or reattach soft tissues. However if the bone is low quality (e.g. osteoporotic) or the fracture is particularly severe, over time the screws can loosen or the bone around the screw can fail, leading to the requirement for revision surgery.

The EXF Screw (Fig. 1) is an expandable orthopaedic screw that can replace conventional screws in fracture fixations to improve strength and consequently reduce revision rate, especially in patients with low bone quality. The EXF Screw is suitable to expand into the spongy central bone (cancellous bone) found in the ends of long bones and in most areas throughout the skeleton except for the mid-shaft of long bones. As a platform technology, the EXF Screw can also be adapted to suit many other applications, which include spinal fusion, revision arthroplasty and soft tissue anchors.

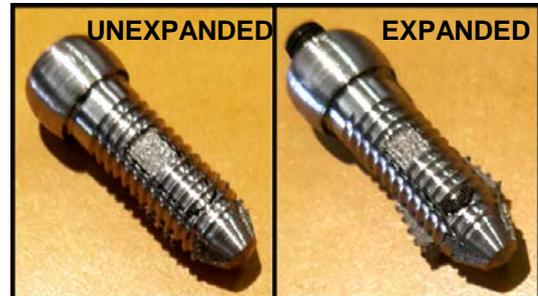


Figure 1 - An EXF Screw prototype, manufactured from titanium through 3D printing, is expanded by screwing in an

The EXF Screw is inserted, by an orthopaedic surgeon, into a drilled hole in the bone of the patient, in the same manner as a standard screw. The EXF Screw is then expanded simply by screwing an additional expansion bolt into its centre splaying open the expansion tabs (Fig. 1 right). If removal is required, for example, for revision surgery, the expansion pin can be removed (by screwing it out) and the expansion tabs will automatically 'un-expand' due to the spring-back in the material (elastic strain). Afterwards the screw can be removed in the same manner as a standard screw (screwing it out). This creates only minimal change to the surgical procedure and is not technically difficult to perform.

The EXF Screw, has increased fixation strength because it distributes the loading force over a larger volume of bone compared to standard screws, which rely only on the fixation strength of the screw thread in the bone. Additionally the stress in the bone that is compressed to make space for the expansion promotes an increase in bone density around the screw and promotes osseointegration, improving the fixation strength over time. The immediate and long term increased fixation strength



Figure 2 – A shoulder fracture that has been fixated by a plate and screw system.

provided by the EXF Screw is likely to reduce the rate of revision surgery, which is an attractive proposition for the manufacturers, patients, surgeons and payers. The EXF Screw could potentially be used for all patients, but would be most advantageous for patients with low quality, osteoporotic bone or patients with severe fractures, providing reduced risk of fixation failure. Additionally for some surgeries achieving equivalent fixation strength with a reduced screw length may reduce or eliminate the risk of the screw over-penetrating the bone and damaging soft tissues such as joints or nerves.

The EXF Screw can replace conventional screws in a broad range of applications, but we have selected shoulder fracture fixation (proximal humeral fractures, see Fig. 2) using locking plate and screw system as the primary indication as it has:

1. one of the largest unmet clinical needs of the common fractures with a 22% complication and 14% revision rate¹ in a systematic review for the general population and a 57% complication rate for patients over 60²,
2. a solid market size, being the third most common fracture (61 per 100,000 of population per year) with a large percentage of osteoporotic patients, estimated at US\$122.7M globally,
3. a commercially attractive market entry because of the low risk of mortality and the relatively short (1 year) clinical follow-up time to demonstrate efficacy,

¹ Sproul et al. (2011) 'A systematic review of locking plate fixation of proximal humerus fractures', Int J Care Injured; 42:408-13.

² Owsley & Gorczyca (2008) 'Fracture displacement and screw cutout after open reduction and locked plate fixation of proximal humeral fractures', J Bone Joint Surg Am; 90:233-40.

4. No other expandable screws currently developed for proximal humerus fracture fixation, and
5. Confirmation from a panel of orthopaedic surgeons that will consider using an expandable screw in proximal humerus fracture cases to reduce surgical complications.

The EXF Screw head can be easily modified to suit proximal humerus plate system from any implant manufacturer as required.

Proximal femur fractures (hip fractures) are the planned second indication. Hip fractures are a larger market (being the most common fracture). However the revision rate is slightly lower, the potential for fatigue failure of the screw is higher (the hip is weight bearing) and there is an expandable screw already on the market with CE Mark approval (not FDA) that is undergoing a large scale multi-centre randomised clinical trial (X-Bolt).

In addition to the first two indications and as a platform technology, the EXF Screw can be adapted to suit many different applications; lumbar pedicle fixation for lower back fusion, fracture fixation in the proximal tibia (lower knee) and distal radius (upper wrist) are a few applications identified. We believe that having flexibility to respond to the specific strategic priorities of implant manufacturers is extremely attractive.

An early unthreaded, square prototype of the EXF Screw has been tested in sheep bone and compared to conventional orthopaedic screws. We have demonstrated its potential to:

1. **reduce screw failure rate** based on a 41% increase in pull-out strength¹,
2. **increase resistance to screw migration** based on a 222% increase in failure energy¹,
3. **improve performance in poor bone quality** (osteoporosis) compared to conventional screws.²

Both of these studies have been accepted for publication. The EXF Screw with these three competitive advantages is expected to reduce the revision rate in proximal humerus fracture application.

Fixation strength: Testing of the EXF Screw in a synthetic bone model has demonstrated superior fixation strength in the three common failure modes with up to 92%, 42% and 22% increase in axial pull-out, push-in and shear tests, respectively, compared to Zimmer NCB locking screws.

Removability: We have developed the EXF Screw to have gapless expansion which prevent bone ingrowth into the fastener mechanism, which has been demonstrated by our latest prototype having a minimum gap size of 125 µm that is lower than the theoretical limit for bone ingrowth in a loaded implant¹. To further demonstrate ease of removability, the EXF Screw was implanted into bone impregnated with PMMA bone cement to simulate bone ingrowth that will occur over time. Removal using the conventional procedure (screwing them out) was very easy with only a marginal increase in removal torque (approximately 10% more torque for a 50mm screw).

Fatigue failure: The EXF Screw has been tested under cantilever fatigue loading and we demonstrated that for a 25mm long screw (smallest for shoulder fractures and worst case scenario) the EXF Screw does not fail at the expanding section, but rather at the head of the screw which is the typical general orthopaedics clinical failure mode. This means that because the EXF Screw has at least equivalent strength at this area we should have equivalent fatigue resistance compared to a predicate screw (a 3.5mm cannulated locking screw). Note that for shoulder fractures plate fatigue only occurs in the case of fracture non-union and screw fatigue is a very rare clinical failure mode as typically the plate fatigues before the screws.

Manufacturing: The EXF Screw is manufactured using Selective Laser Melting (SLM), a 3D printing process, which uses standard biocompatible titanium alloy (See Fig.3). SLM is a high value added, low labour cost, advanced manufacturing process that has been used previously by the team to manufacture medical grade titanium implants. SLM is being invested in by implant manufacturing companies such as Lima orthopaedics and Austofix to cost-effectively manufacture orthopaedic implants.

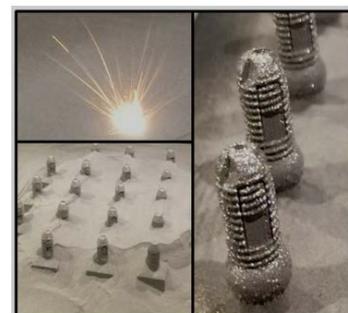


Figure 3 – Selective Laser Melting Process

¹ Itala et al. (2001) 'Pore Diameter of More Than 100 µm Is Not Requisite for Bone Ingrowth in Rabbits', J Biomed Mater Res (Appl Biomater); 58:679-83.

Top 5 most relevant scientific articles

1. **Oldakowski, M, Oldakowska, I, Kirk, TB**, Ford, CT, **Sercombe, TB, Hardcastle, P, Day, RE** 2016, 'Pull-out strength comparison of a novel expanding fastener against an orthopaedic screw in an ovine vertebral body: an ex-vivo study', Journal of Medical Engineering & Technology, DOI: 10.3109/03091902.2015.1127441
2. **Oldakowski, M, Oldakowska, I, Kirk, TB**, Ford, CT, **Sercombe, TB, Hardcastle, P, Day, RE** (in press), 'Influence of bone morphological properties on a new expandable orthopaedic fastener', Journal of Physics: Conference Series.
3. Zeiter, S, Montavon, P, Schneider, E, Ito, K 2004, 'Plate Stabilization With Bone Rivets: An Alternative Method for Internal Fixation of Fractures', Journal of Orthopedic Trauma, vol. 18, no.5, pp. 279-285.
4. Rohl, K, Ullrich, B, Huber, G, Morlock, MM 2009, 'Biomechanical analysis of expansion screws and cortical screws used for ventral plate fixation on the cervical spine', European Spine Journal, vol. 18.
5. Erhardt, JB, Stoffel, K, Kampshoff, J, Badur, N, Yates, P, **Kuster, MS** 2012, 'The position and number of screws influence screw perforation of the humeral head in modern locking plates: A cadaver study', Journal of Orthopaedic Trauma, vol. 26, no. 10, pp. e188-e192.

COMPETITION and COMPETITIVE ADVANTAGE

Competitive advantage: Standard screws

The advantages below apply to both general orthopaedics and our primary application.

Compared to standard orthopaedic screws, the EXF Screw is likely to achieve:

1. Significantly increased immediate fixation strength compared to conventional orthopaedic screws used in surgery today;
2. Increased bone density over time due to passive radial stress;
3. Without compromising removability during revision surgery (critical); and
4. With minimal change to the surgeon's operating procedure.

Superior fixation strength will:

1. Reduce the risk of clinical failure and subsequent complications and a possible costly and traumatic revision surgery (confirmed by a panel of orthopaedic surgeons);
2. Allow surgical treatment of patients with lower quality bone (osteoporotic, elderly patients) who would otherwise have to have joint replacements due to likelihood of screw failure thus improving their functional outcome earlier; and
3. Allow earlier rehabilitation resulting in improved patient outcome and reduced cost burden on the payer (insurance companies and national health services).

EXF Screws will not cost significantly more than existing screws. Based on Rickenbacher et al.'s cost-model for Selective Laser Melting we expect an additional cost of between US\$1-3 depending on whether the whole screw is manufactured using SLM or just the expanding tip, which is then attached using friction welding (more likely)¹.

Reduction in overall cost to the payer is anticipated through a reduction in revision surgeries which can support an increase in implant costs. This scenario has been seen previously in this space with a dramatic (~5 fold) increase in cost for locking plates compared to non-locking plates for shoulder fracture fixation². In this case it is observed that the early adopter of technologies have dominated the

¹ Rickenbacher et al. (2013) 'An integrated cost-model for selective laser melting (SLM)', Rapid Prototyping Journal; 19(3):208-14.

² Handschin et al. (2008) 'Functional results of angular-stable plate fixation in displaced proximal humeral fractures', Int J Care Injured; 39:306-13.

marketplace (e.g. DePuy Synthes' PHILOS, the first locking plate system) and the literature supports the cost effectiveness of payers paying this premium to reduce revision rates in the long term.

Competitive advantage: expandable screws in other applications

The market adoption of currently available expandable screws is limited because they are difficult to remove once implanted. This means that if a surgeon has a patient that needs revision and they have used another expandable screw (other than the EXF Screw) then they will anticipate a challenging revision surgery with possible additional complications to the patient. This is a major stress-point for surgeons and a critical factor in the adoption of the technology, as surgeons may have to remove the screw due to infection, non-union, a fracture adjacent to the plate, periosteal irritation or because the patient specifically requests removal. 655 attendees of the 2008 AO Principles and Masters Courses of Operative Fracture Treatment in Davos, Switzerland were surveyed and 40% believe that fracture fixation plates should be surgically removed *even without any clinical issues present*¹. The majority of surgeons and the key opinion leaders that we have surveyed have also indicated that removability was 'critical'.

Currently there are no expandable screws developed for proximal humerus fracture fixation, with the vast majority of expandable screws being developed for spinal fusion, in particular lumbar pedicle fixation. The X-bolt is the only non-spinal expandable screw and is being developed for hip fracture fixation. None of these expandable screws have a small enough diameter to be feasible for use in conventional shoulder fracture plates.

Although some expandable screws are marketed as 'able to be removed' (because they have a mechanism to retract the expansion), after significant period of time in the bone (i.e. during a typical revision surgery), bone will grow into the expandable mechanism of the fastener, preventing retraction and subsequent removal.

Consequently the literature reports difficulty of removal, breakage of screws during removal (which necessitates leaving a portion of the screw behind, creating an infection risk) and excessive damage to the patient's bone during removal (lumbar pedicle broken off limiting surgical options for revision)². In this case, **no expandable screw on the market or in development, can be removed safely during revision surgery.**

Consequently the primary competitive advantage of the EXF Screw over other expandable screws is safe retraction and removal even after a significant period of time in the body. This addresses the critical concern of surgeons and the major barrier to adoption of this type of technology.

The key to the EXF Screw's advantage over other expandable fasteners is that it is designed to expand in such a way that the deformation of the expanding arms is only temporary (elastic) and occurs without leaving any 'gaps' within the mechanism for the bone to grow into (see Fig. 7 in the intellectual property section). This allows safe and reliable removal during revision surgery. For more detailed information about the technical aspects of the removability of the EXF Screw, see 'Intellectual Property'.

A table of all the competitors on the market and under development is attached as Appendix A.

¹ Hanson et al. (2008) 'Surgeon's beliefs and perceptions about removal of orthopaedic implants', BMC Musculoskeletal Disorders; 9:73.

² Cook et al. (2001) 'Lumbosacral fixation using expandable pedicle screws: an alternative in reoperation and osteoporosis', The Spine Journal; 1(2):109-14.

THE MARKET

The Orthopaedic devices market is a multi-billion dollar market dominated by large implant companies such as DePuy Synthes (part of J&J), Zimmer-Biomet (merged 2015) and Stryker, as illustrated in Figure 4. The global orthopaedic trauma devices market was valued at US\$5.7B in 2013 with internal fixation devices holding the largest market share. This market is expected to grow at a CAGR of 7.2% from 2014 to 2020, to reach an estimated value of US\$9.4B in 2020. It is estimated that US\$6B in screws are sold annually in the orthopaedic device market¹.

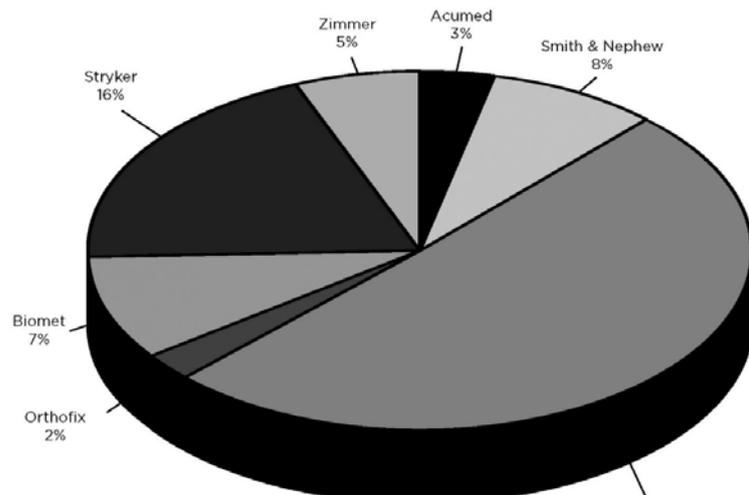


Figure 4 - Market share of fracture fixation companies (2014)

The EXF Screw could ultimately capture a significant market share as a platform technology partnered with a large medical device company and utilised over their entire trauma product range. Capturing just 5% of the market would result in a market share worth US\$300M.

North America has the largest market for orthopaedic trauma fixation devices followed by Asia and Europe. Asia has the fastest growing market for trauma fixation devices. Increases in incidence of fractures, increased healthcare expenditure and positive clinical outcomes act as some of the key drivers for the global orthopaedic trauma fixation devices market. The aging population, rising number of road accidents and increased government funding holds immense potential for this market. The aging population also means that the demand for fixation suitable for osteoporotic bone will increase in the future. Orthopaedic trauma fixation device market is one of the fastest growing segments of the global medical devices market. Plate and screw systems are the most commonly used internal fixation devices for fixing a traumatised fracture.

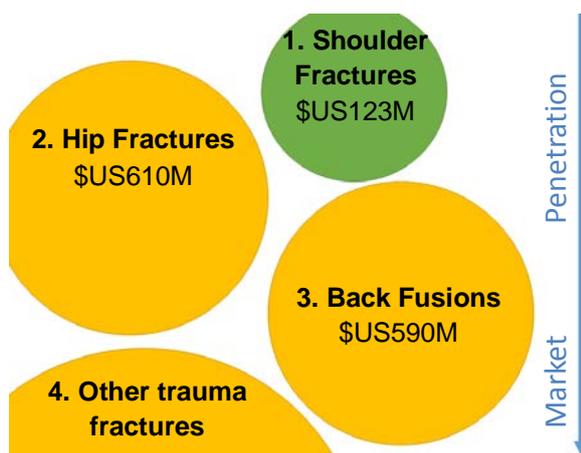


Figure 5 - Relative market sizes of indications.

Our primary indication, proximal humeral fractures, has an incidence of 61 per 100,000 of population per year and an **estimated global market size of US\$122.7M for Proximal Humerus Fracture Fixation hardware alone**. Average cost per surgery is US\$10,000 including US\$830 for the hardware. The market size of our second indication, hip fractures is approximately five times larger at **\$610M**. Figure 5 illustrates relative market sizes per indication and our market penetration strategy.

The EXF Screw can fit within all existing proximal humerus plate systems such as that shown in Figure 2. This provides our licensee partners an opportunity to provide choices for surgeon either to replace one of the screw with the EXF Screw or replace all the screws within the plate system,

which currently can be between 5 and 7 screws per system. Incorporating the EXF Screw within an existing system will have a flow on effect in increasing sales of the whole system and thus the potential to increase the market share of the manufacturer in that indication. Each proximal humerus screw is

¹<http://www.courant.com/health/hc-woven-orthopedic-mainstreet-20150306-story.html>

currently priced at approximately US\$50 whereas the cost of material and manufacturing of each screw will be less than US\$5. The EXF Screw will cost an additional US\$1-3 to manufacture depending on the manufacturing technique employed. DePuy Synthes have confirmed that this increase is acceptable. Other cost of supply such as sterilisation and distribution will not vary significantly between current screws and the EXF Screws. As the EXF Screw will not present a significant increase in the cost of goods, significant margins can be gained with a premium pricing for the EXF Screw within the plate system. Additionally, given the screws only presents a very small cost of an ORIF surgery (US\$350 of US\$10,000 per surgery), a 20-50% screw price uplift will be easily absorbed by the market, as demonstrated by the 5-fold price increase over existing plate system when locking plates for proximal humerus fractures were first introduced. This is especially the case when a clinical trial can demonstrate a reduction in revision rate by using the EXF Screw, as each reduction in revision case presents a US\$11,500 (Hemiarthroplasty) to US\$22,000 (Total Shoulder Arthroplasty)¹ cost savings to the healthcare system for the revision surgery, not including the patient's reduction in function, community involvement and additional pain. In the US alone, the cost burden of revision surgery associated with proximal humerus ORIF is estimated at US\$180M per year. A 1% decrease in the revision rate will present a cost saving of US\$13M per year to the healthcare system.

For our second indication of hip fractures, the cost burden of revision surgery is currently estimated at around US\$638M per year, with a 1% decrease in revision rate presenting a cost saving of approximately US\$80M² per year to the US healthcare system. Additionally, revision of hip fracture fixation surgeries are associated with a high mortality rate.

Aside from screws and plates there are a number of other internal fixation devices used in orthopaedic trauma surgery. The EXF Screw can be adapted to suit many of the internal fixation devices throughout the body, such as those shown in Figure 6.



Figure 6 - Internal fixation devices

KEY TECHNICAL AND COMMERCIAL RISKS

Due to the size of the market, the cost of a clinical trial and onerous nature of regulatory clearances, the development of a medical device is inherently a high risk and high reward proposition. The following technical and commercial risks are listed approximately in order of importance.

