

Development of a low imaging signature cervical disc arthroplasty

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Abstract

Spinal disc replacements have the fundamental goal of pain relief while prolonging lifespan of adjacent intervertebral discs. This study focuses on reducing magnetic resonance (MR) artefacts, thereby improving the post-operative imaging qualities of the Kineflex cervical disc arthroplasty. Magnetic resonance imaging (MRI) is used to evaluate the success of the resulting design, as it provides the greatest distinction between various cellular types, and is the technique of choice for spinal diagnosis.

Initial research includes a survey of the most recent findings regarding cervical kinematics, the pathology of degenerative disc disease, treatments of cervical myelopathy and radiculopathy, and the complications associated with total disc replacement. The influence of modern imaging techniques and the properties of common biomaterials are investigated to obtain the basis for development

Reducing the occurrence of MR artefacts is achieved through material selection and design adaptation. Various biomaterials used in spinal applications are evaluated for their clinical performance. Smaller artifacts are achieved by replacement of cobalt-chromium-molybdenum (CCM) of the original device, with a combination of polyether-ether-ketone (PEEK) and titanium due to a lower magnetic susceptibility

Testing of the device is performed in two phases: verification and validation. The prototype device is successfully verified by means of MR, computed tomography (CT) and fluoroscopy imaging of a human cadaver spine with the device in the C5-6 position. Successful verification of the prototype warranted further development. After reviewing manufacturing techniques, validation is achieved on a production-ready device to characterise the MR signature of the end product.

Artefact area is reduced from 1842mm² to 242mm², allowing for visibility of both spinal nerve roots and adjacent intervertebral discs. The spinal canal remains affected by encroachment of artefacts by 2-3mm, but the improvement in imaging signature over the existing CCM device is significant. The resulting Kineflex product is expected to find considerable application in industry.

Acknowledgements

Enthusiasm generates powers, it generates boldness, courage; kindles confidence, overcomes doubts.

It creates endless energy, the source of all accomplishment.

-Henry Ford-

The work presented here is a result of a stimulating work environment, where product development is powered by open and innovative minds. A project of this nature requires numerous sources of enthusiasm and encouragement. I would like to extend my gratitude to the following people whom have made this work possible. Firstly to my study leader **Leon Liebenberg**, thank you for your support, encouragement and ability to afford guidance where necessary. **Malan de Villiers** has made this project possible by providing our team with both freedom and support to explore conceptual design. To **Jan Hugo**, **Richard Pieterse**, and **Gernot Liebentritt** who provided technical advice on manufacturing. **Yves Arramon** deserves mention for performing the verification and validation tests. **Louis Nel** your assistance with MR image analysis has been a significant contribution to this work. Proof reading has been daunting, **Tamsin Cracknell** and **Doug Velleman** have performed an invaluable contribution to the quality of work. My friends, colleagues and in particular my Family, **Shaz**, **Ben** and **Trev**, your support and understanding cannot be overstated.

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List of symbols

Symbol	Definition	Unit
$^{\circ}$	Angle	degrees
B_0	Applied magnetic field	T
B_1	Secondary magnetic field	T
$\hbar$	Reduced Planks constant	joule-seconds
ℓ	Volume	litre
N	Force	newton
Pa	Pressure	pascal
T	Magnetic field strength	tesla
w	weight	newton
ω	Angular frequency	radians per second
χ	Bulk nuclear magnetic susceptibility	centimetre-gram-second
γ	Gyro-magnetic ratio	radian per second per tesla

Nomenclature

ABS	A polymer, consisting of acrylonitrile butadiene styrene
AL	Anterior ligament
ALL	Anterior longitudinal ligament
ACD	Anterior cervical discectomy
ACDF	Anterior cervical discectomy and fusion
ASTM	American Society for Testing and Materials
ASTM F67	Standard Specification for Unalloyed Titanium, for Surgical Implant Applications
ASTM F136	Standard Specification for Wrought Titanium-6 Aluminum-4 Vanadium ELI (Extra Low Interstitial) Alloy for Surgical Implant Applications
ASTM F2026	Standard Specification for Polyether-ether-ketone (PEEK) Polymers for Surgical Implant Applications
ASTM F2119-07-2010	Standard Test Method for Evaluation of MR Image Artifacts from Passive Implant
C1... C7	Cervical vertebra 1... Cervical vertebra 7
C2-3	Reference to a specific intervertebral disc, for example: between the second and third cervical vertebra
CaP	Calcium phosphate
CCM	Cobalt-chromium-molybdenum
CFR	Carbon fibre reinforced
CL	Capsular ligament
CSF	Cerebro-spinal-fluid, a clear bodily fluid that occupies space around the spinal cord offering physical protection
CNS	Central nervous system
CoCrMo	Cobalt-chromium-molybdenum
CP	Commercially pure
CT	Computed Tomography
cTDR	Cervical total disc arthroplasty
DDD	Degenerative disc disease
E	Energy
EDM	Electrical discharge machining
eV	Electron volt
DOF	Degrees of Freedom
FAR	Finite axis of rotation
FDA	Food and Drug Administration
FEA	Finite element analysis
FSU	Functional spinal unit
g	Grams

GE	Gradient-echo
HA	Hydroxyapatite
IAP	Inferior articular process
IDE	Investigational device exemption
IAR	Instantaneous axis of rotation
ISO	International Organization for Standardization
ISO 13485	A quality management system where an organization needs to demonstrate its ability to provide medical devices and related services that consistently meet customer requirements and regulatory requirements applicable to medical devices and related services.
ISO 18192-1:2005	Defines a test procedure for the relative angular movement between articulating components, and specifies the pattern of the applied force, speed and duration of testing, sample configuration and test environment to be used for the wear testing of total intervertebral spinal disc prostheses.
IVD	Intervertebral disc
KCD	Kineflex cervical disc
L1... L5	Lumbar vertebra 1... lumbar vertebra 5
LF	Ligamentum flavum
M	Nuclear magnetisation
NMR	Nuclear magnetic resonance
MR	Magnetic resonance
MRI	Magnetic resonance imaging
ms	millisecond
NDI	Neck disability index
NP	Nucleolus pulposus
PEEK	A polymer, consisting of Polyether-ether-ketone
PLL	Posterior longitudinal ligament
PMA	Pre-market-approval
PMMA	Poly(methyl methacrylate)
RF	Radio frequency
RoM	Range of motion
S1... S5	Sacral vertebra 1... sacral vertebra 5
SAP	Superior articular process
SP	Spinous process
SE	Spin-echo
T1... T12	Thoracic vertebra 1... thoracic vertebra 12
TDR	Total disc arthroplasty
TE	Echo time
TR	Repetition time

Ti	Titanium
TSS	Twin spine study
UHMWPE	A polymer, consisting of ultra-high molecular weight polyethylene
VAS	Visual analogue scale

Glossary

Analgesic	Any member of the group of drugs used to relieve pain
Anterior	Positioned toward the front
Artefact	Area of an image which is not representative of the specimen
Arthrodesis	Removal of a joint
Arthroplasty	Replacement of a joint
Axial	Either a plane sectioning the body into superior and inferior portions, or the direction perpendicular to this plane
Bioactive	Having a cellular interaction with tissue
Bioinert	Having no cellular interaction with tissue
Bioresorbable	Can be resorbed by the surrounding tissue
Biotolerant	Material that is biocompatible, but will not osseointegrate
Cancellous bone	Soft, porous bone
Cartilage	Flexible connective tissue found in joints and intervertebral discs
Central nervous system	Portion of the nervous system including the brain and the spinal cord
Computed tomography	Medical imaging method employing tomography created by computer processing of X-ray diffraction
Coronal	Plane extending laterally from the midline of the body
Cortical bone	Hard, dense bone
Disc herniation	A portion of the nucleus pulposus has now extended outside of the confines of the annulus fibres
Discectomy	Procedure to reduce herniation by removing a portion of the nucleus pulposus
Distal	Positioned away from a reference point; extremity
Dorsal	Posterior side
Dural	Relating to the dura or membrane
Extension	Bending into an upright position by means of abdominal muscle relaxation, in the sagittal plane
Ferromagnetic	Metal containing iron which can be magnetized
Flexion	Bending forward by means of abdominal muscle contraction, in the sagittal plane
Fluoroscopy	Imaging technique used to obtain real-time moving images of internal structures through the use of a fluoroscope
Foraminal disc	A disc herniation on the side of the spinal canal where the nerve roots leave the spinal canal through the foramina
Foraminal stenosis	Narrowing of the foramen
Fusion	See arthrodesis
Inferior	Lower or below
<i>in situ</i>	In between
<i>in vitro</i>	Not performed in a living organism but in a controlled environment
<i>in vivo</i>	Performed on a whole, living organism
Kinematics	The study of motion
Kyphosis	Forward curvature of the spine, in the sagittal plane

Laminectomy	Removal of the lamina to reduce stenosis
Lateral	Away from the midline of the body
Lateral bending	Bending over sideways, in the coronal plane
Lordosis	Backward curvature of the spine, in the sagittal plane
Magnetic resonance	Medical imaging technique interaction of magnetism
Magnetic susceptibility	The degree of magnetisation in response to an applied magnetic field
Medial	Towards the midline of the body
Myelopathy	Damage to the spinal cord
Nerve root	A smaller nerve which exits the spinal cord through the intervertebral foramen
Neurological	To do with the science of nerves
Osseointegration	Intimate contact between the surface of the implant-bone interface, providing ridged attachment for long term fixation
Osteoconductive	Susceptible to the passive process whereby bone grows onto a surface
Osteogenesis	Process of bone tissue formation
Osteolysis	Resorption or dissolution of bone in tissue
Osteophytes	Bone spurs
Posterior	Toward the back
Postero-lateral	Situated on the side and toward the posterior
Post-operative	After a surgical operation
Pre-operative	Before a surgical operation
Primary fixation	Method of mechanical fixation of an implant, e.g. using screws
Prolapse	To move out of place and protrude
Proximal	Toward a reference point (not at an extremity)
Radiculopathy	Impaired nerve function
Radiolucent	Transparent to X-rays
Radiopacity	The relative inability of X-rays to pass through a material
Sagittal	Plane extending in an anterior-posterior direction from the midline of the body
Scoliosis	Lateral curvature of the spine
Secondary fixation	Maintenance of implant position by osseointegration
Spinal stenosis	Narrowing of the spinal cord
Spondylolisthesis	A slippage of one vertebra against the vertebra directly below
Spondylolysis	Process where bone supporting the facet joints becomes weak and fractures
Subsidence	Act of sinking to a lower level
Superior	Upper or above
Synovial fluid	A fluid found in joints that reduces friction between cartilage
Synovial joint	An encapsulated joint surrounded by synovial fluid
Tribology	Science of interaction of surfaces in relative motion
Ventral	Anterior side
Young's modulus	Coefficient of elasticity of a solid substance
Zygapophyseal	Also known as a facet joint, a synovial joint between the inferior and superior vertebral spinous processes

Chapter 1: Overview of the Study

1.1 Introduction and Background

In the USA, pain associated with the spine is the third most frequent reason for physician consultation. Neck and back pain account for approximately 65% of disability claims. A survey conducted in 2000 indicated that in North America, 54% of respondents had experienced neck pain in the preceding six months (Roth *et al.* 2009).

Over the past six years, motion preservation technologies have started to supersede fusion procedures worldwide. Growth in market revenue of 15% to 20% is predicted for the next four years. The reason for this growth is the recent introduction of new technologies such as dynamic stabilisation, disc and nucleus arthroplasty and less invasive surgery (Federico and Bros. 2006). Successful treatment of spinal disorders is consequently essential to improving the lives of an increasing number of people.

It has been postulated by developers of disc arthroplasties that preserving natural biomechanical motion between vertebrae will reduce the rate of adjacent level segment disease (Murrey *et al.*, 2008). In 2005 there were a total of seven disc arthroplasties that were under investigation by the Food and Drug Administration (FDA) board in the USA. Owing to the age of arthroplasty technology, 'two-year results' or longer comparisons between spinal fusion and disc replacement have only recently been published (Murrey *et al.*, 2008, Guyer *et al.*, 2009).

The Kineflex Cervical Disc (KCD) was developed in 2001 by Southern Medical (Pty) Ltd as a second-generation spinal disc arthroplasty indicated for one- or two-level anterior cervical compression with axial neck pain, radiculopathy or myelopathy. Figure 1¹ is a rendering of the current device, showing posterior and exploded views.

¹ Unless otherwise stated all images in this document have been produced by the author.



Figure 1: Kineflex Cervical Disc, posterior and exploded views

Kineflex technology utilises a three-piece device (Figure 2A), consisting of two endplates and a bi-convex bearing in the centre. The KCD device is an all-metal construction. The material used is cobalt-chromium-molybdenum (CCM), which is titanium plasma-coated for osseointegration onto the vertebrae. The core is a highly polished CCM mobile bearing, which allows for five degrees of freedom, that is translation and rotation about each axis, with no translation in an axial direction.

Figures 2B and 2C illustrate how the mobility of the core features the necessary geometry to allow for uncoupled translation and articulation between the superior and inferior endplates.

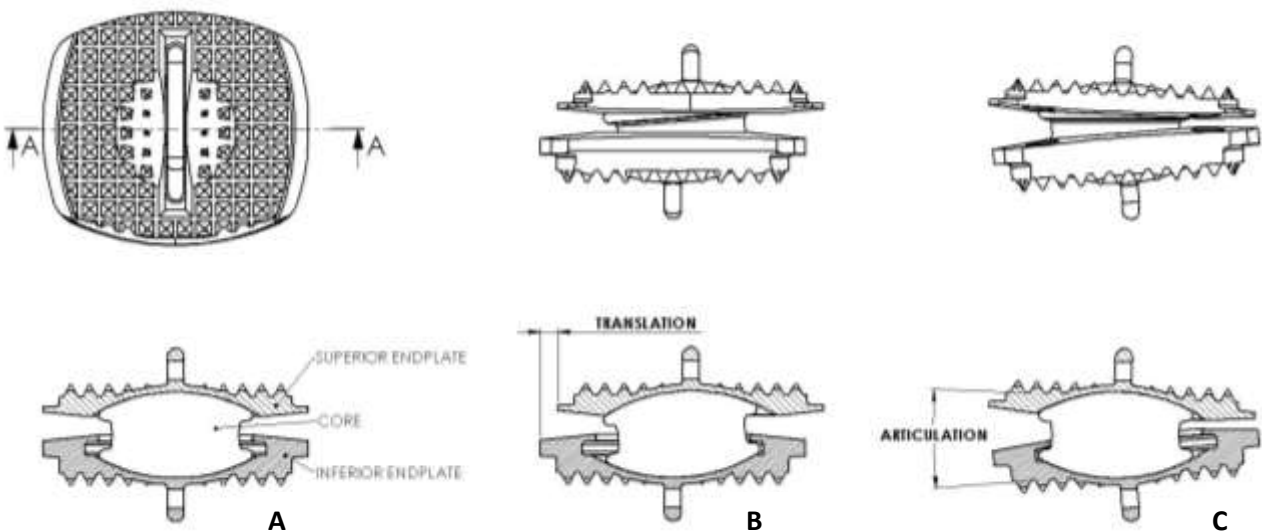


Figure 2: Section view of KCD in (A) centred, (B) pure translated and (C) articulated positions.

1.2 Motivations for Development

In general, implants constructed from CCM or stainless steel **produce** large artefacts, and are thus not considered imaging compatible. Artefacts are a well-known complication for radiologists and neurosurgeons; they appear on magnetic resonance (MR) and computed tomography (CT) scans as black or white flares. Figure 3 compares a MR image **without** artefact, and with a typical MR artefact produced by a ProDisc™-C implant. It is noted that the presence of the artefact reduces the amount of detail available for accurate diagnosis. Artefacts are more prevalent on MR scans than other imaging techniques such as CT or X-ray (Sekhon 2006).

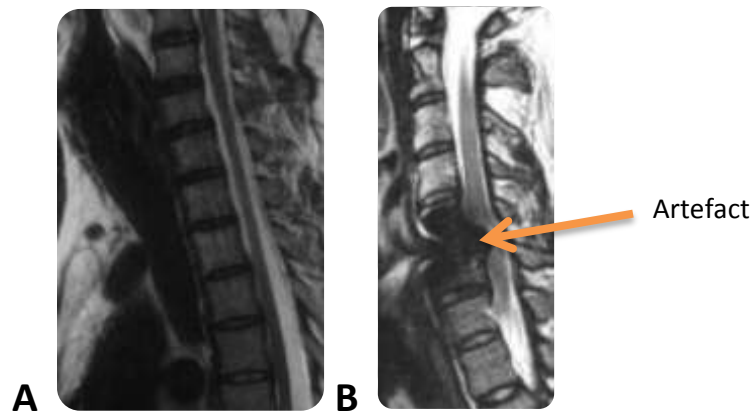


**Figure 3: (A) MR image of a healthy cervical spine (Srivastava *et al.* 2010)
(B) MR artefact (Sekhon and Ball, 2005)**

Devices with a low imaging signature would improve the value of post-operative images. A definitive competitive advantage would be gained should the artefact **produced** by the device not encroach over tissue structures.

Figure 4 shows the presently FDA-approved cervical discs arthroplasty devices: the Bryan® (BRYAN® Cervical Disc - P060023 2009), the Prestige® (PRESTIGE® Cervical Disc System - P060018 2007) and the ProDisc™-C (ProDisc™-C Total Disc Replacement - P070001 2007). The Bryan® device produces the smallest MR signature of the approved devices; however none of these products provide satisfactory magnetic resonance imaging.



Figure 4: Presently Approved Cervical Arthroplasties:

(A) BRYAN® (Artificial Disc Explained 2005);

(B) PRESTIGE® (PRESTIGE® Cervical Disc System - P060018 2007);

(C) ProDisc™ (ProDisc™-C Total Disc Replacement - P070001 2007)

Medical device manufacturers are under increasing pressure to provide evidence-based research that the long term prognosis for the patient outweighs the risk associated with the procedure.

Spinal disc arthroplasty is beginning to provide results which show that arthroplasty has a more consistent reduction in pain over a two-year period when compared with anterior cervical fusion for **one-** or two-level cervical disc disease (Coric *et al.* 2010:93). Competition within this market segment is consequently increasing and the need to provide innovative products persists.

Locally in South Africa, the KCD has established a place in the market; the new product will therefore be aimed at existing surgeons. This strategy is considered to be an acceptable marketing risk. The disc will be developed on an existing technology platform, thereby building on existing understanding and mitigating development costs.

In future, disc replacements (both lumbar and cervical) will be achieved by a device that enables the manufacturer to provide objective evidence of the procedure's success. A device with an imaging signature allowing for post-operative diagnosis of symptoms will be a key part to providing objective evidence of the efficacy of the surgery.

1.3 Objective of the Study

The primary objective of the study is to further develop Kineflex technology into a position whereby the device generates a low imaging signature.

In this context, a device with low imaging signature is defined as one which does not excessively obscure soft tissue structures. The assessment of the concept will be on the basis of the detail visible on typical imaging techniques. Visualisation of surrounding neurological tissue by means of standard magnetic resonance imaging techniques will provide clinically useful images.

Development of the arthroplasty device will be done in two phases: proof of concept or verification and implementation of concept or validation.

1.4 Scope of the Study

The scope of this study includes a review of contemporary literature on the requirements for cervical arthroplasties, clinical efficacy and development, manufacture and imaging testing of a prototype device as well as a production ready device.

Prediction of magnetic resonance artefact of spinal disc arthroplasties within cervical anatomy is to the **author's** knowledge essentially impractical and largely undocumented. Verification is therefore performed on a prototype device in an actual situation. Validation is performed on a production ready device, which therefore is representative of the final product.

Imaging testing will be by means of the most popular techniques used; magnetic resonance (MR), computed tomography (CT), and fluoroscopy. Detailed evaluation of neurological structures and artefact size will only be performed on MR images.

Chapter 2: Literature Review

This chapter reviews up-to-date literature about spinal and disc surgery, ensuring the recent findings are taken into consideration. These topics include the functioning and anatomy of the spinal column, as well as the kinematics of the cervical spine and intervertebral disc degeneration.

2.1 Introduction

The vertebral column is also known as the backbone or spine. It extends from the base of the skull to the tip of the coccyx. The spine fulfils two seemingly contrasting functions: supporting the weight of the body, while providing flexibility, and nerve protection (Bao *et al.* 1996) (Moore and Dalley 1999).

The functional spinal unit (FSU) consists of hard tissue, in the form of vertebral bodies, and soft tissue including the intervertebral discs, interconnecting ligaments, and cartilage (Narayan Yoganandan *et al.* 2000). Vertebral columns are approximately 730mm long, between a third and a quarter of the length is made up of intervertebral discs (Davis *et al.* 2006). The hard tissue provides structure to the spinal column while protecting the neurological and circulatory structures. The soft tissue provides restricted mobility to the spine by connecting the vertebral bodies and muscles to each other.

2.2 Anatomical Planes

Three planes are used to describe anatomical motion or positions. Figure 5 illustrates the arrangement of the planes with respect to the anatomy. The sagittal plane cuts through the midline of the body in an anterior-posterior direction. The coronal plane extends laterally, while the axial plane sections the body into superior and inferior portions.

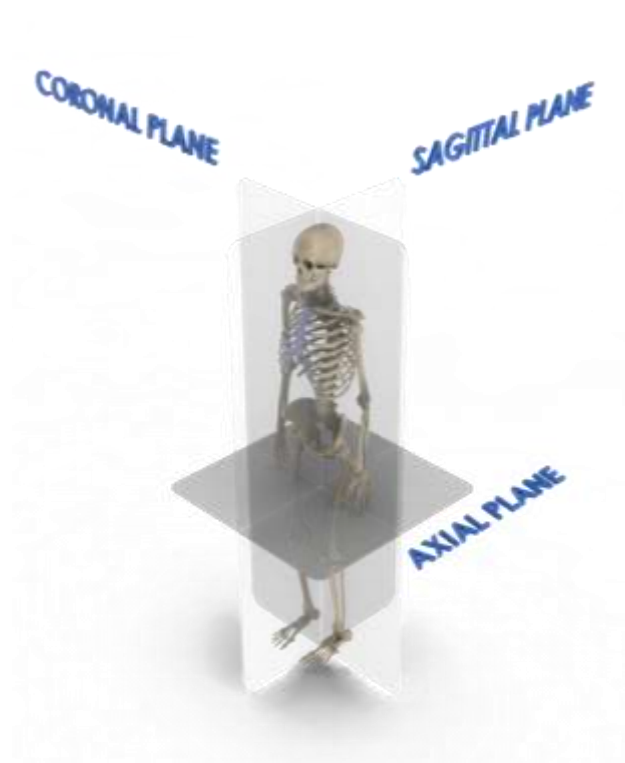


Figure 5: Anatomical planes: coronal, sagittal and axial

Figure 6 demonstrates normal motion of the spinal column in the modes of extension, flexion, lateral bending, axial rotation and distraction / compression. Extension-flexion can be described as bending backwards and forwards in the sagittal plane. Lateral bending is observed from the coronal plane. Twisting of the spine is observed from the axial plane.

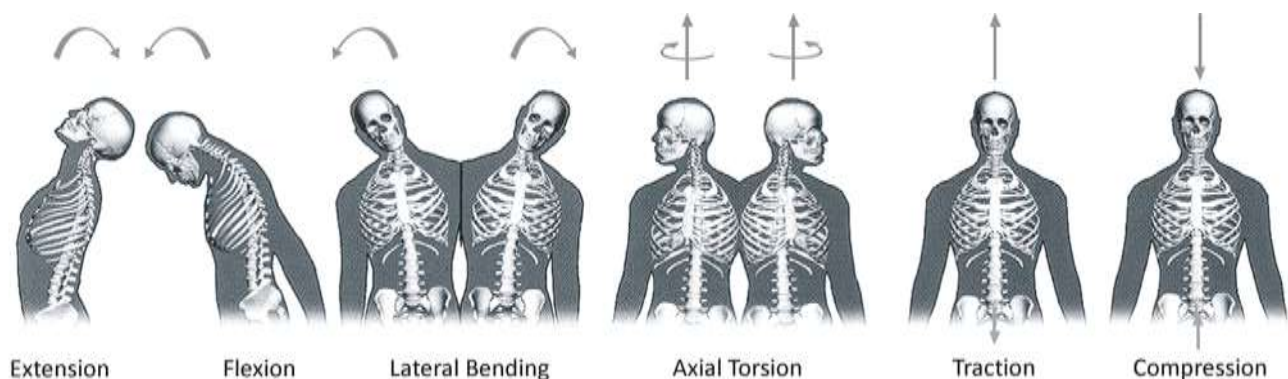


Figure 6: Movements of the spine (Adapted from Austin 2008)

2.3 Functional Spinal Unit

Figure 7 illustrates the spinal column, which consists of 33 vertebrae and 23 intervertebral discs. The spine can be divided into five regions: the cervical spine (vertebrae C1-C7), thoracic spine (T1-T12), lumbar spine (L1-L5), sacrum or sacral spine (S1-S5) and coccyx or coccygeal spine (3-5) (Gray and Lewis 1918).

Biomechanical loads increase from the cervical to lumbar spine, and the size of vertebral bodies therefore increases accordingly (ASTM F2423-05). The lower two regions (sacral and coccygeal) are fused to withstand comparatively high loads but do not allow for movement within the region

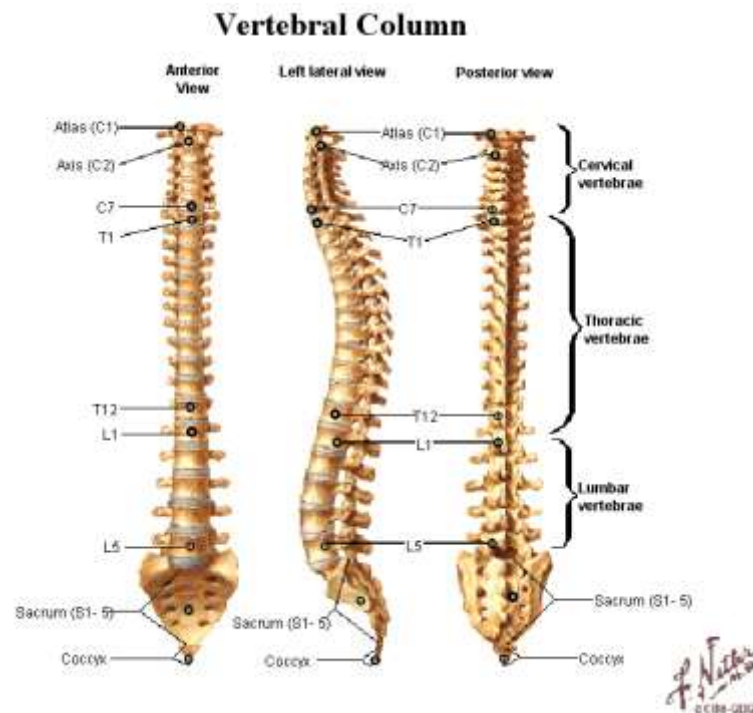


Figure 7: Artist's impression of the spinal column, anterior, left lateral, and posterior views. (Netter 1990)²

² "Celebrated as the foremost medical illustrator of the human body and how it works, Dr. Frank H. Netter's career as a medical illustrator began in the 1930's when the CIBA Pharmaceutical Company commissioned him to prepare illustrations of the major organs and their pathology. Dr. Netter's incredibly detailed, lifelike renderings were so well received by the medical community that CIBA published them in a book. This first successful publication in 1948 was followed by the series of volumes that now carry the Netter name - The Netter Collection of Medical Illustrations. Even 12 years after his death, Dr. Netter is still acknowledged as the foremost master of medical illustration." (Netter)

Figure 7 illustrates the natural curvature of the spinal column when viewed laterally, from the sagittal plane. This backward curvature is termed lordosis, and is found in both the lumbar and cervical spinal regions. The thoracic spine sees a curvature in the opposite direction known as kyphosis.

When viewed in the coronal plane the FSU should ideally lie in a straight vertical position, indicating that the lateral balance has been achieved. Excessive lateral imbalance leads to a condition known as scoliosis.

The FSU demonstrates a spring-like behaviour when the soft tissue stores and releases energy during stretching and contracting. Excessive amounts of lordosis or kyphosis are termed hyperlordosis or hyperkyphosis respectively. With an excessive curvature of the spine, the biomechanical behaviour is compromised such that the spring mechanism fails, and buckling of the spinal column occurs.

2.3.1 Cervical Spine

The cervical spine functions mainly to support the head in a stable orientation (Nabhan *et al.* 2007) while providing a pivot for the head. The cervical spine consists of seven vertebrae, and six intervertebral discs (Gray and Lewis 1918). The first intervertebral disc is between the C2-C3 level. The articular facets for the first rib are found on the first thoracic vertebra (T1).

Figure 8 is a lateral view of the cervical spine, illustrating the vertebral bodies of the cervical spine. It is notable that the angle of the zygapophyseal joints becomes more vertical and the size of the spinous processes increases at lower levels of the cervical spine.