Technical risks:

Risk 1 - Failure to translate increased fixation strength into improved clinical outcomes: It is possible that the increased fixation provided by the EXF Screw might not correspond to significantly better clinical outcomes. However this is unlikely, given that we have a very large unmet clinical need both in proximal humerus and proximal femur fractures and a large increase in performance demonstrated in benchtop testing. Furthermore other expandable screws have demonstrated significantly improved clinical results corresponding to their increased fixation strength in benchtop testing. The clinical trial of the EPS for pedicle fixation in the lumbar spine reported a significantly lower rate of screw loosening at 4.1% compared to 12.9%³. Furthermore, although synthetic bone is well recognised as a suitable testing medium due to its repeatability, performance increase in synthetic bone

¹

<http://www.ucsfcmec.com/2013/MMJ13008/slides/29ShearerTheCostEffectivenessOfSurgicalMgmtForComplexHumerusFractures.pdf>

² Song et al. (2011) 'Cost burden of second fracture in the US Health System', Bone; 48:828-36

³ Wu et al. (2012) 'A comparative study on screw loosening in osteoporotic lumbar spine fusion between expandable and conventional pedicle screws', Arch Orthop Trauma Surg; 132(4):471-6.

may not correspond to equal performance increase in human cadaveric bone due to differences in structure (cortical layer, variable cancellous bone density) and material properties (elasticity).

Risk 2 - Removability: Removability is critical for our competitive edge and a key feature to allow mainstream adoption of expandable screws with orthopaedic surgeons. The EXF Screw is designed to be *unconditionally* removable (even after long term implantation) due to a combination of elastic expansion (guiding the screw to return to its original position without any permanent deformation) and gapless expansion (preventing bone from growing inside the fastener). Manufacturing a watertight interface between metals on a microscopic level is difficult to achieve due to micro-surface roughness. Despite these manufacturing limitations, we have demonstrated using high resolution computed tomography (HR-CT) a gap-size of 125µm with our current prototypes, which is below the theoretical limit to which bone can grow into a loaded implant. We have also tested in ex-vivo animal model and simulated bone/implant osseointegration using bone cement, and have successfully removed the EXF Screw with minimal increase in removal torque compared to a conventional screw. Robust testing of fastener removability after bone ingrowth requires a live sheep study, as the bone needs to have the time to grow into the voids in the fastener to simulate removal after a significant amount of time in the patient (revision surgery). In the unlikely event of poor removability results from our live animal studies, we have identified a number of additional proprietary methods of ensuring removability after bone ingrowth including; redesigning the profile of the expanding section, increasing the 'un-expansion' force using a forced contraction mechanism and adding silicone rubber to provide hematic sealing of the interface (successfully prototyped). Consequently we are confident that we can achieve unconditional removability of the EXF Screw.

Risk 3 - Cost of integrating SLM manufacturing into standard screw manufacturing process: Standard screws are manufactured from long rods using a CNC (Computer Numerically Controlled) lathe and then post processed (adding cutting flutes and screw-driver connections). The easiest way to integrate into this manufacturing process would be to manufacture rods using Selective Laser Melting (SLM). However, to save cost the tips of the EXF Screw could be manufactured using SLM and then connected to titanium rods using friction welding. Additionally Hot Isostatic Pressing should be performed to the parts manufactured using Selective Laser Melting to increase fatigue performance and eliminate the risk of particle detachment. The total increase in manufacturing cost is estimated to be *less than* US\$4 per screw, which is within the threshold of cost increase, based on our conversation with implant manufacturers.

Commercial risks:

Risk 1 - Difficulty in identifying and engaging with potential licensee: A critical risk of this project relates to our ability to identify and engage with potential licensee with strategic alignment that can see the potential of the EXF Screw as a platform technology. To mitigate this risk we have initiated discussions with several major global implant manufacturers, receiving positive feedback and will continue to engage these and others throughout the development process. We will explore partnering with an Australian-based contract manufacturing company to explore the opportunity to market the EXF Screw screws which increases the attractiveness to a potential manufacturing company partner.

Risk 2 - Freedom to operate: Required searches related to the intended application of the technology can be conducted as required. Further details can be found in the Intellectual Property Section. No relevant IP has been discovered when conducting prior art searches or during patent examinations to date.

Risk 3 - The project takes longer and costs more than planned: The most critical risk with all early stage projects is that of project planning and execution and budget control. To mitigate this risk we have created and will continue to develop, update and maintain detailed planning documents and budgets along with strong policies and procedures around expenditure controls. We are also applying for several grants and incentives from a range of funders (see Fund Sought) and this non-diluting funding, where awarded, will contribute to delivering the development plan.

Risk 4 - Regulatory clearances: We have engaged a regulatory specialist to establish a quality management system for the company and ensure the development outlined within this proposal satisfies all regulatory requirements prior to product validation. We also plan to have a pre-submission meeting with FDA at the end of the proof of concept phase to further ensure all testing requirements have been addressed. The company's strategy is to collate all documentation required for a regulatory clearance submission in the relevant jurisdictions to significantly de-risk the product and drive up deal value. The licensee will then only need to validate the product based on their manufacturing system for the final submission. Further details on the regulatory strategy can be found on the commercial strategy, returns and exits section.

Risk 5 - Intellectual Property Rights: A commercial risk is companies infringing the project's intellectual property. To mitigate this risk we are working closely with potential commercial partners early in order to respond to their expectations and requirements to create an attractive licensing proposition. Furthermore we are filing multiple patents to ensure that every aspect of our intellectual property is as robust as possible. We will retain a US patent lawyer to advise on optimal IP strategy.

INTELLECTUAL PROPERTY

Key inventors and ownership structure

The Intellectual Property in the EXF Screw is owned and managed by Curtin University, through its IP Commercialisation team. The company ownership structure is proposed to be Curtin 47.5%, the inventors 47.5% and DoH 5% equity pre-money.

Patent applications

Using national IP Attorney firm Griffith Hack and their international associates the technology has been protected by three patent families:

1. 'A Fastener' – PCT/AU2015/000099 filed 24 February 2015, Published as WO2015237726 covering the design and uses of the EXF Screw.
2. 'A Component' – Provisional Australian patent application number 2016901032 filed 18 March 2016, covering the additional design features of the EXF Screw.
3. An orthopaedic Stabilisation device – PCT/AU213/000943 filed 23 August 2013 published as WO2014028981, covering an implantable stabilisation device, which incorporates the key design feature of the EXF Screw.

Patent 1 ('A fastener') covers parallel and largely rectangular dedicated bending sections (see Fig. 7). This allows the fastener to expand by a large amount (we have expanded by 100% of our diameter), within the elastic region of the material, in a controlled fashion (no uneven expansion) and when unexpanded return to exactly the original shape to facilitate easy removal. On 24th August 2016 this application entered National phase in the United States, Europe via the European Patent Convention and Australia. We are considering expedited prosecution of Patent 1 in the US having received a clear International Search Report (ISR) and Written Opinion.

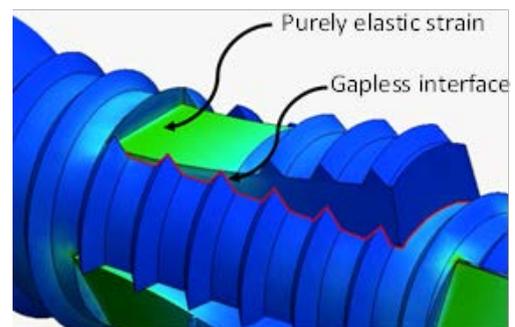


Figure 7 - Key design features of the EXF Screw covered by patents 1 & 2.

Patent 2 ('A Component') covers gapless expansion (see figure 5, above), which prevents bone ingrowth and allows 'un-expansion' of the EXF Screw for example during revision surgery. This is achieved by a multitude of related innovative features and this patent specification outlines additional proprietary methods of preventing bone ingrowth, increasing the elastic response force and removal methods. Features described in this patent can be applicable to other expandable fasteners to improve their removability, thus providing cross-licensing opportunities. The next major patent application

deadline for Patent 2 is 18 March 2017 (PCT filing) with an estimated cost of \$15,000. Patent 2 has not been examined

Patent 3 ('An orthopaedic stabilisation device') covers integration of an expandable fasteners (incorporating key EXF Screw features) into a single unit implantable device, compared to a conventional implant which has the screws separate from the stabilising element (plate or rod). This is claimed for use in small joints such as neck, foot and hand. Patent 3 is pending examination in the United States and Australia, and we have received a clear ISR and Written Opinion.

Extensive patent searching has been performed by the inventors using search terms "expandable screw" and "orthopaedics" in the International Patent Classification *A61B 17/00 Surgical instruments, devices or methods, e.g. tourniquets*. Freedom to Operate (FTO) searches related to the intended application of the technology can be conducted and we have received quotes from Griffith Hack and recognised searching companies to complete these as required.

In order to evaluate the possibility to engineer around our patents we convened a group of inventors, manufacturing specialists and design engineers for a 'rock throwing exercise'. The outcome of this discussion was that the IP was robust and no obvious technical work around was identified.

We will retain a US patent lawyer experienced in litigation of medical device and orthopaedic products to provide advice on robust IP strategies for protecting the EXF Screw.

KEY PEOPLE AND MANAGEMENT

Inventors

Matthew Oldakowski and **Intan Oldakowska** are PhD students at Curtin University who are the lead designers of the EXF Screw and have conducted all the biomechanical testing and analysis, Matthew and Intan have won numerous awards for their work including the John Black Student Award (2008 and 2015), the Young Biomedical Engineers Award (2008, during undergraduate studies), winner of the US ambassador innovation grant (2015), and Second Prize, Curtin Innovation Awards (2013). They are supported by an experienced academic supervisory team including **Professor Brett Kirk** (Engineering) and **Professor Garry Allison** (Health Sciences). Matthew and Intan will continue to drive the design and testing for the project and are keen to work in commercial roles.

Professor Philip Hardcastle, a retired spinal surgeon and adjunct Professor at Curtin University, invented the first stand-alone anterior lumbar interbody fusion "STALIF®" device (Patent: US4904261), creating a new market for integrated interbody spacers and commercialised by Surgicraft Ltd. He also invented the IntExt (Patent: US6579290) for anterior cervical fusion, developed by Centinel spine into the STALIF C™. Prof Hardcastle will hold an advisory role in the project, given his extensive relevant experience.

Professor Gabriel Lee, a Neurosurgeon at St John of God Hospital and Sir Charles Gairdner Hospital (DoH), is involved in refining the design of the fastener for the spinal applications. Professor Lee is an advisor for the Clinical Training and Evaluation Centre at UWA and DePuy Synthes and will advise the company on clinical testing.

Commercialisation team

Ian Brown MBA, FAICD, FAIM, is retained as a commercialisation consultant, and will manage the company as CEO. He is an experienced and successful entrepreneur. Ian is an Entrepreneur in Residence at INSEAD and has experience including as CEO of medical device and orthopaedic product spin out from Imperial College London. Ian will deliver on the strategy and commercialisation plan and facilitate deals through his extensive network.

Russell Nicholls, GAICD, RTTP is Deputy Director, IP Commercialisation at Curtin and is managing the commercialisation of the EXF Screw. Curtin has established 15 companies based on its IP, which

employ over 100 people and generate revenues in excess of \$15 M p.a. Russell is a director of Selvax Pty Ltd and has previously served on the board of MiReven Pty Ltd.

Dr Rosemary (Roz) Thompson is a consultant supporting the regulatory approval process. Roz is a research engineer and project manager with extensive experience in orthopaedic medical device R&D, regulatory affairs and quality management systems. She has worked in Switzerland for the AO Research Institute, Zimmer GmbH and as a regulatory consultant for Medisonos.

Scientific Advisors

Professor Markus Kuster is an orthopaedic surgeon at Royal Perth Hospital (DoH) with extensive implant design and commercialisation experience, having developed to market four orthopaedic implants: the Non-Contact Bridging (NCB) and the periprosthetic NCB (NCB-PP) plating systems (Zimmer) and the LCS posterior stabilised and LCS revision Total Knee Replacement (DePuy Synthes). Professor Kuster will provide clinical development advice and perform the phase 1 clinical trial.

Dr Greg Roger FIEAust is the founder and CEO of Vestech Medical Pty Ltd and Cryptych Pty Ltd, and was CEO and Founder of Advanced Surgical Design & Manufacture Ltd (ASDM). He invented the RCI Screw, Active Total Knee Replacement, CCS Clavicle Fixation System, Carpal Plate Fixation System, the Revision Total Knee Implants for the Active Knee and a High Tibial Osteotomy opening wedge device. Greg is a Member of the TGA's advisory group, Strategic Industry Leaders Group for the Medical Devices Action Agenda, Board of AusBiotech, Therapeutic Innovation Australia, Biomaterials Biopharmaceuticals and Medical Devices Advisory Committee, Board of AIMS Research and Swinburne University Biodevices Advisory Board.

Rob Day is a biomedical engineer at Royal Perth Hospital (DoH), and has extensive knowledge of clinical testing and mechanical testing which will be used in the development of the EXF Screw. Mr Day worked on the development of the NCB plates and the design and manufacture of patient specific cranioplasty implants.

Professor Tim Sercombe (Mechanical and Chemical Engineering) at The University of Western Australia specialises in Selective Laser Melting (SLM) technology. Prof Sercombe will manufacture the prototype fasteners using the latest SLM techniques.

Professor Allen Goodship is an outstanding internationally recognised academic at University College London with an extensive and commercial track record including the formation of 3 spinout companies (Stanmore Implants, Vetcell and Litethru) and has advised a large number of major orthopaedic companies. Prof Goodship will provide scientific advice to assist translation of the product to market.

Professor Gordon Blunn is a world leader in innovation for surgical implants and prosthetics and has held key roles at Stanmore Implants, Fitzbionics and Accentus. Professor Blunn is the Director of the Institute of Orthopaedics at University College London at the forefront of translation research. Prof Blunn will provide scientific advice to the company.

Ross Garrett was a Senior Director, Zimmer Biomet (2007 - 2012). Ross is an experienced executive in medical devices and drug development who has led a management team focused on business development and technology commercialisation of musculoskeletal R&D products.

Our global network of scientific advisors also include Jonny Johnson, Consultant Spinal Surgeon at Princess Grace Hospital, London, UK and Professor Philip Procter, a commercialisation consultant and ex-industry executive with extensive experience in product design and development currently researching device fixation and performance enhancement in compromised bone at Uppsala University, Sweden.

COMMERCIAL STRATEGY, RETURNS AND EXITS

We have identified a significant problem in the orthopaedic surgical market and we have developed a compelling solution that can be used without changing standard surgical practice. The market opportunities are significant and market growth is strong. Estimates on the cost of manufacturing and

the potential market price provide a compelling commercial prospect. Whilst the technology is at an early proof of concept stage, it has already demonstrated the potential to have a strong competitive edge. We have built an international multidisciplinary team with the skills and knowledge to ensure the development plan is as robust as possible and risks are mitigated as much as possible. The network of contacts of the team facilitates direct access to multinational orthopaedic implant manufacturers for further development input, access to equipment for testing and partnering.

Four very large multinational orthopaedic implant manufacturers dominate the orthopaedic trauma market that we have focused our strategy around. Each of the multinational orthopaedic implant manufacturers has invested heavily in large-scale manufacturing and distribution capabilities. Their business model is to take product iterations, line extensions and innovative new products, developed internally or externally (in-licensed), scale up manufacturing and push them out through their distribution network. In harmony with this, we will explore a partnership with an Australian-based contract manufacturing company to market EXF Screws before partnering with a major multinational implant manufacturer with a considerable market share.

The team has ongoing discussions with DePuy Synthes and Zimmer Biomet, the top 2 multinational orthopaedic implant manufacturers in the global trauma market (combined 54% share). The feedback on the EXF Screw and first indication has been positive, and they also recognise the potential for the technology to be applied as a platform technology across their product range. DePuy Synthes has outlined in their support letter that they are “interested in evaluating this concept further once the preclinical data is available” and that they will be “willing to take these devices to the next level of testing for potential commercialization”. The developmental plan and commercialisation pathway of the EXF Screw is in line with these requirements. They have demonstrated their intent on being involved with the project by supplying screws for comparison testing.

The EXF Screw has broad applicability to most orthopaedic procedures throughout the body. Strategically, we have selected proximal humerus fractures, which requires a plate coupled with our EXF Screws, as our primary lead indication, to progress to pre-clinical and clinical development. The reason for this approach is that proximal humeral fractures are an attractive commercial proposition in terms of length of clinical follow up and clear clinical unmet need (currently up to 57% complication rate).

The team recognise that surgeons have a significant decision making power on the use of a particular device within the health system. So we have ensured that the development of the EXF Screw is continually guided by surgeon feedback within our team as well as within the WA Orthopaedic community. We have presented the EXF Screw technology at the WA Australian Orthopaedic Association Annual Meeting in 2015 and 2016 with positive feedback from Orthopaedic surgeons. We have also recently conducted a survey of *independent* surgeon’s attitude towards expandable screws and the EXF technology. Feedback on our survey has indicated that the majority (86%) of surgeons are likely or will use an expandable screw with demonstrated cadaveric benchtop and animal *in vivo* study (without clinical data).

Commercialisation Strategy

The new company will seek a partner to manufacture and sell the technology globally. We have already engaged with potential partners to gain development plan design input and have received strong interest. We anticipate more formal discussions with potential partners interested in evaluating the EXF Screw further once the preclinical testing is complete. At that time we will be discussing the potential partners’ willingness, which they have already indicated, to take part in the clinical development. We envisage partnering with the same large multinational medical device company working towards an acquisition by them within 4 years.

While recognising our core technology is at an early stage, we are undertaking further development to reduce risk, commencing with bench-top testing to be completed by Q2 2017. Further de-risking will be achieved through further development and testing in in-vivo animal models (Q4 2017) and design

verification testing (Q4 2018). A key value inflection point will be achieved upon completion of phase 1 clinical trial (10-20 patients), which will be conducted in conjunction with the DoH and St John of God Hospital, that we anticipate will conclude in Q3 2020, allowing initiation of the regulatory approval.

The major milestones of the commercialisation strategy for the EXF Screw are outlined in Appendix B. Other key events driving up value are grant of a patent in the US (estimate 2018/9) and human ethics approval for phase 1 clinical trial.

Regulatory Strategy

Our strategy is to develop the EXF Screw within a lean Quality Management System (QMS) that selectively draws on requirements from ISO 13485 and Good Manufacturing Practice (GMP) that serve a dual purpose:

1. Fulfil the requirements to gain clearance for a Phase I clinical trial in Australia
2. Create a supporting quality system package that combines the EXF Screw design and can be seamlessly integrated into a fully compliant QMS (e.g. that of an implant manufacturer).

A risk management plan as part of the QMS will be implemented to ensure conformity with the regulatory pathway in the US, Europe and Australia. When coupled with a plate to treat a proximal humerus fractures, the EXF Screw is categorised as a Class II device and eligible for 510(k) clearance with the FDA. For this type of application, the system needs to demonstrate equivalence to existing systems, typically through bench-top testing. However, a formal regulatory opinion will be obtained from US based consultants to confirm this. Although a phase 1 clinical trial may not be required for a 510(k) application, the conversations with the implant manufacturers have indicated that clinical data is important prior to initiating partnering deal term negotiations. The development plan described here are in line with the requirements of these regulatory bodies and can contribute to the Technical File that will be required to demonstrate compliance and allow market approval for the device product (the EXF Screw used in conjunction with a plate).

Reimbursement Strategy

Our reimbursement strategy will be driven by our commercialisation partner, subject to the stage of regulatory clearance, and can be designed as an initial like-for-like reimbursement strategy and then a reimbursement augmentation strategy. The like-for-like reimbursement strategy will allow for the substituting of one screw for the EXF Screw under the existing indication procedure reimbursement code. The augmentation reimbursement strategy will allow for the augmentation of existing indication procedure reimbursement code fee or a new indication procedure reimbursement code fee, as more performance data is available e.g., following phase 2 clinical trials.

Once minimal clinical evidence is available an application to the relevant authorities can be made. We will retain a reimbursement consultant to guide the initial process.

Licensing and Exit Strategy

Successful completion of preclinical and clinical testing will enable strong negotiating position in discussions with potential partners.

As stated earlier, US\$6B of orthopaedic screws are sold annually and we estimate that use of EXF Screw is suitable and advantageous in approximately 50% of cases. If a multinational orthopaedic implant manufacturer acquired the EXF Screw platform technology, a 5% increase their market share could be worth US\$150M a year.

For proximal humerus fractures, US\$122M of orthopaedic plates and screws are sold annually and we estimate that use of our expandable screw (EXF) is suitable and advantageous in 100% of cases. In this scenario the use of EXF Screws and an orthopaedic plates in combination will increase sales of both. An increase of 5% of market share represents a potential increase in sales of US\$6M a year. In our proposed second indication Proximal Femur, a 5% increase in market share represents a potential increase in sales of US\$30m per year.

The new company will seek an exclusive partnership with a top 5 medical device company to manufacture and sell the EXF Screws globally. We already have strong interest from potential partners who have provided input to our development plan and have expressed a willingness to participate in clinical development and commercialisation.

We expect to transact the technology within 4 years, once we have phase 1 clinical data and first sales, allowing our partner to drive the remaining clinical development and incorporate the technology into their product portfolio and develop a full range of indications. The deal will include an upfront fee and payments for reaching key milestones (market launch in 1st indication, market launch in 2nd indication, reaching US\$1M sales, etc). The deal size is anticipated to be in the range of 5-10 times the initial investment, based upon comparable deals in the sector (listed in Appendix D).

FUNDING SOUGHT

We are seeking AU\$2.5M to support the formation of a start-up company focused on the development of the EXF Screw product. The funding is for pre-clinical (2 years) and clinical (2 years) testing and the data will be incorporated in a technical file supporting for a regulatory filing with the TGA and European Commission (CE Mark) for the EXF Screw used in proximal humerus fracture fixation.

We are also actively pursuing up to AU\$3.21M non-diluted funding to support the R&D through several schemes including:

1. NHMRC Development grant for the pre-clinical testing – submitted for AU\$439K (3 years)
2. CRC-Project grant for the manufacturing protocol development activities – in preparation approx. \$750K
3. State Health Research Advisor Council Funding for the phase 1 clinical trial – up to AU\$270K
4. Accelerating Commercialisation grant for technical file development and commercialisation activities – up to AU\$1M
5. R&D Tax incentive to offset 45% of the cost associated with milestones 1 to 4 - approximately \$750K.

A Gantt chart indicating the timing of the developmental milestones with their respective costs can be found in Appendix C.

Milestone 1: Completion of the human cadaveric testing, which establishes the mechanical performance of the EXF Screw compared to conventional screws by bench-top mechanical tests on human cadaveric shoulder bones under different loading conditions.

Milestone 2: Completion of the in vivo animal study to demonstrate biocompatibility and compare the EXF Screw against conventional screws in terms of removability after a significant implantation period and the effect of passive radial stress on osseointegration and subsequently on the fixation failure forces. Mechanical testing and imaging of the bone/implant interface will be conducted to quantitatively analyse these parameters.

After completion of the animal study, the EXF Screw will be ready for manufacturing at a Good Manufacturing Practice (GMP) accredited facility and a series of mechanical design verification tests will be conducted at a facility complying to NATA standard to establish the mechanical risk safety margin for the product. The mechanical testing conducted will be in accordance with the FDA and TGA/CE Mark standard testing requirements for bone screws and plate construct.

Milestone 3: Completion of the pre-clinical technical file summarising the human cadaveric, animal *in vivo* and design verification testing data, which will be required to initiate the phase 1 clinical trial.

Conversations have been initiated with contract manufacturers in Australia (Cryptych/Vestech Medical and Objective3D), testing facilities (Royal Perth Hospital) and hospitals (St John of God) to conduct the clinical trial. We have also been in conversation with DePuy Synthes who has expressed their willingness to supply implant materials (i.e. plate system) for the clinical trial, provided we can

demonstrate positive pre-clinical data. We have recently received 20 screws to the market value of approximately US\$13,000 from DePuy Synthes to conduct mechanical testing, which shows their willingness to collaborate in this capacity. Additionally, Professor Kuster has a long standing relationship with Zimmer Biomet, for possible provision of a plate for clinical testing purposes.

Milestone 4: CE Mark and reciprocal TGA approval for the EXF Screw and a plate system for use in proximal humerus fracture fixation. We anticipate the EXF Screw will be manufactured by an Australian-based contract manufacturing company allowing the EXF Screw and a plate system to enter the market by 2020.

Milestone 5: Completion of a Phase 1 clinical trial to show safety and efficacy. After successful design verification testing we will obtain human ethics approval for a phase 1 clinical trial of the EXF Screw for proximal humerus fracture. The EXF Screw and a plate system manufactured by an Australian-based contract manufacturing company and recruitment of approximately 15 patients with proximal humerus fracture from a WA hospital affiliated with the WA Department of Health (e.g. St John of God, Royal Perth, Sir Charles Gardner) will begin. Prof Kuster will be involved in the development of the clinical trial and recruitment of WA shoulder surgeons for the trial. Based on the feedback on our surgeon survey, given favourable outcome in our pre-clinical testing data, surgeons are likely to use the EXF screw. The EXF Screw will be coupled with an existing plate system to assess the safety and efficacy based on complication rate, which typically occurs within 12 months of surgery. Removability can also be assessed if early revision of the screw is required as the majority of complications in this indication occur within 12 months of surgery. The completion of a one year follow-up for the final patient will allow finalisation of the technical file containing the pre-clinical and clinical data of the EXF Screw in proximal humerus fracture fixation.

The development plan outlined will work within the lean QMS with a simplified, four tier hierarchy framework. The primary tier will be the management tier and the secondary tier will be the subject level, which requires the areas to comply to the QMS; project management, research, manufacturing, cleanliness and sterility, regulatory affairs, documentation, labelling, tracking and surveillance. The third tier of the QMS will be the standard operating procedure level and the fourth tier will contain all working instructions and forms that need to be controlled within the QMS.

Commercialisation support has been costed at:

AU\$50K per year for regulatory consultants and fees

AU\$75K per year for patent prosecution, maintenance and strategic advice, plus legal costs

AU\$15K per year for travel and marketing

AU\$15K per year for corporate costs such as insurance, accounts and compliance.

AU\$70K per year for a part time CEO and board expenses

These commercialisation support activities will include business development, establishing contact and interest and progressing potential partnership negotiations and further engagement with KOLs and surgeons, including attending key conferences such as the American Association of Orthopaedic Surgeons annual meeting.

Appendix A

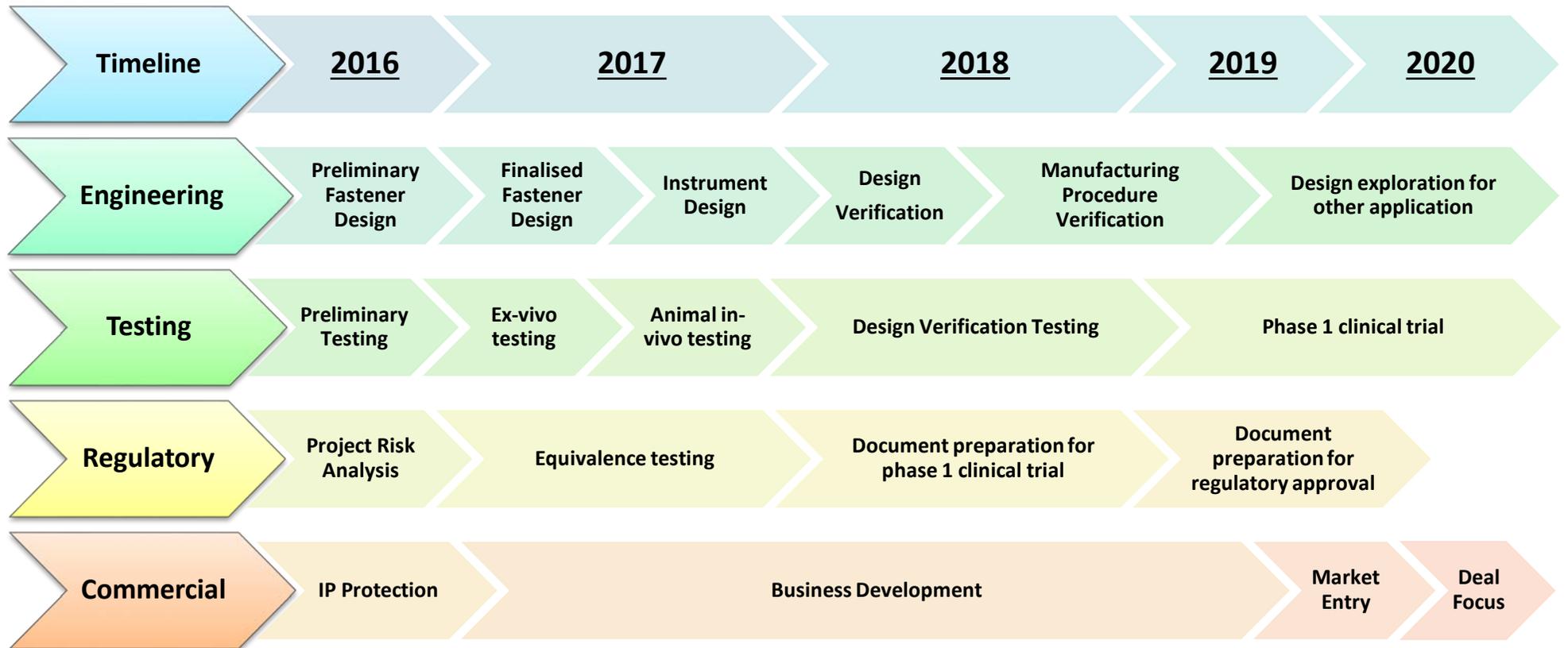
Competitors on the market and in development (Note that we define removability as follows: un-removable (no method of removal), actively removable before ingrowth (can be un-expanded but not after bone ingrowth), passively removable before ingrowth (cannot be un-expanded but can be forcibly removed but not after bone ingrowth), removable (can be removed even after bone ingrowth)).

Name	Company	Diameter	Stage of Development	Removability	Additional Comment
PROXIMAL HUMERUS FRACTURE FIXATION					
Locking Compression Plate (LCP) System	DePuy Synthes	3.5 mm	CE Mark and FDA Approved	Removable (non-expandable)	Can accommodate up to 7 screws. Screws can be locked in a number of pre-set configurations. Established market leader.
NCB Polyaxial Locking Plate System	Zimmer Biomet	4 mm	CE Mark and FDA Approved	Removable (non-expandable)	Can accommodate 5 screws. Individual polyaxial screw placement. Can use either locking or lag screws. Plate not indirect contact with the bone surface to reduce risk of impairment to the periosteal blood supply.
PERI-LOC Periarticular Locked Plating System	Smith & Nephew	4.5 mm - 5.7mm	CE Mark and FDA Approved	Removable (non-expandable)	Can accommodate 5 optionally larger diameter screws. Screws are locked in a pre-set configuration.
AxSOS Plating System	Stryker	4 mm	CE Mark and FDA Approved	Removable (non-expandable)	Can accommodate up to 7 screws. Screws can be locked in a pre-set configurations. Universal screw hole for locking or lag screws. Population based anatomically contoured plates.
Polarus Proximal Humeral Plating System	Acumed	4.5 mm - 5.7 mm	CE Mark and FDA Approved	Removable (non-expandable)	Can accommodate 5 larger diameter screws. Screws are locked in a pre-set configuration.
Conventus Cage	Conventus Orthopaedics	N/A	FDA Approved	Actively removable before bone ingrowth	Nitinol Cage within the fracture fixated with screws. Minimally Invasive procedure with minimal tissue disruption. Very different to existing system in this indication
PROXIMAL FEMUR FRACTURE FIXATION					
X-Bolt	X-Bolt Orthopaedics	9mm diameter	CE Mark approved. Clinical trial in EU. Not for sale in US	Actively removable before bone ingrowth	Additional bone reaming required to make space for the device inside the femoral head (surgically unattractive). Known difficulty for removal after long term implantation.
LCP DHS	DePuy Synthes	9mm diameter	CE Mark and FDA approved	Removable (non-expandable)	The established market leader in hip fracture fixation
LUMBAR PEDICLE SPINAL FIXATION					
XPed	Expanding Orthopedics	6.5mm diameter	Commercially available in EU. Not FDA cleared	Actively removable before bone ingrowth	4 fold increase in pull-out strength (significant) compared to conventional screw in saw bone. Clinical trial (2nd year) in Germany and Israel. In mid-2013 they announced 2000th implantation.
Osseo-screw	Alphatec Spine	6.5mm Diameter	Commercially available in EU, not	Actively removable before bone ingrowth	Significantly greater ultimate pull-out strength compared to standard titanium pedicle screw (~30%) in cadaveric bone

			FDA cleared and for sale in the US		
EBI Omega-21	Electro-Biology, Inc	6.5mm diameter	510(k) cleared in 1998. Not found in the market anymore	Passively removable before bone ingrowth	Significant 47% increase in pull-out strength in human cadaveric low quality bone compared to conventional pedicle screw. But not significant 19% increase in healthy bone. Clinical outcome similar to other conventional pedicle screw system
EPS	Sofamor-Weigao Orthopaedic Material	6.5mm diameter	Clinical trial	Passively removable before bone ingrowth	In-vivo lumbar sheep study, osteoporotic induced, EPS provided 59.6% increase in pull-out strength over conventional screw Clinical trial – Expandable (EPS) vs Conventional (CPS): <ul style="list-style-type: none"> The rate of screw loosening in the EPS group (4.1%) was significantly lower as compared with the CPS group (12.9%) The fusion rate in the EPS group (92.5%, 74/80) was significantly higher than that of the CPS group (80.5%, 62/77)
SMArt	University of Toledo		Research	Not removable.	This fastener concept actuates using a Shape Memory Alloy (SMA) wire. However the team has subsequently disbanded, probably due to technical difficulties in expanding the fastener. Although they say that it is retractable they themselves admit in their paper that after osseointegration it would be impossible to retract.
ANTERIOR CERVICAL SPINAL FIXATION					
Osmium	Ulrich Medical	5mm diameter	Commercially available in EU	Passively removable before bone ingrowth	have a comparatively large diameter compared to 3.2mm for typical screws in the cervical vertebral body, and only expands very marginally (~10% increase), which means that it's only suitable for revision surgery.
SOFT TISSUE ANCHORS					
Appian Fx	KFx Medical	5.5 mm diameter	Commercial. FDA 510(k) approved	Not removable.	No dedicated bending sections, limited expansion size, depth penalty
Morphix	Medshape	2.5, 3.5, 4.5, 5.5mm diameter	Commercially available in the US	Not removable.	Using exotic shape memory alloy material that needs to be heated to change its shape. Not removable.
GENERAL ORTHOPAEDIC					
Active	Intelligent implant systems	3 to 7.5 mm diameter	510(k) cleared in 2012	Possibly removable after bone ingrowth	No data for pull-out strength increase, unlikely to increase strength significantly
Woven Screw Sleeve	Woven Orthopaedics Technology	All sizes	In development	Removable.	No testing paper found

Appendix B

Development timeline



Appendix C

Budget and Milestones

Milestone	Developmental Plan	Year 1		Year 2		Year 3		Year 4		COST
1	Cadaveric human bench-top testing									\$359,132
2	Animal In-vivo study									\$401,145
3	Final product design and testing verification									\$256,152
4	Regulatory approval and market entry									\$266,200
5	Phase 1 Clinical Trial									\$524,552
	IP and legal									\$300,000
	Commercialisation costs									\$400,000
COST		\$734,705		\$697,925		\$699,552		\$375,000		\$2,507,181

Appendix D

Table of comparable deals

Year	Company/tech	Acquired by	Product Stage	Indication	Amount (US\$ M)
1995?	RCI Screw	Smith & Nephew	Early market	Knee	5 + undisclosed royalties
2007	Setagon Inc	Medtronic	Development	CV metal implant	20
2008	Restore Medical Inc	Medtronic	Early Market	Soft tissue implant	29
2014	Solana	Wright Medical	Early market	Foot/ankle	90
2011	Ascension Ortho	Intergra	Mid-market	Shoulder/foot/hand plus materials platform	65
2014	OrthoPro	Wright Medical	Mid-market	Foot/ankle	35
2016	Stanmore Implants	Stryker	Established market	Multiple/platform	52
2016	Tornier Hip and Knee range	Corin	Established market	Hip/Knee	38
2016	Biotronic	Nuvasive	Established market	Spinal	98
2014	Optimised Ortho	Corin	Early market	Platform	undisclosed
2016	Biomedical Enterprises	DePuy Synthes	Mid-market	Platform	undisclosed
2016	SafeWire	Stryker	Early market	Spinal	undisclosed

Product stage definitions:

Early Market = 1 – 3 yrs sales

Mid market = 4 – 8 years yrs sales

Established Market = 9+ yrs sales

Appendix G EXF Screw PCT submission

AN EXPANDABLE FASTENER FOR ORTHOPAEDIC APPLICATIONS

Field of the Invention

5 The present invention relates to an expandable fastener for orthopaedic applications.

Background of the Invention

10 Expandable fasteners in bore holes in bone have been used in the past for orthopaedic applications in order to increase fixation strength and decrease the risk of failures.

It is usually required to remove the fasteners from the bore holes after a period of time, which requires contracting the fasteners from an expanded configuration to a contracted configuration. However, ingrowth of bone often makes it impossible to
15 contract the fasteners, which results in complications.

Summary of the Invention

The present invention provides an expandable fastener for orthopaedic applications
20 and arranged for fastening when positioned in a bore hole in bone, the fastener comprising:

a body having an axis; and
an expansion portion moveable between a contracted configuration and an expanded configuration such that, in use, the expansion portion urges outwardly from
25 the body towards the bone surrounding the bore hole;

wherein the fastener is arranged such that ingrowth of bone between the expansion portion and the body is substantially avoided when the expansion portion is in the expanded configuration.

30 The fastener may be arranged such that, when the fastener is in the expanded configuration, the expansion member is in contact with the body along at least a majority of a length of the expansion portion.

In one specific embodiment of the present invention the expansion portion contacts the
35 body along the length and typically also across the width of the expansion portion

whereby the fastener is arranged such that a gap between the expansion portion and the body is substantially avoided.

5 The expansion portion may be partially or entirely surrounded by the body when the expansion portion is in the expanded configuration. A gap, or any gap, between the expansion portion and the body may be sufficiently small such that ingrowth of bone is substantially or entirely avoided when the fastener is in the expanded configuration.

10 In one specific example any immediately adjacent surface regions of the expansion portion and the body are in direct contact with each other such that a gap between the adjacent surface regions is substantially avoided.

15 The fastener may also be arranged such that ingrowth of bone along the axis of the body is substantially avoided when the fastener is in the expanded configuration.

20 In one specific embodiment of the present invention the fastener is arranged such that at least a portion of a thickness of the expansion portion overlaps with a portion of the body along a length of the expansion portion when the fastener is in the expanded configuration.

25 In another specific embodiment of the present invention the fastener comprises an element arranged to cover or fill at least a portion of a gap between the expansion portion and the body when the fastener is in the expanded configuration. In this specific embodiment at least some or all immediately adjacent surface regions of the expansion portion and the body are in indirect contact via the element.

The expansion portion may be a part of an expansion member that is separate from the body. Alternatively, the expansion portion may be attached to the body.

30 In one specific embodiment the expansion portion is one of a plurality of expansion portions. In this embodiment the expansion portions are typically attached to the body. The element may be arranged to cover or fill at least a portion of a gap between adjacent expansion portions.

35 The expansion portions may be positioned at different angular positions around an axis

of the fastener. Further, at least some of the expansion portions may be positioned at different longitudinal positions or levels along the axis of the fastener. In addition, at least some of the expansion portions may be positioned at substantially the same longitudinal position along the axis of the fastener.

- 5 At least a portion of the length of the expansion portion may comprise a threaded or corrugated outer surface.

Further, the expansion portion may have an end surface that is substantially arc shaped.

10

The expansion portion may have wedge-shaped contact surfaces that extend along at least a portion of the length of the expansion portion and wedge against the body at contact surfaces of the body when the fastener is in the expanded configuration.

- 15 Alternatively or additionally, the body may have wedge-shaped contact surfaces that extend along at least a portion of the length of the expansion portion and wedge against the expansion portion at contact surfaces of the expansion portion when the fastener is in the expanded configuration.

- 20 The expansion portion may have an actuating surface and the fastener may be arranged such that the expansion portion is urged outwardly away from the axis of the fastener when an actuating member is received along the axis and urges against the actuating surface. The fastener may comprise the actuating member.

- 25 The actuating surface may be convexly shaped or may have a projection or the like. Alternatively, the actuating surface may have an indentation or may be concave and arranged such that the actuating member actuates within the indentation or within the concave shaped surface whereby the fastener is arranged such that an overlap between the body and the expansion portion is increased for a given expansion of the expansion portion compared with an expansion portion that has a convexly shaped
30 actuating surface and is thinner at side surfaces of the expansion portion.

- In one specific embodiment the expansion portion is part of an expansion member that is moveable relative to the body along an axis of the body. In this embodiment the
35 expansion member is typically not attached to the body. The fastener may also

comprise an actuating element. The actuating element may be positioned at a distal end of the fastener and the fastener may be arranged such that the expansion member is moveable towards or away from the actuating element along the axis of the body. Further, the fastener may be arranged such that, when the expansion member is moved towards the distal end of the fastener and towards the actuating element and engages with the actuating element, further movement of the expansion member towards the actuating element urges the expansion portion of the expansion member away from the axis of the body and forwardly to transfer the fastener into an expanded configuration and provide a penetrating force into the bone.