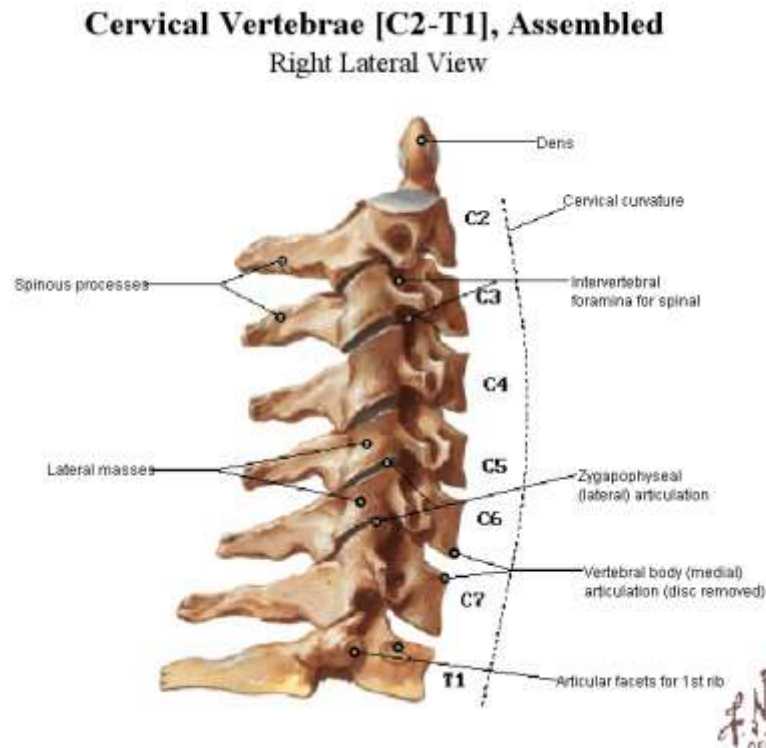


Figure 8: Artist's impression of the cervical spine, excluding C1 (Netter 1990)

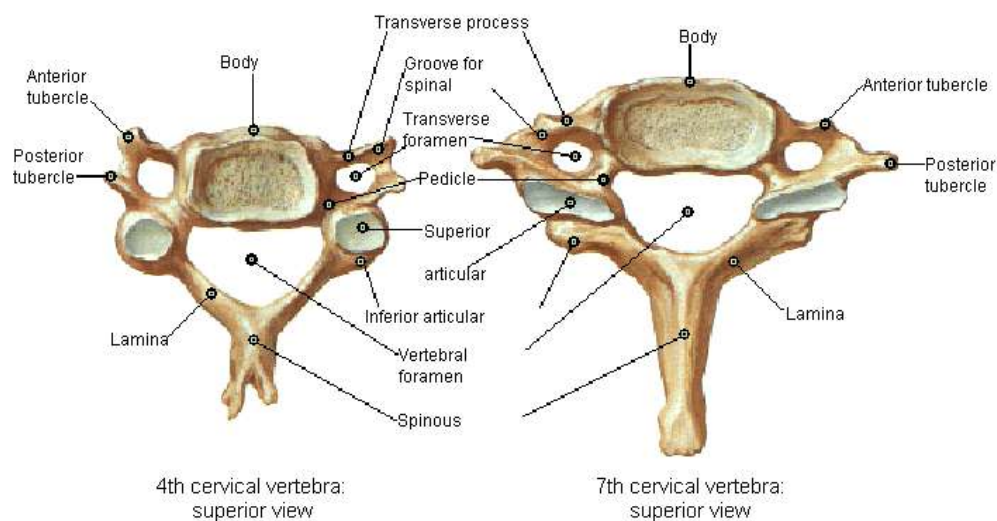
2.3.2 Anatomy of the Cervical Vertebrae

The distinguishing feature of each cervical vertebra and thoracic vertebra is the oval foramen of the transverse process. The morphology of the upper two cervical vertebrae is unlike the rest of the cervical spine (Figure 8). A high degree of rotation is achieved by synovial joints between the skull, atlas (C1) and axis (C2) (Yoganandan *et al.* 2001).

Vertebral bodies C3 through C6 are typical in morphology and are characterised by; a rectangular vertebral body with a concave superior surface and concave inferior surface; large vertebral foramina due to the enlargement of the spinal cord; and nearly horizontal facets. The C7 vertebra is characterised by a significantly longer spinous process and a smaller foramen size. The foramen is sometimes absent in the C7 vertebra (Moore and Dalley 1999).

Cervical Vertebrae [C4 and C7]

Superior Views



F. Netter M.D.
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Figure 9: Artist's impression of the C4 and C7 vertebrae (Netter 1990)

The density of the vertebral bodies was examined by Link *et al.* (2004) by studying the distribution of mineralisation. Figure 10 compares the mineral distribution between cervical and lumbar vertebrae. Lumbar and cervical vertebrae show that the perimeter of the vertebral bodies has a higher density than the centre. This distribution of bone density provides a strong yet light construction.

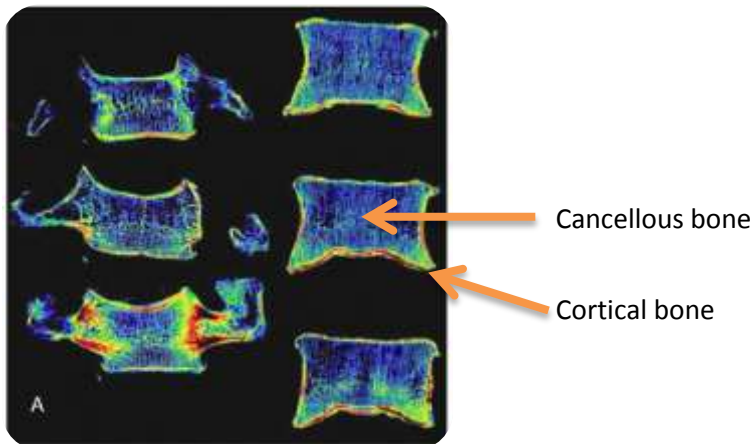


Figure 10: Equi-density images of the middle regions of sections through a cervical (left) and lumbar vertebral bodies. Red and black colours indicate high density; blue indicates low density (Link *et al.* 2004)

Higher density bone is termed cortical bone; lower density bone is termed cancellous bone. Figure 10 and 11 illustrate that higher density is located around the perimeter of the bone.

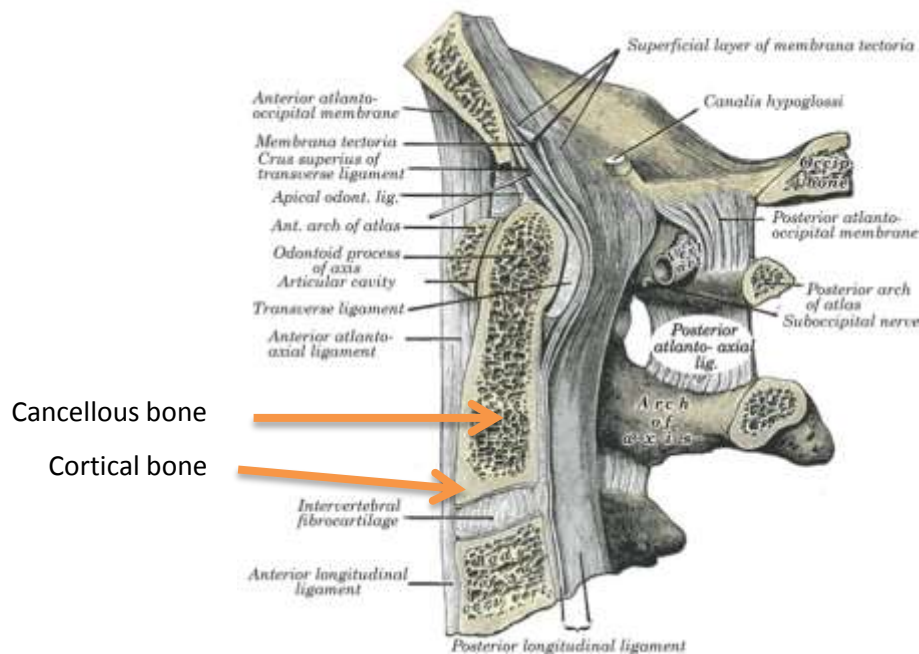


Figure 11: Sagittal section of upper cervical spine (Adapted from Gray and Lewis 1918)

2.3.3 Ligaments

The functional ability of the spinal column depends on the stability of the spine (Panjabi *et al.* 1998; Gunzburg *et al.* 2001). Ligaments provide the primary restraints of the vertebral bodies. They also however serve as sensory organs, having significant input to sensation and activation of the muscles (Waldman 2009). The combinations of ligaments and muscles have the most significant role in stabilising the skeleton (Moshe Solomonow 2009).

Figure 11 is a sagittal section of the cervical spine illustrating ligaments and their connection locations. The anterior longitudinal ligament (ALL) runs the entire length of the vertebral column and constrains hyperextension. The posterior longitudinal ligament (PLL) runs in the posterior side of the vertebral body. The ligamentum flavum (LF) connects posterior arches from C2 to C7. Intertransverse ligaments lie between the transverse spinous processes and are the primary constraints for lateral bending. In the cervical spine, the intertransverse ligaments are not particularly well developed, consisting of only a few scattered fibres (Waldman 2009). The capsular ligament (CL) surrounds the facet joint to contain synovial fluid, which provides a low friction surface for articulation (N Yoganandan *et al.* 2001).

Mechanical behaviour

Kirby *et al.* demonstrated in 1989 that the tensile mechanical properties of spinal ligaments depend on the differing orientations of collagen fibres and proportion of elastin cells. The high elastin content of the ligamentum flavum provides a higher degree of flexibility at lower strain levels. The ligament structure features closely packed parallel fibres, which have various degrees of helical form along the length of each fibre. Short cross fibrils connect the axial fibres to one another (Solomonow 2004; Ivancic *et al.* 2007).

Due to this arrangement of collagen fibres within the ligament, the tensile response is highly non-linear. Figure 12 illustrates how the tension increases exponentially as the collagen fibres become less helical and more axial in their orientation.

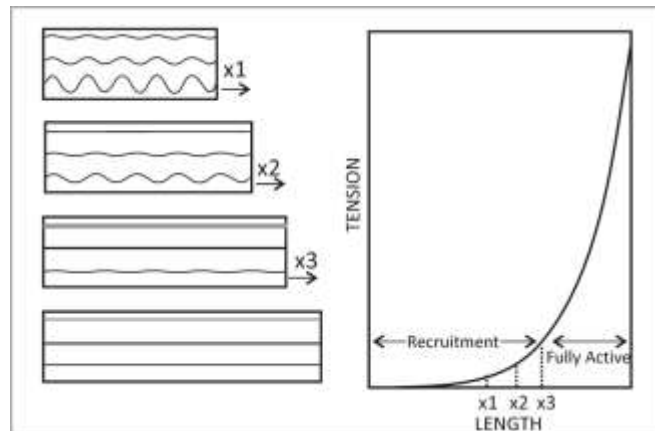


Figure 12: Tensile response of a typical ligament structure (Redrawn from Solomonow 2004)

Solomonow (2004) demonstrates that due to the nature of the tissue of which the ligament tissue is comprised, the tensile response is also dependent on the histology of the loading which that ligament has undergone. The mechanical properties of ligaments are subject to creep, tension relaxation, and frequency of loading (Lucas *et al.* 2008). Fortunately, ligaments are also adaptive to repetitive functions in that, given sufficient recovery time; the strength of the ligament should increase by altering the amount of collagen.

Ligaments as Sensory Organs

Ligaments are primarily known for their tensile strength, but they also have an important sensory input to locomotion (Solomonow 2004). Motion of the spine requires various levels of neural control; to maintain balance or propel the body forward, muscle coordination is controlled by the nervous system. Load-sensitive nerve endings (mechanoreceptors) found in muscle and tendons provide feedback to the nervous system to better control the muscle action (Holm *et al.* 2002).

2.4 Spinal Nerves

The spinal cord forms part of the central nervous system (CNS), sensory information is transmitted from the target organs, controlling voluntary muscles of the limbs and trunk. Sensory information is relayed from these regions to the brain. Blood vessels are also controlled by the spinal cord. The

cord is described as a series of segmental components, but is actually a continuous cylinder of central nervous tissue running within the vertebral canal (Watson and Kayalioglu, 1996).

Along the entire length of the spinal cord, pairs of spinal nerves develop at regular intervals, leaving the vertebral column through the intervertebral foramina. The human CNS contains 31 pairs of spinal nerves; eight in the cervical spine, twelve thoracic, five lumbar, five sacral and one coccygeal. (Watson 2005)

The cervical spinal, the first seven nerves emerge above their respective vertebrae; the remaining nerve roots emerge below their respective vertebrae. Each spinal nerve is attached to the spinal cord by a ventral and a dorsal root. Each root is formed by six to eight rootlets, extending the entire length of the corresponding spinal cord segment. Figure 13 illustrates the dorsal and ventral nerve roots emerging from the spinal cord (Watson 2005).

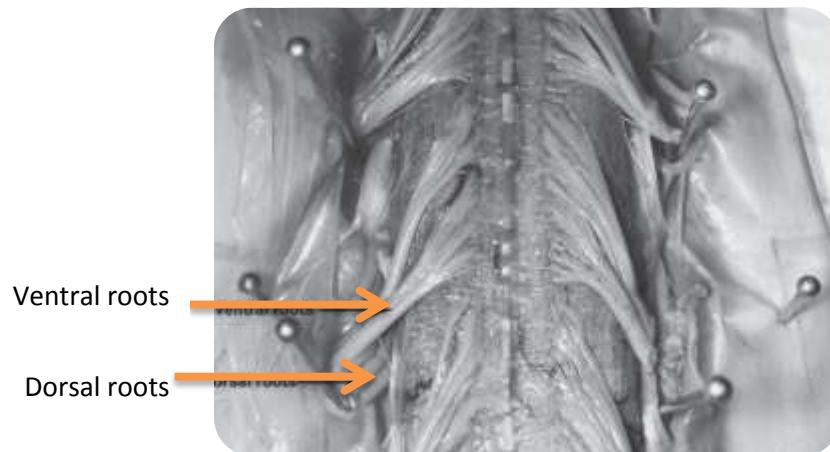


Figure 13: Dissection of a spinal column, illustrating the ventral and dorsal nerve roots (Watson 2005)

2.5 The Intervertebral Disc

Figure 14 illustrates the various components that function with the intervertebral disc. The intervertebral disc consists of the disc annulus and nucleus pulposus. The annulus is a ring-like structure that retains the nucleus pulposus between the two cartilaginous vertebral endplates. The nucleus pulposus is a hydrated jelly-like substance that transfers load by means of pressure between vertebral bodies. (Shankar *et al.* 2009)

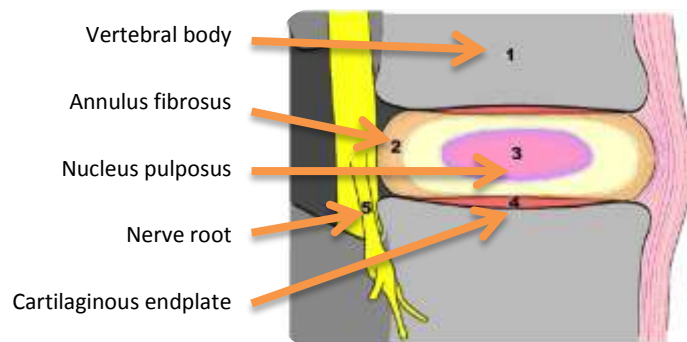


Figure 14: Illustration of a sagittal section of the intervertebral disc; (1) vertebral body; (2) annulus fibrosus; (3) nucleus pulposus; (4) cartilaginous endplate; (5) nerve root (Shankar *et al.* 2009)

Figure 15 illustrates an axial section through the cervical spine. The annulus fibrosus consists of 15-25 concentric rings of collagen fibres oriented radially at approximately 60° to the vertical axis in alternating directions. The vertebral endplates are covered by cartilage approximately 1mm thick to which the nucleus pulposus is attached. (Shankar *et al.* 2009)

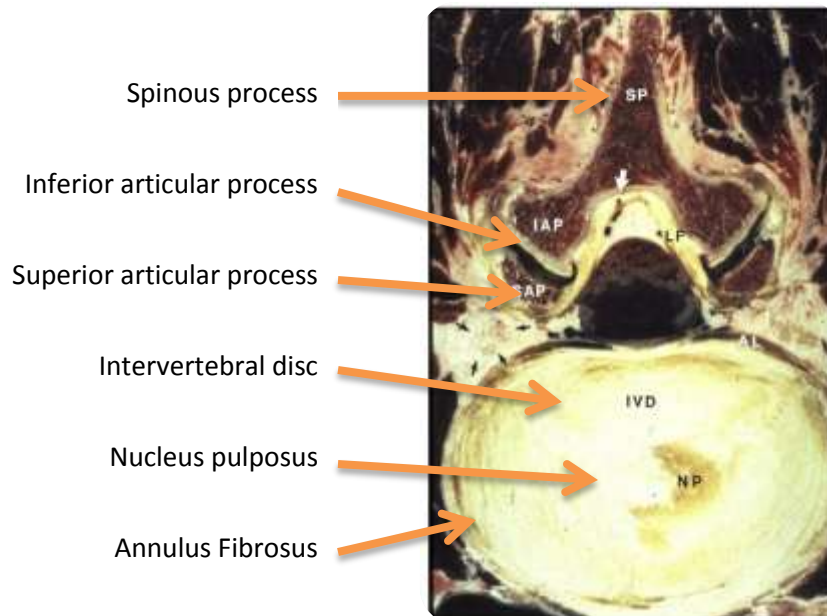


Figure 15: Axial section through a FSU; (NP) nucleus pulposus; (IVD) intervertebral disc; (AL) annulus fibrosus; (SAP) superior articular process; (IAP) inferior articular process; (SP) spinal process (Shankar *et al.* 2009)

2.6 Vertebral Loading

In 2009, Harper *et al.* noted that there have been few reports describing the typical daily loading of cervical or lumbar spines. There is, however, an appreciation of load magnitudes and range of motion, but not the motion combinations.

Finite Element Analysis (FEA) has been utilised to obtain improved insight into the biomechanics of the spinal column's response to loading and injury mechanisms (Panzer and Cronin 2009). Finite element studies have necessitated detailed evaluation of various tissue types; Zhang *et al.* (2006) used 1200MPa and 450MPa as Young's modulus for cortical and cancellous bone, respectively.

Spinal disc arthroplasties require extensive wear and fatigue testing according to International Standards Organisation (ISO) or American Society for Testing and Materials (ASTM) standards. These tests are an attempt to reproduce the physiological stresses experienced in daily activities to ensure that the device has sufficient endurance. Devices may fail by wearing out or producing a significant biological reaction to wear debris generated by the tribology of the device. Figure 16 provides the loading pattern as required by the ISO18192-1:2005 test standard. Loads vary between 50 and 150N in a sinusoidal pattern.

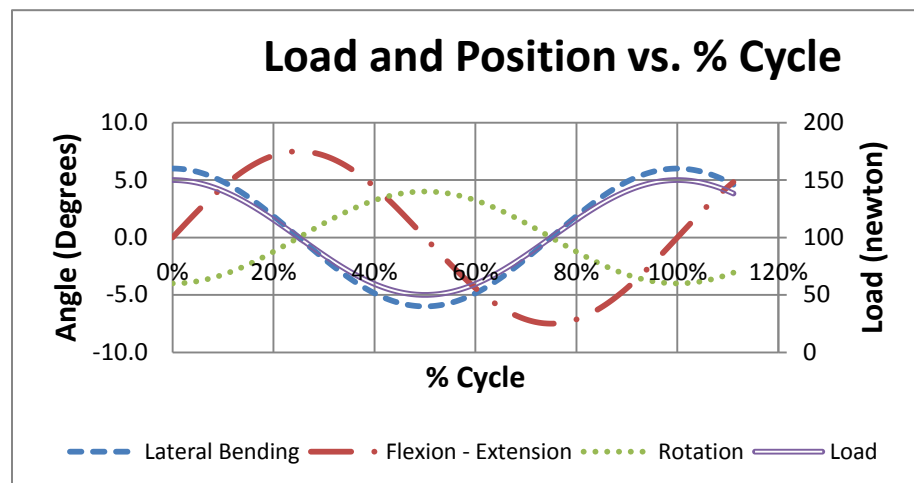


Figure 16: Sinusoidal loading cycle for wear tests for the cervical disc arthroplasties (Redrawn from ISO 18192-1 2005)

The body of the vertebra is the area that bears the majority of the axial loads (Moore and Dalley 1999). Link *et al.* (2004) suggest that the footprint size of the device implanted should be maximised to reduce pressure on the superior and inferior endplates. Figure 17 illustrates typical areas of high bone density, where the capacity to bear loads is comparatively high. Should the bearing pressure become too high the implant may subside into the vertebral bone, as was observed by Marshman *et al.* (2007) and by Adams and Dolan (2005).

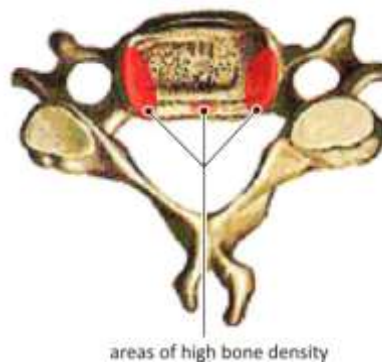


Figure 17: Superior view of C5 vertebrae, red regions indicates example areas of high bone density (Link *et al.* 2004)

2.7 Kinematics of the Cervical Spine

Kinematics is the study of motion applied to an object in three-dimensional space. This principle is applied to the cervical spine to develop an understanding of its biomechanics. Vertebral bodies are subjected to motion in all six possible degrees of freedom, being rotation and translation along each anatomical plane (sagittal, coronal and axial) (Sears *et al.* 2006).

In an attempt to understand normal motion patterns of the spine and the influence of pathologic conditions on these motion patterns, significant research has been concentrated on cervical spine motion. Essentially, two methods exist in determining the range of motion (RoM) and finite axis of rotation (FAR) in the spine: *in vitro* (cadaver) and *in vivo* studies. Measuring functional activities accurately *in vivo* remains a significant challenge (McDonald *et al.* 2010). The most studied parameter is the RoM, in degrees between physiological extremes (Galbusera *et al.* 2008). Flexion-extension, lateral bending and axial rotation are the degrees of freedom which are typically reported.

The combination of tough collagen fibres encasing the softer core allows for six degrees of freedom between vertebral bodies. The cable-like fibres of the annulus fibrosus tend to limit the range of motion between the vertebrae, which provides the spinal column with the biomechanical strength to support the upper body during flexion and extension, lateral bending, rotation and compression. Table 1 shows the modes of motion relevant to each anatomical plane.

Table 1: Anatomical plane and degree of freedom

Plane	Bending Motion	Translation	Translation
Sagittal	Flexion-extension	Anterior posterior	Vertical
Coronal	Lateral bending	Lateral	Vertical
Axial	Axial Rotation	Anterior posterior	Lateral

2.7.1 Range of Motion (RoM)

The RoM and FAR vary between spinal levels. Flexion-extension motion is concentrated around the C5-C6 level, making this the most studied level. A summary of these results were compiled by Fabio Galbusera *et al.* in 2008, as shown in Table 2, and compared with the ISO 18192-1:2008 (Implants for surgery – wear of total intervertebral spinal disc prosthesis) and ASTM F2423-05 (Standard Guide for Functional, Kinematic, and Wear Assessment of Total Disc Prostheses) standards. These standards do not distinguish between various spinal levels; a conservatively high value in all but flexion-extension is used to ensure that the testing is rigorous.

Table 2: Summary of range of motion

Degree of Freedom	Galbusera <i>et al.</i> (2008)	ISO 18192-1:2008	ASTM F2423-05
Flexion-extension	20°	15°	15°
Lateral Bending	4-11°	12°	12°
Axial Rotation	2-7°	8°	12°

2.7.2 Finite Axis of Rotation

The calculation of the finite axis of rotation (FAR) is a geometrical exercise where the perpendicular bi-sections of the paths of two points moving over a time interval are extended to their point of intersection. Figure 18 illustrates how the FAR is obtained when the vertebrae are moved from position a to a' and from b to b' (Bogduk and Mercer 2000). The complications involved in measurement of the motion of the vertebral bodies will directly translate into complications in measurement of the FAR (Sears *et al.* 2006).

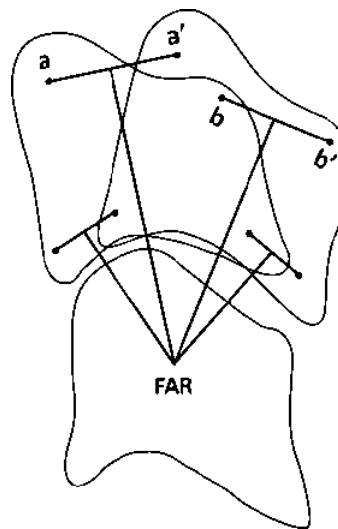


Figure 18: A sketch of cervical vertebrae illustrating how the location of the FAR is obtained (Adapted from Bogduk and Mercer 2000)

Figure 19 compares two recent studies, which investigate the kinematics of the cervical spine. The points indicate the location of the FAR while the spinal column is in a neutral position. The coupling between soft and hard tissue causes the location of the FAR to vary during motion of the spine, which is indicated by the circle around the centre point. Research on cadavers has allowed the coupling effects to be studied accurately, but does not account for the muscle activity or loading effects (Gibbons and Tehan 1998). Figures 19A and 19B show similar results between the two studies, the location of the FAR varies depending on the cervical vertebra.

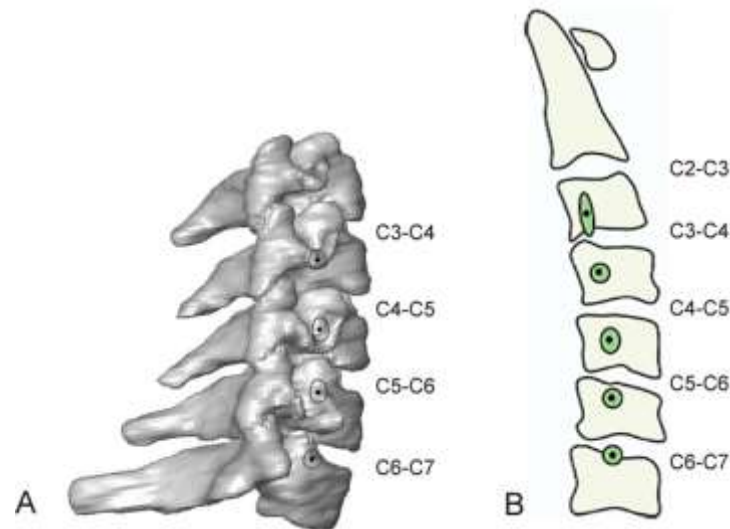


Figure 19: Comparison between two FAR studies, (A) Galbusera F *et al.* (2008) and (B), Sears *et al.* 2006

2.8 Disc Degeneration

For the FSU to maintain mobility, it is necessary that both soft and hard tissues remain healthy. Aging is a natural process whereby these flexible elements lose their mechanical integrity. Disc degeneration is an active process which mimics the passive natural aging process but occurs at a much higher rate. The aging process typically begins in the early twenties (Rumboldt 2006).

The various functional entities of the spinal column operate in concurrence, supporting each other to provide their function. Disc degeneration causes the kinematics of the spinal unit to change, which in turn places even higher loads on the zygapophyseal (Figure 8) joints which may lead to pain associated with impingement (Link *et al.* 2004).

Degenerated discs fail to bear normal daily loading due to a breakdown of the extracellular matrix (Zhao *et al.* 2007). Should the disc annulus deteriorate sufficiently, a prolapse of the disc may occur. This could lead to significant pain as the annulus may press against the spinal cord, as indicated in Figure 20 by the arrow.

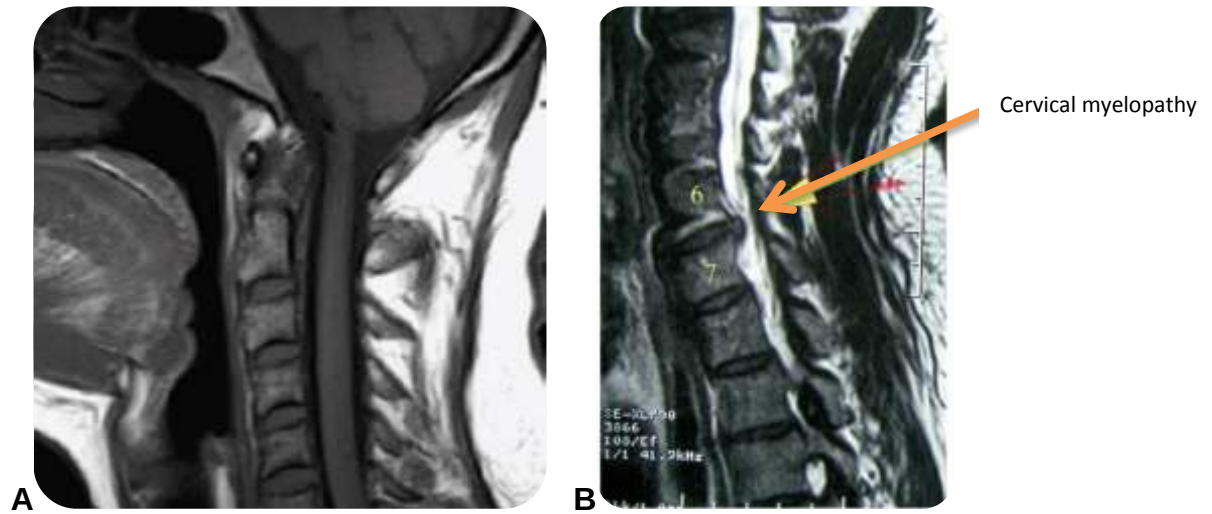


Figure 20: Sagittal section magnetic resonance images of the cervical spine;
(A) healthy cervical spine (Adapted from Moeller and Reif 2005);
(B) cervical myelopathy of C6-C7 level (Hannallah *et al.* 2007)

The exact mode of Degenerative Disc Disease (DDD) is not yet fully understood (An *et al.* 2006). Theories and models of pathology of DDD have been adopted over the past half century (Battié *et al.* 2009). Consensus has been reached that no single factor alone can result in disc degeneration. Three main phenomena can be considered as the contributing factors of DDD, namely mechanical loading, genetic predisposition and nutritional effects (Paesold *et al.* 2007).

2.8.1 Mechanical Loading

Biomechanical loads are transmitted and absorbed by the annulus, nucleus and endplate in a hydraulic mechanism. The rate at which disc aging occurs is influenced by mechanical loads imposed on the disc structure (Zhao *et al.* 2007). Damage to the annulus tends to propagate as the mechanical capacity is reduced when collagen fibres tear as a result of high biomechanical loading conditions. Annulus fibrosus damage (radial tears for example) tends to leave the disc more prone to herniation and the cycle continues (Iatridis and Gwynn 2004).