10

In one variation the actuating element has a tapered surface that has an apex and is positioned to facilitate an outward urging of the expansion portion of the expansion member when the expansion portion of the expansion member contacts the tapered surface of the actuating element, and when the expansion member is further moved toward the actuating element.

15

In another embodiment the fastener comprises an actuating member that is separate from the body and is moveable along the axis of the body. The fastener may be arranged such that the expansion portion urges outwardly away from the axis of the body when an actuating member is received along the axis and urges against the actuating surface portion of the expansion portion.

20

The expansion portion may be one of a plurality of expansion portions and at least two expansion portions may be oriented in opposite directions. When in the expanded configuration, the at least two expansion portions oriented in opposite directions and urged outwardly present the advantage that the fixation strength of the fastener may be increased where the surrounding bone is hard and dense.

25

In one embodiment the fastener comprises at least two pairs of expansion portions. In this embodiment the expansion portions of one pair are oriented opposite to the expansion portions of the other pair such that ends of the expansion portions of one pair oppose ends of the expansion portions of the other pair. A first pair of expansion portions may be attached to the body and a second pair of expansion portions may be separate from the body. The expansion portions of both pairs may be arranged to urge outwardly when the ends of the expansion portions of one pair are moved against the

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opposing ends of the other pair. In this embodiment, the fastener may be arranged such that an actuating member, moveable along the axis of the body, can move the ends of the expansion portions of one pair that are against the opposing ends of the other pair. The fastener may be arranged such that the ends of both pairs of
5 expansion portions urge outwardly in a manner such that a gap between the opposing ends of the expansion portions is substantially avoided.

Further, the fastener may be arranged such that elastic forces caused by an inwardly urging first pair of expansion portions against the second pair of expansion portions
10 facilitate removal of the fastener when in the expanded condition and when the actuating member is removed.

The expansion portion may comprise a bending region at which the expansion portion predominantly bends when the expansion portion urges towards the expanded
15 configuration and the bending region may be positioned inside an outer periphery of the body and may be at least partially overlapped by a portion of the body.

At least portions of the body or the expansion portion may comprise an outer deformable layer of a material, and may be arranged such that, when the expansion
20 portion urges outwardly, contact surfaces of the body or sidewalls of the expansion portion fractionally engage with each other thereby allowing the outer deformable layer of material to deform and fill or overlap at least a portion of a gap that may otherwise form between the expansion portion and the body. The outer deformable layer of the material may comprise titanium.

25 The fastener may be formed using a 3D printing process such as a process including Selective Laser Melting or Electron Beam Melting.

The fastener may comprise an outer elastic layer, such as an elastic membrane. The
30 elastic membrane may be arranged to overlay gaps that may form between the body and an expansion portion or between adjacent expansion portions when in the expanded configuration and thereby avoid ingrowth of bone. The elastic layer or membrane may or may not be separate from the body and the expansion portion and may surround both the body and the expansion portion.

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The fastener may also comprise a material that may be non-viscous and may be positioned between the body and the expansion portion or between adjacent expansion portions so as to fill a gap. For example, the material may initially be injected into an interior portion and may be positioned to penetrate into a gap between the body and the expansion portion or between adjacent expansion portions when the actuator is received by the fastener and urges the expansion portion or the expansion portions outwardly.

A deformable material may be infused into an interior of the fastener and may comprise an antibacterial substance arranged to substantially prevent formation or accumulation of bacteria. The deformable material may also be used to fill a gap along the axis of the body when the fastener is in the expanded configuration. The deformable material may comprise a polymeric material such as rubber.

Alternatively or additionally, the fastener may also comprise a coating that has chemical properties that substantially inhibit or reduce growth of bone at the coating such that the ingrowth of bone between the expansion portion and the body is reduced when the fastener is in the expanded configuration.

The fastener is typically formed from bio-compatible materials.

The fastener may be arranged such that the expansion member urges inwardly when an actuating member is removed.

If the expansion portion fails to contract when the fastener should be removed, the fastener may be arranged such that contraction of the expansion portion can be triggered. For example, the fastener may comprise a removal element arranged to engage with the expansion portion wherein the removal element is arranged to contract the expansion portion when removal of the fastener from the bore hole in bone is initiated.

The fastener may comprise a removal element arranged for insertion into the body and structured to engage with the expansion portion when the fastener is in the expanded configuration wherein the removal element is arranged to contract the expansion portion when the removal element is moved in a direction away from the bore hole

along an axis of the fastener.

In one example the removal element is attached to, or part of, the body, and the fastener is arranged such that, when the expansion portion is moved along the axis of
5 the body, the expansion portion is moved inwardly.

Alternatively, the removal element may be part of, or may be coupled to, another device (such as a plate, an intramedullary nail or a rod), and the fastener may be arranged such that, when the removal element with the other device is moved along
10 the axis of the body, the expansion portion urges inwardly if not fully contracted.

The removal element may be a spring element or an elastic element that urges the expansion portion inwardly when the actuating member is removed. For example, the spring element or elastic element may be provided in the form of an elastic ring, or
15 spring clip that surrounds at least a portion of the fastener.

The fastener may comprise an actuating element that also functions as a removal element.

20 One of the expansion portion and the actuating element may comprise a hole and the other one of the expansion portion and the actuating element may comprise a suitable projection for engagement within the hole. Either one or both of the hole and the projection may be tapered in a manner to facilitate engagement.

25 The actuating element and the expansion portion may be arranged such that the actuating member engages with the expansion portion and forces the expansion portion to move from an expanded to a contracted configuration when the actuating element is moved in a direction away from the bore hole along an axis of the fastener.

30 The actuating element may comprise a central rod that is coupled to the expansion portion via a linkage, wherein the fastener is arranged and the linkage is positioned such that the expansion portion moves between the contracted configuration and the expanded configuration when the actuation element moves to different positions along the axis of the fastener.

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The body of the fastener may have a threaded or corrugated outer surface along at least a portion of its length.

5 The expansion portion may have a thickness that is tapered in a direction around the axis of the fastener such that, when the expansion portion is in the expanded configuration, the expansion portion projects at one side portion further away from the axis than at an opposite second side portion.

10 A person skilled in the art will appreciate that the fastener may be used for various orthopaedic applications.

For example, the fastener may be used for bone fracture fixation and spine fixation, or as intramedullary nail and hip stems.

Brief Description of the Figures

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Embodiments of the present invention will now be described, by way of example only, with reference to the accompanying Figures, in which:

20 Figures 1 (a) and (b) show a fastener in accordance with an embodiment of the present invention;

Figures 2 (a) and (b) show a portion of the fastener shown in Figure 1;

25 Figures 3 (a) to (c) show cross-sectional views of a fastener in accordance with an embodiment of the present invention;

Figures 4 (a) and (b) show perspective cross-sectional views of portions of a fastener in accordance with an embodiment of the present invention;

30 Figure 5 shows cross-sectional views of a fastener in accordance with an embodiment of the present invention, (a) in a contracted configuration, and (b) and (c) in an expanded configuration;

35 Figure 6 shows a side view of a fastener in accordance with a further embodiment of the present invention;

Figure 7 shows a side view of a fastener in accordance with an embodiment of the present invention;

5 Figures 8(a) to (d) show cross-sectional views of portions of a fastener in accordance with an embodiment of the present invention;

 Figures 9(a) and (b) show perspective views of an end portion of an expansion portion and an end portion of a removal element in accordance with an embodiment of the present invention;

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 Figure 9(c) shows a cross-sectional view of portions of an expansion portion and a removal element in accordance with an embodiment of the present invention;

15 Figure 10(a) shows a cross-sectional view of a fastener in accordance with an embodiment of the present invention;

 Figure 10(b) shows a side view of the fastener of Figure 10(a); and

20 Figure 11 shows a cross-sectional view of a fastener in accordance with an embodiment of the present invention.

 Figures 12(a) and (b) show cross-sectional views of portions of a fastener in accordance with an embodiment of the present invention;

25 Figure 13 shows cross-sectional views of a fastener in accordance with an embodiment of the present invention, (a) in a contracted configuration, (b) in an expanded configuration, and (c) in a contracted configuration;

30 Figure 14 shows a side view of a fastener in accordance with an embodiment of the present invention;

 Figure 15 shows cross-sectional views of a fastener in accordance with another embodiment of the present invention (a) in a contracted configuration, and (b) in an expanded configuration;

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Figure 16 shows cross-sectional views of a fastener in accordance with another embodiment of the present invention (a) in a contracted configuration, and (b) in an expanded configuration.

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Detailed Description of Specific Embodiments

Embodiments of the present invention generally relate to an expandable fastener. For example, the fastener may be used for orthopaedic applications to secure stabilisation members used to stabilise fractured bones. The fastener is arranged for positioning in a bore hole in bone.

The fastener has a body and expansion portions that are moveable between a contracted and an expanded configuration such that, in use, the expansion portions urge outwardly from the body towards the bone surrounding the bore hole. The fastener is arranged such that ingrowth of bone between the expansion portions and the body or into the internal section of the body is substantially avoided when the expansion portions are in the expanded configuration.

The fastener may be arranged such that a thickness of each of the expansion portions overlaps with the thickness of the body when the fastener is in the expanded configuration. Each expansion portion typically contacts the body along the length of the expansion portion (and typically also across the width) such that a gap is avoided when the expansion portion is in the expanded configuration. Alternatively or additionally, the fastener comprises an element, such as a layer or a fill material, which is arranged to cover or fill at least a portion of a gap between the expansion portion and the body or between adjacent expansion portions when the fastener is in the expanded configuration.

The fastener has a hollow interior region for receiving an actuating member that engages with the expansion portions and urges the expansion portions outwardly when the actuating member is moved into the interior region of the fastener.

In general, such a fastener may be inserted into a provided predrilled bore hole in bone as follows. The fastener is provided in a contracted state and engaged with a suitable

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tool that holds the fastener and prevents translational or rotational movement relative to the fastener. The tool is then used to insert the fastener into the predrilled bore hole. As will be described in further detail below, the fastener may comprise an actuating member. The tool is kept engaged with the fastener while the actuating member is
5 inserted into the fastener to stop relative translational or rotational movement between the fastener and the bone. The actuating member is then inserted into a hollow space within the fastener along an axis of the fastener and moved towards a distal portion of the fastener. Alternatively, the fastener may be arranged such that the actuating member is rotated within the body of the fastener. In either case, one or more
10 expansion portions urge outwardly during movement of the actuating member towards an expanded configuration in which the one or more expansion portions engage with the bore hole.

The fastener may be removed from the bore hole as follows. Initially the tool is
15 engaged with the fastener in a manner such that rotational or translational movement of the fastener relative to the tool is prevented. The tool will also prevent translational and rotational movement of the fastener relative to the bone. The actuating member is then removed either by rotational movement or translational movement along the axis of the fastener whereby the one or more expansion portions contract into the
20 contracted configuration so that the fastener can be removed from the bore hole. In an alternative variation which will be described in further detail below, the actuating member may also function as a removal member and may engage with the one or more expansion portions to move the one or more expansion portions to the contracted configuration.

25 Specific examples of the fastener will now be described with reference to Figures 1 to 16.

Referring initially to Figure 1 (a) and (b), there is shown an expandable fastener 10 for
30 fastening when positioned in a bore hole in bone. The fastener 10 has a body 14 which has an axis A and multiple levels L1, L2, L3 and L4 at which expansion portions 16 are positioned. Each expansion portion 16 is moveable between a contracted configuration and an expanded configuration of the fastener 10. Figure 1 (a) shows the expansion portion 16 in a contracted configuration and Figure 1(b) shows the expansion portion
35 10 in an expanded configuration.

In use, each expansion portion 16 urges outwardly from the body 14 towards the bone surrounding the bore hole (not shown). In this embodiment, the fastener 10 has a substantially circular cross-sectional shape in a plane that is transversal to the axis A.

5 The fastener 10 is formed from bio-compatible materials.

Further, the body 14 of the fastener 10 has a threaded or corrugated outer surface along its length and at least a portion of the length of the expansion portions comprises a threaded or corrugated outer surface.

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Referring now to Figure 2 (a) and (b), there is shown a portion of the fastener 10 with the expansion portion 16 in the contracted configuration (a) and in the expanded configuration (b). The expansion portion 16 is arranged to urge from a contracted configuration outwardly away from the body 14 such that at least a portion of the thickness "t" of the expansion portion 16 overlaps with a portion of the body 14 along the length "L" of the expansion portion 16. In one specific embodiment the expansion portion overlaps with the body and contacts the body such that a gap between the expansion portion and the body is substantially or even entirely avoided.

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20 Referring now to Figure 3, there are shown cross-sectional views of a fastener 30 in accordance with a further embodiment of the present invention. Figure 3 (a) shows the fastener 30 in the contracted configuration, Figure 3 (b) shows the fastener 30 in an intermediate configuration and Figure 3(c) shows the fastener 30 in an expanded configuration. Expansion portions 32 are positioned between body portions 34 and have arc-shaped end surfaces 35 at which they contact the bone when in use. The body portions 34 have wedge-shaped contact surfaces 37 that wedge against the expansion portions 32 at contact surfaces 36 when the expansion portions 32 are in the expanded configuration.

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30 Figure 4 (a) shows a perspective cross-sectional view of a fastener 40 in accordance with a further embodiment of the present invention. The fastener 40 comprises body portions 42 and expansion portions 44 and 45. The expansion portions 44 and 45 have inner actuating surfaces 46 and 48, respectively. The expansion portions 44 and 45 urge outwardly when an actuating member (not shown) is received along an axis of the fastener 40 and urges against the actuating surfaces 46, 48, respectively. The

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actuating surface 46 of each expansion portion 44 is in this embodiment tapered to a tip (or may for example be convexly curved). In contrast, the actuating surfaces 48 of the expansion portion 45 is instead concavely curved such that a thickness of the expansion portion 45 at the side portions of the expansion portion 45 is increased
5 compared with that of the expansion portion 44. Side portions of the expansion portions 44, 45 overlap with surfaces of the body 42 in either embodiment at least along a portion of the length of the expansion portions 44, 45 when the expansion portions 44, 45 are in the expanded configuration. However, because the actuating surfaces 48 of the expansion portions 45 is indented or concavely shaped and the
10 thickness is increased at the side portions of the expansion portions 45, the expansion portions 45 can expand further without formation of a gap between the expansion portions 45 and the body 42 compared to expansion portions 44 with convexly shaped actuating surfaces, which reduces the likelihood of ingrowth of bone between each expansion portion 45 and the body 42 when the expansion portions 45 are in the
15 expanded configuration.

In a variation of the above described embodiment the expansion portions have a thickness that is tapered in a direction around the axis of the fastener such that, when the expansion portions are in the expanded configuration, each expansion portion
20 projects at one side portion further away from the axis than at an opposite second side portion. This embodiment provides the advantage that the contraction of the expansion portions is facilitated when the actuating member is removed and the fastener is rotated about the axis in a direction towards the thinner side portions of the expansion portions.

25 In general, each expansion portion has a bending region at which the material is thinner and at which the expansion portion predominantly bends when the expansion portion moves into the expanded configuration. Further, each expansion portion has an actuating surface that is sloped inwardly. The bending section should be as short as
30 practical for providing elastic or substantially elastic deformation. A shorter bending section allows more expansions per unit length, which increases fixation strength. A shorter bending section also provides a stiffer spring-back force, which helps removability. Further, a shorter bending section also increases an expansion angle, which further increases fixation strength.

35 Figure 4 (b) shows a cross-sectional perspective side view of a portion of the fastener

40. The Figure shows a bending region 49 and a sloped actuating surface 46 of the expansion portion 44. As mentioned above, it is advantageous to design the bending region of an expansion portion relatively short. Further, it is advantageous to design an upper region with the actuating surface relatively long and/or the slope of the actuating surface relatively gradual and extending along a relatively large length portion as then, when the expansion portion 44 is in the expanded configuration, the thickness of the side portions of expansion portion 44 overlaps along a longer length portion (or along the entire length) of the expansion portion 44 to avoid any gap.

10 Figure 5 shows cross-sectional views of a fastener 50 in (a) contracted configuration and (b) expanded configuration in accordance with a further embodiment of the present invention.

The fastener 50 comprises a body 52 and expansion portions 54. In this example, the surface of the body 52 comprises an outer thin deformable layer of material 56 that is arranged such that, when the expansion portions 54 urge outwardly, contact surfaces of the body 52 fractionally engage with sidewalls of the expansion portions 54 thereby allowing the outer thin deformable layer of material 56 to deform and fill or overlap at least a portion of a gap that may otherwise form between the expansion portions 54 and the body 52. This results in accumulation of material, which is schematically indicated in figure 5(c) by a "lip" 58 that overlaps a portion of the expansion portion 54. The outer thin deformable layer of material may, for example be formed from the same metallic material as the material comprising the body 52, and may possibly be formed from titanium. The outer thin deformable layer of material surrounding the body 52 may be an extension of the body 52, built in during the manufacturing process.

A person skilled in the art will appreciate that alternatively portions of the expansion portion 54 may comprise this outer thin deformable layer of material.

30 Figure 6 shows a side view of a fastener 60 comprising a body 62 and an expansion portion 64. In this example, a sealant 66 is injected in the areas in which bone ingrowth is not desirable, such as between the body 62 and the expansion portion 64. The sealant 66 is squeezed between the body 62 and the expansion portion 64 when the expansion portion 64 urges from a contracted configuration to an expanded configuration, so as to cover or fill a gap between the body 62 and the expansion

portion 64 and thereby avoid ingrowth of bone between the body 62 and the expansion portion 64. The sealant 66 is in this embodiment a polymeric or an elastomeric compound, and may be non-viscous. The sealant 66 may also comprise a substance that inhibits growth of bone at the sealant and thereby inhibits ingrowth of bone.

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Figure 7 shows a side view of a fastener 70 comprising a body 72 and an expansion portion 74 in accordance with an embodiment of the present invention. An outer surface of the fastener 70 is coated with a thin membrane 76. The thin membrane 76 is arranged to stretch as the expansion portion 74 moves from a contracted to an expanded configuration, thereby covering any gap and avoiding the undesirable ingrowth of bone when the expansion portion 74 is in the expanded configuration. The thin membrane 76 is in this embodiment a resilient elastomer such as silicone rubber.

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Figures 8(a) to (d) show section views of a fastener 80. The fastener comprises expansion portions 82. In this embodiment, the expansion portions 82 have actuating surfaces 84 that are arranged to receive an actuating member 86 along an axis A of the fastener 80 whereby the expansion portions 82 are urged outwardly away from the axis A as seen in Figure 8(b). The expansion portions 82 having actuating surfaces 84 are also arranged to urge inwardly from the bone towards the axis of the fastener 80 when the actuating member 86 is removed whereby the fastener 80 moves to the contracted configuration, such a configuration illustrated in Figure 8(a). The expansion portions 82 are structured such that, when the actuating member 86 is received or removed, the expansion portions 82 urge elastically outwardly and inwardly, respectively.

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If an expansion portion 82 fails to contract, a removal element 89 that couples with the fastener 80 may be used. The expansion portions 82 comprise in this embodiment holes 88 that taper inwardly. The removal element 89 comprises projections that are arranged for engagement with the expansion portions 82 and within the holes 88 of the expansion portions 82 such that when the removal element 89 has engaged with the expansion portions 82 in the expanded configuration as shown in Figure 8(c) and is pushed forwardly, the expansion portions 82 are moved inwardly and the fastener 80 is moved to a contracted configuration as shown in Figure 8(d).

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Figures 9(a), (b) and (c) show portions of a fastener 90 in accordance with a further

embodiment of the present invention. The fastener 90 comprises an actuating member 92 that functions as a removal element and has recesses 94. The fastener 90 further comprises the expansion portion 96 that has an engaging portion 98. The actuating member 92 and the expansion portion 96 are arranged such that recesses 94 engage
5 with the engaging portion 98 of the expansion portion 96 when the actuating member 92 is received along the axis A and urges against the expansion portion 96. As the expansion portion 96 and the actuating member 92 are engaged, the expansion portion 96 moves outwardly when the actuating member 92 is inserted and moves inwardly from the bone surrounding the bore hole to the body when the actuating
10 member 92 is retracted.