The effect of axial torque combined with flexion-extension was studied by Marshall and M McGill (2010). Purple dye was injected into the nucleus pulposus to illustrate the areas of disc damage under various loading conditions. A combination of repetitive flexion motion and axial torque was applied

to simulate biomechanical loading conditions. Figure 21 illustrates the progression of the die through the intervertebral disc. The findings were that repetitive flexion alone encourages radial delamination within the annulus. Repetitive flexion motion alone encourages postero-lateral damage through the annulus (Marshall and McGill 2010). This study illustrates that various types of loading patterns may affect the failure mode of the intervertebral disc.



Figure 21: Axial dissection of intervertebral disc (IVD) (Marshall and McGill 2010):
(A) no herniation;
(B) posterior herniation;
(C) posterior herniation and radial delamination

Figure 22 is a sagittal section through a herniated cadaveric lumbar L2-L3 section. The anterior side **is on the left**, with the posterior side of the disc prolapsing. It is observed that the nucleus pulposus has broken through the annulus with the result that stenosis of the canal occurs. Herniation of cervical intervertebral discs follows a similar mode of failure to lumbar discs.

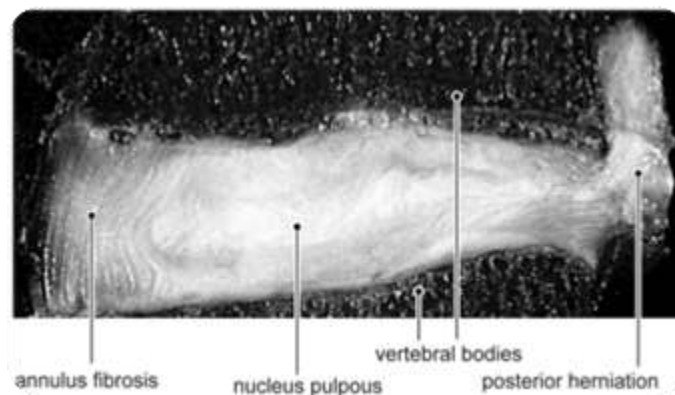


Figure 22: Sagittal section through a herniated cadaveric lumbar disc; note the annulus fibrosus and nucleus pulposus (Adapted from Adams and Dolan (2005))

2.8.2 Genetic Predisposition

Since the exact etiology of DDD is not yet completely understood, numerous theories have been proposed. N Boos cites seven studies which indicate a strong familial predisposition for degenerative disc disease.

A significant contribution to evaluating the etiology of lumbar disc degeneration was made by Battié *et al.* (2009). It is plausible that a particular gene (or set of genes) is responsible for accelerated aging of the intervertebral disc. The Twin Spine Study (TSS) investigates certain risk factors between ‘exposure-discordant identical twins’. These exposures include smoking, posture and physical demands imposed on the FSU such as working environment.

The outcome of the TSS was that there was a substantial hereditary and environmental influence on lumbar disc degeneration. Although the TSS focused on the lumbar region, studies which are cited by Boos (2007) indicate that similar findings may result in the cervical spine.

2.8.3 Nutritional Effects

The largest avascular structure in the human body is the intervertebral disc. Nutritional supply travels from the borders of the annulus and endplates, inwards towards the central nucleus pulposus (Cassar-Pullicino 1998).

After the first year of life, blood supply to the disc is provided only by the longitudinal ligaments on either side of the disc, and occasionally in the outermost portions of the annulus. Branches of the segmental artery provide blood supply to the vertebral body (Shankar *et al.* 2009).

Vertebral endplates may become sclerotic and less porous, inhibiting the transfer of nutrients and water (Bao *et al.* 1996). This, combined with evidence which suggests that a decrease in nutrient supply leads to disc degeneration (Bibby and Urban 2004), leaves the intervertebral disc with roughly a 30-year life before degeneration begins.

2.9 Conclusion

The spinal cord relays sensory information between the brain and target organs. Spinal nerves emerge at regular intervals from the spinal cord, leaving the vertebral column through the intervertebral foramina. Misalignment of the vertebral bodies or reduction of disc height may lead to impingement of spinal nerves, leading to pain.

To reduce the likelihood of subsidence, the loads transferred to the vertebrae should be distributed over as large an endplate area as possible. The outer surface of vertebral bodies contains bone of a higher density, and should be used for load bearing if possible.

The IVD serves as a spring to support the upper body. Maintaining the function of the intervertebral discs is necessary to preserve quality of life. The kinematics of the intervertebral disc are difficult to obtain *in vivo* and are dependent on the patient, for this reason the regulatory authorities (ISO and ASTM) have conservatively assumed the range of motion to be $+12^\circ$ to -12° for flexion-extension and lateral bending, similarly the loading is assumed to be 150N.

The finite axis of rotation is approximately in the centre of the IVD, below the surface of the inferior endplate. The natural disc in combination with ligaments and muscles provides six degrees of freedom. This soft and hard tissue combination causes the location of the FAR to vary as the FSU moves.

Intervertebral disc degeneration is a natural process, with disc degeneration beginning at the age of 20, and the rate of **it** increasing after the age of 30. DDD is thought to occur due to a combination of two or more of the following factors; by high mechanical loading, genetic predisposition and insufficient nutrient supply. It is essentially a natural process which is difficult to prevent.

In the **author's** opinion, an artificial disc should provide as near to healthy kinematics as possible. The following ideal kinematic requirements are summarised; Mobile centre of rotation, six degrees of freedom, self-centering geometry and 12° range of motion.

Chapter 3: Neck Pain

Neck pain is usually defined as stiffness and/or pain felt dorsally in the cervical region (Ferrari and Russell 2003). The cause of neck pain is due to compression or damage of a neurological structure, such as the spinal cord and or a nerve root due to disc degeneration. Pain relief is achieved by removing the source of neurological compression, known as decompression.

Treatment is usually first administered conservatively, surgical treatment is offered as a last resort in the event of persistent (over six months) discomfort. Conservative treatment typically consists of rest, heat, analgesics and physical therapy. Surgical treatment is placed in the following categories: decompression surgery, decompression and fusion, fusion, or spinal arthroplasty. Each of these surgical procedures achieves pain relief by removing the source of neurological compression. The method of decompression is selected based on the individual indications and contra indications of the patient.

The Neck Disability Index (NDI) was introduced in 1991 as the first self-rated disability index of patients with neck pain (Vernon 2008). The NDI is the most commonly used questionnaire for the assessment of neck pain disability. It contains ten questions, which investigate patients' symptoms and the effect of neck pain on functional activities (En *et al.* 2009). In this way, a reasonably objective evaluation can be obtained which can be used for comparison at a later stage of treatment.

Visual Analogue Scale (VAS) is a popular method to investigate subjective pain. When using VAS as a method of pain assessment, subjects are asked to indicate pain intensity by marking a 100mm line, marked 'no pain' on the left hand side, and 'worst pain possible' on the right hand side (Briggs and Closs 1999).

3.1 Axial Neck Pain

Axial neck pain does not radiate into the arms or upper extremities, but rather is situated in the base of the skull, neck and/or back of the shoulders. The cause of this type of pain is typically damage to the soft tissue structures. This type of disorder is also referred to as musculoskeletal. The extent of musculoskeletal pain ranges from temporary to chronic with regenerative injection therapy presently being the most commonly administered treatment (Linetsky and Manchikanti 2005). Treatment of axial neck pain is usually conservative, i.e non-surgical.

3.2 Cervical Myelopathy

Myelopathy is gradual degradation and loss of function of the spinal cord; this may be caused by either disease or damage to the spinal cord. Myelopathy is the most common cause of spinal cord dysfunction among those over the age of 55 (Baptiste and Fehlings 2006; Hillard and Apfelbaum 2006)

Damage to the spinal cord may be caused by an intervertebral disc prolapse or herniation. Osteophyte formation may also lead to stenosis of the canal (Edwards *et al.* 2003). Static and dynamic forces combined with disc degeneration contribute to the direct compression of the spinal cord (Komotar *et al.* 2006).

The diagnosis of cervical myelopathy is challenging (Salvi *et al.* 2006) as patients present a broad spectrum of symptoms. The symptoms include diminished balance and dexterity, and numbness. The magnitude of spinal dysfunction could further complicate the diagnosis due to patients being asymptomatic (Edwards *et al.* 2003).

3.3 Radiculopathy

Radiculopathy refers to pain caused by nerve root compression; symptoms are similar to those of myelopathy, including neck and/or arm pain. (Salvi *et al.* 2006). Cervical radiculopathy results from foraminal encroachment of the spinal nerves (Haitham Al-Khayat *et al.* 2007).

3.4 Treatment of Cervical Myelopathy and Radiculopathy

The most common treatment methodology of cervical myelopathy and radiculopathy is cervical discectomy (Shih *et al.* 2010). There are three anterior variations in the procedure: Anterior Cervical Discectomy (ACD) alone, Anterior Cervical Discectomy with Fusion (ACDF), and anterior cervical discectomy with fusion and plating (Mobbs *et al.*, 2009). Figure 23A illustrates a lateral cervical radiograph of a multilevel spondylosis with radicular symptoms (Jaramillo-de La Torre *et al.* 2008). Figure 23B illustrates a common treatment by means of ACDF.

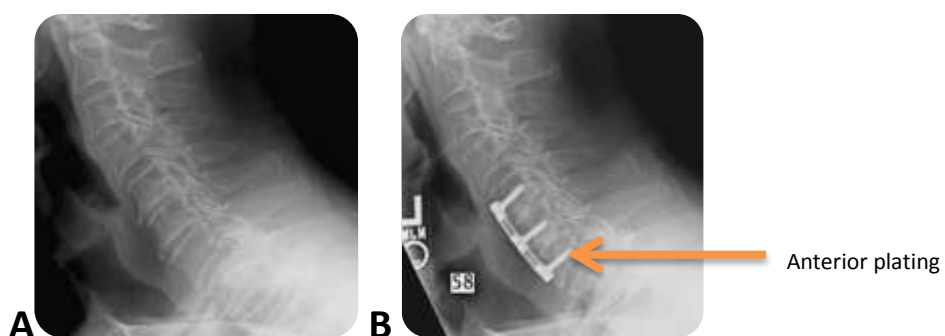


Figure 23: Lateral cervical X-ray image of a multilevel (A) spondylosis; (B) ACDF with plating at C5-6, C6-7 level (Jaramillo-de Torre *et al.* 2008)

Posterior treatment is also possible using lateral mass screws and rods (Komotar *et al.*, 2006) as illustrated in Figure 24. A laminectomy may also be used to alleviate the pressure by removing the lamina.

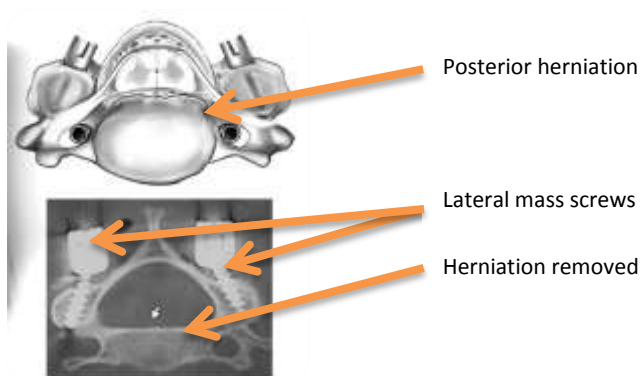


Figure 24: Cervical stabilisation by means of lateral mass screws (Komotar *et al.* 2006)

The aim of these surgical procedures (arthroplasty, arthrodesis, and laminectomy) is to remove the source of the pressure on the spinal cord, which would alleviate progression of neurological damage.

In the short term, fusion of the diseased level ‘is one of the most successful procedures’ to treat cervical myelopathy (Albert and Eichenbaum 2004), however, over the longer term osteophytes may develop on adjacent levels. Figure 24 illustrates how the stenosis of the spinal canal is removed (as indicated by the arrow).

3.5 Rationale for Cervical Arthroplasty

Adjacent level disease combined with functional disability has been the driving force behind the development of intervertebral disc replacement. The discontinuity in flexibility caused by a single or multiple level fusion increases motion on non-operated adjacent levels (Ishihara *et al.* 2004; Pickett 2008; Kasimatis *et al.* 2009). Traynelis (2006) and Jaramillo-de Torre *et al.* (2008) reference four biomechanical studies which illustrate an increased intradiscal pressure in adjacent discs due to the increased motion.

In recent years, interest in cervical arthroplasty for the treatment of myelopathy has been increasing (Mobbs *et al.* 2009) due to the theory that maintaining normal biomechanical motion will reduce intradiscal pressure and thereby the rate of degeneration (Albert and Eichenbaum 2004). Fusion of one or multiple levels influences the kinematics of the adjacent intervertebral discs. Figure 25 illustrates how RoM is maintained under flexion and extension at the surgical level.

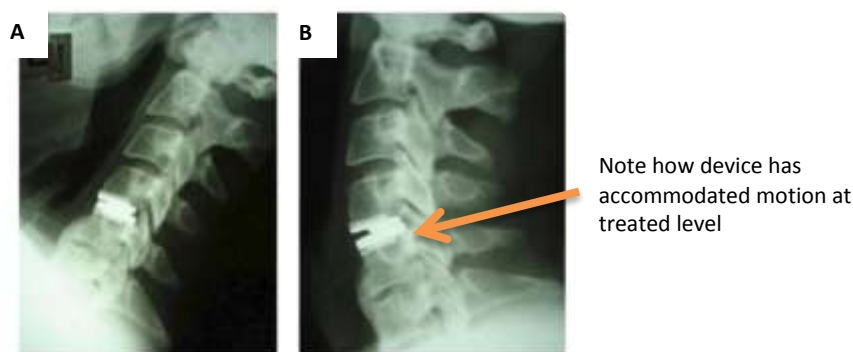


Figure 25: Post-operative dynamic lateral (A) flexion and (B) extension X-rays. Disc arthroplasty at C4-5 level (Mobbs *et al.* 2009)

3.6 Indications and Contraindications for Cervical Arthroplasty

All FDA approved cervical disc arthroplasties are indicated for the treatment of intractable radiculopathy and or myelopathy (BRYAN® Cervical Disc - P060023 2009).

Conservative treatment for radiculopathy such as manipulation remains controversial, but studies by Murphy *et al.* in 2006 and Whalen in 2008 report that six month post-operative relief is obtained by approximately half of patients whose cases have been effectively followed up. The guidelines for candidacy for manipulation treatments are not universally agreed on.

Auerbach *et al.* (2008) has summarised the indications and contraindications from clinical trials of four different cervical disc arthroplasties; Prodisc-C™, Prestige-LP®, Bryan®, and PCM. The summary for indications and contraindications can be obtained in Appendix A, Table 23 and 24 respectively.

3.7 Clinical Results of Cervical Arthroplasty

Validation that the various devices perform as intended can only be conclusively proved or disproved by means of a clinical trial. This section reviews two clinical trials which compare pain measures of cervical disc arthroplasty (commonly called total disc replacement (TDR)) and fusion by means of ACDF. The surgical approach is alike with these procedures and therefore is not expected to be a variable between arthroplasty (TDR) and arthrodesis (ACDF).

A non-biased clinical trial requires random patient selection; the size of the study needs to be large enough for a statistically insignificant variance between treatments under investigation. The trial aims to prove or disprove a hypothesis setup by the investigator, which has an associated confidence in obtaining a test statistic.

The results of these two studies are typical of those published in ‘Spine’ or ‘The Spine Journal’. They have been selected because they are both randomised studies. The first being a comparison between TDR and fusion, the second being comparison between different TDR and ACDF devices.

3.7.1 TDR and ACDF comparison

Table 3 presents results from a prospective randomized comparison between TDR and fusion (Guyer *et al.* 2008). A total of 40 patients were followed up, with six-month results reported. The ratio between TDR and fusion was 1:1. The KCD device was used to replace the disc, and fusions were performed anteriorly. The results illustrate that over the short term:

- Average reduction of pain score is 80% for TDR and 65% for fusion.
- Range of motion is increased by 36.5% with arthroplasty, but reduced with fusion.
- Disc height has been increased by over 85% for both TDR and fusion.

Table 3: Results of a randomised 40 patient disc arthroplasty and fusion comparison (Guyer *et al.* 2008)

	Procedure	Pre-op.	6 month post-op.	% Change
VAS	TDR	79.8	15.9	80.1%
	Fusion	74.8	24.8	66.8%
NDI	TDR	63.7	12.8	79.9%
	Fusion	63.7	24.0	62.3%
ROM	TDR	7.4	10.1	36.5%
	Fusion	6.4	1.9	70.3%
Disc Height	TDR	3.1	6.2	100.0%
	Fusion	2.7	5.0	85.2%

3.7.2 TDR Device Comparison

Coric *et al.* (2010) performed a randomised study comparing three TDR devices as well as ACDF from a single investigational site (hospital). Ninety eight patients with indications for either TDR or ACDF treatment for cervical radiculopathy and/or myelopathy were selected for the study. Both groups showed a ‘significant improvement’ over the baseline with regard to NDI. Table 4 summarises the results from the study performed by Coric *et al.*

Table 4: Clinical indices pre and post-op (data sourced from Coric *et al.* 2010)

	No. of Patients	Pre-operative			Post-operative (24 month)			
		Month	NDI	ROM (°)	Month	NDI	ROM (°)	> 20% NDI improvement
Bryan®	57	0	62	7.6	48	13	8.5	96%
Kineflex		0	63	7.9	24	22	13.0	85%
Discover™		0	54	8.2	24	20	6.9	87%
ACDF	41	0	62	8.1	24	23	0.8	unknown

3.7.3 Discussion of Selected Studies

These and other recent studies (such as Zigler (2007), Auerbach *et al.* (2008), Murrey *et al.* (2008)) illustrate that pain indices as a result of cervical radiculopathy and/or myelopathy can be significantly reduced over at least a two-year period by either anterior fusion or total disc replacement. In the period studied there does not seem to be a significant statistical difference of clinical results between the variations of device kinematics and materials adopted by various manufacturers.

3.7.4 Complications of TDR

Surgery strategy is dependent on several factors, neurologic presentation, pathologic anatomy and medical comorbidity. The urgency of the surgery will depend on the rate of neurological deterioration (Komotar *et al.* 2006).

All surgical procedures have an associated risk; these include anaesthesia complications, blood clots, and allergic reactions. Surgery may introduce undiagnosed complications. Complications of an anterior surgical include (Cervical Artificial Disc Surgery, Medtronic):

- Allergic reaction or hypersensitivity to device material
- Device may physically fail
- Open surgery may lead to local and/or systemic infection
- Pain
- Neurological injury or dural tear

- Reduction of range of motion, or fusion
- Disc degeneration may develop or progress at other levels
- Swelling
- Swallowing dysfunction
- Altered mental state
- Pregnancy complications
- Death

Careful consideration from the surgeon and patient should be used to mitigate the risks to an acceptable level. Patient selection and surgical technique based on careful radiographic and clinical assessment are the primary methods of mitigating the associated risk to an acceptable level.

3.8 Conclusion

Neck pain ranges from temporary to chronic, with treatment ranging from conservative methods to invasive surgery. As a general rule, surgical intervention should only be administered as a last resort after six months of failed conservative treatment.

Patient selection in combination with surgical strategy is an important requirement to successful treatment of cervical radiculopathy and/or myelopathy. Treatment may be performed with total disc replacement or fusion, with a significant improvement over pre-operative pain indices.

It can be expected that the range of motion at the treated level will increase after a diseased disc is replaced, but will reduce with fusion. An increase in range of motion of the treated level is expected to reduce the onset of adjacent disc degeneration.

Two-year post-operative pain index scores between arthroplasty and fusion do not show a statistical difference. There does not seem to be a significant variation in clinical outcomes between the Bryan[®], Kineflex, and Discover[™] arthroplasties.

Presently there seems to be no clinical evidence which illustrates that the long term outcome of TDR is superior to ACDF for treatment of cervical radiculopathy and/or myelopathy. Further study of the

treatment of this symptom, with a larger sample size, over a longer period is required to conclusively determine which surgical procedure is the most effective.

Chapter 4: Imaging Techniques

This chapter evaluates three imaging techniques which are commonly used for imaging of the cervical spine: plane X-ray, computed tomography (CT) and magnetic resonance imaging (MRI). X-rays were first discovered in 1895, and were initially used for theatrical performance. From this period until the First World War diagnostic radiography matured (Hessenbruch 2002). Each of these technologies has proven to be a vital component to accurate diagnosis. Their development continues to advance.

Artefacts may appear on MR and CT images as combinations of black or white areas (flares) where the image does not represent the item being scanned. Artefacts are a well-known problem, typically caused by metallic implants. Artefacts may also be caused due to motion such as blood flow or movement during the scan.

4.1 Plane X-ray

Plane X-rays are ideal for high risk (trauma) patients as a primary technique to provide quick and effective diagnosis on the extent of injury (Lee 2003). Although plane X-rays do not provide the necessary contrast for soft tissue evaluation, they continue to be the most commonly used type of imaging (McGill and Yingling 1999).

X-ray imaging measures the density distribution of an object according to the strength of the penetration. Longer and thus less energetic are more easily absorbed by bone than shorter wavelengths (Hessenbruch 2002). Dimensional data is generated by radiating the object from various directions and measuring the response (Nukaga *et al.* 2008). X-ray imaging is not as sensitive to metallic artefacts, but is subjected to artefact formations (Gomi *et al.* 2009).

X-ray energy is measured as electron volt³ (eV), Figure 26A illustrates the artefacts formed at three different energy values, 40, 80 and 120keV. The shape of the sample (Figure 26B) does not match

³ 1 eV = 1.602176487(40)×10⁻¹⁹ joule

the image produced. Artefacts are present with each of the energy settings, higher energy X-rays provide for a 'brighter' image, and the higher intensity also increases the intensity of the artefact.

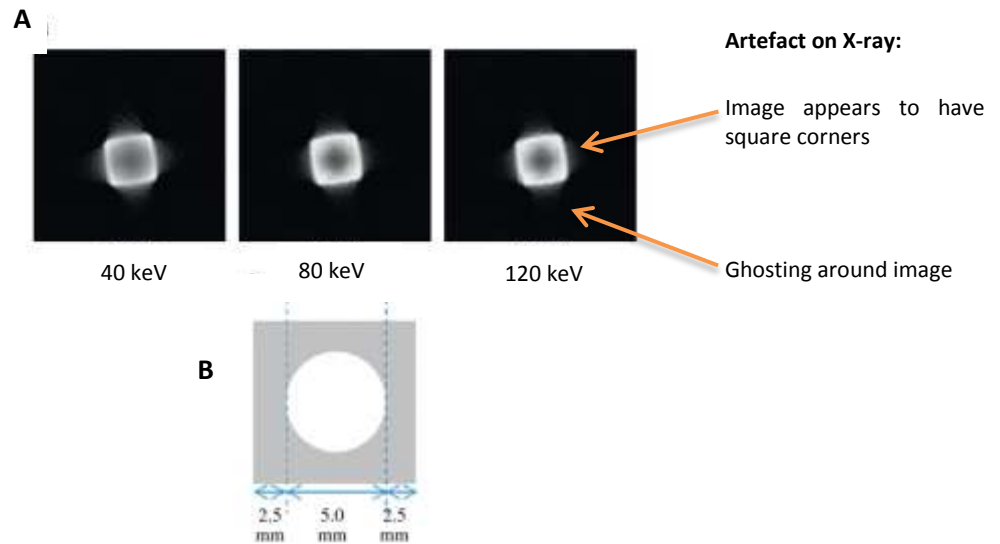


Figure 26: (A) X-ray CT images of molybdenum at 40, 80, and 120 keV; (B) detail drawing of sample (Matsumoto *et al.* 2010)

Neat polymers such as polyether-ether-ketone (PEEK) and ultra-high-molecular-weight-polyethylene (UHMWPE) are radiolucent. Image contrast additive may be added to the polymer to alter the degree of visibility during screening. Figure 27 illustrates varying degrees of radiopacity of an intervertebral fusion device under X-ray screening.

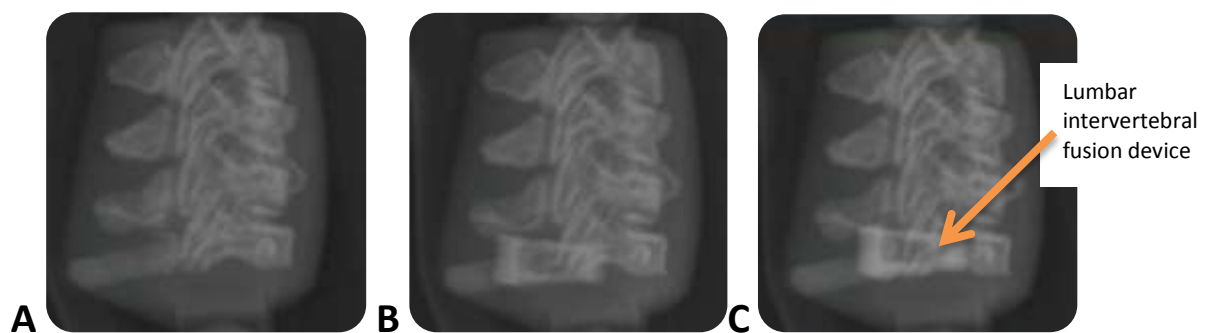


Figure 27: Varying degrees of radiopacity of sample intervertebral device; (A) Neat or unfilled; (B) Low radiopacity; (C) High radiopacity (PEEK-OPTIMA Material Properties 2010)

4.2 Computed Tomography

The **advances** in computational power in the 1960's made the development of Computed tomography possible. A series of two-dimensional images are assembled into a three-dimensional volume which **may be** sectioned and viewed in any desired manor (Hessenbruch 2002).

CT is an effective method for trauma evaluation due to the rapid scan time, as well as a higher resolution in bone and soft tissue than plane X-ray. CT lacks sensitivity in detecting intrinsic pathology of the spinal cord (Gilbert *et al.* 2006). Fisher and Young (2008) suggest that the greater accuracy of CT is necessary for the assessment of trauma, and plane X-rays should be eliminated from trauma protocols.

4.3 Magnetic Resonance Imaging

The development of MRI technology has improved the ability to correctly diagnose pathogenic mechanisms (McCormack and Weinstein 1996). MRI is the fastest developing imaging technique (Lewin 2003). Owing to its ability to differentiate between soft tissue structures, MR has become the preferred imaging method for assessment of spinal disorders (Westbrook and Kaut 1998, Bozzali and Cherubini 2007). The quality of modern MR images is such that common pathologies can be assessed clinically (Wessely 2004). **The clinical value of the MRI would be reduced if an artefact is present in close proximity to the area under investigation.**

The author believes that the ideal case for an imaging compatible implant is therefore a device which is visible during trauma imaging, and invisible during soft tissue evaluation. Device migration as a result of trauma could be assessed using standard trauma imaging techniques. Soft tissue evaluation would be possible by means of MRI. Due to MR providing the clearest distinction between tissue types, artefacts have been investigated in the context of MR.

Figure 28 is a typical MR mid-sagittal image of the cervical spine. Note the contrast of the various tissues. The differing composition and density of tissues causes the contrast which makes for clear distinction of tissue types.

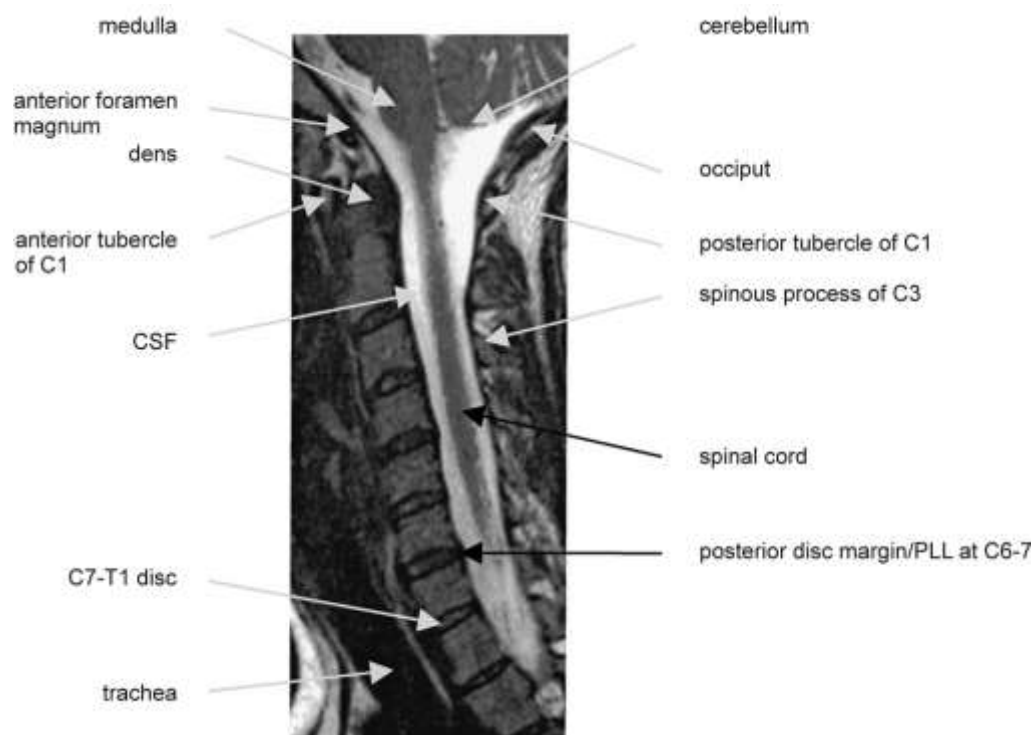


Figure 28: T2-weighted mid sagittal MRI scan of a cervical spine (Adapted from DeVries 2003)

Figure 29 illustrates an example of a T2-weighted axial image, showing the anatomy of the cervical spine. The spinal cord is cylindrical, with eight spinal nerves composed of a dorsal sensory root and a ventral root for motor impulses (DeVries 2003).

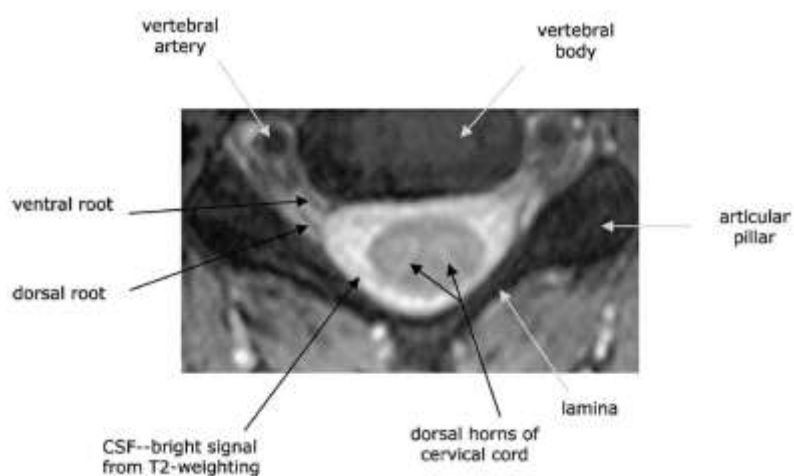


Figure 29: Axial T2-weighted image of the cervical spine (DeVries 2003).

4.3.1 Basic Principle of MRI

The basis of Nuclear Magnetic Resonance (NMR), more commonly known as magnetic resonance imaging is the interaction between an external magnetic field and atomic nuclei of the test subject with a nonzero magnetic moment (Kuperman 2000).

Alignment

In the absence of an external magnetic field, the magnetic alignments of the nuclei are randomly distributed. Figure 30 illustrates how the introduction of a strong external field brings about alignment of the nuclei to the external field. The alignment may either be in the same direction (parallel) or in the opposite direction (anti-parallel) alignment (Westbrook and Kaut 1998).

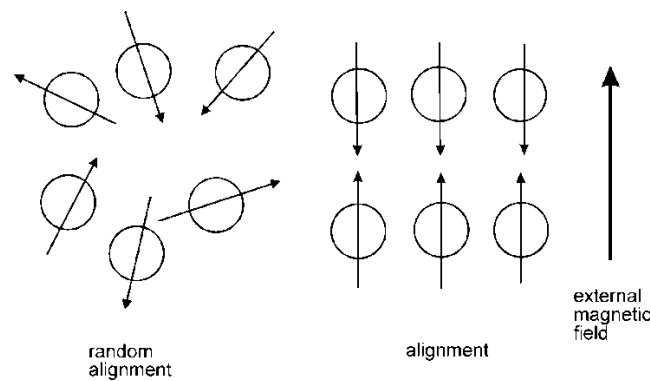


Figure 30: Diagram illustrating magnetic alignment of nuclei with no external field, and when an external field is present (Redrawn from Westbrook and Kaut 1998)

The energy of interaction with a magnetic field depends on the direction of nuclear moments, in such a way that the minimum energy corresponds to the state in which the moments are parallel to the external magnetic field (Kuperman 2000).

When the patient is positioned in the magnetic field, the hydrogen nuclei within the patient align to the external field in a parallel and anti-parallel manner. A small excess of nuclei with parallel alignment contribute to the patient's net magnetisation vector (Westbrook and Kaut 1998). Bloch (2000) explained it succinctly as:

$$M = \chi B_0 \quad (1)$$

where M is the nuclear magnetisation, B_0 is the external static magnetic field, and χ is the bulk nuclear susceptibility of the sample. If an oscillating field is applied to the sample, a resonating frequency could be achieved which corresponds to the nuclear susceptibility of the nucleus. Magnetic susceptibility is defined as the degree of magnetisation in response to an applied magnetic field (Kuperman 2000).

Precession

Classical electromagnetic theory dictates that the motion of individual nuclear moments in a static magnetic field is a precession at a particular angular frequency. This characteristic precession frequency ω_0 is given by the Larmor equation (Kuperman 2000):

$$\omega_0 = B_0\gamma \quad (2)$$

Where B_0 is the external static magnetic field strength, and γ is the gyro-magnetic ratio. The gyro-magnetic ratio defines the relationship between the angular momentum and the magnetic moment of each MR active nucleus. The gyro-magnetic ratio is specific to the type of MR active nucleus. For example, hydrogen is 42.57 MHz/T (Westbrook and Kaut 1998). MR active nuclei for biological applications have been listed in Table 5.

Table 5: NMR constants for biological applications (Kuperman 2000)

Element	Mass number	Gyro-magnetic ratio: γ ($10^6 \omega/T$)	Resonant frequency: $\gamma/2\pi$ (MHz/T)
Hydrogen	1	267.5	42.573
Carbon	13	67.26	10.705
Oxygen	17	-36.264	-5.772
Fluorine	19	251.66	40.052
Sodium	23	70.77	11.263
Phosphorus	31	108.29	17.237

Quantum physics dictates that electromagnetic radiation is not propagated in continuous waves (classical theory), but emitted in discrete bundles of energy called quanta or photons:

$$E = \hbar\omega_0 \quad (3)$$

where the energy (E) is dependent only on the frequency (ω_0) of the nucleus and the reduced Plank constant ($\hbar$). Applying quantum physics to MRI, hydrogen nuclei possess only two energy states, low and high. Low energy state relates to nuclear moments parallel to the external field, high energy state to the anti-parallel direction. To maintain thermal equilibrium, there are always fewer high-energy nuclei than low energy nuclei, and the magnetic moments of the parallel nuclei cancel out the smaller number of anti-parallel moments (Westbrook and Kaut 1998).

Resonance

Resonance occurs when a body encounters an oscillating force which has a frequency equal to its own natural frequency of oscillation. Only nuclei with frequencies matching the applied field will resonate due to the impulse. The existence of a particular type of nucleus can be shown by applying an oscillating field at a particular frequency. The coil which applies the resonant excitation pulse is named the radio frequency (RF) coil and is referred to as B_1 (Westbrook and Kaut 1998).

The summation of in-phase resonating magnetic nuclei causes a magnetic induction, which the receiver captures as a voltage. The frequency at which the voltage oscillates is equal to the Larmor frequency, which makes it possible to differentiate between various types of nuclei (Westbrook and Kaut 1998).

Pulse sequences and Motion of Magnetic Moments

The motion of nuclei occurs about a nuclei percussion axis, the direction of which is determined by the sum of magnetic fields, namely the static and RF fields. The RF pulse is linearly polarised and perpendicular to the static field. The RF pulse therefore causes the axis of rotation to move away from the static field, toward the perpendicular axis. The difference between the static field and nuclei percussion axis is termed the flip angle. The longer the duration of the RF pulse, the closer the flip angle is to 90° (Kuperman 2000).

Decay of Free Induction

The short duration between RF pulses allows the axis of precession to realign with the static field, losing energy gained by the RF pulse. The process of realignment is called relaxation, thereby decreasing the perpendicular field strength and increasing the static field strength. Recovery of static magnetic field strength is termed T1 recovery; decay of the perpendicular magnetic field is termed T2 decay.

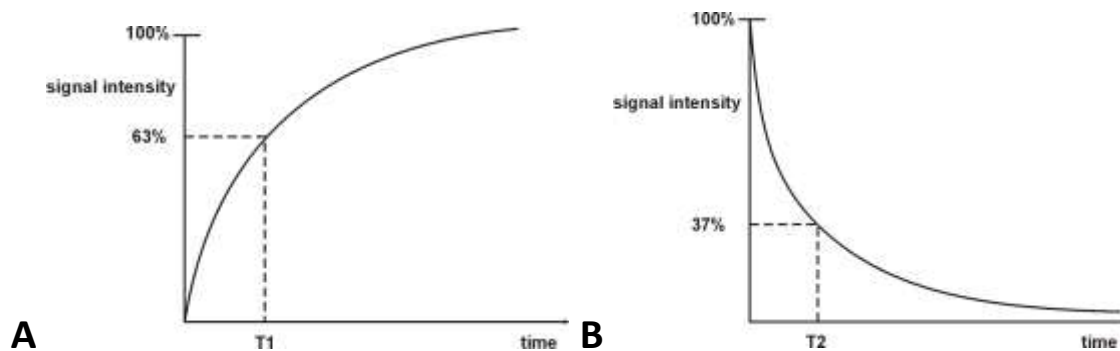


Figure 31: Exponential decay and recovery of signal intensity (Westbrook and Kaut 1998):
 (A) T1 recovery, time taken for 63% of signal intensity to recover in the tissue
 (B) T2 decay, time taken for signal intensity to reach 37% in the perpendicular plane

Spin-echo

Signal loss due to magnetic field non-uniformity can be avoided by recovering some of the oscillation decay by the application of a spin-echo (SE) refocusing pulse. This is a second application of the B_1 field which acts to turn the spins 180° so that the phases are reversed. Spin-echo pulse sequences include T1 and T2-weighting (Kuperman 2000; Liney 2006).

Gradient-echo

T2-weighted images can also be obtained with gradient-echo (GE) pulse sequences. The advantage of GE is primarily reduced acquisition time over SE. GE images have similar intensity as SE T2-weighted images (Liney 2006).

Contrast Mechanisms

Contrast between tissue types is predominantly obtained through mechanisms of T1 recovery, T2 decay and proton or spin density. T1 recovery occurs when nuclei **dispersing** their energy to the surrounding tissue (Westbrook and Kaut 1998).

Proton density is the amount of hydrogen nuclei per unit volume. Image intensity is directly related to proton density, and proton density within soft tissue is fairly consistent, varying by only a few percent. T1 and T2 relaxation times vary by more than 100%. Table 6 lists T1 and T2 relaxation times for various tissue types (Kuperman 2000).

Table 6: Approximate relaxation times for tissue types at 1.5 Tesla (Kuperman 2000)

Tissue	T1 (ms)	T2 (ms)
Gray matter	920	101
White matter	790	91
Cerebrospinal fluid (CSF)	2650	280
Kidney	650	58
Liver	40	43
Skeletal Muscle	870	47

T1 and T2 Contrast

When subjected to a sequence of excitation pulses, tissues with a short T1 will restore their longitudinal magnetisation more rapidly and will have a larger steady-state transverse magnetisation than tissues with a long T1. As a result, tissues with short T1 provide a high signal and therefore are brighter on T1-weighted images (Kuperman 2000).

Similarly, variations in T2 relaxation time between tissue types can be used to produce images with predominant T2 contrast. Tissues with a bright appearance will have long T2 relaxation times, and tissues with short relaxation times are darker in appearance (Kuperman 2000).

Depending on the type of contrast desired, either a T1 or T2 weighted image will be utilised. On T1-weighted images, fat and marrow appear white, while **water**, CSF, cortical bone and ligaments appear darker. T1-weighted images are normally used for showing anatomical detail. In T2-weighted

images water, marrow and CSF appear white, while darker areas represent fat, cortical bone and air. T2 images are more commonly used for detecting pathology (DeVries 2003).

4.3.2 MRI Safety

In 2006 Liney notes that there is no known long-term or irreversible biological effect from exposure to static fields of less than 10 Tesla at this stage in the development of MR technology. Presently, the FDA allows for MR equipment induced magnetic fields with strength of up to three tesla⁴. Future regulations may further increase the allowable field strength to obtain higher image qualities. Not all devices are MR compatible; these include pacemakers, implanted defibrillators, infusion pumps and cochlear implants. Obesity and claustrophobia are also conditions which make imaging problematic (DeVries 2003).

The strength and/or fluctuation of the applied magnetic field may lead to heating, force or a torque being generated by the medical device (Shellock 1996; Shellock and Valencerina 2005; ASTM F2119-07 2010). This energy may cause the temperature of the implant to increase to a level which may damage surrounding tissue. Similarly, should the torque or force being imparted be large, the device may become dislodged at a severe risk to the patient.

Starcuková *et al.* (2008) states that according to literature, all non-ferromagnetic materials pose negligible forces or torques that can cause patient discomfort or danger. This is in agreement with the compatibility of numerous types of permanent implants seen on MR images. Selection of a non-ferromagnetic material therefore makes the device MR compatible.

MRI differs from computed tomography in that no radiation is used during the imaging process (DeVries 2003). The patient is therefore not exposed to radiation, making the MR technology safer than either CT or X-ray in that respect.

⁴ Based on the assumption that the Earth's magnetic field is approximately $5 \times 10^{-5} \text{T}$, a field strength of 3T is therefore 60 000 times stronger than is experienced naturally.

4.3.3 MR Artefacts

Figure 32 illustrates the presence of artefacts in an image produced by the MR equipment. The image is expected to show a circle in the centre of the image; however, it is observed that various shapes are reported by the MRI – these are known as artefacts.

Image contrast ranges between black and white, high signals are represented by white and low signals are represented by black on the image. Intermediate signals are a grey-scale between these two extremes. Signals are measured in the transverse plane; a large transverse magnetisation therefore is displayed **as a bright area** on the image. Small signal amplitude in the transverse plane is displayed as a dark area on the image (Westbrook and Kaut 1998).

The size of the artefact can be reduced to some extent by proper MRI equipment setup; however, this is impractical mainly due to time constraints. The size of artefacts is measured as ‘the maximum distance (mm) from the edge of the implant to the fringe of the resulting image artefact’ (ASTM F2119-07 2010).

Figure 32 illustrates the effect of gradient-echo (GE) and spin-echo (SE). It was observed that for materials with a magnetic susceptibility significantly larger than water, SE artefacts extend further than GE. Low transverse signals were observed with the GE pulse sequence, while high transverse signals were present with the SE pulse sequence. It is however not known if the orientation of the sample in the test setup would have an influence on the artefact produced due to the asymmetric influence on the static and RF fields.

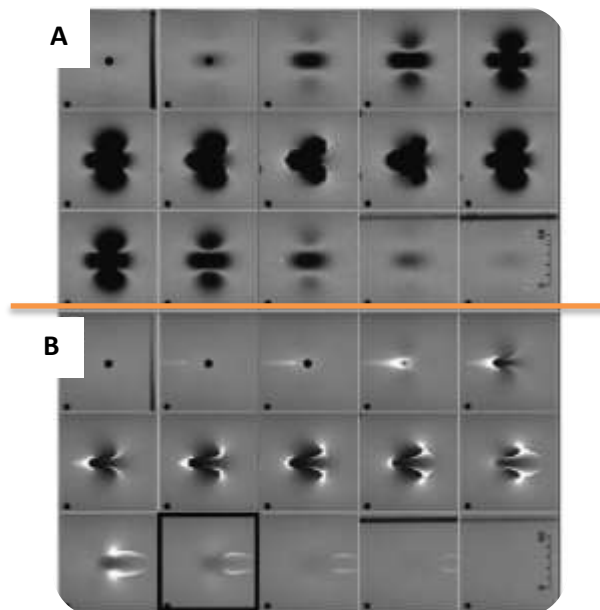


Figure 32: Bronze alloy cylinder immersed in CuSO_4 -doped ($1.25\text{g}/\ell$) water, axial slice thickness 3mm: (A) gradient-echo; (B) spin-echo. (Starcuková *et al.* 2008)

4.3.3.1 Material Influence

The distortions of the images are caused by a distortion in the magnetic field within the MR field (Brown and Semelka 2003). The significant variances in magnetic properties between the natural tissue and metallic objects cause a non-predictable field (Viano *et al.* 2000) which tends to obscure the MR image. The signal-to-noise ratio is one of the most important image characteristics as it defines the ability to distinguish between different structures in the image (Westbrook and Kaut 1998).

Starcuková *et al.* found that precious metals displayed an artefacts size of less than 5mm, with titanium being the next most imaging-compatible material with artefacts of approximately 12mm as illustrated in Figure 33. Materials with a low magnetic susceptibility are therefore expected by definition to produce smaller artefacts than higher susceptibility.

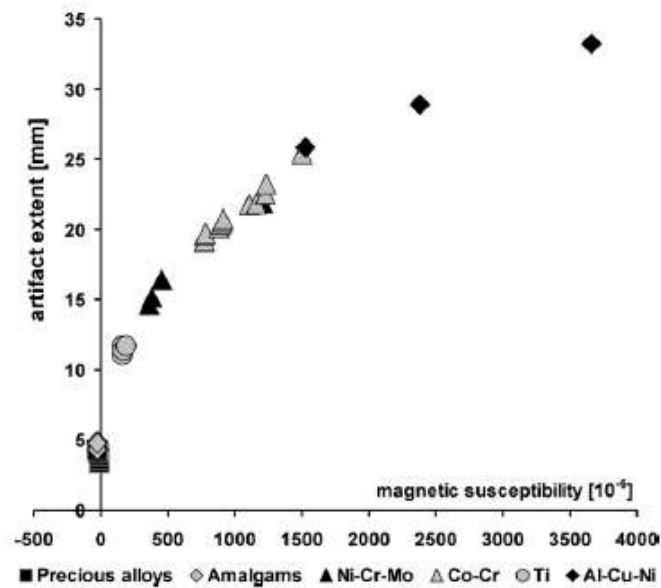


Figure 33: Artefact's extent (Starcuková *et al.* 2008)

Titanium or tantalum produces localised distortions, whereas stainless steel can produce large distortions (Brown and Semelka 2003). Cobalt-chromium-molybdenum as commonly used in implants tends to cause large artefacts (Sekhon 2006).

The choice of materials available for permanent implant is limited to highly bio-compatible materials. Cervical disc arthroplasty devices **are** presently manufactured from a combination of metals, elastomers, polymers or ceramic material (Morrison *et al.* 1995; Perrin 2005; Sekhon and Ball 2005:446).

4.3.4 Artefact Size

The size of the artefact is dependent on the material selection, volume and geometry of the device being scanned (Shellock 1996, Viano *et al.* 2000). Figure 34 demonstrates an example of a MRI with a titanium test specimen, with varying volume (A-B), and with varying geometrical shape but equal volume (B-C). Figure 35 can be used as a comparison between dissimilar materials. Geometrically similar test specimens are manufactured from carbon in this test.

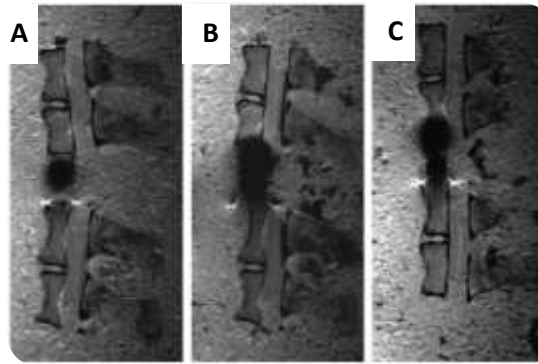


Figure 34: MRI artefact example for titanium: (A) small cylinder; (B) large cuboid; (C) medium cylinder with equivalent cuboid volume (Shellock 1996)

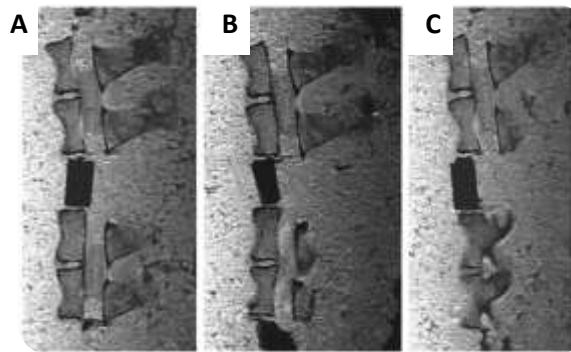


Figure 35: MRI artefact example for carbon: (A) small cylinder; (B) large cuboid; (C) medium cylinder with equivalent cuboid volume (Shellock 1996)

The size of the artefact is therefore related to the amount of magnetic field distortion, which is a function of the magnetic properties, volume and mass of the device.

4.4 Conclusion

Each imaging modality has its niche, where its strengths should be applied for the particular scenario (Gilbert *et al.* 2006; Verlaan *et al.* 2005). Magnetic resonance imaging is the most popular method for imaging soft tissue structures. Demand for MR imaging is increasing, and will continue to be the imaging technique of choice for the foreseeable future. It is therefore necessary that implanted devices are not only MR compatible, but also produce as small artefacts as possible.

Artefact size is dependent on material composition, volume and shape. These variables are to be optimised under the constraints of the device requirements:

- The volume of metallic material should be kept to a minimum.
- Selection of a non-ferromagnetic material will result in very low torques, forces and heating which ensures compatibility.
- Titanium generates the least amount of MR artefacts among the biocompatible materials which is commonly used in spinal arthroplasties. Polymers do not generate artefacts and must also be considered for the development of an imaging compatible device.

On the basis of the literature reviewed, non-ferromagnetic material must be selected for development of this device.

Chapter 5: Biocompatible Materials

Biocompatible materials (or biomaterials) were developed to direct, supplement, or replace the functions of living tissues of the human body (Ramakrishna 2001; Dorozhkin 2010). Biomaterials can be categorised into three classes: metals, plastics and ceramics. Progress in the biomaterial field has increased due to the advance of material, biological, chemical, medical and mechanical sciences. Figure 36 illustrates the introduction of biomaterials between 1920 and 1980; recently more focus has been placed into the development of bioceramics (Niinomi 2002; Kady *et al.* 2009).

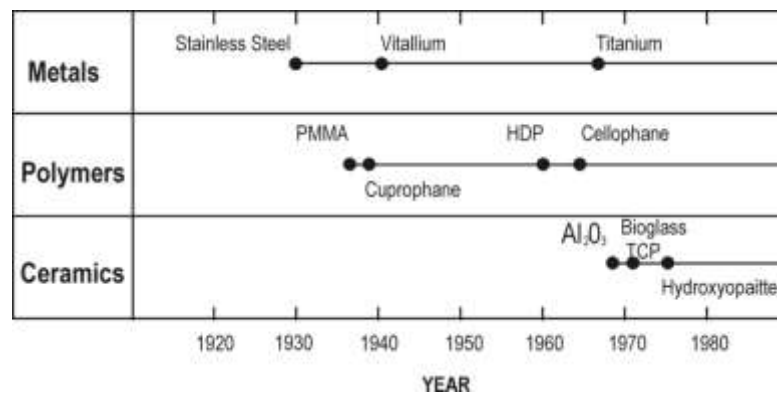


Figure 36: History of biocompatible materials (Adapted from Niinomi 2002)

5.1 Material Selection

Biocompatible materials used in orthopaedic applications have the following selection criteria: mechanical properties, biocompatibility, high corrosion and wear resistance, and osseointegration (Geetha *et al.* 2009). From a practical point of view it is also necessary for the material to be universally available and manufactured by known techniques.

This section explores various aspects of material properties, although they should by no means be considered in isolation. The selection of the biomaterial is based on the intended application of the device. By combining various materials a hybrid can be achieved, thereby obtaining particular mechanical or biological properties where necessary.

5.1.1 Mechanical Properties

Due to a variance between Young's Modulus of Elasticity of an implant and natural tissue, a strain difference exists between the implant and the bone. This occurrence is known as stress shielding, which may lead to implant loosening (Simoes and Marques 2005; Chevalier and Gremillard 2009).

Figure 37 lists several common orthopaedic biomaterials and their modulus of elasticity; note the distribution of the material types. In an effort to reduce stress shielding PEEK was developed by closely matching the elasticity of the polymer to that of the cortical bone (Kurtz and Devine 2007).

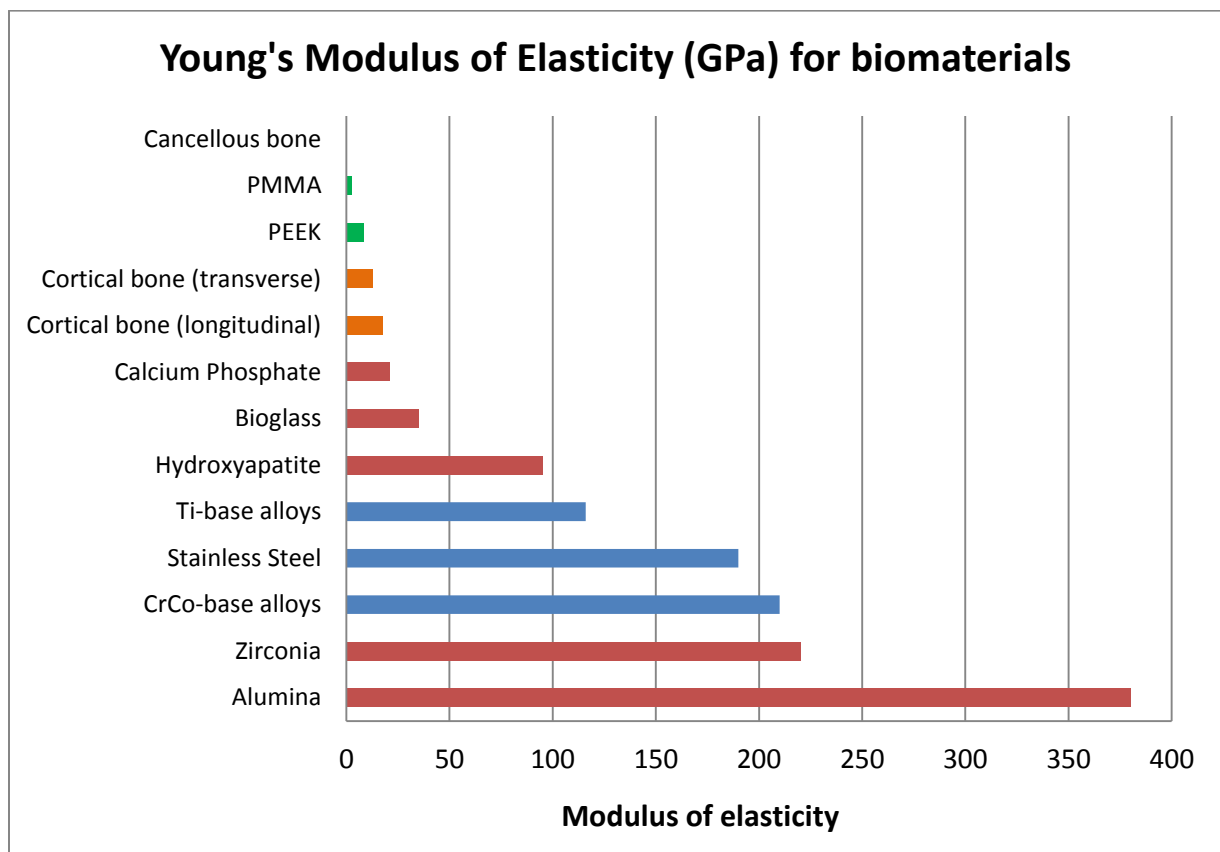


Figure 37: Young's Modulus of Elasticity (GPa) of various biomaterials (Adapted from Ramakrishna 2001)

Mechanical performance of material are dependent on their environment. It must therefore be considered that temperature, and acidity of surrounding fluid may adversely influence the mechanical properties.

5.1.2 Biocompatibility

Materials used for long-term implants are expected to be highly non-toxic, and should not cause any inflammatory or allergic reactions (Geetha *et al.* 2009). Biomaterials are also categorised by the response of tissue in intimate contact with the material. The extent of biocompatibility was assessed by experimental animal studies. The degree of biocompatibility is classified into biotolerant, bioinert, bioactive, and bioresorbable (Kienapfel *et al.* 1999).

Biotolerant materials do not cause a negative response but will be surrounded by fibrous tissue when embedded into the body (Kady *et al.* 2009). Bioinert materials have a higher degree of biocompatibility than biotolerant materials and as such promotes contact osteogenesis and osseointegration. The highest form of biocompatibility is found in bioactive and bioresorbable materials. Table 7 illustrates various biomaterials and their extent of biocompatibility and degree of osteogenesis. Bioresorbable materials are not considered in the context of the requirement of the device to be a long term implant (Kurtz and Devine 2007).

Table 7: Biomaterials and their extent of biocompatibility (Adapted from Kienapfel *et al.* 1999; Niinomi 2002; Kurtz and Devine 2007)

Material	Material Classification	Extent of Biocompatibility	Reactive Bone Formation
PMMA	Polymer	Biotolerant	Intervened osteogenesis
PEEK	Polymer	Biotolerant	Intervened osteogenesis
Stainless steel	Metal	Biotolerant	Intervened osteogenesis
CrCo-base alloys	Metal	Biotolerant	Intervened osteogenesis
Ti-base alloys	Metal	Bioinert	Contact osteogenesis
Alumina	Ceramic	Bioinert	Contact osteogenesis
Calcium phosphate	Ceramic	Bioactive	Bonding osteogenesis
Bioglass	Ceramic	Bioactive	Bonding osteogenesis
Hydroxyapatite	Ceramic	Bioactive	Bonding osteogenesis

Titanium has traditionally been the most attractive biomaterial due to the high degree of biocompatibility, machinability and availability. Titanium of various grades has been the subject of experiments for over half a century. Its biocompatibility is caused by an instantaneous build-up of a stable and inert oxide layer (Huang 2003; Elias *et al.* 2008).

PEEK biomaterials have over a decade and a half of successful clinical history in load-sharing fusion applications in the spine (Kurtz and Devine 2007). Ceramic materials exhibit a good combination of biocompatibility and hardness, and as such toughened Alumina has been used extensively as a femoral head replacement.

5.1.3 Osseointegration

The term osseointegration is presently accepted as intimate contact between the interface of the implant and bone. Cellular proliferation onto the surface of the implant is the primary requirement for osseointegration (Kienapfel *et al.* 1999).

Osseointegration is commonly used for long-term fixation of medical devices. Micro movement between the device and adjacent bone results in implant loosening. A fibrous tissue develops at the implant-bone interface if the implant is not well integrated (Geetha *et al.* 2009).

Micro movement may also be caused by a mismatch of strain experienced by the bone and implant surface. The device-bone interface should match the anatomy closely to increase the area of osseointegration as much as possible. This results in a reduced stress shielding and stronger anchorage of the device.

The quality of osseointegration may be improved by roughening the implant's surface or by applying a porous titanium-plasma, grit blasting, acid etching or anodising. Rough surfaces favour bone anchoring, which increases the stability of the device (Le Guéhennec *et al.* 2007).

The rate at which osseointegration occurs can be improved by providing a scaffold for new bone formation. Calcium phosphate (CaP) and Hydroxyapatite (HA) coatings have been developed as a surface treatment to induce a biological apatite for the surface of the device. These scaffolds are known as osteoconductive, calcium phosphate is the most common type used (Le Guéhennec *et al.* 2007; Cunningham *et al.* 2009). Neither porous nor nonporous calcium phosphate ceramic coatings have satisfactory long term durability (Kienapfel *et al.* 1999). Dorozhkin (2010) suggests that the reason for limited use is due to poor fatigue resistance and high brittleness.