Figure 10 shows (a) a cross-sectional view and (b) a side view of a fastener 100 comprising a body 102, an expansion portion 104 and a removal element 106 coupled to a portion of the outer surface 105 of the fastener 100. In this embodiment the
15 removal element 106 is coupled to the body 102 and the expansion portion 104 to increase the contraction force and induce contraction of the expansion portion 104 when the actuation member is removed from an interior of the fastener 100. The removal element 106 is an elastic ring, such as an O-ring formed from a polymeric material. Alternatively, the removal element 106 may also be a suitable spring clip,
20 such as a spring clip formed from a metallic material (such as titanium).

Figure 11 shows cross-sectional views of a fastener 110 comprising a body 112 and two opposite expansion portions 114. The expansion portions 114 are coupled to an actuating element 113 that also functions as a removal element. The actuating element
25 113 comprises a central rod 116 connected to stiff radial linkages 118. The actuating element 113 is arranged and the linkages are positioned such that the expansion portions 114 move between a contracted configuration (a) and an expanded configuration (b) when the actuating element 113 moves to different positions along the axis A of the fastener 110.

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Figure 12(a) and (b) show cross-sectional views of portions of a fastener 120 in accordance with an embodiment of the present invention. In this embodiment, an expansion portion 122 has an end surface 123 that is substantially arc shaped such that, when the expansion portion 122 is in the expanded configuration, interference of
35 the expansion portion 122 with the surrounding growing bone (not shown) is

minimised. Further, the expansion portion 122 comprises an upper section 124 with a threaded or corrugated outer surface, and a bending section 125 at which the material is thinner than the material of the upper section 124 and at which the expansion portion 122 predominantly bends when the expansion portion 122 urges towards an expanded configuration. The bending section 124 is positioned inside the outer periphery of a body 126 and is overlapped by a portion of the body 126.

This embodiment allows a greater expansion angle of the expansion portion 122 while substantially avoiding any gap between the body 126 and the expansion portion 122 when the expansion portion 122 is in the expanded configuration, which further increases the fixation strength of the fastener 120.

This embodiment further allows a section 127 with a threaded or corrugated outer surface to be positioned at the outer surface of the bending section 125 to cover or fill a gap at the bending section 125 between the body 126 and the expansion portion 122 when the expansion portion 122 is in the expanded configuration. Thereby, ingrowth of bone between the body 126 and the expansion portion 122 when the expansion portion 122 is in the expanded configuration is prevented in the area surrounding the bending section 125 and the threaded or corrugated outer surface of the additional section 127 further increases the fixation strength of the fastener 120 in the bore hole of a bone (not shown).

In this embodiment, when an actuating member 128 is received along an axis A of the fastener 120 and urges the expansion portion 122 outwardly, it is also possible to fill in the gap along the axis A of the body 126 of the fastener 120 with a deformable material 129 infused with an antibacterial substance to prevent growth of bacteria along the axis of the body 126 of the fastener 120 when the expansion portion 122 is in the expanded configuration. The deformable material 129 may comprise rubber.

Figure 13 shows cross-sectional views of a fastener 130 in accordance with an embodiment of the present invention, (a) in a contracted configuration, (b) in an expanded configuration, and (c) in a contracted configuration. In this embodiment, an actuating member 132 functions as a removal element. The actuating member 132 engages with expansion portions 134 in a "tulip" design (a), such that the expansion portions 134 are forced to move from an expanded (b) to a contracted (c) configuration

when the actuating member 132 is moved in a direction away from the bore hole along an axis A of the fastener 130.

5 Figure 14 shows a side view of a fastener 140 in an expanded configuration when inserted in a bore hole of a bone 141, in accordance with an embodiment of the present invention. The fastener 140 comprises a body 142 and three levels of expansion portions 144, 146, and 148, distributed along the length of the fastener 140, for fixation in the bore hole of a bone 141. In this embodiment, at least two levels of expansion portions such as 144 and 146 are facing in opposite directions along the axis A of the body 142 (the expansion portions 144 are rotated by 180 degrees
10 compares to the expansion portions 146). The expansion portions 144, 146, and 148 urge outwardly from the body 142 towards the bone 141, when an actuating member (not shown) is received along the axis A of the body 142 and urges against the actuating surface portions (not shown) of the expansion portions 144, 146 and 148.
15 The two levels of expansion portions 144 and 146 that face in opposite directions allow increasing the fixation strength of the fastener 140, when in the expanded configuration, onto the bone 141 surrounding the bore hole, in particular where the bone 141 is hard and dense such as cortical bone, which is harder and denser than cancellous bone.

20 Figure 15 shows cross-sectional views of a fastener 150 in in accordance with another embodiment of the present invention, (a) in the contracted configuration and (b) in the expanded configuration. In this embodiment, two pairs of expansion portions 152 and 154 are positioned at different longitudinal positions along the axis A of the fastener 150. The pair of expansion portions 152 is oriented opposite to the pair of expansion portions 154 such that ends 157 of the expansion portions 152 oppose respective ends 158 of the expansion portions 154. The expansion portions 152 have actuating surfaces 159 that are arranged to receive an actuating member 156 along the axis A of the fastener 150, from a proximal end of the expansion portions 154 towards the ends
25 157 of the expansion portions 152, whereby the expansion portions 152 are urged outwardly away from the axis A. The ends 157 of the expansion portions 152 contact the ends 158 of the expansion portions 154 such that the expansion of the expansion portions 152 urges the expansion portions 154 outwardly. Further, when the actuating member 156 is removed, the expansion portions 154 elastically urge inwardly away
30 from the bone (not shown) towards the axis A. The ends 157 and 158 are in contact
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such that the expansion portions 152 are urged inwardly together with the expansion portions 154 when the inwardly urged ends 158 move against the opposing ends 157. The pairs of expansion portions 152 and 154 urge outwardly towards an expanded configuration (b) in a manner such that a gap between the opposing ends 157 and 158 is substantially avoided.

Figure 16 shows cross-sectional views of a fastener 160 in accordance with another specific embodiment, (a) in the contracted configuration and (b) in the expanded configuration. In this specific embodiment, the fastener 160 comprises a body 162 and expansion portions 164, wherein the expansion portions 164 are part of an expansion member 166 positioned within the body 162, the expansion member 166 being moveable with the expansion portions 164 relative to the body 162 along an axis A of the body 162 of the fastener 160. The fastener 160 further comprises an actuating element 167 positioned at a distal end 168 of the fastener 160, and the expansion member 166 with the expansion portions 164 are moveable towards or away from the actuating element 167. The actuating element 167 has a tapered surface with an apex such that when the expansion member 166 with the expansion portions 164 are moved towards the distal end 168 of the fastener 160 and towards the actuating element 167, an outward urging of the expansion portions 164 is facilitated, and the expansion portions 164 are urged outwardly away from the axis A of the fastener 160 when the expansion member 166 with the expansion portions 164 are further moved towards the actuating element 167, which is received by actuating surfaces 169. The fastener 160 is thus transferred to an expanded configuration (b).

Further, when the expansion element 166 is moved away from the actuating element 167, the expansion portions 164 are urged to move inwardly and away from the actuating element 168, such that the fastener 160 is transferred to a contracted configuration (a).

Numerous variations and modifications will suggest themselves to persons skilled in the relevant art, in addition to those already described, without departing from the basic inventive concepts. All such variations and modifications are to be considered within the scope of the present invention, the nature of which is to be determined from the foregoing description. For example, the fasteners may not necessary have a substantially circular cross-sectional shape and may alternatively have any other

suitable cross-sectional shape. Further, the fasteners may be formed from any suitable material.

Claims:

1. An expandable fastener for orthopaedic applications and arranged for fastening
5 when positioned in a bore hole in bone, the fastener comprising:
 a body having an axis; and
 an expansion portion moveable between a contracted configuration and an
expanded configuration such that, in use, the expansion portion urges outwardly from
the body towards the bone surrounding the bore hole;
10 wherein the fastener is arranged such that ingrowth of bone between the
expansion portion and the body is substantially avoided when the expansion portion is
in the expanded configuration.
2. The fastener of claim 1, wherein the fastener is arranged such that, when the
15 fastener is in the expanded configuration, the expansion member is in contact with the
body along at least a majority of a length of the expansion portion.
3. The fastener of claim 1 or 2 wherein the expansion portion is at least partially
surrounded by the body when the expansion portion is in the expanded configuration
20 and wherein a gap between the expansion portion and the body is substantially
avoided such that ingrowth of bone is substantially avoided.
4. The fastener of any one of the preceding claims wherein any immediately
adjacent surface regions of the expansion portion and the body are in direct contact
25 with each other such that a gap between the adjacent surface regions is substantially
avoided.
5. The fastener of any one of the preceding claims wherein the fastener is
arranged such that at least a portion of a thickness of the expansion portion overlaps
30 with a portion of the body along a length of the expansion portion when the fastener is
in the expanded configuration.
6. The fastener of any one of claims 1 to 3 comprising an element arranged to
cover or fill at least a portion of a gap between the expansion portion and the body
35 when the fastener is in the expanded configuration.

7. The fastener of any one of the preceding claims wherein the expansion portion is a part of an expansion member that is separate from the body.

5 8. The fastener of any one of the preceding claims wherein the expansion portion has wedge-shaped contact surfaces that extend along at least a portion of the length of the expansion portion and wedge against the body at contact surfaces of the body when the fastener is in the expanded configuration.

10 9. The fastener of any one of claims 1 to 7 wherein the body has wedge-shaped contact surfaces that extend along at least a portion of the length of the expansion portion and wedge against the expansion portion at contact surfaces of the expansion portion when the fastener is in the expanded configuration.

15 10. The fastener of any one of the preceding claims wherein the expansion portion has an actuating surface and the fastener is arranged such that the expansion portion is urged outwardly away from the axis of the fastener when an actuating member is received along the axis and urges against the actuating surface.

20 11. The fastener of any one of the preceding claims wherein the expansion portion is part of an expansion member that is moveable relative to the body along an axis of the body.

25 12. The fastener of claim 11 comprising an actuating element attached to the body at a distal end of the fastener, wherein the fastener is arranged such that the expansion member is moveable towards or away from the actuating element along the axis of the body, and wherein the fastener is arranged such that, when the expansion member is moved towards the distal end of the fastener and towards the actuating element and engages with the actuating element, further movement of the expansion member towards the actuating element urges the expansion portion of the expansion member away from the axis of the body to transfer the fastener into an expanded configuration.

35 13. The fastener of claim 11 comprising an actuating member that is separate from the body and is moveable along the axis of the body, wherein the fastener is arranged

such that the expansion portion urges outwardly away from the axis of the body when an actuating member is received along the axis and urges against the actuating surface portion of the expansion portion.

5 14. The fastener of any one of the preceding claims wherein the expansion portion one of a plurality of expansion portions.

10 15. The fastener of claim 14 comprising at least two pairs of expansion portions, wherein the expansion portions of one pair are oriented opposite to the expansion portions of another pair such that ends of the expansion portions of one pair oppose ends of the expansion portions of another pair, and wherein the expansion portions of the pairs are arranged to urge outwardly when the ends of the expansion portions of one pair are moved against the opposing ends of another pair.

15 16. The fastener of claim 15 wherein the fastener is arranged such that an actuating member, moveable along the axis of the body, can move the ends of the expansion portions of one pair are against the opposing ends of another pair, whereby the fastener is arranged such that the ends of the pair of expansion portions urge outwardly in a manner such that a gap between the opposing ends of the expansion portions is substantially avoided.

20 17. The fastener of any one of the preceding claims wherein the expansion portion comprises a bending region at which the expansion portion predominantly bends when the expansion portion urges towards the expanded configuration and the bending region is positioned inside an outer periphery of the body and is at least partially overlapped by a portion of the body.

25 18. The fastener of any one of the preceding claims wherein at least portions of the body or the expansion portion comprises an outer deformable layer of a material, and is arranged such that, when the expansion portion urges outwardly, contact surfaces of the body or sidewalls of the expansion portion fractionally engage with each other thereby allowing the outer deformable layer of material to deform and fill or overlap at least a portion of a gap that may otherwise form between the expansion portion and the body.

35

19. The fastener of any one of the preceding claims comprising an outer elastic membrane arranged to overlay gaps that may otherwise form between the body and an expansion portion or between adjacent expansion portions when in the expanded configuration and thereby avoid ingrowth of bone.

5

20. The fastener of any one of the preceding claims comprising a material that is non-viscous and is positioned between the body and the expansion portion or between adjacent expansion portions so as to fill a gap.

10

21. The fastener of any one of the preceding claims wherein a deformable material is infused into an interior of the fastener and is an antibacterial substance arranged to substantially prevent formation or accumulation of bacteria.

15

22. The fastener of any one of the preceding claims comprising a coating that has chemical properties that substantially inhibit or reduce growth of bone at the coating such that the ingrowth of bone between the expansion portion and the body is reduced when the fastener is in the expanded configuration.

20

23. The fastener of any one of claims 1 to 6 wherein the expansion portion is attached to the body.

Abstract

The present disclosure provides an expandable fastener for orthopaedic applications and arranged for fastening when positioned in a bore hole in bone. The fastener
5 comprises a body having an axis. The fastener further comprises an expansion portion moveable between a contracted configuration and an expanded configuration such that, in use, the expansion portion urges outwardly from the body towards the bone surrounding the bore hole. The fastener is arranged such that ingrowth of bone
10 between the expansion portion and the body is substantially avoided when the expansion portion is in the expanded configuration.

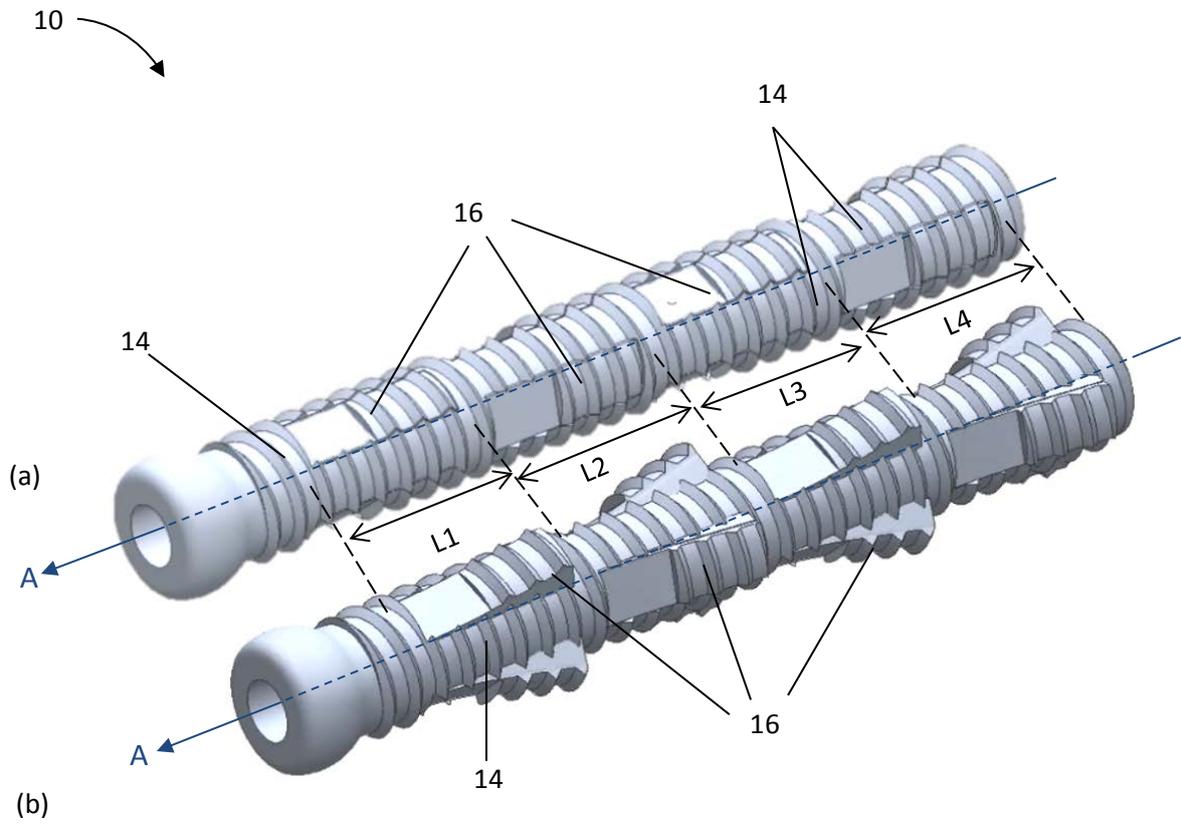


FIGURE 1

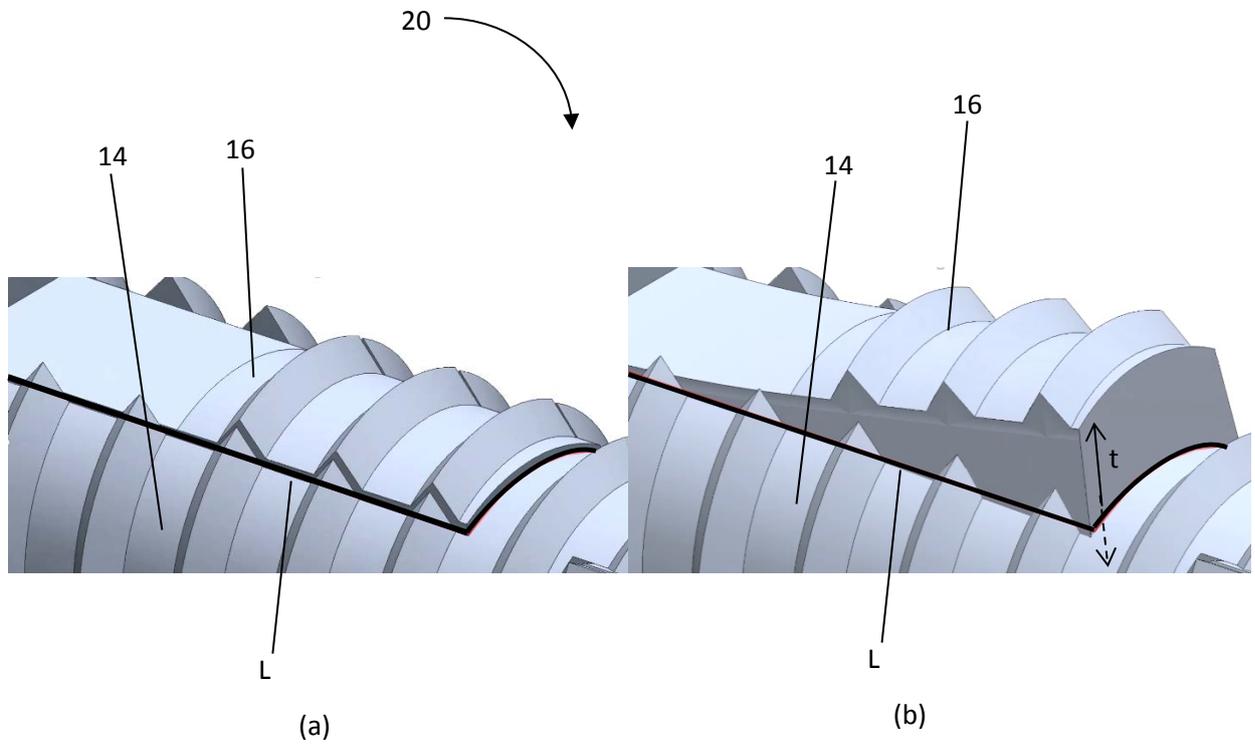
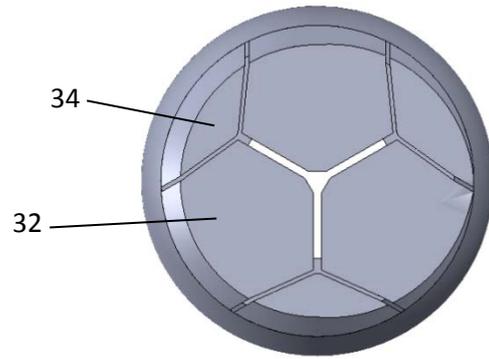
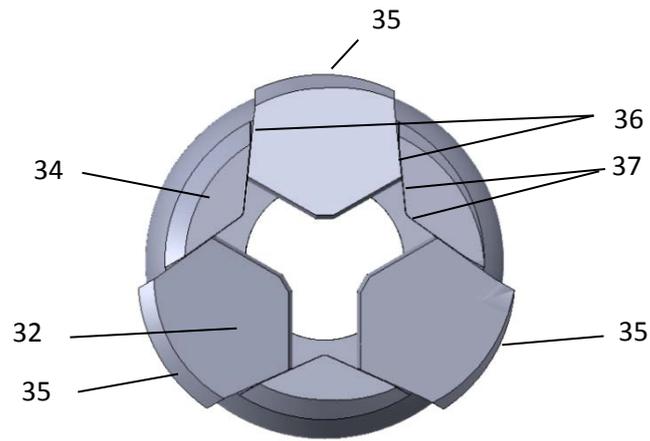


FIGURE 2

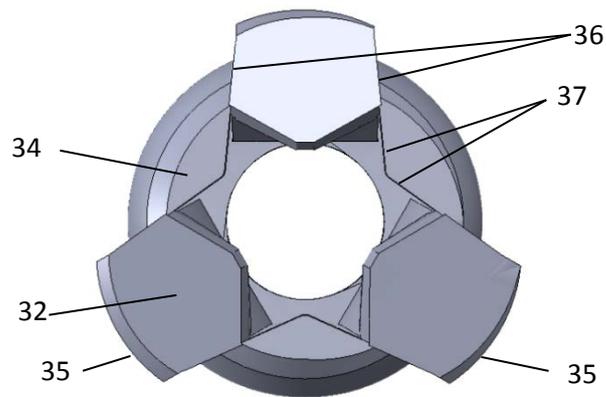
30 ↘



(a)

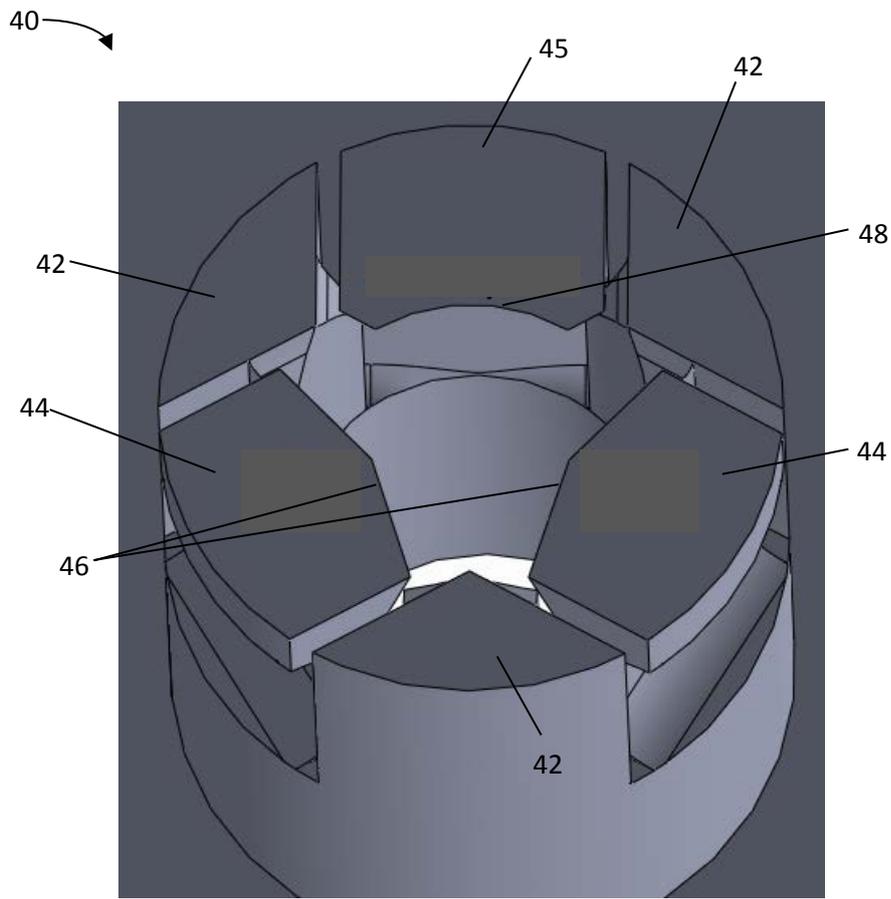


(b)

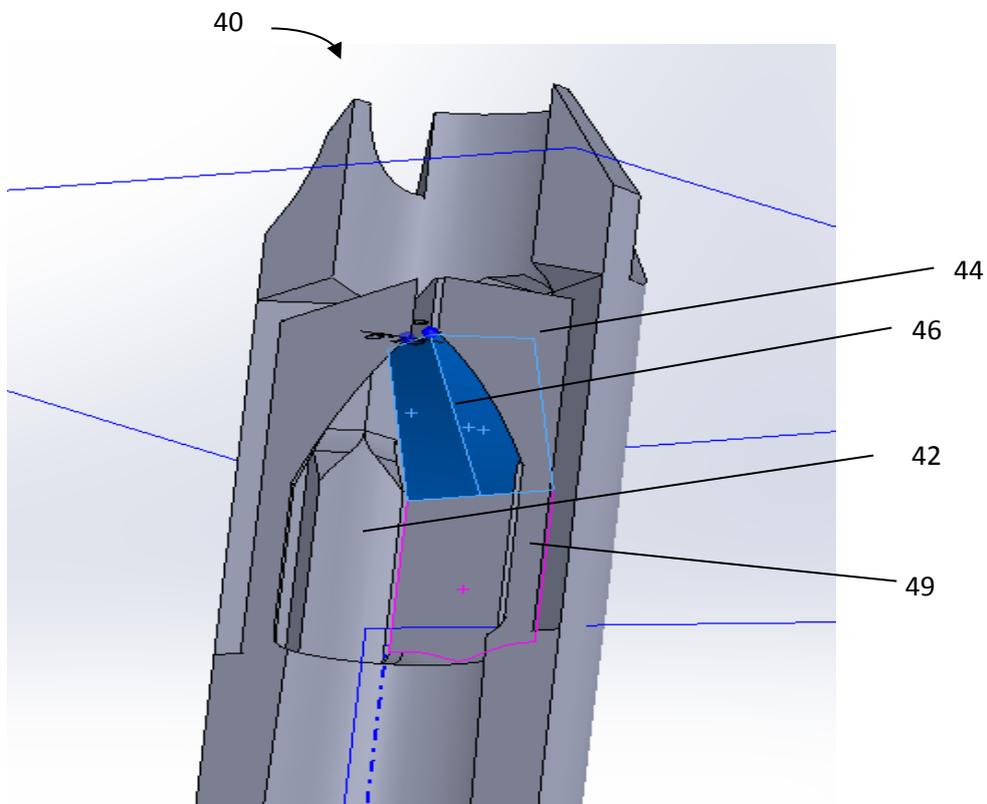


(c)

FIGURE 3



(a)



(b)