5.1.4 Wear Resistance

Mechanical wear may be defined as material removal or a surface damage process resulting from two surfaces in contact and encountering relative motion with each other. The rate of wear is dependent on the applied load and hardness of the material surfaces (Paital and Dahotre 2009).

Obtaining high wear resistance is required for two reasons: to increase the lifespan of the device and reduce the volume of wear debris and **thereby lessen biological reaction**. Should the bearing surfaces wear out, the device may no longer maintain its intended purpose.

The shape of the wear debris has an effect on the biological reaction; elongated fibres are more pro-inflammatory than round particles (Hallab 2009). Due to the variability of the debris morphology, biological reaction should be tested by means of *in vivo* studies.

The most common type of wear couple for hip arthroplasties has been highly polished polyethylene-metal or polyethylene-ceramic (Paital and Dahotre 2009). Polyethylene wear debris is released into the surrounding tissue, which leads to loosening of the implant in 10% of the cases (Borruto 2010). This inflammatory response is known as osteolysis (Raimondi and Pietrabissa 2000; Harper *et al.* 2009; Kurtz *et al.* 2009; Grupp *et al.* 2010). Scholes and Unsworth (2010) noted that aseptic loosening caused by osteolysis is the most common reason **for** hip revision surgery. It is therefore conceivable that implantation loosening occurs within the spinal column due to osteolysis.

Kurtz *et al.* (2009) have studied wear mechanisms by means of retrieval analysis. The study notes that the dominant wear mechanism for metal-on-polyethylene is a combination of abrasion and adhesion.

Owing to outstanding thermomechanical properties, PEEK has been under scrutiny as a wear couple surface since the 1980's where it was used in industrial and military applications. Peer-reviewed results for PEEK as an arthroplasty application are limited (Kurtz and Devine 2007).

In an attempt to reduce osteolysis of traditional UHMWPE, the 1990s saw CFR-PEEK being used as an alternative material in hip arthroplasties. The wear rate was found to be an order of magnitude

less than that of the control. To validate the biological reaction to the CFR debris a 30-patient clinical study was started in April 2001, with promising results which was expanded in 2003 to 121 patients. In 2007 the trial was on-going; preliminary data supports the short-term efficacy of CFR PEEK as a bearing material. At the time of writing the results had not yet been published (Kurtz and Devine 2007).

Grupp *et al.* (2010) **explore** alternative polymer-on-polymer wear couples for cervical arthroplasty. It is noted that fibre-reinforced PEEK displays superior wear characteristics when compared to unfilled PEEK. Biocompatibility of reinforcement fibres (or materials) has also to be considered; early results by Utzschneider *et al.* (2010) determine that carbon fibre-reinforced PEEK (CFR-PEEK) is comparable to UHMWPE with respect to biological response.

5.1.5 Other Considerations

Should mutual solubility between the two wear surfaces be similar, a higher wear rate is expected. Hence the wear rate is generally higher for wear couples of similar materials. Implants are naturally surrounded by saline, which may lead to a galvanic reaction between dissimilar materials. A galvanic reaction leads to corrosion, which may further increase the wear rate, and cause an inflammatory response (Paital and Dahotre 2009).

Mechanical properties may be affected by the rate of water absorption, sterilisation techniques (such as autoclave, gamma irradiation). Polymer materials are subject to water absorption, which may have an effect on the mechanical properties. Cyclic loads may lead to fatigue failure; a comprehensive fatigue test validation is required to mitigate the risk as far as possible.

5.2 Conclusion

Material selection should take cognisance of mechanical, biocompatibility, wear resistance, and osseointegration properties. The functional performance of a particular area or surface of the component can be improved by selecting a combination of materials.

Osseointegration is the accepted means for long-term device fixation. Titanium is the most widely used surface for osseointegration, and non-active surface enhancing techniques should be applied to further improve the fixation. Primary and secondary fixations are used in combination to achieve successful osseointegration.

Due to the clinically proven biocompatibility of PEEK material, research is being conducted into using this polymer as a wear surface for spinal disc arthroplasty devices.

Chapter 6: Competitor Products

Cervical disc arthroplasties can be grouped by their biomechanics, fixed axis of rotation or mobile axis of rotation. Table 8 summarises spine arthroplasty devices which are presently in clinical trials. The following design considerations **are included for** comparative purposes; material, constraint, primary fixation, and degrees of freedom (DOF).

Table 8: Cervical prosthetic disc comparison (Anbarani *et al.* 2010)

Manufacturer	Device Name	Regulatory Status	Wear Couple	Articulation Design	Fixation	DOF
Amedica	ALTIA [®] TDR-C	IDE began: 2009	Silicon nitride ceramic	Ball & Socket	Keel, unknown	3
Cervitech	PCM	US clinical trial enrolment compl.	CoCrMo-UHMWPE	Mobile Core	Screw & Rib, TiCa Phosphate	3
DepuySpine	Discover [™]	IDE began: 2006	Ti-UHMWPE	Ball & Socket	Ti Beads & Pin, Ti Plasma	3
Globus	Secure [®] -C	FDA Cleared	Metal-PE	Ball & Socket	Keel, Ti Plasma	5
LDR	Mobidisc-C [®]	PMA submission: 2010	CoCrMo-UHMWPE	Mobile Core	Keel, Ti Plasma	5
Medtronic	Bryan [®]	FDA Approved 2009.05.12	Ti-UHMWPE	Mobile Core	Screw, Ti beads	5
Medtronic	Prestige [®]	FDA Approved 2007.07.16	Stainless Steel	Ball & Socket	Screw, Ti Plasma	5
Medtronic	Prestige [®] -LP	unknown	Titanium	Ellipsoid & Saucer	Keel & screw, Ti beads	5
Nexgen Spine	Physio-C	unknown	None: Flexible Polymer	unknown	unknown	6
NuVasive	CerPass [™]	IDE began: 2008	Ti-Ceramic	unknown	Plasma HA	3
Pioneer Surgical Technology	NuNec [™]	unknown	PEEK-PEEK	Ball & Socket	Cam-screw, HA coating	3
Rainer	Cadisc [™] -C	Under development	None: Flexible Polymer	Flexible Polymer	Unknown	6
Scientix	Discocerv [®] / Cervidisc	IDE began: 2008	Ti-Ceramic	Ball & Socket	Rib, Ti Plasma	3
SeaSpine	Catalina [™]	IDE began: 2008	PEEK-PEEK	Ball & Socket	unknown	5
Spinal Motion	Kineflex C	IDE enrolment complete	CoCrMo-CoCrMo	Mobile Core	Keel, Ti Plasma	5
Spinal Kinetics	M6	Feasibility study underway	Flexible Polymer	Polymer & Filament	Keel, Ti Plasma	6
Stryker	Cervicore [™]	PMA submission 2009	CoCrMo-CoCrMo	Saddle	Keel & screw, Ti Plasma	3
Synthes	Prodisc [™] -C	FDA Approved 2007.12.17	CoCrMo-UHMWPE	Ball & Socket	Keel, Ti Plasma	3

6.1 Material Selection

Material selection for present cervical arthroplasty devices is limited to stainless steel, titanium, cobalt-chromium-molybdenum, PEEK, UHMWPE, ceramic, or a flexible proprietary polymer.

Devices which have been constructed chiefly from either stainless steel or CCM are not imaging compatible. Figure 38 illustrates the size of MRI artefacts for the Bryan[®] (titanium), Prestige[®] (stainless steel), and Prodisc-C[™] (CCM) disc replacements. It is noted that in Figure 38A the Bryan[®] cervical disc has been implanted at the C5-6 level. Although an artefact is present, the spinal cord and adjacent discs can be visualised for all levels. This degree of visualisation is not possible with the Prestige[®] and Prodisc-C[™] due to their material selection (Sekhon and Ball 2005).

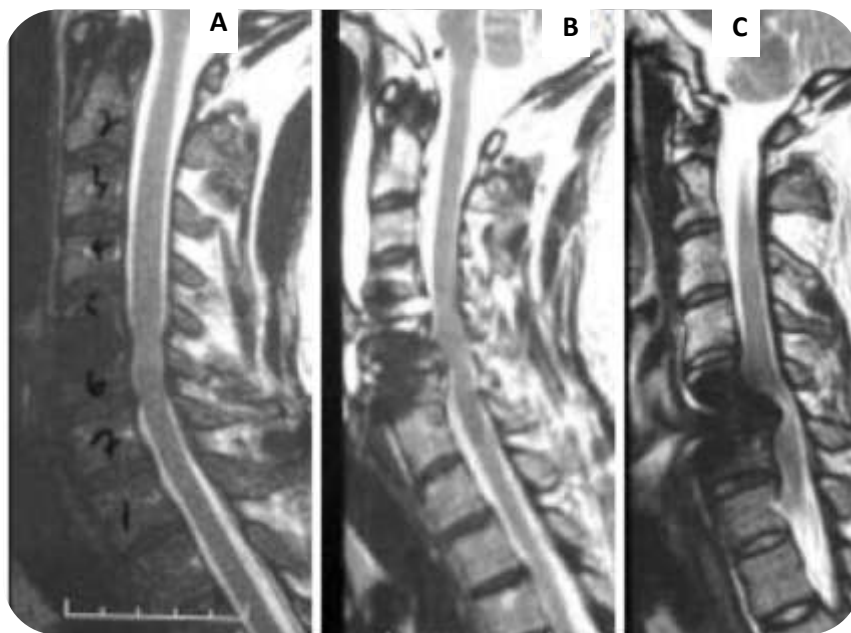


Figure 38: Comparison of artifact size for (A) Bryan[®]; (B) Prestige[®]; (C) Prodisc[™]-C (Sekhon and Ball 2005)

6.2 Device Constraint

The kinematics of the device should mimic the natural motion as closely as possible. The primary kinematics under consideration is range of motion; finite axis of rotation; bending moment vs. displacement; degrees of freedom.

Since the location of the FAR changes during motion of the spine, the FAR of the device can only be matched if the device allows for uncoupled translation and rotation (these devices include the Bryan[®], Kinelfex, M6, Mobidisc-C[®], Prestige[®], Prestige[®]-LP). Moumene and Geisler (2007) investigated that facet loading is reduced in the lumbar spine with a mobile FAR, and is expected to play a major role in long term clinical outcomes.

Devices which provide increasing resistance as movement progresses are considered to have biomechanics which more closely mimic natural biomechanics. This biomechanical quality of motion is obtained by replacing a wear couple with a flexible polymer.

Both fixed and mobile FAR devices show an improvement of neck pain scores over a two-year period (Siddiqui *et al.* 2006, Coric *et al.* 2010). Due to the relatively short follow-up period, a clear distinction between the advantages and disadvantages of constraint type has not yet been drawn. Long-term studies which compare device constraint were not found.

6.3 Primary and Secondary Fixation

In order for osseointegration to take place the device requires primary fixation, which is achieved by a constraining mechanism such as a screw or keel which allows sufficient time for cellular proliferation (Sekhon and Ball 2005).

Primary fixation should be obtained by removing as little as possible bone mass from the vertebrae; bone compaction of weight-bearing implants has been found to be advantageous by Kold *et al.* (2006).

Secondary fixation of devices listed in Table 8 is achieved by osseointegration onto a titanium or ceramic surface. Osteoconductive coating such as HA or CaP has been used by Cervitech, NuVasive, Pioneer Surgical Technology. Uncoated osseointegration is used by Medtronic, Spinal Motion, Spinal Kinetics, Stryker and have a longer clinical history.

Risks associated with anaesthesia range from trivial to permanent injury, a general requirement for a reduced operative time therefore exists (Lakshmanan and Fischer 2007). Devices which use screws

for fixation are by definition more invasive than those which use keels or pins for primary fixation and should therefore expect a shorter operative time.

6.4 Conclusion

Table 8 illustrates that there are presently 18 known cervical disc arthroplasties undergoing clinical trials. Within the next two years, there may be nine devices which have completed the two-year minimum follow up required for FDA clinical trials.

Keel fixation is used on one approved and eight investigational devices, making it the most popular choice for primary fixation. The use of keels facilitates accurate placement as well as minimal bone mass loss, but may be considered to be traumatic from a placement perspective.

Table 8 references devices which use flexible polymers to provide six degrees of freedom; this technology is gaining popularity and should be considered for future development.

The technology pipeline includes:

- PEEK-PEEK and Ceramic-Ceramic, Ceramic-Polymer wear couples or better still, the elimination of wear debris
- by the use of flexible elements (such as polymers) providing six degrees of freedom, while eliminating wear debris,

Material choices are limited to a combination of titanium, stainless steel, CCM, polyethylene, PEEK, flexible polymer, or ceramic.

There are two design philosophies regarding the kinematics; fixed FAR and mobile FAR, with no conclusive result about which kinematic arrangement has superior performance, due to the short duration of the technology.

Chapter 7: Product Development Process

The scope of this project does not include all the essential requirements for an ISO 13485 approved medical device, but only those relevant to the title of this dissertation. The scope of the user needs pertains only to the topic of this dissertation.

7.1 Design Control

Design control of medical device development is intended to ensure that the result of the development process is a device with predictable satisfactory performance. Verification and validation of the essential design requirements **mitigate** the risk of clinical failure as far as possible. The design control for medical devices is outlined in Figure 39.

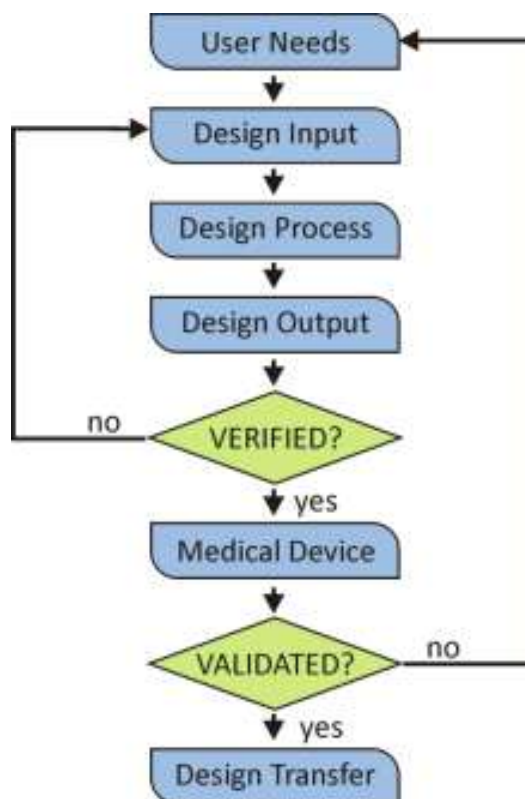


Figure 39: Design control process (adapted from Harnack 1999)

This process is applicable to product development with the aim to obtain FDA approval (Harnack 1999). The following progression is followed:

- User needs and intended uses serve as the design initiation.
- User needs are interpreted into design inputs.
- Design inputs are translated into design outputs.
- Verification will be performed to ensure that the design outputs satisfy the design inputs. This task may be performed by means of a literature or design review in the European regulatory context.
- If the design output fails verification, new design outputs must be generated.
- Validation of the design outputs will be obtained experimentally, which ensures that the design outputs satisfy the user needs.

7.2 User Needs and Design Initiation

Obtaining user needs (or requirements) with a receptive market forms the basis of project initiation; these requirements are classically high-level requests to the design team from marketing. Figure 40 illustrates the starting point to the design process.

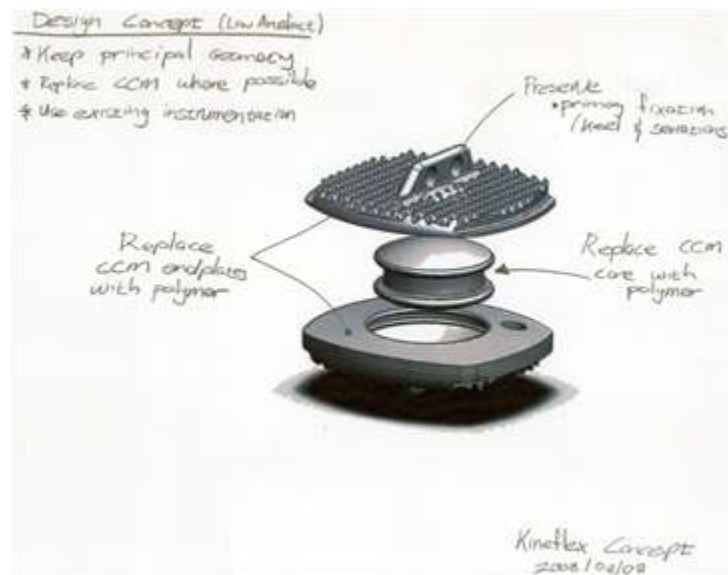


Figure 40: Design initiation, conceptual input for envisioned design.

Figure 41 illustrates the size of the artefact for the CCM Kineflex device. Spin-echo and gradient-echo pulse sequences produced an artefact with sizes of 57.25mm (sagittal plane) and 40.98mm (coronal plane) and 73.10mm (sagittal plane) and 63.98mm (coronal plane) respectively. The shapes of the artefacts are roughly ellipsoid, with the affected area calculated as 1842mm² and 3671mm².

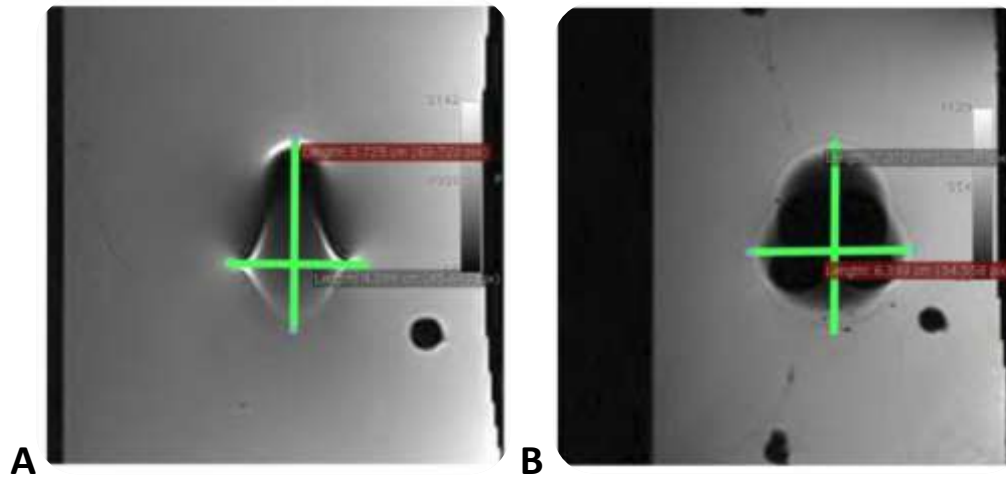


Figure 41: MR test results as per ASTM 2119, 1.5T MR axial images of size 1 Kineflex cervical disc; (A) Spin-echo; (B) Gradient-echo pulse sequences

The user needs are listed in Table 9.

7.3 Design Input

Design inputs are listed in Table 9.

Table 9: Design input, output, verification and validation matrix

Customer Requirements	Design Input	Verification / Validation	
User Need / Intended Use	Design Requirement	Design Verification	Design Validation
Marketing Requirements			
1. Post-operative imaging capability	a. Adjacent intervertebral discs and spinal cord to be clear on post-operative image	Chapter 7.5	Chapter 7.7
2. Ease of use	d. Use current instrumentation as far as possible	Surgical procedure comparison with competitor products	Device interfaces with existing instrumentation
Safety Requirements			
3. Device is biocompatible	e. Meet biocompatibility standards for tissue/bone implant device (permanent)	Chapter 7.4.1	2-year clinical evaluation
1. Post-operative imaging capability	b. Device is MR safe: heating, torque, force	Chapter 4.3.2	-
	c. Implant must be visible under X-ray and CT	Chapter 7.5	Chapter 7.7
Functional Requirements			
4. Device to fit C2-C6 disc space	f. Multiple heights, footprints	Chapter 7.4.6	Clinical experience documentation
5. Range of motion equal to CCM KCD	g. Match CCM geometry where possible	Chapter 7.6.1	-
Manufacture Requirements			
6. Device to be designed for manufacturability	h. Dimensions and tolerances assessed for ease of manufacturing, functional requirements, and cost savings	Review of manufacturing process	Product has repeatable quality
		Chapter 7.4.6	

7.4 Design Output

The starting point to this design was material selection. The design of the disc assembly was divided into the following sections:

- Material selection
- Primary fixation
- Secondary fixation
- Wear couple
- Connection between “Integration Screen” and “Bearing Body”

7.4.1 Material Selection

Material selection is the primary means of reducing MR artefact (see section 4.3.3.1 Material Influence), and forms the basis of the conceptual design. The selection of the material must satisfy related user requirements; biocompatibility, long term fixation, load-bearing, and manufacturability.

Table 7 lists orthopaedic biomaterials, which have been used in cervical disc arthroplasties and which are presently undergoing clinical trials. Figure 33 was applied as an input for material selection with respect to relative artefact size. Neat biopolymers do not generate artefacts, and will therefore be used as the material to replace original CCM where feasible.

The device will be subject to *in vivo* cyclic loadings; fatigue is therefore a reliability consideration for all components of the device. Although not part of the scope of this dissertation, reliability is a requirement which cannot be over-emphasised for a device of this nature. Reliability of the product can largely be assured by considering practical manufacturing processes. Manufacturing process validation ensures that the mechanical and dimensional output of the device remains consistent, which therefore provides predictable performance.

7.4.2 Primary Fixation

A review of primary fixation methods of competitor products reveals similar techniques for the majority of cervical disc arthroplasty devices. Lateral ribs, screws, barbs, keel, and serrated surface are used in the majority of devices, sometimes in combination with one another. Figure 42 illustrates some of the variations on the listed methods.

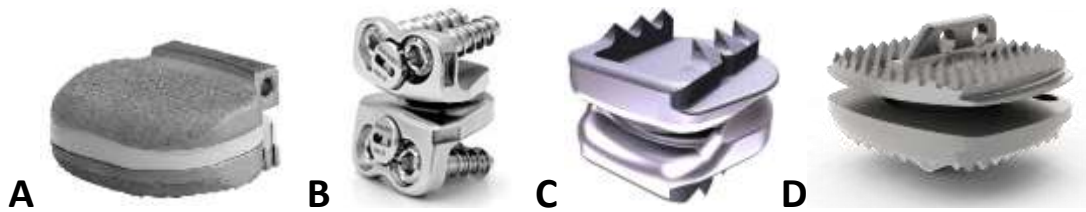


Figure 42: Primary fixation techniques:

- (A) PCM, lateral ribs (Traynelis 2006);
- (B) PRESTIGE®, screws (PRESTIGE® Cervical Disc System - P060018 2007);
- (C) Stryker, barb-keel combination (Anbarani *et al.* 2010);
- (D) Kineflex|C, keel-rough surface combination

The author is of the opinion that adequate primary fixation should not come at the expense of an invasive surgical procedure. It must be considered that it may be necessary to remove the device at a later stage. More recently developed devices (PCM, Cadisc™-C, Discocerv®, Prodisc™-C, Mobidisc®-C) have less invasive primary fixation than older designs such as Prestige® and Bryan®.

On the basis of the clinical results from Guyer *et al.* (2008) and Coric *et al.* (2010), primary fixation of the device under development will be by similar means as the current Kineflex|C. The combination of keels and roughened serrated surface will be utilised. This allows for slots being cut into the vertebrae with a surgical technique which is familiar to the majority of surgeons.

7.4.3 Secondary Fixation

Successful clinical outcome can only be achieved with adequate secondary fixation. Disc arthroplasty devices typically (as listed in Table 8) feature an intermediate material to facilitate the bone integration indirectly onto the bioinert material. Titanium (or titanium plasma) and ceramic coatings (Calcium Phosphate (CaP); hydroxyapatite (HA)) have been applied as means of secondary fixation by osseointegration. The long term success of HA and CaP coatings is questionable (refer to section 5.1.3 Osseointegration). For this reason ceramic coatings will not be considered as an osseointegration surface/medium.

Kurtz and Devine (2007) review literature on the addition of HA particles mixed into PEEK resin in an attempt to osseointegrate PEEK. They observed that PEEK-HA composites show great promise as bioactive implants as cellular proliferation occurs into the pores of the composite. At the current stage of material development the poor adhesion between the HA and PEEK particles reduces tensile strength by 45%. The mechanical properties need to be improved to be of use in spinal applications.

Titanium is inherently bioinert. The risk of osseointegration surface failure due to delamination at the bone-implant or integration surface-implant interface is therefore mitigated as far as possible with the use of titanium. Osseointegration is satisfactory, provided there is adequate primary fixation, low stress shielding, and sufficient surface roughness.

In light of the literature reviewed, secondary fixation of the design concept under consideration will be achieved by means of a titanium-bone osseointegration surface similar in nature to the Kineflex|C.

7.4.4 Titanium Selection

In this instance, material selection is based on: mechanical properties, quality of osseointegration, imaging characteristics and machinability. The selection will be based on the best compromise between the mentioned material properties.

Mechanical properties may be improved with the addition of alloying elements into titanium, unalloyed and alloyed (Ti-6Al-4V, known as grade 5) long-term implant grades are described in ASTM F67 and ASTM F136 respectively. Table 10 lists the mechanical properties for pure and alloyed titanium in various conditions. Grade 5 titanium has a fatigue endurance limit of more than double that of pure titanium.

Table 10: Material properties of implant grade titanium (Paital and Dahotre 2009)

ASTM Designation	Condition	Young's modulus (GPa)	Yield strength (MPa)	Tensile strength (MPa)	Fatigue endurance limit (MPa)
F67 (Grade 4)	30% cold-worked	110	485	760	300
F136 (Grade 5)	Forged annealed	116	896	965	620
	Forged, heat treated	116	1034	1103	620-689

Fatigue endurance is also dependant on external factors, such as temperature, corrosion environment and surface finish of the component (Fleck and Eifler 2010). The introduction of residual compressive surface stresses by means of shot blasting improved fatigue endurance (Gil *et al.* 2007; Pazos *et al.* 2010). This has an additional benefit of improving integration due to a rougher surface.

The strength of osseointegration has been investigated by Johansson *et al.* (1998) by means of torque tests performed on screw shaped dental implants in rabbit bone. Over the short term there was no significant difference between commercially pure (CP) and alloyed titanium (grade 5). Over a twelve month period of implantation, the CP grade displayed a 92% greater removal torque over the grade 5 sample. With this in mind device reliability is the driving consideration when selecting a particular grade of titanium.

Taksali *et al.* (2004) notes that alloyed titanium has better material properties than pure titanium and **has** ‘excellent’ imaging qualities. This concurs with the literature reviewed in section 4.3.3.1 Material Influence.

Materials which have been heat treated tend to distort during machining. Milling in particular removes material in an un-balanced sequence, which tends to distort the component if internal stresses exist within the material. Milling of thin components is therefore susceptible to distortion. In order to reduce distortion, the internal stresses should be eliminated which is achieved by annealing. Annealing relieves internal stresses by heating to a temperature above the recrystallization temperature and slowly cooling to room temperature. Forged annealed condition ASTM F136 will therefore be selected due to fatigue endurance and machinability considerations.

7.4.5 Wear couple

In general, positive tribological performance is related to a combination of low surface energy, high stiffness, toughness and hardness, and smooth surface finish, and low friction coefficient (Zhang and Schlarb 2009). Polymers with a higher degree of crystallinity tend to have a lower wear rate (Stuart and Briscoe 1996). Table 11 lists typical material properties of biomaterials. It is noted that PMMA does not lend itself to favourable tribological performance, which corresponds to the factors noted by Zhang and Schlarb (2009).

Table 11: Typical physical properties of PEEK (adapted from Kurtz and Devine 2007)

Property	Unfilled PEEK	30% (w/w) chopped CFR	UHMWPE	PMMA
Polymer Type	Semi-crystalline	Semi-crystalline	Semi-crystalline	Amorphous
Flexural modulus (GPa)	4	20	0.8-1.6	1.5-4.1
Tensile strength (MPa)	93	170	39-48	24-49
Tensile elongation (%)	30-40	1-2	350-525	1-2
Degree of crystallinity (%)	30-35	30-35	39-75	Non-crystalline

Biological reaction to wear debris is influenced by the composition, volume, and morphology. Composition is selected by a designer, however the volume and morphology of the debris is unknown until physical wear tests are performed.

It would seem that the rate of osteolysis has been reduced with the usage of CFR-PEEK compared with UHMWPE. PEEK with various additives is becoming increasingly popular (Zhang 2004; Scholes and Unsworth 2010). Filled PEEK has a higher wear resistance than unfilled PEEK (refer to 5.1.4 Wear Resistance); however biological reaction to wear debris requires further study.

For the reasons mentioned, Neat PEEK has been selected as the wear couple for conceptual development.

7.4.6 Concept Generation

Concept generation is a creative process whereby different ideas are developed and evaluated against a scoring matrix. Design inputs are addressed as far as possible with design output. The device matches the principal dimensions of the Kineflex|C.

Concepts were evaluated on the following weighting criteria, based on achieving a device without performance compromise; manufacturing complexity (3), PEEK quality (8), secondary fixation area (10), fixation connection (10), and titanium volume (10). Table 25 (Appendix B) summarises the salient points of the concept generation process; concepts are arranged in chronological sequence.

Constraining the dimensions to that of the existing device ensures that the device will fit into the disc space due to the clinical experience obtained thus far, and therefore maintain similar kinematics to the existing device.

The four concepts from 2008.04.08 to 2009.06.11 were considered for the verification phase. Concept 2009.03.04 as expected scored higher than the other concepts, however would not be selected due to the poor performance of bioactive mediums as an integration surface.

Integration Surface

Concept 2009.06.11 was selected as it seemed to show the most probable configuration for titanium integration. This concept retained the keel and serrated surface as primary fixation. The original CCM KCD has an integration area of 318.91mm²; the selected concept has an area of 265.32mm² per endplate for the smallest size, a reduction of 17%.

Figure 43 illustrates that the occurrence of stress raising sharp corners is eliminated with the use of a ball nose end mill, thereby creating concave radii at the base of the serrated surface.

Titanium-PEEK connection

Connection between the titanium and PEEK should maintain structural integrity under compressive and shear loading patterns. Numerical assessment of the strength of the metal-polymer interface does not form part of the scope of this project.