FIGURE 4

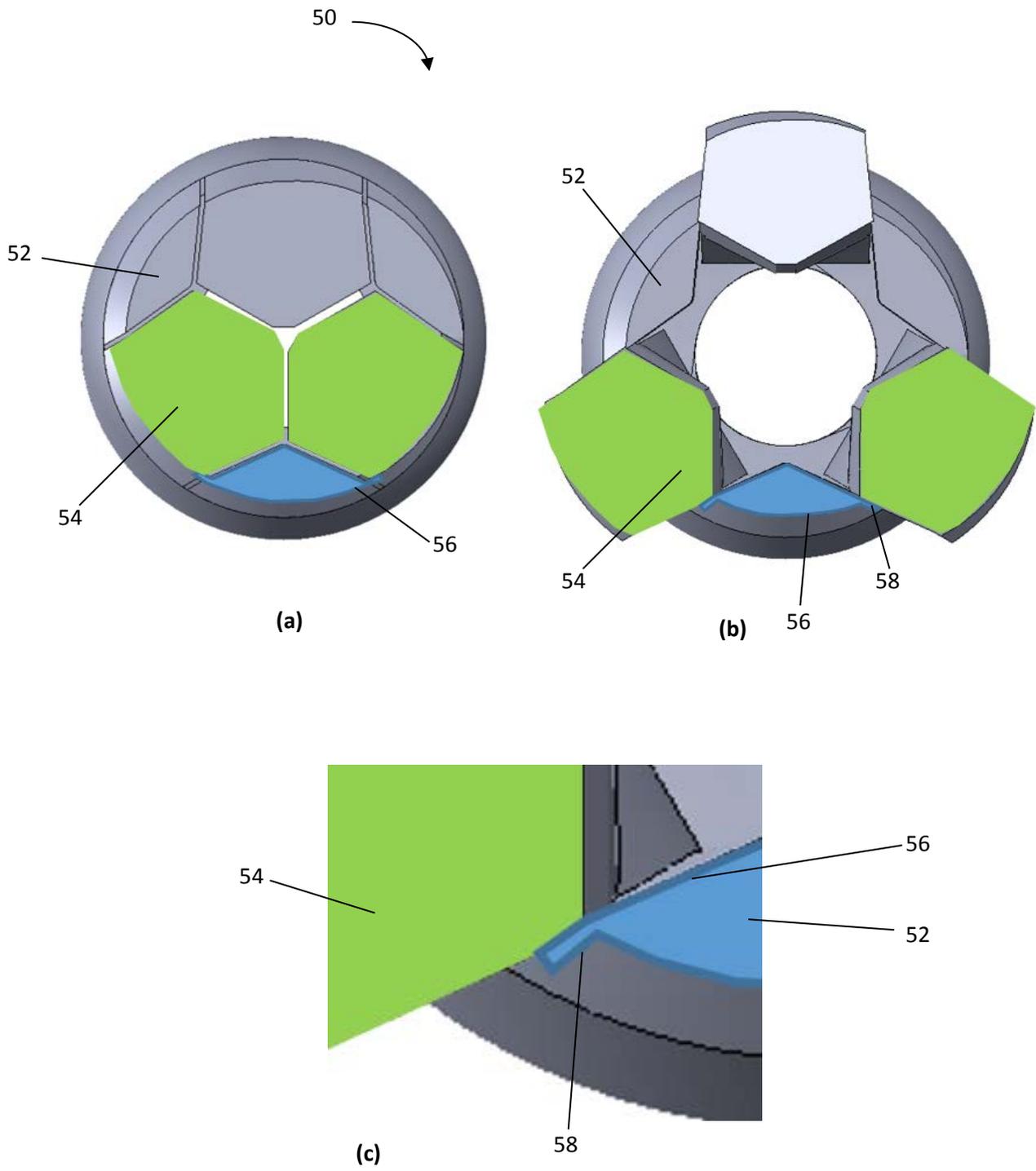


FIGURE 5

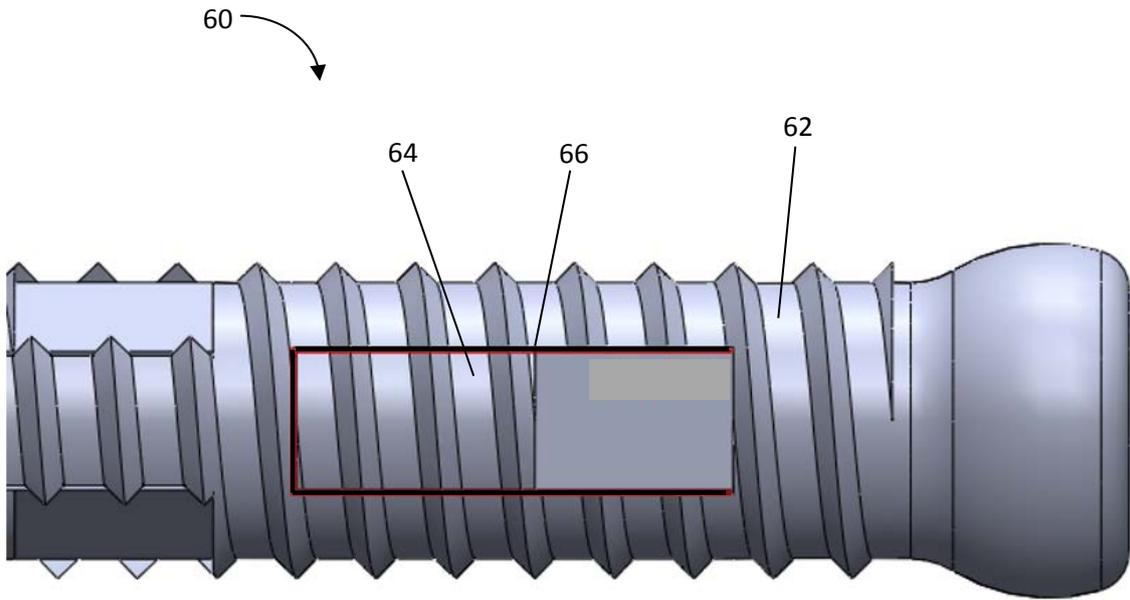


FIGURE 6

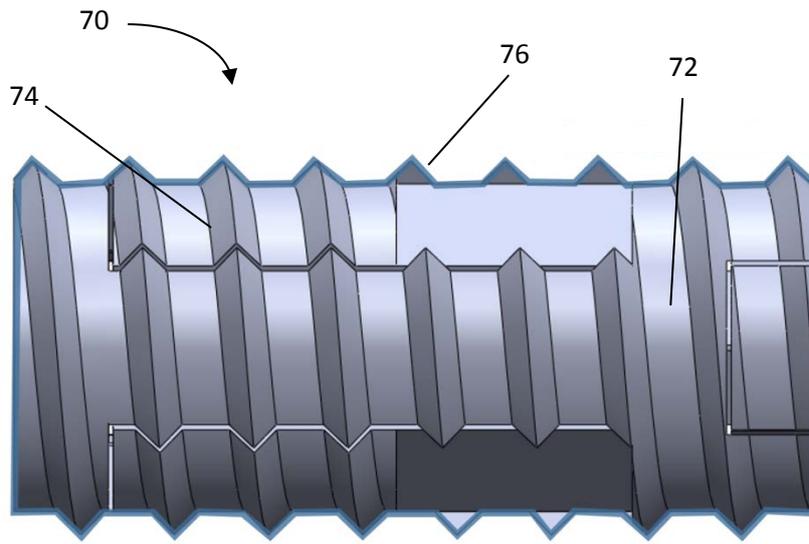


FIGURE 7

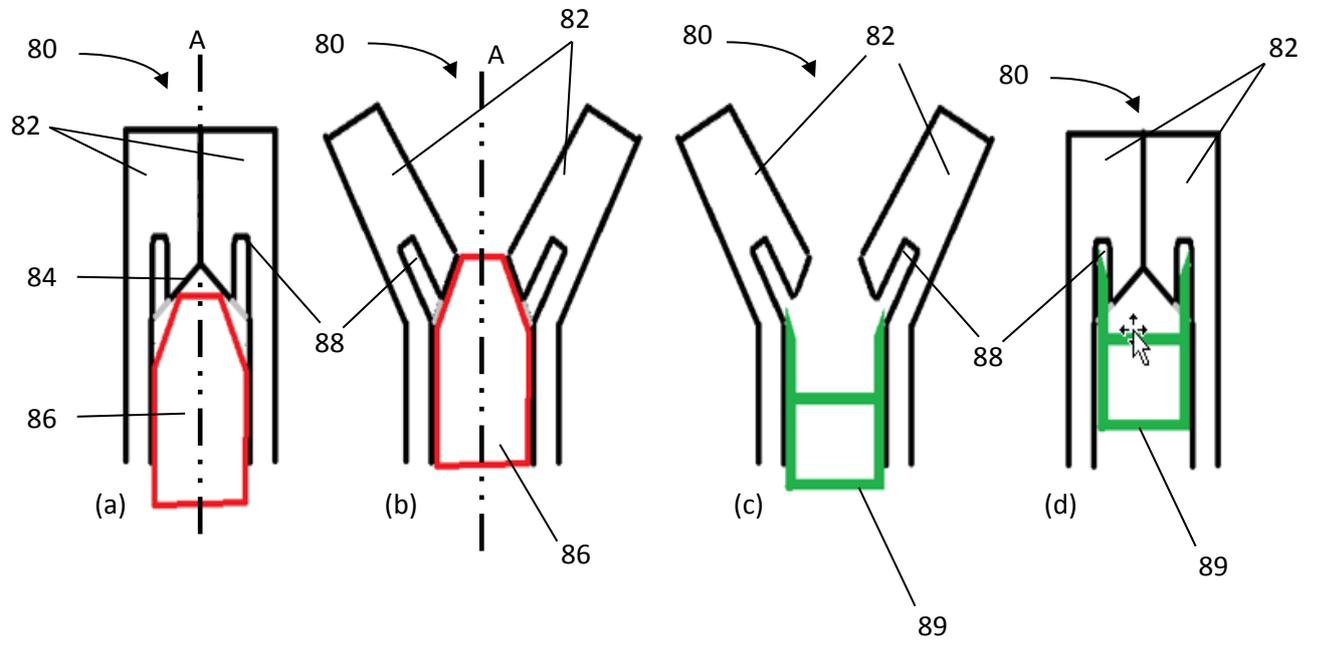


FIGURE 8

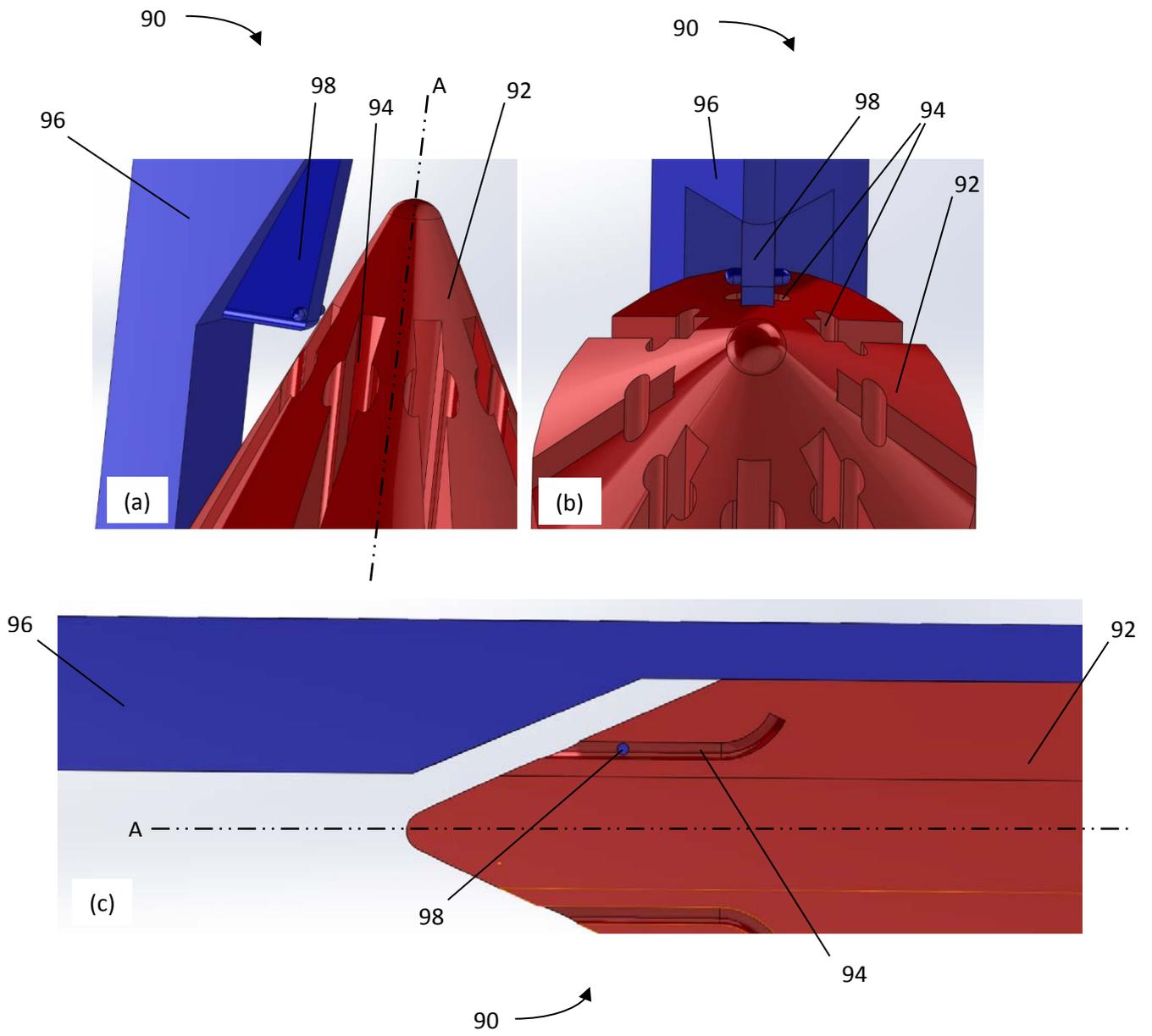


FIGURE 9

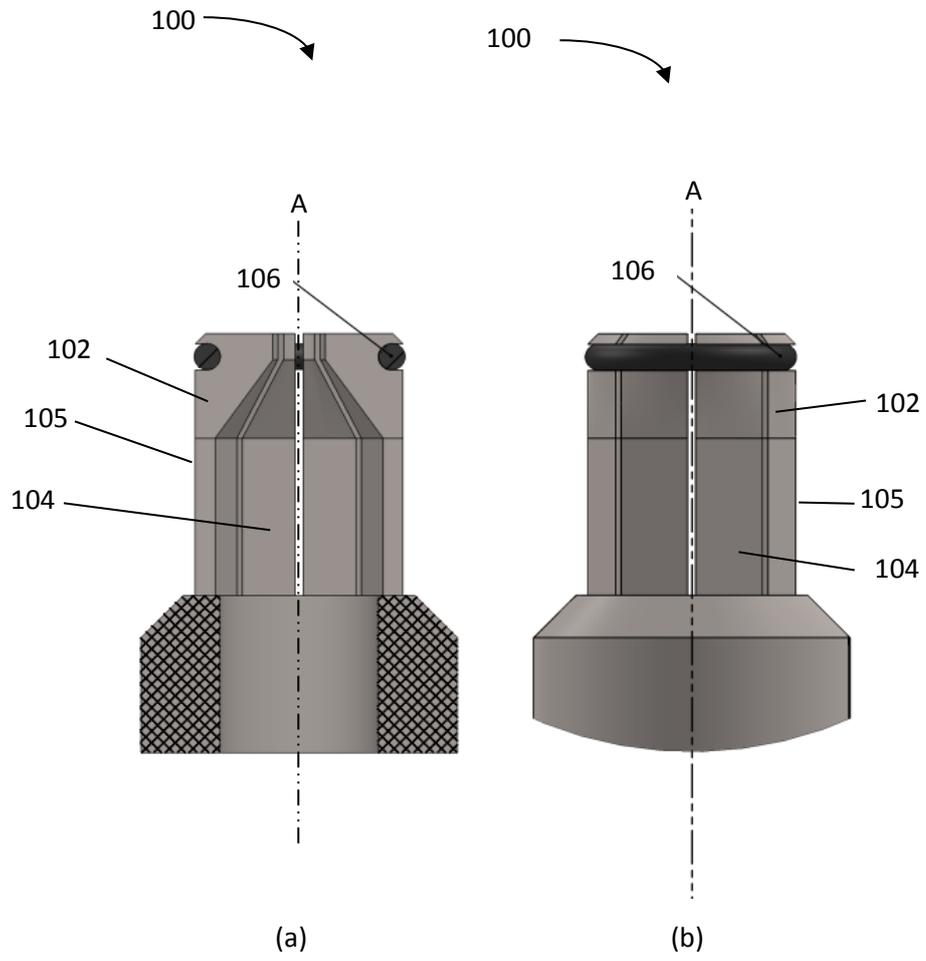


FIGURE 10

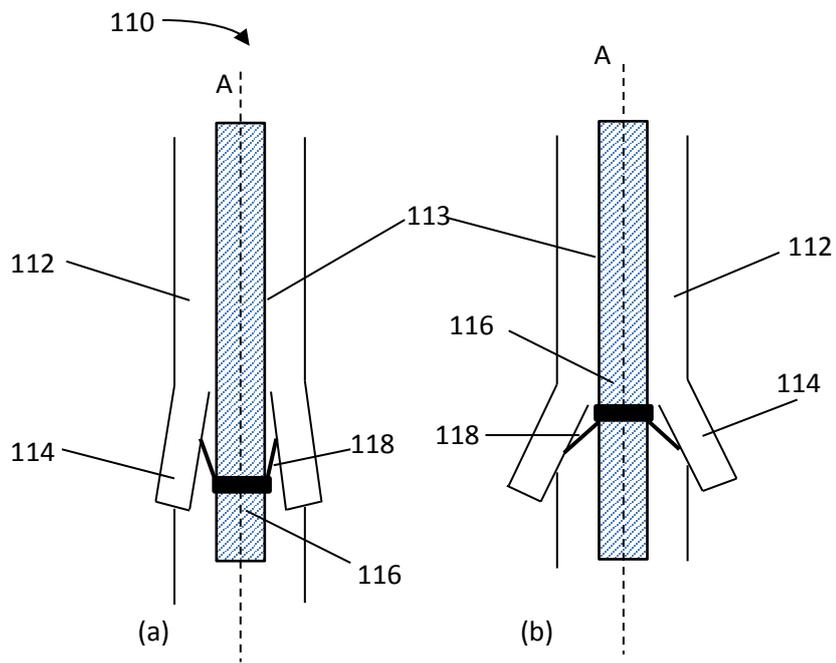


Figure 11

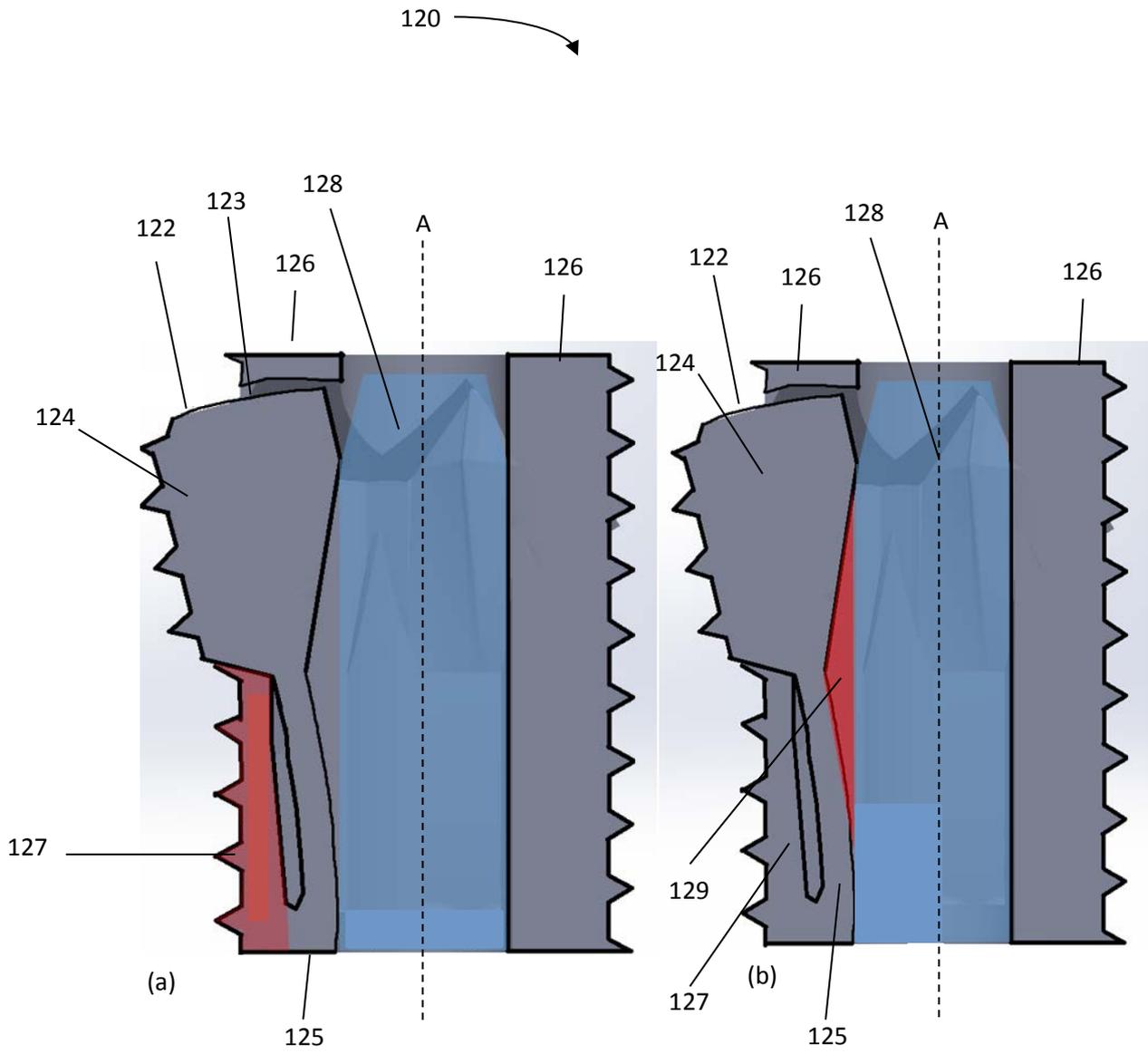


FIGURE 12

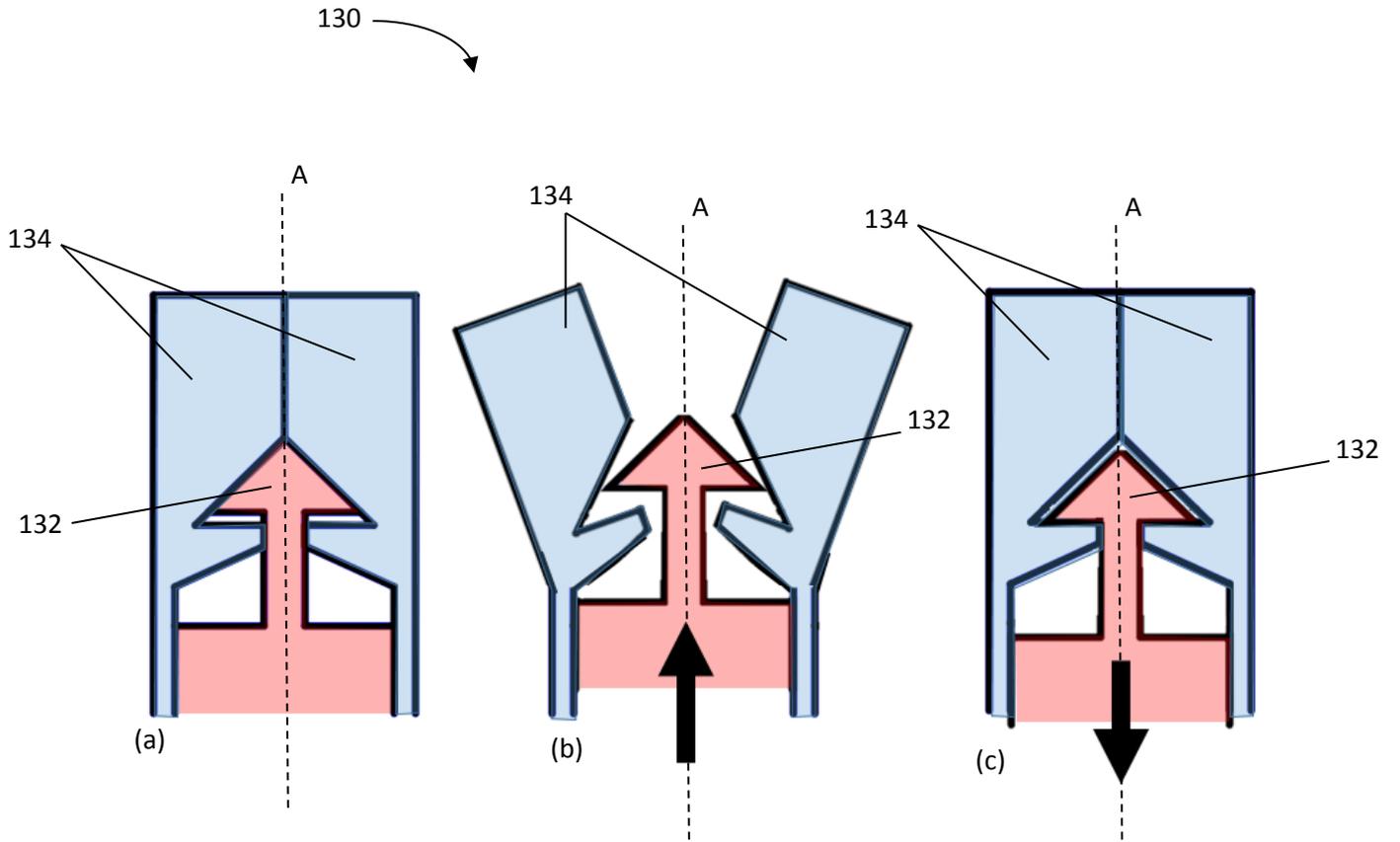


FIGURE 13

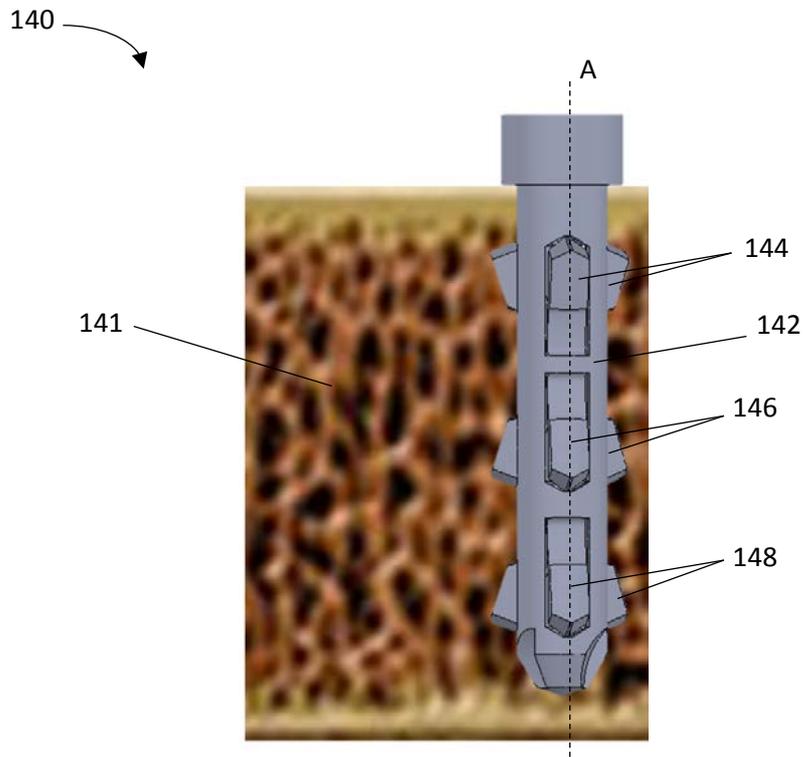


FIGURE 14

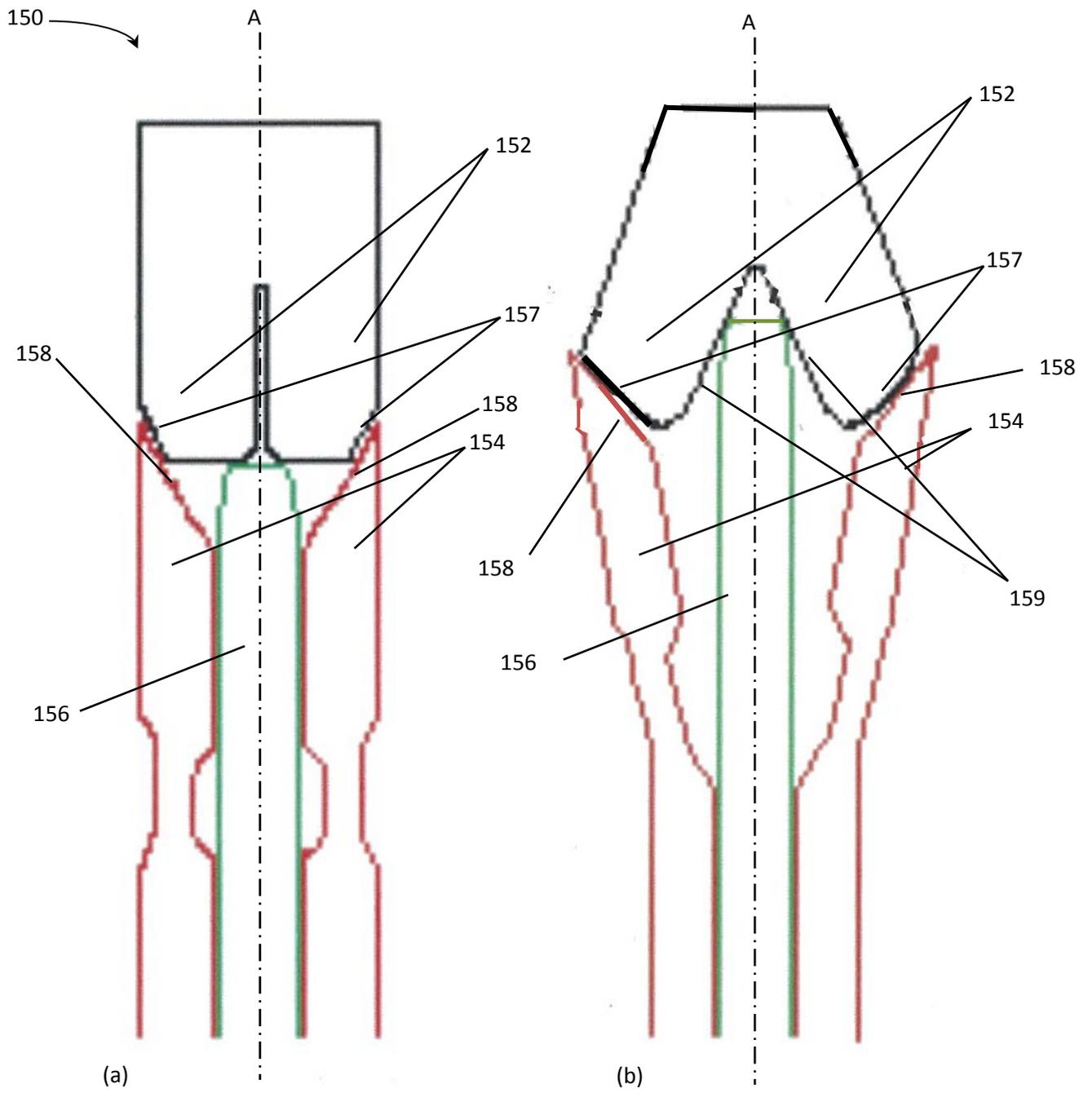
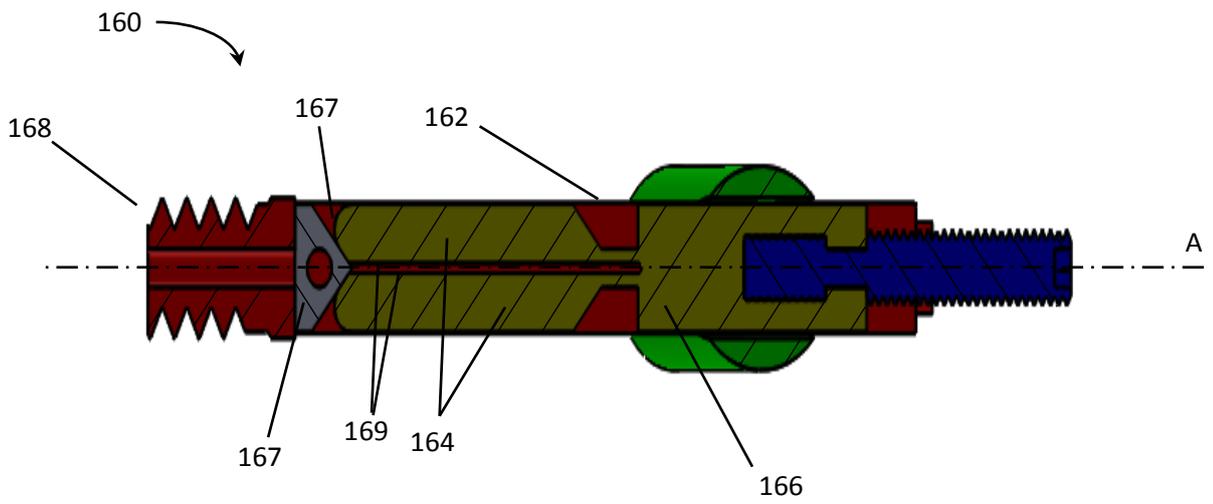
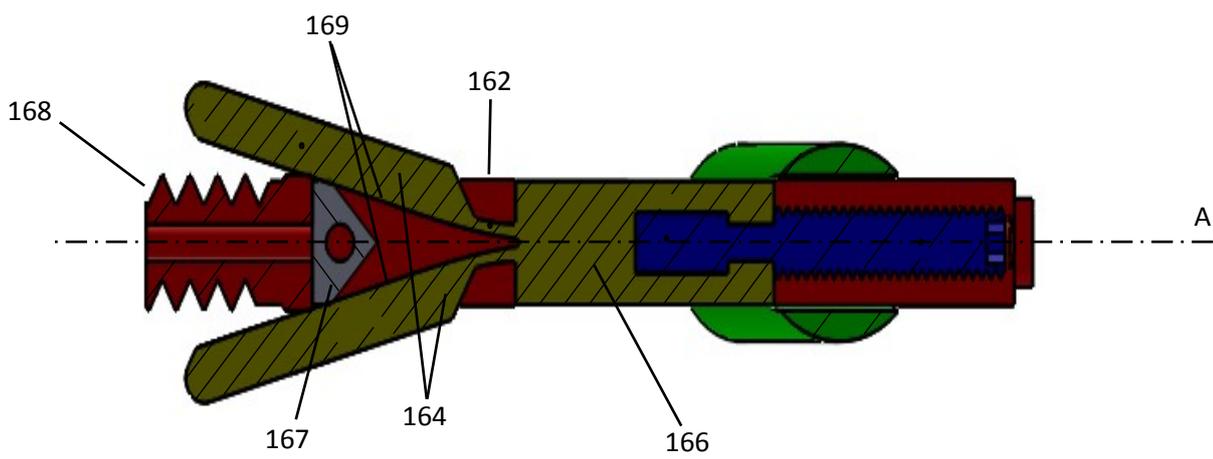


FIGURE 15



(a)



(b)

FIGURE 16

Appendix H Poster presented at the
Australia New Zealand
Orthopaedic Research
Society in 2015

FEASIBLE EXPANSION SIZE OF A NOVEL EXPANDABLE FASTENER IN THE CERVICAL SPINE



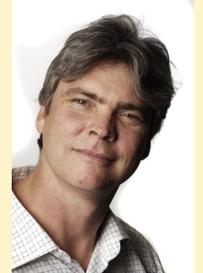
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Introduction

Studies [1,2] have reported the potential for expandable fasteners to provide increased pull-out strength compared to conventional screws in bone. The author's previous work on a novel expandable fastener for cervical spine fixation (see figure 1) demonstrated a 41% increase in pull-out strength against an equivalent sized orthopaedic screw [3] in ovine bone. This study investigates the maximum potential expansion size and expandable fastener length along common fastener trajectories in the cervical lateral mass and vertebral body, the first application of the novel expandable fastener.