Methods of attaching the metal to the polymer are considered: Screw and or pin, interference or snap fit, ultrasonic welding, and injection moulding. The interference fit conceptual design presented here is the final result of an iterative design process; early concepts can be seen in Appendix B.

Interference Connection

A circumferential step (or skirt) with an acute angle was evaluated as a means of connecting the integration surface to the polymer. Figure 43 illustrates the conceptual design; each endplate consists of three components, two symmetrical integration screens and the wear body.

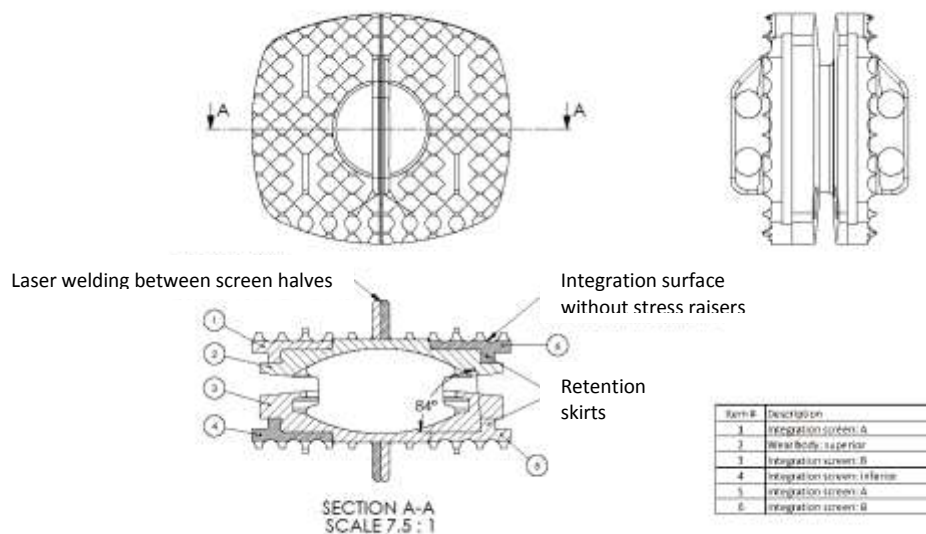


Figure 43: Circumferential interference connection, revision A-005

Endplate assembly is performed by sliding the integration screens toward the centre. Micro-movement is prevented by preloading the titanium-PEEK connection. Preload is applied by slightly under-sizing the titanium screens, which fit tightly over the PEEK insert. The two screens are thereafter laser-welded to each other, which maintain the three components as a unit. Figure 44 illustrates this assembly.

The disadvantage of preloading the assembly is that the spherical wear surface may become distorted. The extent of the distortion is expected to influence wear rate negatively, and will be evaluated by means of surface measurement as well as wear testing.



Figure 44: Illustration of endplate assembly

Material used for the production version (Revision A-005) would be from annealed ASTM F136 titanium and extruded ASTM F2026 PEEK bar stocks. Manufacture would be performed by turning, milling and wire electric discharge machining (EDM) processes.

7.5 Design Verification

Design verification is the process of physical testing or literature review, to warrant that the design output satisfies the design inputs. The process of verification should demonstrate that the specifications are satisfactory for the design. Verification can be satisfied by means of a literature study, or proving equivalence with competitor products, physical testing or alternative calculations.

One of the purposes of design verification is to limit the amount of capital and time expenditure associated with physical manufacture and testing of devices. It is therefore acceptable that testing be performed on a prototype unit, which is representative of the final production device.

7.5.1 Testing Protocol

Aim: The performance of the proposed design concept is at this stage largely unknown. The aim of the verification is to:

- Obtain representative MR, CT, and fluoroscopy images of the device *in vitro* for qualitative assessment of the design proposal in a human cervical cadaver spine
- Identify neurological structures by means of MR images
- Determine the surface area of the MR artefact

Materials and Methods:

The test was conducted with the prototype device, in a human cadaver spine, with typical imaging equipment. Three types of imaging equipment were utilised, namely magnetic resonance, computed tomography and fluoroscopy.

Imaging Equipment

Table 12 lists imaging equipment used, the type of equipment is typical as would be found in modern hospitals.

Table 12: Testing devices and apparatus for first verification

Imaging Method	Imaging Equipment
Magnetic Resonance	General Electric, HDe 1.5T
Computed Tomography	General Electric, LightSpeed VCT
Fluoroscopy	Philips, BV Pulsera

Analysis of MR and CT images is performed with “eFilm Lite™ V2.0.1 build 5” software. This analysis includes measurement and section plane visualising.

Device Description

The device under investigation is rendered in Figure 45. Producing the required tooling to manufacture the skirt geometry proved to be impractical for the quantity required. Rapid-prototype manufacture technique was used to produce the first off component.



Figure 45: Rendering of prototype device (revision A-005)

Table 13 lists the specifications of relevance to the imaging verification testing.

Table 13: Summary of tested components

Verification test component description	
Date tested	2008-09-17
Device revision	A-005
Components	KCD-R1-5.0
	KCD-R-CORE
	KCD-R1-5.0-WR
Manufacture method	Rapid-prototype
	Polymer: ABS
	Metal: Ti Grade 5
Titanium volume (mm ³)	Superior: 138.37
	Inferior: 138.37
	Total: 274.74
Implanted level	C5-6
Device position	As per surgical procedure

Variance between production methods of the prototyped and final production unit is listed in Table 14.

Table 14: Discrepancies in method of manufacture and materials between prototype and production units

	Prototype	Production
Process	Laser sintered	Milling, Turning, Welded
Polymer	ABS	Neat PEEK (ASTM F2026)
Metal	Ti Grade 5 (Sintered)	Ti Grade 5 (ASTM F136)

Device Positioning

The keels of the prototype were wider than the original KCD, which combined with the flexibility of the spine made cutting of the keel slots difficult. **For** this reason, slots were cut by means of hand tools into the C5-6 vertebral bodies. The accuracy of the final positioning was therefore not as high as during surgery. Figure 46 illustrates the device placed in situ, at the C5-6 level.

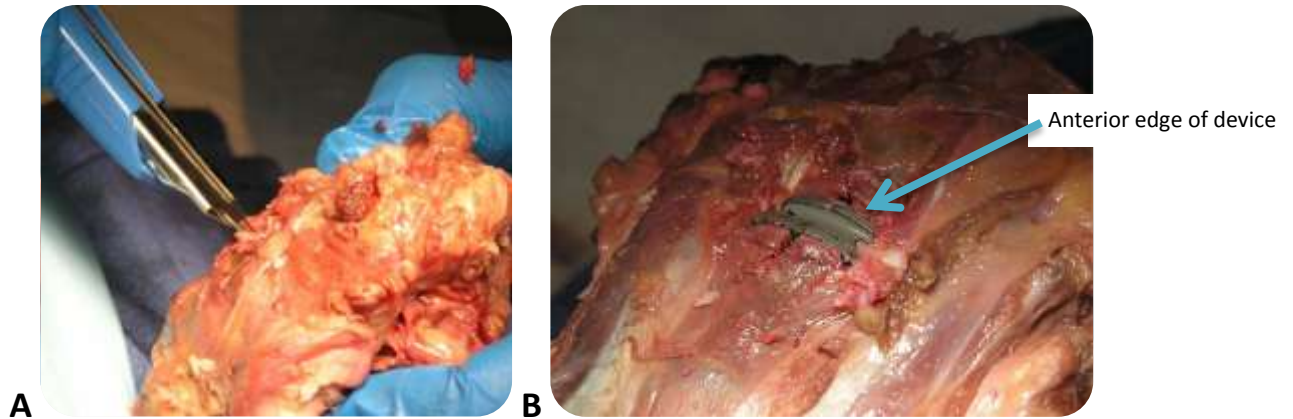


Figure 46: Placement of Prototype A-005:

(A) Cutting of keel slots into human cadaver cervical spine;
(B) Device positioned *in-vitro* C5-6 level

Device Imaging

The device under investigation is then imaged **under the following conditions**.

Table 15: Verification settings

MR settings		
Parameter	T1-weighting	T2-weighting
Field strength	1.5 tesla	1.5 tesla
Bandwidth	256×256	256×192
TR (ms)	4000	500
TE (ms)	97	25

To determine the size of the MR artefact, images were studied. Since the edge of the artefact is not always clearly defined, a perimeter is estimated. The area is obtained from importing the image into computer aided design software, and using the standard measurement tools of the software.

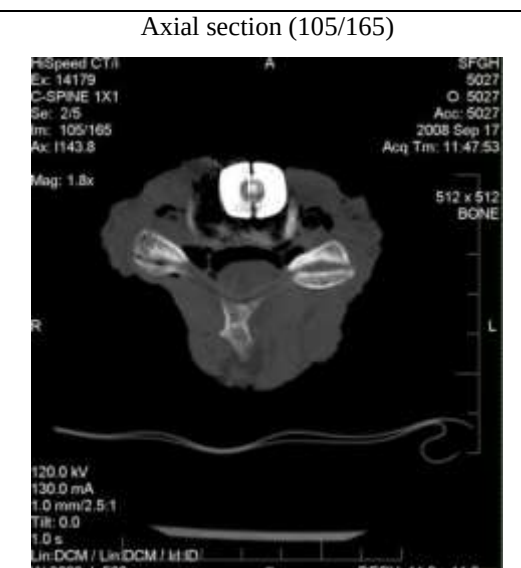
7.5.2 Results

The results presented in this section are divided into qualitative and quantitative types. Qualitative assessment is necessary from a surgical and marketing perspective. Quantitative results are required from a development point of view.

Qualitative Results

- The location of MR sagittal and axial slices is in Appendix C.
- The distance between axial slices was determined to be 4mm with the aid of MR imaging software (eFilm Lite V2.0.1, build 5).
- Qualitative results are by means of MR, CT, and fluoroscopy images, presented in Table 16. The slides which have been selected are representative of the largest artefact found within the series.
 - T2-weighted MR images display a dark artefact obscuring the location of the device.
 - CT images display each of the titanium integration screens clearly
 - Fluoroscopy displays the location of the keel and device perimeter, enabling sufficiently accurate placement during surgery.
- T1-weighted axial images were not accessible
- The full sets of images, unmodified are available in Appendix C.

Axial and sagittal plane section images are useful to view the condition of the spinal cord, dorsal and ventral neurological structures. To this end their discernibility has been indicated in Table 17 and Table 18. Bearing in mind that device placement was too far anterior, the neurological structures being unaffected.

Magnetic Resonance (MR)	Computed Tomography (CT)	Fluoroscopy
Sagittal section (7/13)  1.5T GEMRGEMR Ex: 18729 *FSE SAG T2 Se: 2/4 Im: 7/13 Sag: L21.8 (COI) Mag: 3.6x ET: 14 TR: 3400.0 TE: 102.0 CTLTOP 3.0thk/1.0sp Id:DCM / Lin:DCM / Id:ID W:500 L:250 DFOV: 20.0 x 20.0cm	Coronal section (19/100)  HiSpeed CT/i Ex: 14179 Average Se: 401/5 Im: 19/100 Cor: P8.4 (COI) Mag: 1.8x 120.0 kV 130.0 mA Tilt: 0.0 1.0 s Lin:DCM / Lin:DCM / Id:ID W:2050 L:817 DFOV: 16.4 x 15.7cm	Lateral view  PHILIPS BN Pattern uCM "750-Beam" Patient: Study: Series: Image: Date of Ref: 09-11-2008 Ref: 00027 09-11-2008 M CARTAS/00000000 Orthopaedics 09-11-2008 11 (124)
Axial section (20/27)  1.5T GEMRGEMR Ex: 18729 FSE AX T2 Se: 4/4 Im: 20/27 Ax: IS.1 (COI) Mag: 5.4x ET: 8 TR: 4000.0 TE: 97.0 CTLTOP 3.0thk/1.0sp Id:DCM / Lin:DCM / Id:ID W:828 L:414 DFOV: 10.8 x 10.6cm	Axial section (105/165)  HiSpeed CT/i Ex: 14179 C-SPINE 1X1 Se: 2/5 Im: 105/165 Ax: I143.8 Mag: 1.8x 120.0 kV 130.0 mA 1.0 mm/2.5:1 Tilt: 0.0 1.0 s Lin:DCM / Lin:DCM / Id:ID W:2000 L:500 DFOV: 11.9 x 11.9cm	Coronal view  PHILIPS BN Pattern uCM "750-Beam" Patient: Study: Series: Image: Date of Ref: 09-11-2008 Ref: 00027 09-11-2008 M CARTAS/00000000 Orthopaedics 09-11-2008 21 (125)

Quantitative Results

The extent of the artefact is determined from the colour contrast of the MR image. Artefact perimeters were generated for selected images in the series. Estimates of the plan and section areas of the disc were generated in this fashion. Conservative estimates were taken where exact artefact extent could not be precisely judged.

Axial Sections

The locations of the axial sections have been illustrated in Figure 65. Images were imported as a texture into SolidWorks computer aided design software, and scaled to size. This allowed the device to be superimposed onto the artefact with matching scale. Figure 47 illustrates the method used to determine the surface area of the artefact. To gain insight into the shape of the artefact, the position of the device has been super-imposed onto the artefact.

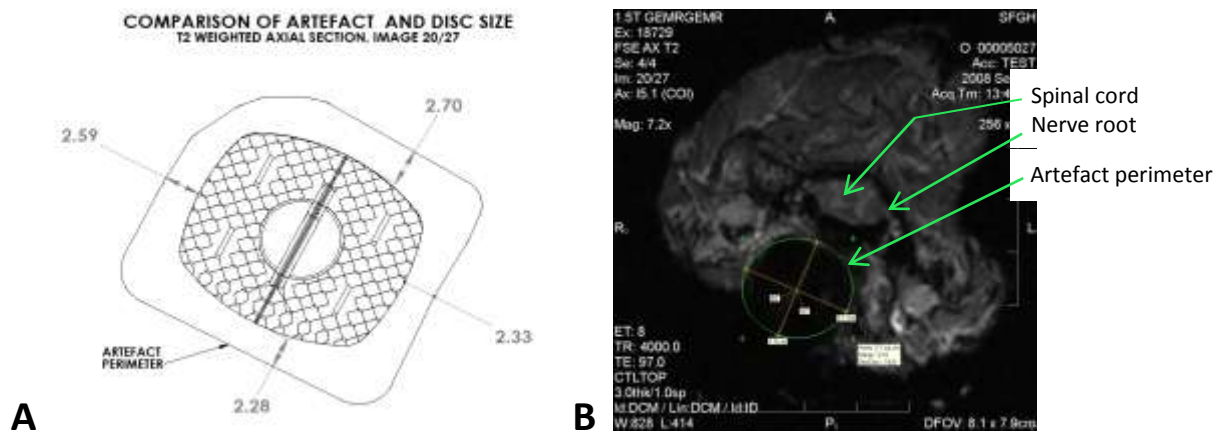


Figure 47: (A) Comparison between estimated disc position and artefact of T2-weighted axial section image 20/27 (B) MR Image for convenient reference (scale between (A) and (B) are not equal)

Table 17 and 16 summarise the results obtained with analysis on T2-weighted axial images 16 to 23. The estimation of device area was performed with the assumption that:

- Images 19 and 20 were sections through the maximum plan area of the device, in a direction normal to the integration surface, with an area of 194.0mm²
- Images 18 and 21 were sections through the keel of the device, the largest plan area of the keel was assumed to be a rectangular shape of 1.2×8.5mm

- Images 16, 17, 22, and 23 no artefacts were visible, and were therefore not sections through the device.

This image set therefore contains the entire area which may have been affected by the device.

Table 17: Analysis of MR artefacts generated in axial plane

T2-Weighted, Axial Plane				
Image #	Device Area (mm ²)	Artefact Area (mm ²)	% Increase	Spinal Canal Intrusion (mm)
16/27	-	N/A	-	0
17/27	-	N/A	-	0
18/27	10.2	30.0	194%	0
19/27	194.3	350.0	80%	0
20/27	194.3	310.0	60%	0
21/27	10.2	39.0	282%	0
22/27	-	N/A	-	0
23/27	-	N/A	-	0

Sagittal Sections

Figure 66 (Appendix C) illustrates the orientation of sagittal sections; the spine was rotated approximately 23.5° from the vertical. Figure 48 illustrates the device super-imposed onto the perimeter of the sagittal artefact.

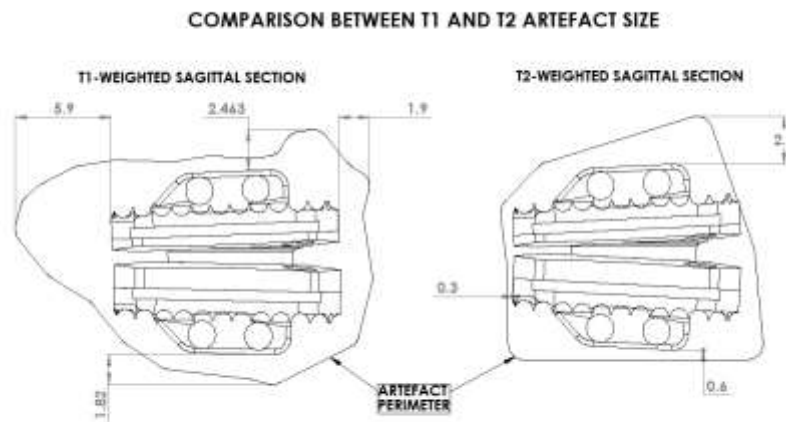


Figure 48: Comparison between MR slide 7/13, with T1 and T2-weighted sagittal section artefacts (refer to for MR images).

Table 18 summarises results of the sagittal plane analysis on T1 and T2-weighted sections. The images are available in Appendix C.

Table 18: Analysis of MR artefacts generated in sagittal plane

Image #	Device Area (mm ²)	Sagittal Plane							
		T1-Weighted				T2-Weighted			
		Artefact Area (mm ²)	% Increase	Spinal Canal Encroachment (mm)	Adjacent Disc Encroachment (mm)	Artefact Area (mm ²)	% Increase	Spinal Canal Encroachment (mm)	Adjacent Disc Encroachment (mm)
6/13	99	136.6	37%	0.0	0.0	159.1	60%	0.0	0.0
7/13	138	241.1	75%	0.0	0.0	194.9	41%	0.0	0.0
8/13	99	211.9	113%	0.0	0.0	293.5	195%	0.0	0.0
9/13	99	130.3	31%	0.0	0.0	200.8	102%	0.0	0.0

7.5.3 Verification Test result Discussion

Due to the void around the anterior side of the spine, precise artefact size estimation was not possible. From a qualitative point of view this does not pose a significant problem, since the area around the spinal cord (posterior edge of disc) is of greatest interest.

The use of a cadaver spine over a known grid or matrix as a means of a test did however make for a practical evaluation of image quality. The absolute location of the device in relation to the artefact is unknown. Due to symmetry of the device (unlike hip stems) it could be assumed that the device was located near the centre of the artefact. A smaller artefact would therefore also provide the radiographer with a higher confidence level of the location of the device.

Magnetic Resonance

T2-weighting provides the highest contrast between soft tissue types and is suggested for viewing pathological detail such as neurological structures. The resolution of the images produced during testing was not as high as that in Figure 28 and 29, which makes identification more challenging.

Table 27 compares T1 and T2-weighted images, it is observed that the contrast ratio is different, as well as the shape of the artefacts.

The position of images 18 and 21 (Appendix C) are sections through the superior and inferior keels. The high percentage increase of artefact area in the axial plane is due to the void created by the slot cut into the vertebrae. Over time, this void would fill with new bone formation. It was therefore difficult to **judge** the extent of artefact accurately. Furthermore, the location of the artefact is not close to any neurological elements. For this reason the author feels that their results may be disregarded.

Axial images 19 and 20 (Appendix C) illustrate the artefact size is less than 75% larger than the device area. The perimeter of the artefact is estimated to be 2.5mm offset larger than the perimeter of the device.

Axial and sagittal section images should be interpreted by taking cognisance that the device was not positioned sufficient posteriorly in the disc space. Axial section images provided for clear identification of the spinal cord, dorsal and ventral nerve roots. Sagittal sections illustrated that both adjacent intervertebral discs were visible. Disc height could be measured on the posterior edge of the vertebral bodies.

Computed Tomography and Fluoroscopy

X-ray images produced by either CT or fluoroscopy provide a clear indication of the presence and location of the device. CT imaging results indicate that the position of the device **was** lateral of the midline.

Table 16 illustrates that all components excluding the core are clearly visible. In the case of these forms of X-ray imaging this is a positive result, since the device is easily located in the case of trauma.

7.5.4 Conclusion on Verification Testing

Due to difficulties with cutting of the keels, the position of the sample device was strictly too far anterior, and not positioned on the midline (3mm and 2mm lateral) of the spine. The spine was also not perpendicular with respect to the sagittal imaging planes, which made for difficulty in estimating

the cross-sectional area of the device. The location and size of the artefact does however suggest that the neurological structures will be visible on axial sections with the device correctly positioned.

When compared with competitor products such as those shown as illustrated in Figure 38, there is a significant improvement over the stainless steel and CCM devices. Compared to the current Kineflex device the, reduction in artefact area is approximately 81%. The Bryan[®] has a low signature but requires screws for primary fixation, and is therefore estimated to have a higher volume of titanium. It is therefore expected that the Bryan[®] would have a larger artefact than the prototype device tested.

Characterisation of a cervical disc arthroplasty of this configuration, material selection and construction is to the author's knowledge undocumented. As a first iteration of the imaging qualities of the disc, knowledge has been gained on volume of titanium with a shape and size, which is useful for cervical disc arthroplasty fixation.

Imaging characteristics of the prototyped device have been obtained; the goal of reducing the MR artefact size to a level which is clinically useful has been achieved. Given that the volume of titanium may be further reduced with further design refinement, this is an encouraging result. Future work must be carried out to further reduce artefact and improve the titanium-peek connection.

7.6 Design Review

Review of the design output as well as verification methodology is necessary for continuous development and improvement while the design control procedure is underway.

7.6.1 Wear Surface Geometry

Design input reference 7 dictates that the translation and articulation range of motion of the KCD is maintained. Figures 49 and 50 verify that the translation and articulation has been maintained with geometry adaptation.

In order to reduce contact stress between the core and retention ring the contact area was increased. The shape of the undercut of the retention ring has been designed for manufacture, as this profile can

be generated with a single tool on a lathe. This simplifies the setup of the machine and eliminates surface discontinuities with tool changes.

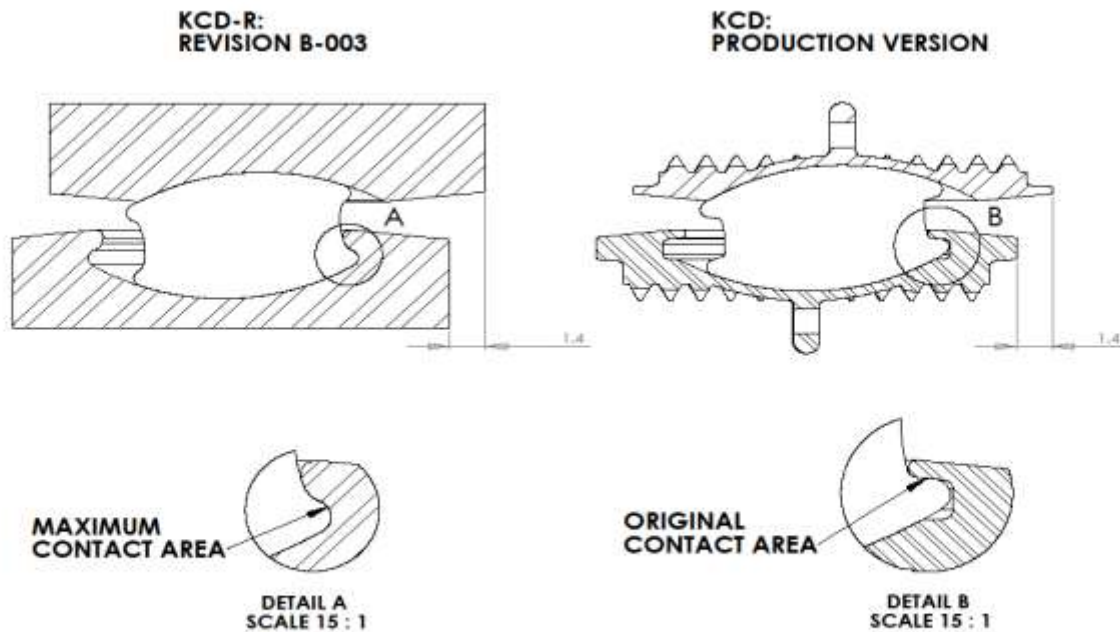


Figure 49: Revision of core and retention ring geometry for reduced contact stress, equal translation

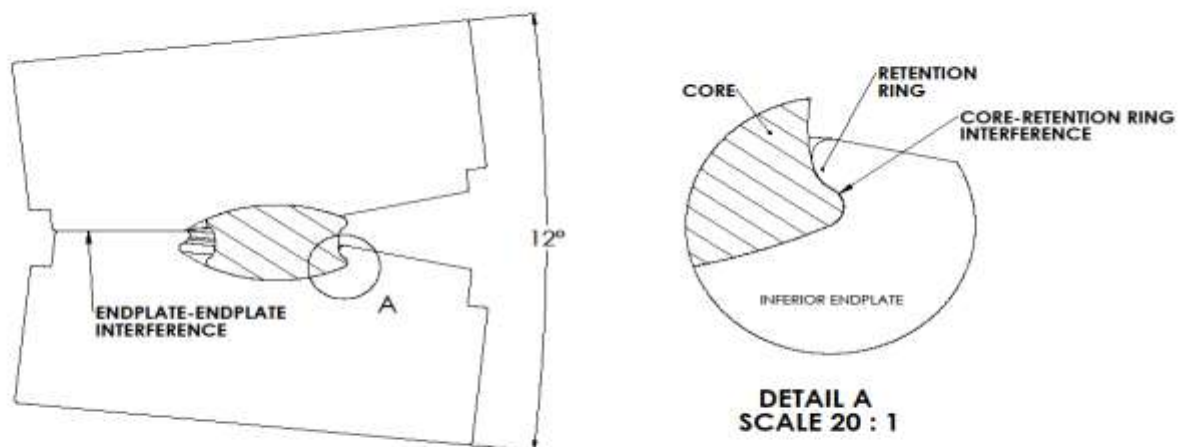


Figure 50: Articulation of endplates, 12° of articulation with endplate-endplate contact occurring at the same time as core-retention ring contact

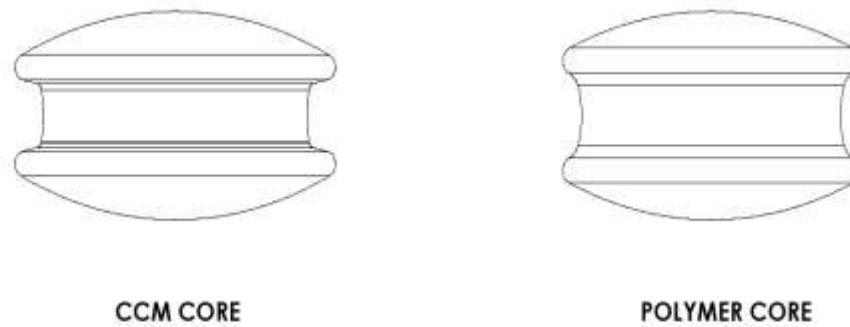


Figure 51: Adaptation of core geometry, maintaining principal dimensions while removing thin retention rim.

7.6.2 Artefact Size

Sagittal section (6-9) and Axial section (18-21) images illustrate a large proportion of the artefact is generated by the keel. After viewing the set of verification MR images, a further reduction of artefact was **thought necessary** to improve post-operative evaluation. Replacement of titanium material of the keel with PEEK would further reduce artefact.

To further reduce the encroachment of the artefact on the spinal canal the posterior edge of the titanium has been moved anteriorly. Figure 52 illustrates how this has been achieved.

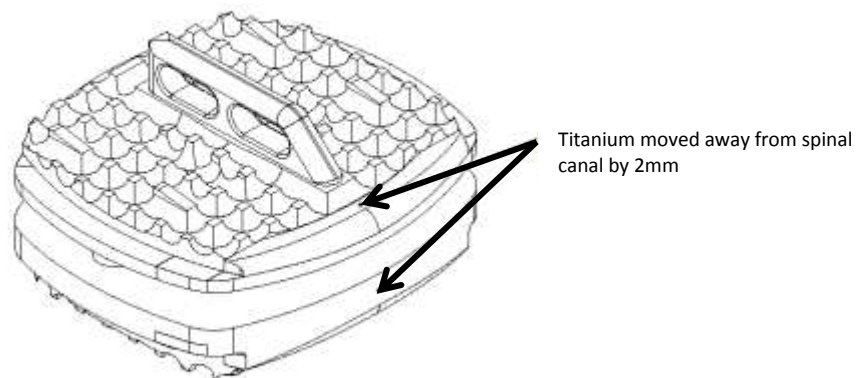


Figure 52: Location of artefact has been moved anteriorly by shortening the screen on posterior edge of disc.

7.6.3 Titanium-PEEK Interface

Assembly of the prototype illustrated that the overlap of the skirt was too little, and may be prone to dislocation. Manufacturing tolerances would become too critical for predictable reliability. Figure 53 illustrates the interference.



Figure 53: Titanium-PEEK interface, acute angle encapsulating wear body

Injection moulding of the PEEK would be able to introduce other connection types. A moulded connection was developed which incorporated a PEEK keel. Figure 54 illustrates the moulded connection concept. Moulding of PEEK allows for an overlap of the integration screen.

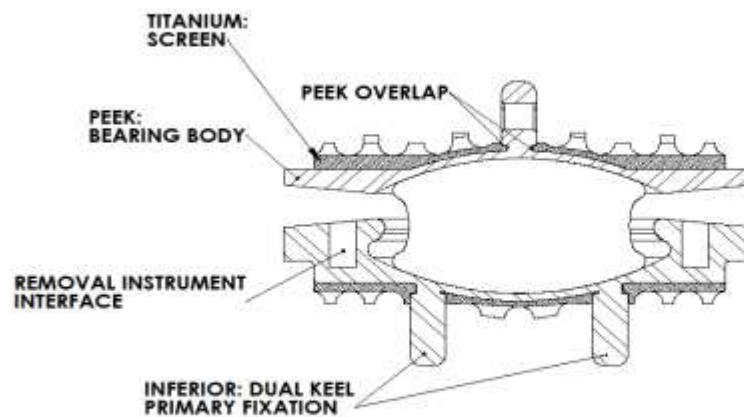


Figure 54: Moulded connection between titanium and PEEK

Figure 55 illustrates design concepts with regard to the titanium screen; these serve to improve the attachment between the two bodies as well as improve manufacturability.

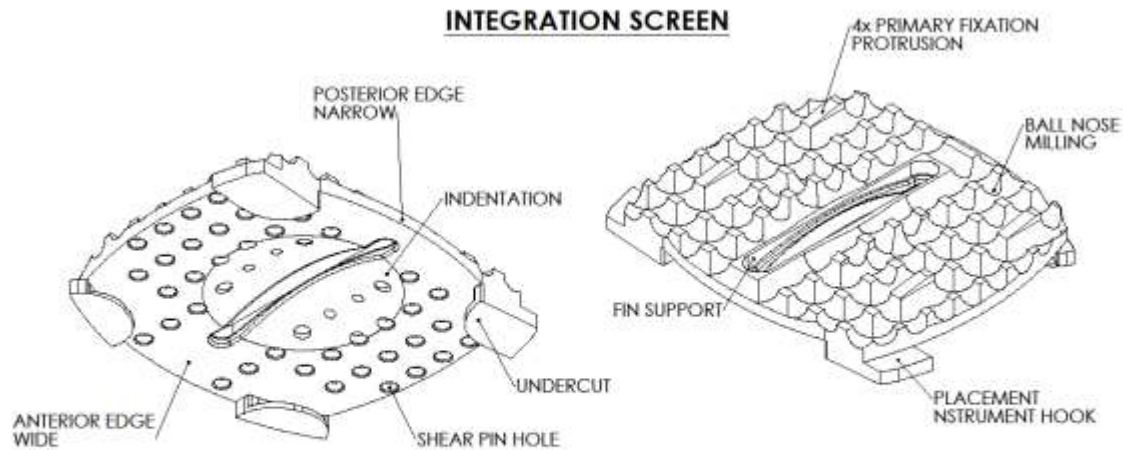


Figure 55: Detail of superior integration screen

The outcome of the design review process is a reduction of titanium volume from 276.74mm³ to 171.81mm³, a reduction of 38%. Surface area of integration was reduced from 318.91mm² of the CCM KCD to 222.73mm², 16% less. Plan area has been maintained by keeping the principal dimensions as per the user input.

On the basis of the concept selection matrix, the final design output is deemed to be the best compromise between the various design inputs.

7.7 Design Validation

Design validation is the process of testing a low-volume production run, to ensure that the design functions fulfil the user needs and intended uses. The successful result of the verification provided the impetus to proceed with the validation of the design concept.

The concepts conceived during the design review were implemented for a production-ready device. Testing the device in production state ensures that seemingly unrelated factors do not influence the product. The validation testing followed the same testing protocol as the verification tests.

7.7.1 Device Description

Table 19 lists the specification of the components used for validation testing. Revision B denotes that the verification and review phases have been completed. Figure 56 shows the device as tested; note the inferior endplate features a dual keel; the core and wear surfaces are highly polished to reduce the degradation of the wear couple.

Table 19: Description of validation test components

Validation test component description	
Date	2009-10-23
Device revision	B-003
Components	KCD-R-5.0
	KCD-R-CORE
	KCD-R-5.0-WR
Manufacture method	Injection Moulded, NC milled
	Polymer: PEEK ASTM F2026
	Metal: Ti Grade 5 ASTM F136
Titanium Volume (mm ³)	Superior: 92.53
	Inferior: 79.28
	Total: 171.81
Implanted level	C6-7
Device position	As per surgical procedure



Figure 56: Photograph of production ready device, inferior endplate on the left, core in the centre, superior endplate on the right.

7.7.2 Device Positioning

The experience gained with the verification positioning was applied to achieving more accurate device placement. The device was placed into a full cadaver, which increased stability of the spine, enabling improved cutting of the keel slots. Figure 57 illustrates the device placement into a cadaver neck. Final depth positioning was performed with the aid of fluoroscopic imaging.

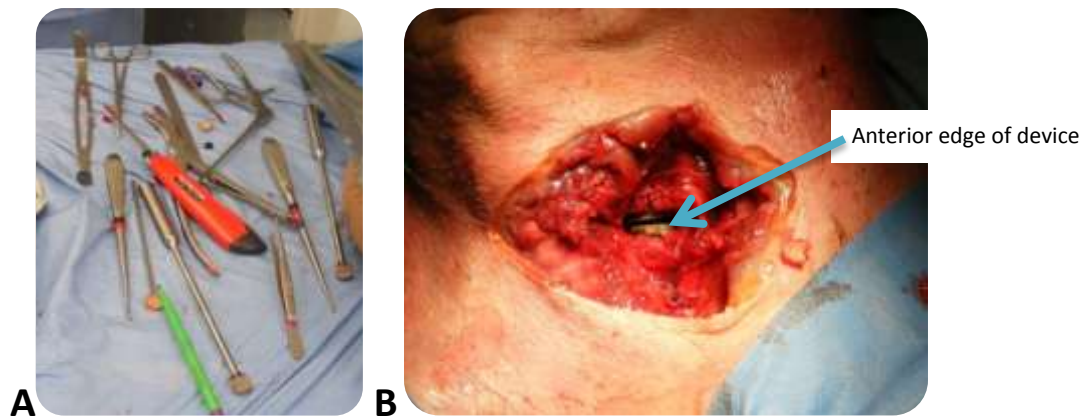


Figure 57: Photograph of (A) instrumentation used for device insertion (B) device positioned *in vitro*

7.7.3 Validation Testing Results

The results of validation testing were divided into qualitative and quantitative. Due to the CT and fluoroscopy being less susceptible to artefact, the focus of the investigation was on MR imaging results. It should be noted that the cadaver used for validation testing displayed posterior

osteophytes, which intrude into the spinal canal. The full set of images used for validation results are available in Appendix D.

Qualitative Result

The positioning of the device relative to the vertebral bodies can be accurately seen on CT images. The device was positioned sufficiently posteriorly, with the posterior edge of the endplate located over the cortical bone, 2mm from the spinal canal. Laterally the position was less than 2.5mm off the ideal medial position.

Axial Results

Axial MR sections were spaced with 3.8mm between each other. This distance between images is typical of MR scans. The assembled disc height was 10mm; two or three sections were therefore expected to intercept the device. Axial sections 8 to 12 have been selected from sagittal section 9, these five sections encompass the device and artefact.

Figure 58 displays an artefact which does not extend into the region of the nerve root or spinal canal. In this case, clinical value of image 9 is not deteriorated due to artefact.

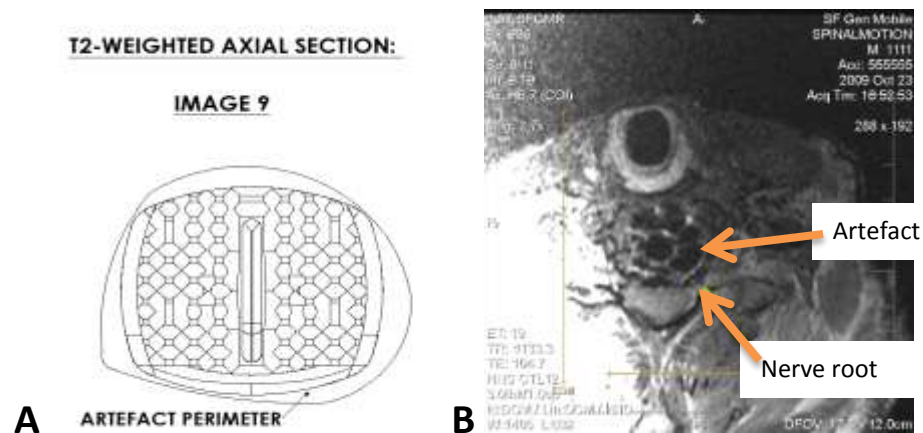


Figure 58: T2-weighted artefact (A) size and position for image 9; (B) Nerve root remains outside of affected area.

Figure 59 illustrates the most distinct artefact found in the selected axial sections. Although larger than the titanium portion, the size and shape of the artefact is similar to the total footprint of the disc. Figure 59 A illustrates that the artefact may intrude into the spinal canal in the axial section.

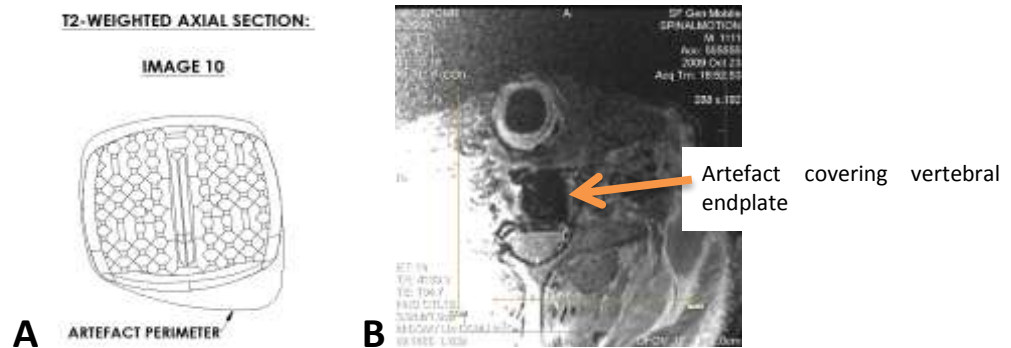


Figure 59: T2-weighted artefact size and position for image 10

Sagittal Results

Sagittal MR sections were spaced at 3mm; the lateral width of the device was 16mm. Five sagittal images were therefore expected to section the device. Artefacts were present in images five to ten, the two largest artefacts were obtained with images seven and eight. This result corresponds with the location of the slice and position of the device (Figure 68, Appendix D).

Figure 60A provides the estimated artefact size, shape, and device position for image 7 in the sagittal plane. The artefact was concave-convex shaped, which matches the natural anatomical disc space. The artefact penetrates into the spinal cord by a margin of between two to three millimetres.

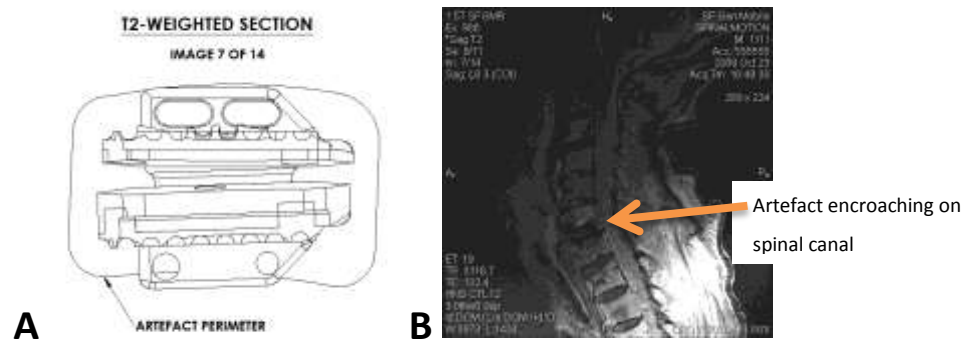


Figure 60: T2-Weighted sagittal section, image 7 of 14

Figure 61 is 3mm lateral of image 7, the artefact encroaches by 2mm into the spinal canal; obscuring the anterior edge of the spinal cord. The shape of the artefact maintains the anatomical disc-space on the superior endplate, while obscuring the interior disc-space to a larger amount.

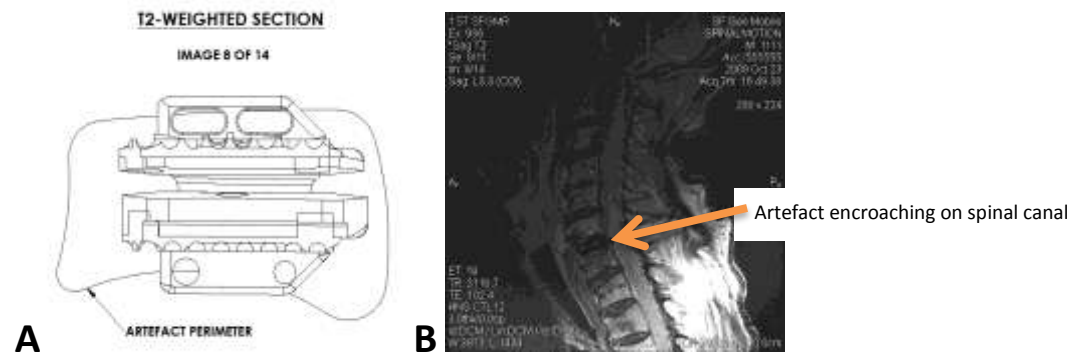
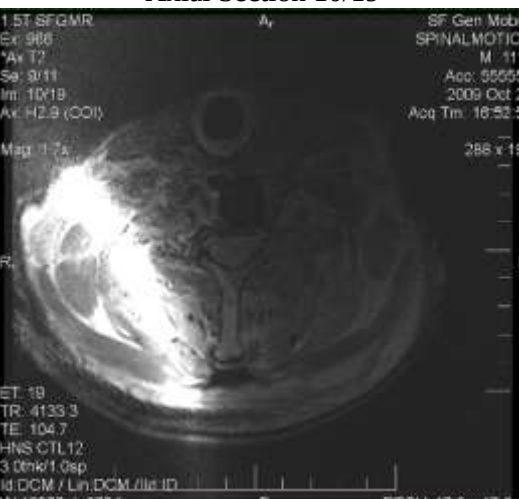
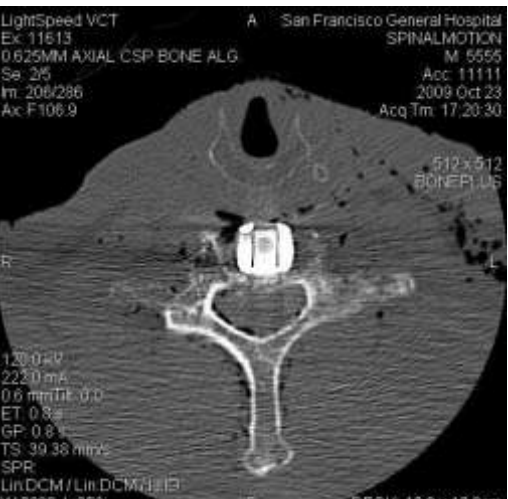


Figure 61: T2-Weighted sagittal section, image 8 of 14

The substitution of titanium with PEEK as a means of primary fixation has significantly reduced the artefact in the sagittal plane. It is noted that the artefact does not extend past the height of the keels.

Table 20 includes a representative image for each of the imaging modalities. Artefact is visible on both axial and sagittal sections with CT imaging. The flare generated is not significant, with the bony structures remaining clearly visible close to the device. Fluoroscopy is used during surgery to provide rapid images of the location of the device. The slots for the fins provide a landmark for final positioning of the device.

Table 20: Validation imaging results

Magnetic Resonance (MR)	Computed Tomography (CT)	Fluoroscopy
Sagittal section 8/14  1.5T SFGMR Ex: 986 *Sag T1 Se: 7/11 Im: 8/14 Sag L3.3 (CC) SF Gen Mobile SPINALMOTION M: 1111 Acc: 555555 2009 Oct 23 Acq Tm: 16:45:06 286 x 192 ET: 3 TR: 466.7 TE: 16.0 HNS CTL12 3.0mm/0.0sp Id DCM / Lin DCM / Id ID W:4441 L:1776 DFOV: 20.0 x 20.0cm	Sagittal section 51/108  LightSpeed VCT Ex: 11613 1.25MM SAG SPINE Se: 602/5 Im: 51/108 Sag L38.8 (CC) San Francisco General Hospital SPINALMOTION M: 5555 Acc: 111111 2009 Oct 23 Acq Tm: 17:20:30 512 x 512 BONEPLUS 120.0 kV 0.0 mA Tilt: 0.0 ET: 0.8 s GP: 0.8 s TS: 39.38 mm/s SPR Lin DCM / Lin DCM / Id ID W:2000 L:350 DFOV: 17.8 x 17.8cm	Lateral view  PHILIPS 98 Fluoro University of Cal. SF Patient: SPINALMOTION 10-23-2009 11 Superior: 10-23-2009 60 (G430) 1
Axial Section 10/19  1.5T SFGMR Ex: 986 *Ax T2 Se: 9/11 Im: 10/19 Ax H2.9 (COI) SF Gen Mobile SPINALMOTION M: 1111 Acc: 555555 2009 Oct 23 Acq Tm: 16:53:53 286 x 192 ET: 18 TR: 4133.3 TE: 104.7 HNS CTL12 3.0mm/1.0sp Id DCM / Lin DCM / Id ID W:10377 L:3754 DFOV: 17.9 x 17.8cm	Axial Section 206/286  LightSpeed VCT Ex: 11613 0.625MM AXIAL CSP BONE ALG Se: 2/5 Im: 206/286 Ax F106.9 San Francisco General Hospital SPINALMOTION M: 5555 Acc: 111111 2009 Oct 23 Acq Tm: 17:20:30 512 x 512 BONEPLUS 120.0 kV 222.0 mA 0.6 mm Tilt: 0.0 ET: 0.8 s GP: 0.8 s TS: 39.38 mm/s SPR Lin DCM / Lin DCM / Id ID W:2000 L:350 DFOV: 12.8 x 12.8cm	Coronal view  PHILIPS 98 Fluoro University of Cal. SF Patient: SPINALMOTION 10-23-2009 11 Superior: 10-23-2009 60 (G430) 1

Quantitative Result

The analysis performed on the validation provides insight into the outcome of the design review. Estimates of device area were calculated under the following assumptions:

- Axial sections were parallel to the serrated surface of the device. The plan area, including PEEK regions was used as the estimated device area.
- Sagittal sections were parallel to the keel of the device.

Axial Section

Analysis of axial section MR images have been summarised in Table 21. Nerve roots are visible in images 8, 9, and 11. No artefact was visible in images 8 and 12; image 11 displays a unique artefact with little disruption of the vertebral body.

Maximum artefact area obtained was conservatively estimated to be 242mm² (Figure 58), an increase of 25% over the estimated device area. The maximum encroachment of the artefact into the spinal canal was three millimetres (image 10).

Table 21: Analysis of MR artefacts, in axial plane

T2-Weighted, Axial Plane					
Image #	Device Area (mm ²)	Artefact Area (mm ²)	% Increase	Spinal Canal Encroachment (mm)	Nerve Root Visible
8/19	0	0	-	0	Y
9/19	194	242	25%	2	Y
10/19	194	234	21%	3	
11/19	194	225	16%	0	Y
12/19	0	0	-	0	

Sagittal Section

Device area was estimated to be 125mm² and 866mm² for section through the keel and through the serration surface only. The encroachment into the spinal canal was between 2-3 millimetres for

images 5 to 19, which correspond with axial section results. Table 22 summarises the results obtained in the sagittal plane.

Table 22: Analysis of MR artefacts in sagittal plane

T2-Weighted, Sagittal Plane					
Image #	Device Area (mm ²)	Artefact Area (mm ²)	% Increase	Spinal Canal Encroachment (mm)	Adjacent Disc Encroachment (mm)
4/14	0	0	0%	0	0
5/14	99	163	64%	0	0
6/14	126	177	40%	3	0
7/14	126	179	42%	2	0
8/14	126	168	33%	2	0
9/14	126	162	28%	3	0
10/14	99	102	3%	3	0
11/14	0	0	0%	0	0

Figure 62 has been rendered by assembly of T2-weighted sagittal images 5 to 10, producing a three-dimensional representation of the artefact extent. The value of this image is that unexpected results can be taken into context and compared with each other.

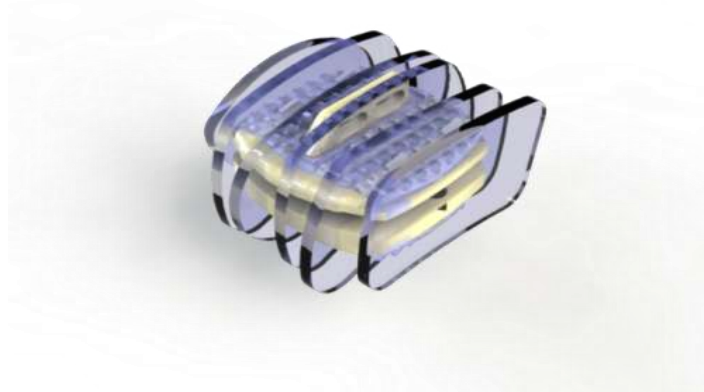


Figure 62: Assembly of T2-weighted sagittal artefact sections 5 to 10

7.7.4 Validation Test Result Discussion

The aim of validation testing is to ensure the result of the development process satisfies the user needs. Tests performed on revision A-005 illustrated that T2-weighted images provide the most clear axial and sagittal images. With this in mind, T2-weighted magnetic resonance images were evaluated to assess the impact of the artefact on the contrast of the spinal cord and nerve roots.

Magnetic Resonance

Artefact size and area estimation performed *in vitro* proved to be challenging due to the artefact obscuring the position of the implant. Voids within the scan area present themselves as dark areas, which under conservative assessment are included in artefact area and encroachment estimation. Since the anatomical shape of the disc space does not precisely match the device, a void volume is created.

Figure 63 illustrates the result of artefact area analysis; three axial images of the MR series displayed a maximum artefact size 25% larger than the device, with an average increase of 20%. In the axial plane, the artefact extends posteriorly less than two millimetres. The perimeter of the artefact did infringe into the spinal canal, however it did not deteriorate the area where spinal nerve roots are expected to be visible.

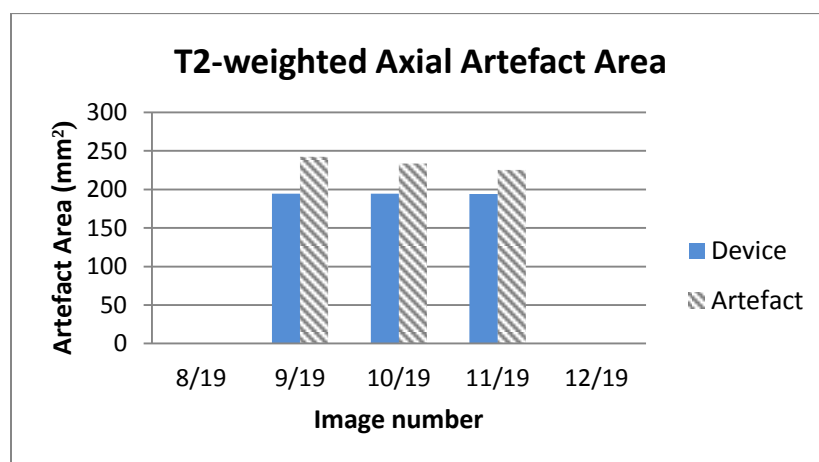


Figure 63: Graphic representation of axial artefact and device areas

Figure 64 illustrates the outcome of sagittal artefact analysis on images 4 to 11. Image 5 displays an artefact area which has a large discrepancy between artefact and device size. The superior shape of the artefact perimeter is likely to be the anatomical shape of the superior vertebral body. Excluding image 5, the average artefact area is 33% larger than the device.

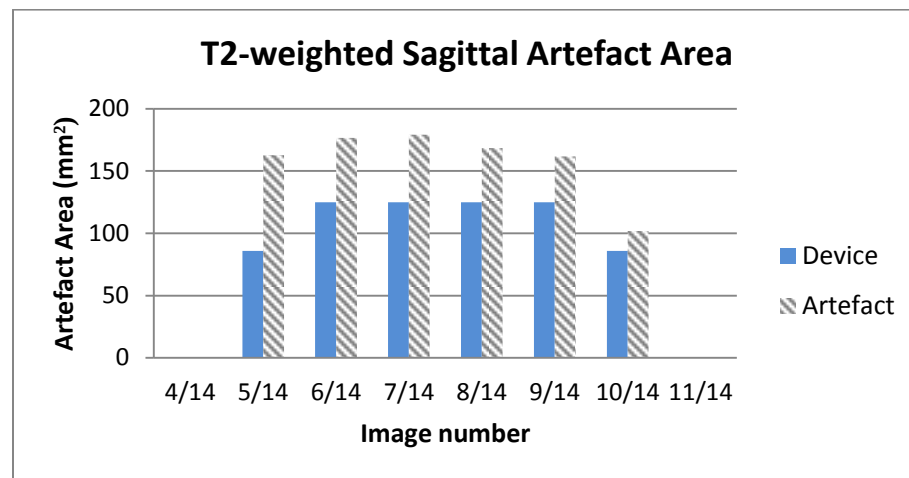


Figure 64: Graphic representation of sagittal artefact and device areas

Comparing devices revision A-005 and B-003, artefact was reduced from 70% to 20% in the axial plane, and from 100% to 43% in the sagittal plane. In the author's opinion, this is due to the thin body of titanium (primary fixation keel) increasing the cross sectional area thereby affecting the magnetic field.

Computed Tomography and Fluoroscopy

Either CT or fluoroscopy images provided satisfactory indication of the devices position. There was not a significant difference between revision A-005 and B-003 with these two imaging modalities.

7.7.5 Conclusion on Validation Testing

The aim of the validation testing was to obtain MR, CT, and fluoroscopy images in order to ensure that the user's needs have been fulfilled. The user **requirements** were that after implantation the clinical value of MR imaging was not drastically reduced.

In the author's opinion the user needs have been addressed agreeably; nerve roots and adjacent intervertebral discs are not affected by the presence of artefact. The intrusion into the spinal canal is not desired; however the likelihood of stenosis of the spinal cord being a source of pain is limited due a full discectomy being performed at the treated level.

Chapter 8: Conclusion

The functional spinal unit serves to relay sensory information between the brain and target organs, as well as to support the upper body. The latter function is achieved in part by the intervertebral discs, the kinematics of which exhibit spring-like behaviour, and enable the patient to move with six degrees of freedom.

Degenerative disc disease

Intervertebral disc degeneration is a natural process, the rate of which increases after age 30. Disc degenerative disease (DDD) speeds up the rate of degeneration, causing misalignment of the spinal column and potentially pain due to strain on the nerve roots or nerves. DDD can be caused by high mechanical loading, genetic predisposition and insufficient nutrient supply.

The exact pathology of DDD has not yet been confirmed, and it is therefore unlikely that the disease can be halted or reversed until its etiology has been identified. The interim solution to restoring quality of life in symptomatic patients is pain reduction through the elimination of neurological stenosis by means of mechanical intervention. The challenge is therefore to apply classical engineering techniques in replicating the natural intervertebral disc.

Spinal Surgery

Successful clinical results of both spinal fusion and disc replacement provide the impetus for a growing number of patients electing to have surgical intervention. At the moment, not enough clinical evidence has been amassed to promote either procedure conclusively as the superior option.

In the author's opinion, spinal disc arthroplasty has not yet reached technological maturity. The amount of clinical evidence collected will therefore always seem to be in short supply due to newer technologies being introduced. Patient selection and the strict application of indications and contra-indications become central to obtaining an un-skewed insight into the efficacy of surgical intervention.

With this in mind, resources need to be applied to further advance the science of cervical disc arthroplasty. Advancement looks toward achieving natural kinematics while reducing the impact of the foreign implant. Natural kinematics include force deflection, range of motion, degrees of freedom while constrained by natural disc geometry. The impact of the device should feature minimal side-effects, including trauma associated with surgical requirements, wear debris generated, cellular proliferation, and long-term effects on facet joint performance.

Spinal Disc Arthroplasty Device Development

While various design philosophies continue to evolve regarding kinematics and device fixation, it follows that low imaging signature is the next logical evolutionary step. To this end, Southern Medical (Pty) Ltd. has researched the goal of achieving an imaging compatible, mobile core device, featuring materials that are commonly used in spinal prostheses in an innovative, robust way.

Artefacts are an occurrence in medical imaging perceived as irregular flares that obscure visibility of the surrounding tissue structures, thereby impairing post-operative diagnosis. Artefacts are the result of an irregular magnetic field caused by the variances in magnetic properties between the implant and surrounding tissues.

Research Methodology

The aim of this work was to reduce MR signature of an existing disc arthroplasty to a level which provides post-operative images of a clinically useful nature, i.e. minimal artefacts. Magnetic resonance imaging is the most popular method for imaging soft tissue structures, owing to the high contrast ratio it can provide between tissue types.

By reviewing and comparing contemporary literature where possible, the following research route was followed.

- The functional spinal unit and the kinematics of a healthy person were investigated
- The influence of mechanical loading on disc degeneration was evaluated
- The origin of neck pain and state-of-the-art treatment modalities were identified

- A comparison of clinical results between disc arthroplasty and arthrodesis was made
- Industry standard imaging techniques were evaluated
- Biomaterials used in spinal applications were selected based on their physical properties
- Competitor products were evaluated to identify areas of improvement
- The design control process for medical devices was applied to achieving verification and validation of the resulting material selection.

From the research, it was found that in order to minimise artefact occurrence:

- The volume of metallic material should be kept to a minimum.
- Selection of a non-ferromagnetic material would ensure compatibility.
- Titanium generates the least amount of MR artefacts among metallic biocompatible materials which are commonly used in spinal arthroplasties. Polymers do not generate artefacts and must also be considered for the development of an imaging compatible device.

Non-active surface-enhancing methods such as keel fixation were considered to improve the primary and secondary fixation. Based on these considerations, as well as those of mechanical properties, biocompatibility, wear resistance and osseointegration properties, a combination of PEEK and titanium was selected as the material for the prototype device.

Design Verification and Validation

A prototype device was manufactured as proof of concept, verifying the feasibility of the attempt to improve imaging compatibility. Testing of the device was performed by MR, CT, and fluoroscopy images of the device in a human cadaver spine. Imaging was performed with equipment which is typical of modern hospitals.