Length Expanded Diameter

Figure 1. Novel expandable fastener dimension schematic

Methods

8 human C5 vertebrae and a single cervical spine (C3-C7) (n=13), as shown in figure 2, were scanned using the Skyscan 1176 micro-CT scanner at the Centre for Microscopy, Characterisation and Analysis at the University of Western Australia with 18 microns resolution and a rotation step of 0.5°.



Figure 2. Example of the human cadaveric cervical vertebra sample

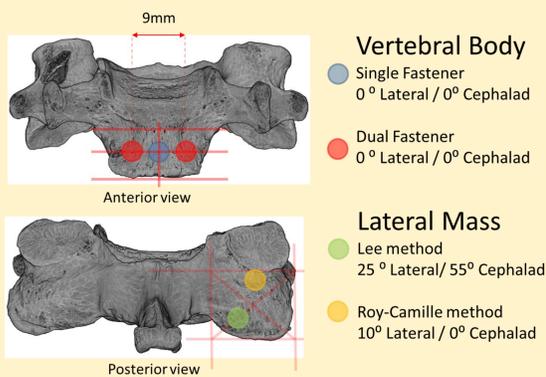


Figure 3. The entry points and angulations of the screw techniques that were assessed

A neurosurgeon marked all the entry points to ensure clinical relevance, as shown in figure 3. A cylindrical volume of interest was digitally created for each fastener trajectory in each sample, that are based on established techniques in the literature. The techniques that were assessed are the Roy-Camille and Lee lateral mass (LM) approaches (posterior) and a conventional, parallel single and dual fastener cervical vertebral body (VB) approaches (anterior). The samples were cortically segmented using a modified Buie method [4]. The maximum expansion diameter at a given fastener depth was defined as the largest diameter circle that could fit without including any cortical bone (see figure 4). This methodology assumes that the fastener can expand right up to the cortex, providing an upper limit to expansion size. The maximum expanded diameter at a particular fastener depth is then recorded and plotted as shown in figure 4.

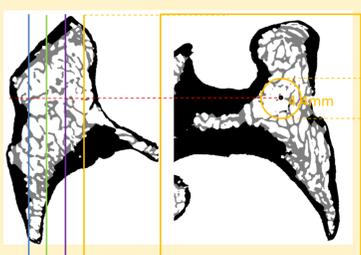
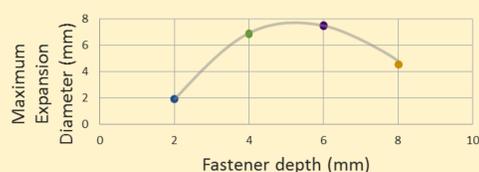


Figure 4. The method for calculating the maximum expansion size at a given fastener depth



Results and Discussions

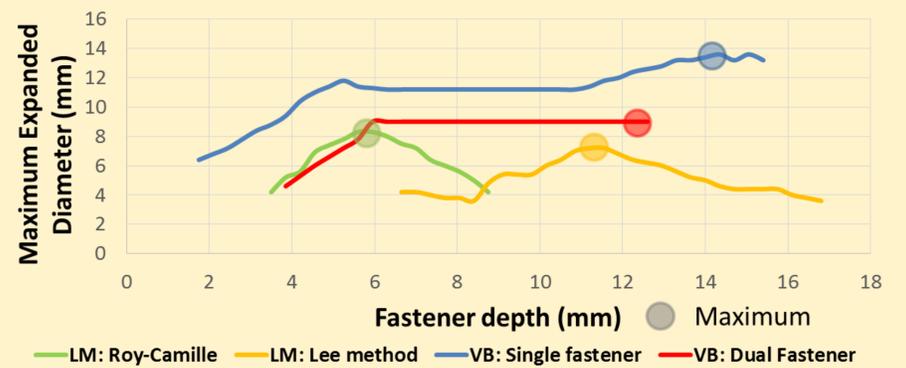


Figure 5. typical traces of maximum expanded diameter at a given fastener depth

	Lateral mass		Vertebral body	
	Roy-Camille	Lee	Single Screw	Dual Screw
Max. Expanded diameter (mm)	7.52±2.43*	5.85±1.57*	8.94±2.84*	8.85±1.10*
Fastener depth (mm)	5.41±1.89*	14.1±5.46*	14.5±2.26*	12.3±2.47*

*95% confidence intervals

Table 1. Summary of maximum allowable expanded diameter

A typical trace of maximum allowable expanded diameter at a given fastener depth for the four investigated trajectories are shown in figure 5. Table 1 summarises the maximum allowable expanded diameter for the four trajectories and the fastener depth at which this occurs. In the vertebral body, significant expansion size is available close to the maximum fastener depth for both the VB single and dual fastener approach. The VB single fastener approach does not significantly increase expansion size ($p=0.762$) but increases fastener depth by 2.2mm on average ($p<0.001$). In the lateral mass, the modified LM Roy-Camille technique allows high expansion only for a limited fastener depth whereas the modified LM Lee method provides only limited opportunity for expansion at a significant fastener depth.

Discussions and Conclusions

The cervical vertebral body has significant potential for a large expansion size at close to maximum depth and is therefore suited to expandable fasteners with a large expansion size. However, the cervical lateral mass has limited potential for significant expansion at significant depth and furthermore the maximum expansion depth is inconsistent, increasing the risk of cortical cracking. The data from this study will be used to select dimensions for future expandable fastener prototypes which will be empirically tested in human cadaveric vertebral bodies to ensure cortical cracking does not occur.

References

- McKoy & An, *J. Orth. Res.* 19(4):545-547, 2001.
- King & Cebon, *J Biomed Eng.* 15:79-82, 1993.
- Oldakowski et al., Manuscript submitted to *J Med Eng & Tech*, 2015.
- Buie et al, *Bone.* 41(4):505-515, 2007.

Acknowledgements

"The authors acknowledge the facilities, and the scientific and technical assistance of the Australian Microscopy & Microanalysis Research Facility at the Centre for Microscopy, Characterisation & Analysis, The University of Western Australia, a facility funded by the University, State and Commonwealth Governments."

Appendix I Poster presented at the
Australian Conference for
Microscopy and
Microanalysis in 2016

Introduction

Segmenting CT scans of bones into the cortical and cancellous components is necessary to accurately evaluate the disparate cortical and cancellous structural properties. Previously this was done by manually contouring the cortical cancellous boundary on each slice (see figure 1¹). However this is difficult, time consuming and prone to variation and inaccuracy. A popular semi-automatic segmentation procedure, created for long bones, is based upon a fixed iteration dilation/erosion cycle, the Buie method^{1,2}. However for vertebral bones with thinner cortices, thicker trabeculae and higher cortical surface curvature (see figure 2² and 3 for comparison) an inappropriate number of dilation/erosion iterations can cause significant error due to either incomplete trabeculae removal or, more commonly, the closing effect of dilation, eliminating cortical regions of high surface curvature (see figure 4).

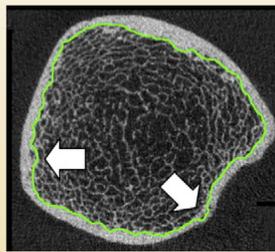


Figure 1: Manual contouring slice-by-slice is onerous and prone to error.



Figure 2: A slice through a typical long bone with a thick cortex, relatively thin trabeculae and low cortical curvature.

We propose a modification of the Buie method to minimise this error by:

1. Calculating the optimal magnitude of dilation/erosion for each sample set; and
2. Introducing an additional dilation/erosion cycle to immediately prior to the calculation of the endosteal surface.

This study will evaluate the reduction in error we can achieve by using the these two modifications.

Method

Five cleaned and dried human and kangaroo cervical vertebral columns (See figure 3) were CT scanned at 35 μ m voxel size using the Skyscan 1176 micro-CT scanner at the Centre for Microscopy, Characterisation and Analysis at the University of Western Australia. The data was filtered with a median filter to remove noise, resampled at 70, 105 & 140 μ m voxel sizes and thresholded using the iterative inter-means histogram method.



Figure 3: A dried and cleaned human (top) and kangaroo (bottom) cervical vertebrae sample.

Conventional Buie segmentation [1,2] was performed using kernel sizes ranging from from 1-20 voxels. The lowest kernel size with complete trabeculae removal, assessed by analysing each image set manually, was taken as the optimal kernel size. The cortical volume using the optimal kernel size is compared against a fixed kernel size, a scaled fixed value taken from the Buie study and the modified method.

Results

The average/maximum optimal kernel size was 0.36/0.84mm and 0.91/1.54mm for the kangaroo and human samples respectively. The fixed method erroneously excluded 15%, 24% & 33% of cortical volume at 70, 105 & 140 μ m voxel size respectively, which was more than the scaled method at large voxel sizes, which erroneous excluded 16%, 22% & 27%. The modification to the scaled method drastically reduces error to 2%, 3% & 6%.



Figure 4: A typical slice through a human vertebrae comparing the error in the conventional Buie method, highlighted in red (left) to the sample processed using the optimal dilation/erosion kernel size and the closing cycle modification

Discussion

The optimal kernel size calculated for vertebral bones differs from the value determined for long bones the previous study¹. The average/maximum optimal kernel size was significantly higher for the human samples than for the kangaroo samples. This was because, being more osteoporotic, the human samples had thinner cortices and larger cortical defects. Scaling the kernel size to account for the data resolution typically reduced error. The additional closing cycle modification had the strongest effect, reducing the scaled method to close to the optimal reduction in error. Our methodology of taking the lowest kernel size with complete trabeculae removal as the optimal is not ideal because minimum total error may occur at some level below this kernel size. However typically any trabeculae exclusion error is large compared to cortical exclusion and the only alternative would be comparing against manual contouring (which has more error than the current methods).

Conclusions

Our modifications to the Buie method allows truly automatic cortical segmentation of vertebral samples with minimal error. However to eliminate all error the optimal kernel size must be found for each sample.

References

1. Buie HR, Campbell GM, Klinck RJ, Macneil JA, Boyd SK. Automatic segmentation of cortical and trabecular compartments based on a dual threshold technique for in vivo micro-CT bone analysis. *Bone*. 2007;41(4): 505-515.
2. Burghardt AJ, Buie HR, Laid A, Majumdar S, Boyd SK. Reproducibility of direct quantitative measures of cortical bone microarchitecture of the distal radius and tibia by HR-pQCT. *Bone*. 2010;47: 519-528

Acknowledgements

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"The authors acknowledge the facilities, and the scientific and technical assistance of the Australian Microscopy & Microanalysis Research Facility at the Centre for Microscopy, Characterisation & Analysis, The University of Western Australia, a facility funded by the University, State and Commonwealth Governments."

Appendix J SZ novelty matrix

	Name of patent	Year of issue	Company	Patent Number	Language	Category	1. Dynamic stabilization provided	2. Compatible with posterior approach	3. Compatible with cervical anatomy	4. Fastener introduced into longitudinal element	5. Longitudinal element formed into a live spring arrangement	6. Device fixated to the bone using expandable fastener	7. Compatible to the bone between anchor points	8. Angular offset between plate and fastener	9. Significantly sized flanges around fastener	10. Device does not require an intervertebral spacer and can support the intervertebral joint not require pre-drilling or sawing	11. Fasteners pointed so as to engage (formally)	12. Multiple fasteners can be simultaneously	13. Multibody	14. Controllable stiffness	15. Controllable end limits	16. C
				5/2 Device		Yes	Yes (posterior)	Yes	yes	Yes	Yes	Yes	Yes	Yes	Yes	Unclear	Unclear	Unclear	Unclear			
046 / A	Spinal dynamic stabilization device		Industrial technology research institute	WO2010091549A1	English	A61B17/86	Yes	Yes	Unclear - Fasteners go through into pedicle into vertebral body (burial anatomy)	No (Intracanal - anchor sleeve with screw)	Yes	No (screw)	Yes	Yes	No (no flange)	Yes	No (screws)	Yes	No	No		
051 / B	Flexible stabilization systems for vertebral columns		Charles V. Burton	US5282863A	English	A61F2/44 & A61F2/04	Yes	Yes	Unclear - Fasteners go through into pedicle into vertebral body (burial anatomy)	no (plate with screws)	Yes	No (screw)	Yes	No	No (no flange)	Unclear	no	No (screws)	yes	No	No	
068 / C	Method for the correction of vertebral deformities through vertebral body tethering without fusion		James Ogilvie	US2002/0007184A1	English	A61B 17/064; A61B 17/170	Unclear (rigid tension provided, however springs mentioned for longitudinal elements)	Yes	Unclear - Staple drawn laterally	Yes (staple element)	Unclear (preferred embodiment right, however springs are mentioned as well)	Unclear (preferred embodiment uses staple fixation, but expansion screw are mentioned as an alternative)	Unclear (staple element without offset)	Unclear	No (no flange)	No (cannot provide support under compression)	Yes (staple)	Yes (staple)	yes	No	No	
069 / D	Bi-directional flexing/locking transvertebral disc spacer/intervertebral cage stand-alone (anterior and posterior), ventral and lumbar intervertebral disc spacer/intervertebral cage	2012	Abraham D Miskowitz	US2012010714A1	English	A61F 2144	No	Yes	No - Specifically stated as lumbar pedicle anatomy	Yes (for staple element)	No	No (screws and staples)	No	No (interlocking)	Yes	No (requires intervertebral spacer to mate with)	Yes (staple)	Yes (staple)	No	No	No	
082 / E	Apparatus and method for anterior spinal stabilization	2004	Gary Karlin Michelson,	US2004/0034453	English	A61B 17/56	No	Yes	Yes	Yes (for staple element)	No	No (screws and staples)	No	No	No (no flange)	No (requires intervertebral spacer to mate with)	Yes (staple)	Yes (staple)	No	No	No	
003	SURGICAL IMPLANT SPINAL SCREW	1977	Downs surgical limited	US4041939	English	A61F 5/00; A61B 17/18	No - correction of scoliosis	Yes	Yes	No (screws with cable)	No (longitudinal element is a cable)	No (screws)	Yes	Yes	No (no flange)	No (cannot provide support under compression)	No (screws)	No (screws)	Yes	No	No	
005	Dynamic spinal stabilization system and method of using the same	2008	Zimmer Spine, Inc.	EP 1 970 031 A2	English	A61 F 2/44; A61B 17/86	Yes	Yes	Yes	No (screws)	Yes	No (screws)	Yes	Yes	No (no flange)	Yes	No (screws)	No (screws)	Yes	Yes	Yes	Centre of rotation moved anteriorly
008	Device for lateral stabilization of the spine	2007	Alain Tornier	US2007/162004	English	A61F 2/30	Yes	No (lateral)	No (no access to vertebral body)	No (screws)	No (tilting mechanism)	No (screws)	No	No	N/A	Yes	No (screws)	No (screws)	Yes	No	No	Tilting motion (zero stiffness between end stops)
009	Device for lateral stabilization of the spine	2007	Alain Tornier	US2007/162003A1	English	A61F 2/30	Yes	No	No (no access to vertebral body)	No (screws)	No (slot sliding mechanism)	No (screws)	No	No	Yes (device is flanged at connection point)	Yes	No (screws)	No (screws)	No	No	No	Slider mechanism
010	Device for stabilizing the spine	2007	Alain Tornier	US2007/0162002A1	English	A61F2/30	Yes	Yes	Yes	No (screws)	No (slot sliding mechanism)	No (screws)	Yes	Yes	No (no flange)	Yes	No (screws)	No (screws)	Yes	No	No	
016	DYNAMIC POSTERIOR STABILIZATION SYSTEMS AND METHODS OF USE	2006	Charles R. Gordon	US2006/0247635	English	A61B17/70	Yes	Yes	Yes	No (screws)	No (slot sliding mechanism)	No (screws)	Yes	No	Yes (device is flanged at connection point)	Yes	No (screws)	No (screws)	No	No	No	
021	Spinal stabilization systems with dynamic interbody devices	2009	Jonathan A Gimbel	US2009/0105759 A1	English	A61B17/58	Yes	Yes	Yes	No (screws)	Yes	No (screws)	Yes	Yes	No (no flange)	Yes	No (screws)	No (screws)	Yes	No	No	
023	DEVICE FOR DYNAMIC POSTERIOR STABILIZATION MAINTAINING THE ANATOMICAL CONDITIONS	2011	Fredrick Fortin	US2011152935A1	English	A61B17/58	Yes	Yes	Yes	No (screws)	Yes	No (screws)	Yes	Yes	No (no flange)	Yes	No (screws)	No (screws)	Yes	No	No	Shock absorber
024	SPINAL STABILIZATION SYSTEMS	2011	Michel H. MALEK	US 2011/0160774 A1	English	A61B 17/70	Yes	Yes	Yes	No (screws)	No (ball socket joint / helical springs)	No	Yes	Yes	No (no flange)	No	No (screws)	No (screws)	Yes	No	No	
025	ARTICULATED INTERVERTEBRAL SURGICAL IMPLANT TO ENCOURAGE CERTAIN INTERVERTEBRAL MOVEMENTS	2011	David Attia	US2011/218571	English	A61B17/70	Yes	No (interspinous)	No (interspinous)	No (screws)	Yes	No	N/A	N/A	N/A	Unclear	N/A	N/A	No	No	No	Interspinous
026	DYNAMIC STABILIZATION SYSTEM USING POLYMER SCREWS	2011	Zimmer Spine, Inc.	US2011/251644A1	English	A61B 17/70; A61B 17/88; A61B 17/86	Yes	Yes	Yes	No (screws)	No (cord)	No	Yes	Yes	No (no flange)	No	No (screws)	No (screws)	Yes	No	No	
027	DYNAMIC STABILIZATION ASSEMBLY WITH FRICTO-CONICAL CONNECTION	2011	Roger P. Jackson	US2011295320A1	English	A61B17/70	Yes	Yes	Yes	No (screws)	No (Elastic spacer)	No	Yes	Yes	No (no flange)	Yes	No (screws)	No (screws)	Yes	No	No	
029	DYNAMIC SPINAL STABILIZATION ASSEMBLY WITH SLIDING COLLARS	2011		US2011307017A1	English	A61B17/70; A61B17/88	Yes	Yes	Yes	No (screws)	Yes	No	Yes	Yes	No (no flange)	Yes	No (screws)	No (screws)	No	Yes	No	
030	FLEXIBLE SPINAL STABILIZATION ELEMENT AND SYSTEM	2011	Warsaw Orthopedic, Inc	US 2011/0513461 A1	English	A61B17/70	Yes	Yes	Yes	No (screws)	No (Elastic spacer)	No	Yes	Yes	No (no flange)	Yes	No (screws)	No (screws)	Yes			