Analysis of imaging focused on MR images for an initial prototype and for a production ready device. The original CCM device produced an artefact of 1842mm². After an initial concept generation and selection process, artefact area was reduced by 81% to 350mm². This positive result provided the affirmation that further refinement should be performed.

Methods of manufacture were evaluated to achieve a repeatable product. A critical review of artefact on axial and sagittal planes provided the direction of refinement. A low-volume production was initiated to perform validation tests. The second iteration of conceptual development further reduced artefact to less than 242mm².

Post-operative MR and CT scans are now capable of producing images which do not negate their clinical value. Sagittal plane MR images encroached 2-3mm into the spinal canal. Axial images do not obscure nerve roots to an extent where clinical value has been deteriorated to an unsatisfactory level.

8.1 Future Work

This study focuses on the imaging performance of the proposed design, it is however only one aspect of the entire project. Future work entails using the results of this study for the basis of further development.

Mechanical Performance

Of particular importance is the volumetric wear rate of the endplates and core. Arthroplasty devices with a PEEK-PEEK wear couple are ball and socket type, mobile COR configuration with any type of polymer-polymer wear couple is yet to be validated. Wear debris validation must be performed by means of a biological study, initially over the short term such as an animal study and ultimately over a long term *in vivo* clinical study.

Due to the reduction of titanium-bone area, secondary fixation requires validation. Similarly the robustness of the design requires extensive *in vitro* and *in vivo* testing before the project is completed. Sufficient primary and secondary fixation

Clinical Performance

The goal of cervical disc replacement is to reduce pain for the patient's lifetime. Reducing pain to a level where the patient would opt to have the same surgery with the same result is used as a measure of clinical success.

8.2 Recommendations

Accelerating development of healthcare product requires that large amounts of accurate information is gathered and assessed. Surgery registries serve as a record of patient outcome, and may be used to evaluate the success of a procedure. The Swedish Spine Registry, (established in 1999) captures patient information such as demographics, symptoms, diagnosis, treatment, results, hospitalisation duration. From these parameters a wealth of information may be assimilated cost effectively (Berg and Tropp, 2010).

It is recommended that a local joint register be implemented. This database should be aligned to European registries. It would be advantageous to publish the results in an interactive manor, whereby patients, practitioners, and manufactures could view the results and serve as a guideline of clinical results.

Chapter 9 References

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Appendix A: Indications and Contraindications

Table 23: Indications for cervical disc arthroplasty (Auerbach *et al.* 2008)

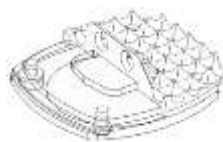
-
- Symptomatic cervical disc disease at one or two vertebral levels between
 - C3–T1 confirmed by magnetic resonance imaging, computed tomography, or myelography showing herniated nucleus pulposus, spondylosis, or loss of disc height
 - Failed six weeks of conservative therapy
 - Between 20 and 70 years of age
 - No contraindications
-

Table 24: Summary of contraindications for cervical disc arthroplasty (Auerbach *et al.* 2008)

-
- Less than 3 vertebral levels requiring treatment
 - Cervical instability (translation >3 mm and/o 11° rotational difference to that or either adjacent level)
 - Known allergy to implant materials (titanium, polyethylene, cobalt, chromium, and molybdenum)
 - Cervical fusion adjacent to the level to be treated
 - Posttraumatic vertebral body deficiency/deformity
 - Facet joint degeneration
 - Neck or arm pain of unknown etiology
 - Axial neck pain as the solitary presenting symptom
 - Severe spondylosis (bridging osteophytes, disc height loss >50%, and absence of motion <2°)
 - Osteoporosis/osteopenia
 - Prior surgery at the level to be treated
 - Active malignancy; any patient with history of invasive malignancy, unless treated and asymptomatic for at least 5 years
 - Systemic disease (AIDS, HIV, Hepatitis B or C, and Insulin-dependent diabetes)
 - Other metabolic bone disease (i.e., Paget's and osteomalacia)
 - Morbid obesity (BMI>40 or weight >55kg over ideal body weight)
 - Pregnant or trying to become pregnant in next 3 years
 - Active local/systemic infection
 - Presently on medications that can interfere with bone/soft tissue healing (ie, steroids)
 - Autoimmune spondyloarthropathies (rheumatoid arthritis)
-

Appendix B: Concept Selection Matrix

Table 25: Concept selection matrix

			Verification				Validation		
									
Date			2008.04.08	2008.06.09	2009.03.04	2009.06.11	2009.05.06	2009.05.13	2009.10.01
Description			PEEK plug in Ti body, pin fixation	Full Ti Screen held into place with pins (half screen shown)	Complete PEEK device coating with Ti / HA / CaP	Screen split in half, with a taper fit. (keel slot and weld to 'hold' screens together)	Circular skirt holding PEEK	PEEK plug moulding into billet coupon	Ti Insert moulding
Manufacture Processes			Milling Screen, Turning PEEK, Welding	Milling Screen, Turning PEEK, Welding	Milling & turning device. Plasma coated	Milling Screen, Turning PEEK, Welding	Milling & turning screen. Injection moulding	Milling billet, Injection moulding, turning, Milling Serrations. Wire EDM perimeter	Milling Screen. Insert moulding.
MR Tested			No	No	No	Yes	No	Yes	No
Design Features			PEEK wear surface surrounded by Ti screen - Very secure fit. Integration surface minimally affected	PEEK protrudes to base on fin - quite a thick section throughout. Pins inserted from bottom, welded onto position - providing anchor also.	The 'ideal' solution from a manuf. and screening point of view since the device is machined completely then coated. A totally unproven concept. New WR shape developed	Fin out of Ti, worried about the strength of weld. Skirt around the edge too thin.	PEEK fin holding screen in centre, moulding shrinkage grip is generated around skirt Revolved skirt attaching outer perimeter. Skirt is too short	PEEK moulded around feet and screen. Good attachment area. Injection moulding results poor thus far.	PEEK moulded around feet and screen. Good attachment area. Injection moulding results poor thus far.
Integration Area mm²			269.65	271.85	298.74	265.32	209.92	222.73	
Weighting	3	Manuf. complexity	7	7	6	8	4	3	5
	8	PEEK quality	10	10	8	10	4	6	6
	10	2 nd Fixation area	6	8	10	8	8	6	7
	10	Fixation connection	7	4	1	6	7	9	9
	10	Ti volume	4	4	10	4	7	7	7
	41	Total	271	261	292	284	264	277	293

Appendix C: Verification Results

Table 26: List of verification results

Reference	Description
Figure 65	Location of MR axial sections, images 18 to 22
Figure 66	Location of MR sagittal sections, images 5 to 10
Figure 67	Location of device
Table 27	Comparison between T1 and T2 weighted sagittal sections, images 6 to 9
Table 28	T2 weighted axial sections, images 17 to 22

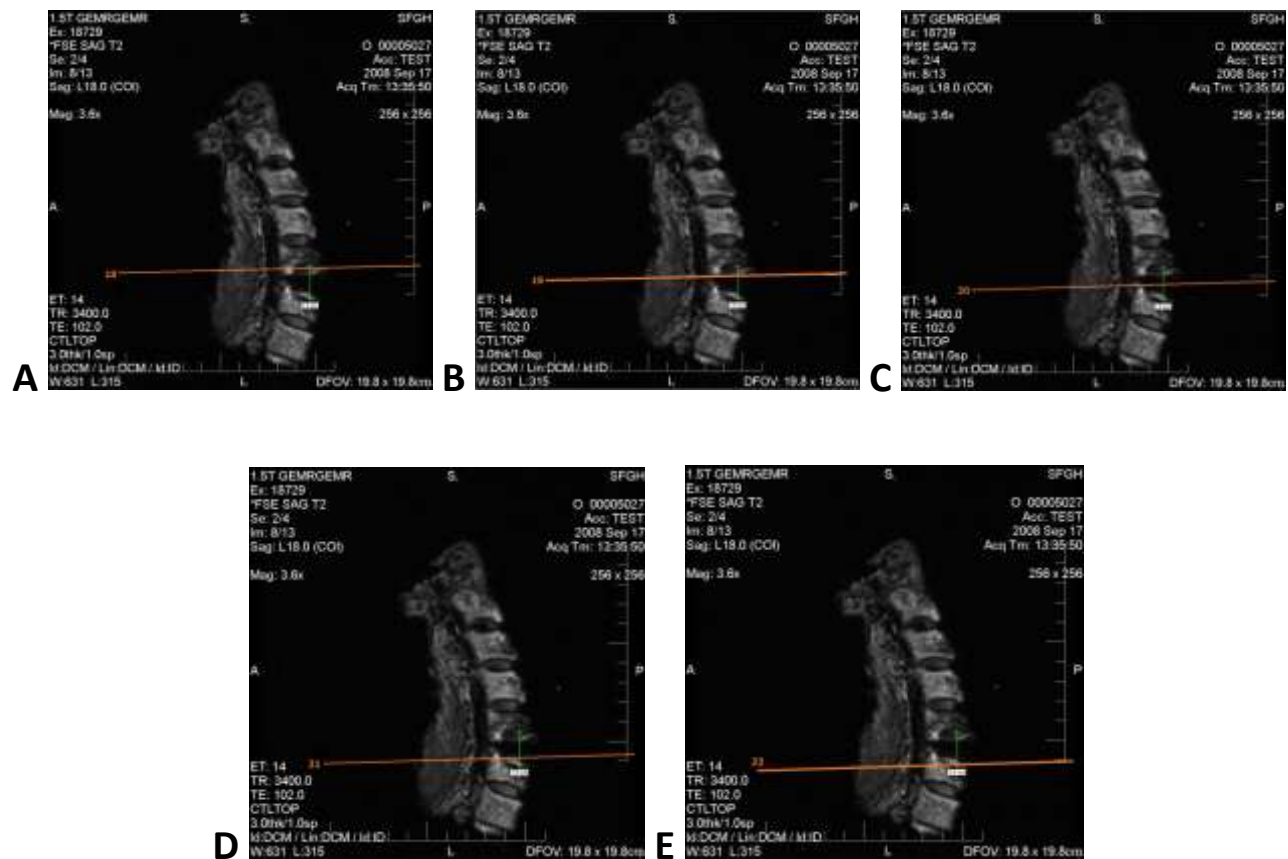


Figure 65: Location of axial planes (A) MR Image 18... (E) MR Image 22

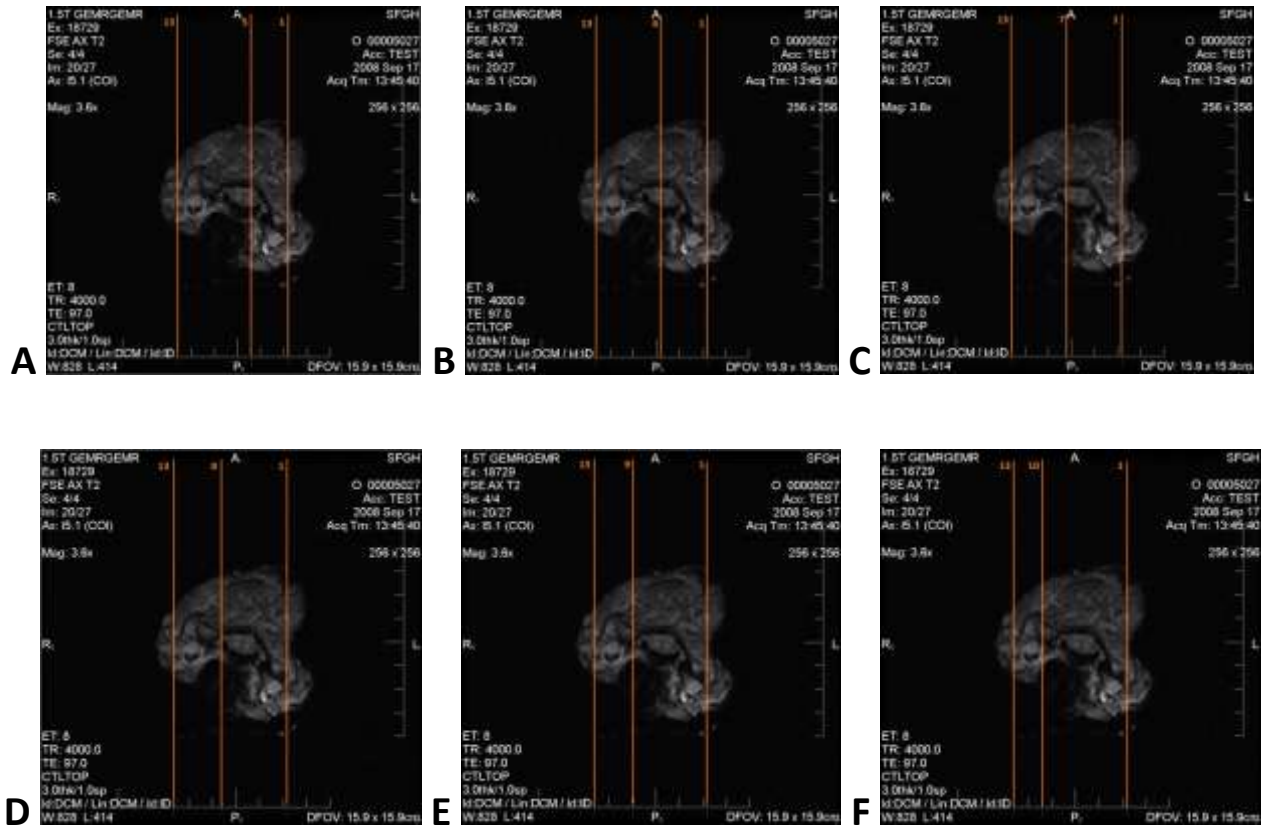


Figure 66: Location of MR sagittal slices; (A) MR image 5... (F) MR image 10

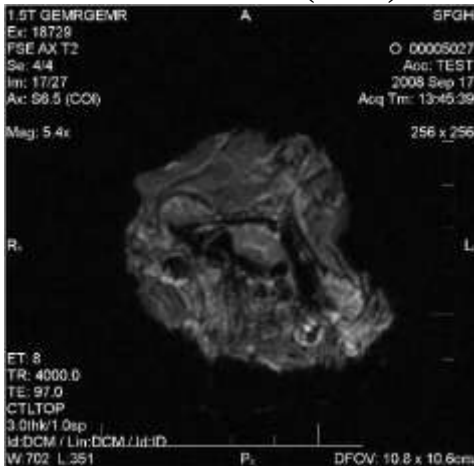
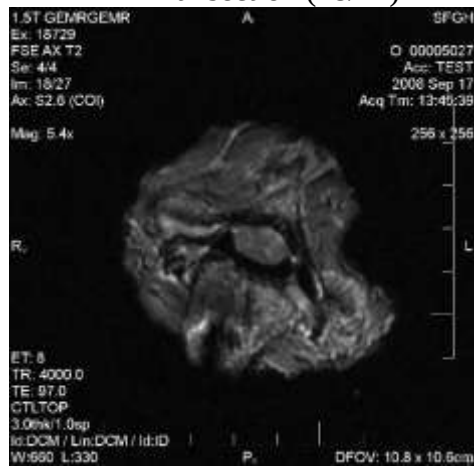
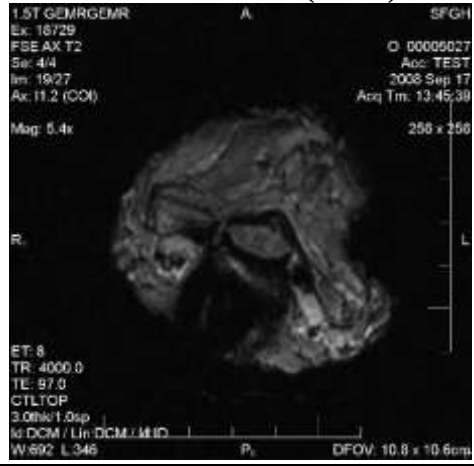
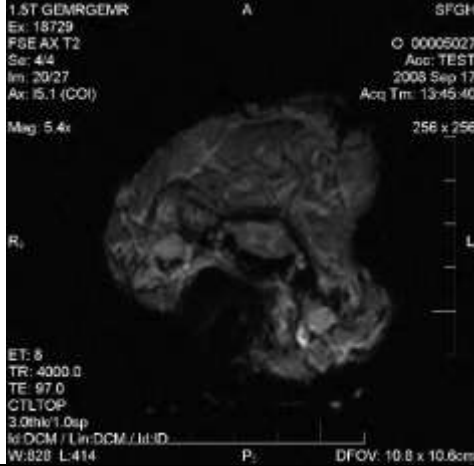
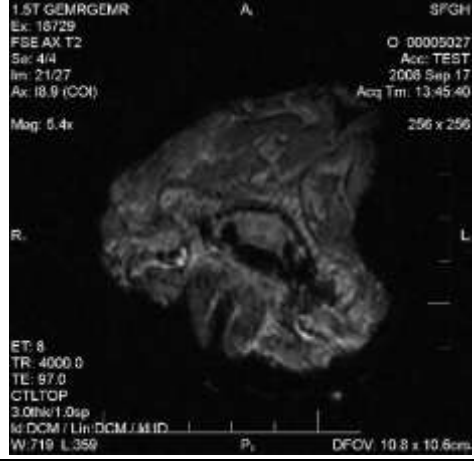
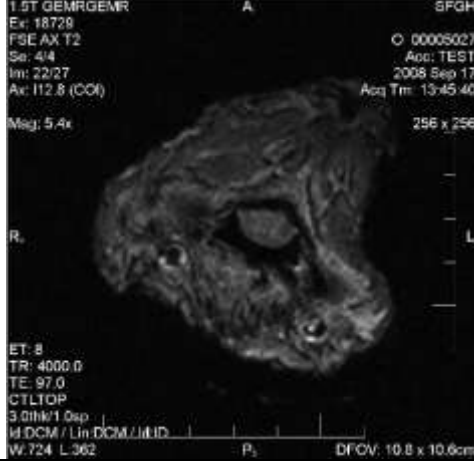


Figure 67: Location of device; (A) 7mm anterior of vertebral endplate, (B) superior 3mm lateral, and inferior 2mm lateral of midline

Table 27: Comparison between T1 and T2 weighted sagittal sections, image 6 to 9.

Magnetic Resonance Images (MRI)	
T1 Sagittal section (6/13)	T2 Sagittal section (6/13)
T1 Sagittal section (7/13)	T2 Sagittal section (7/13)
T1 Sagittal section (8/13)	T2 Sagittal section (8/13)
T1 Sagittal section (9/13)	T2 Sagittal section (9/13)

Table 28: T2 Weighted axial section, image 17 to 22

Magnetic Resonance Images (MRI)	
T2 Axial section (17/27)  1.5T GEMRGEMR Ex: 18729 FSE AX T2 Se: 4/4 Im: 17/27 Ac: S8.5 (COI) Mag: 5.4x 256 x 256 R. L. ET: 8 TR: 4000.0 TE: 97.0 CTLTOP 3.0thk/1.0sp Id:DCM / Lin:DCM / Jit:ID W:702 L:351 P. DFOV: 10.8 x 10.6cm	T2 Axial section (18/27)  1.5T GEMRGEMR Ex: 18729 FSE AX T2 Se: 4/4 Im: 18/27 Ac: S2.8 (COI) Mag: 5.4x 256 x 256 R. L. ET: 8 TR: 4000.0 TE: 97.0 CTLTOP 3.0thk/1.0sp Id:DCM / Lin:DCM / Jit:ID W:680 L:330 P. DFOV: 10.8 x 10.6cm
T2 Axial section (19/27)  1.5T GEMRGEMR Ex: 18729 FSE AX T2 Se: 4/4 Im: 19/27 Ac: I1.2 (COI) Mag: 5.4x 256 x 256 R. L. ET: 8 TR: 4000.0 TE: 97.0 CTLTOP 3.0thk/1.0sp Id:DCM / Lin:DCM / Jit:ID W:692 L:346 P. DFOV: 10.8 x 10.6cm	T2 Axial section (20/27)  1.5T GEMRGEMR Ex: 18729 FSE AX T2 Se: 4/4 Im: 20/27 Ac: I5.1 (COI) Mag: 5.4x 256 x 256 R. L. ET: 8 TR: 4000.0 TE: 97.0 CTLTOP 3.0thk/1.0sp Id:DCM / Lin:DCM / Jit:ID W:828 L:414 P. DFOV: 10.8 x 10.6cm
T2 Axial section (21/27)  1.5T GEMRGEMR Ex: 18729 FSE AX T2 Se: 4/4 Im: 21/27 Ac: I8.9 (COI) Mag: 5.4x 256 x 256 R. L. ET: 8 TR: 4000.0 TE: 97.0 CTLTOP 3.0thk/1.0sp Id:DCM / Lin:DCM / Jit:ID W:719 L:359 P. DFOV: 10.8 x 10.6cm	T2 Axial section (22/27)  1.5T GEMRGEMR Ex: 18729 FSE AX T2 Se: 4/4 Im: 22/27 Ac: I12.8 (COI) Mag: 5.4x 256 x 256 R. L. ET: 8 TR: 4000.0 TE: 97.0 CTLTOP 3.0thk/1.0sp Id:DCM / Lin:DCM / Jit:ID W:724 L:362 P. DFOV: 10.8 x 10.6cm

Appendix D: Validation Results

Table 29: List of validation results

Reference	Description
Figure 68 A	Location of MR axial sections 1 to 19
Figure 68 B	Location of MR sagittal sections 1 to 14
Figure 69	Location of device
Table 30	T2 weighted sagittal sections, images 4 to 14
Table 31	T2 weighted axial sections, images 7 to 12

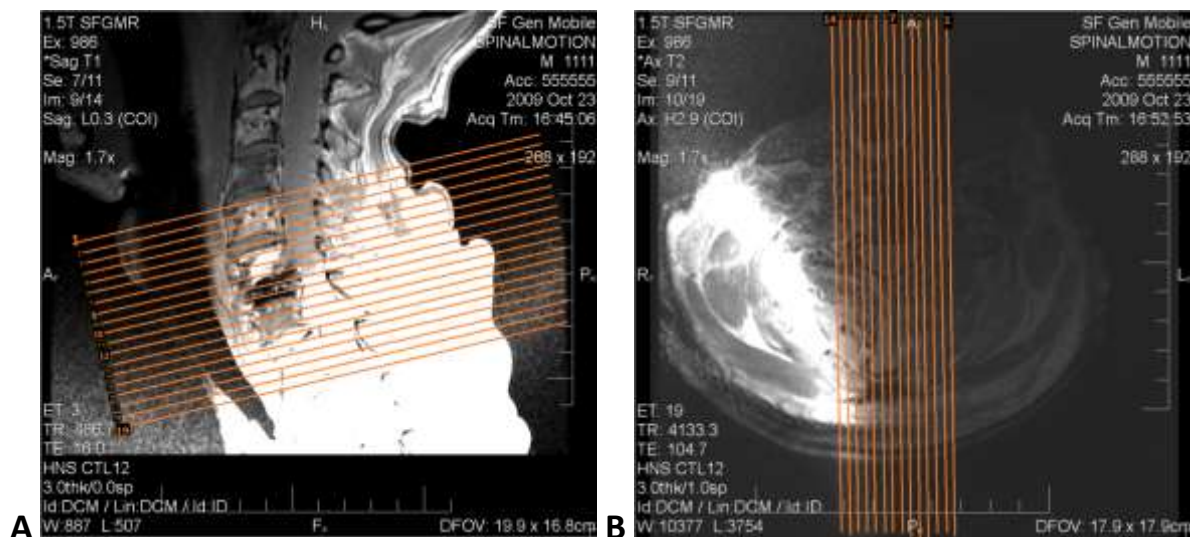


Figure 68: Location of MR image sections, spacing of 3mm between sections
(A) axial sections, images 1 to 19
(B) sagittal sections, images 1 to 14

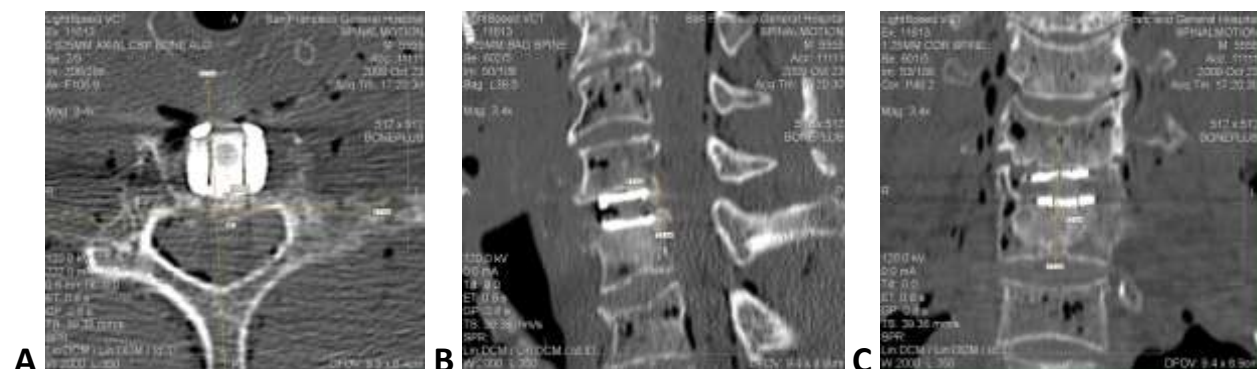


Figure 69: CT scans provide a method for locating the device.
(A) Device is positioned with posterior edge of device on posterior edge of vertebra
(B) Sagittal confirms depth of placement is correct
(C) Coronal plane indicates the midline position; superior and inferior endplates are 0.4 and 2mm lateral

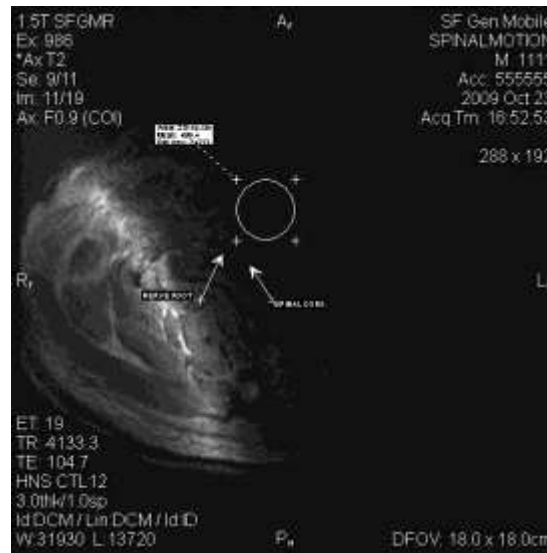


Figure 70: T2 weighted axial image 10/19, approximately through the centre of the disc assembly; artefact size of 17x16mm (A-P x lateral). Soft tissue structures have not been obscured in this image. Soft tissue structures are identifiable as labelled.

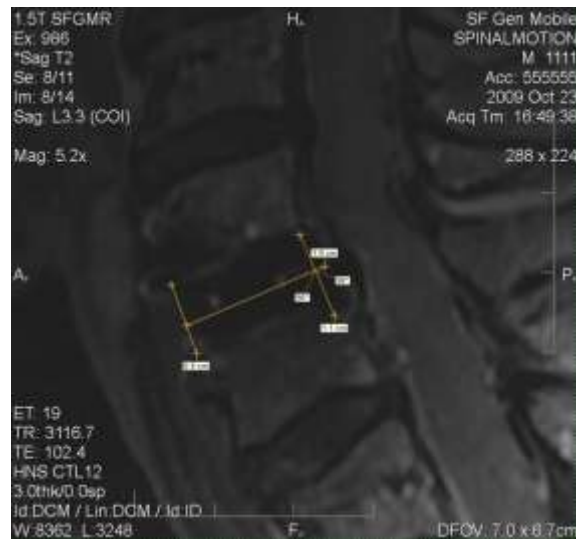
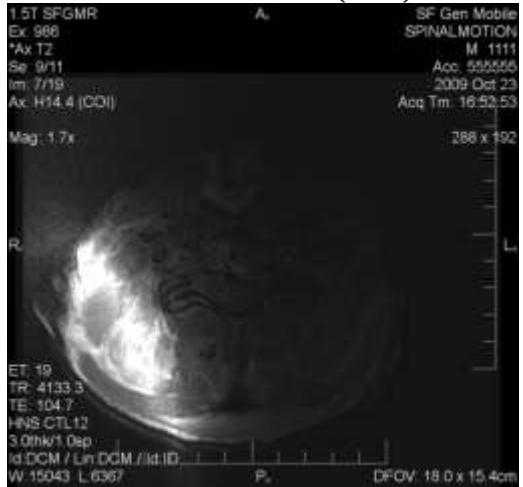
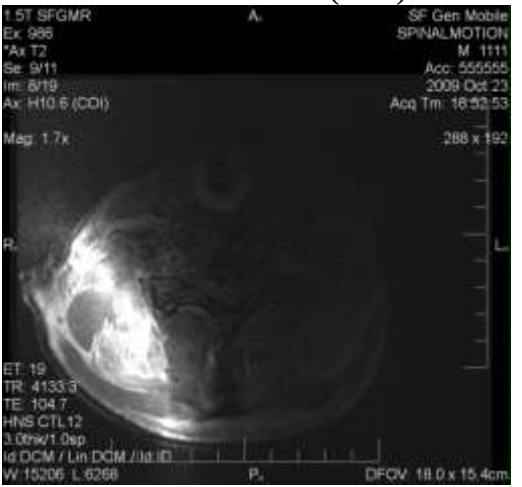
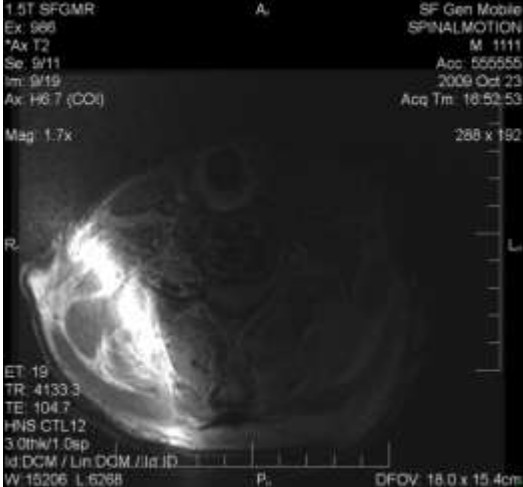
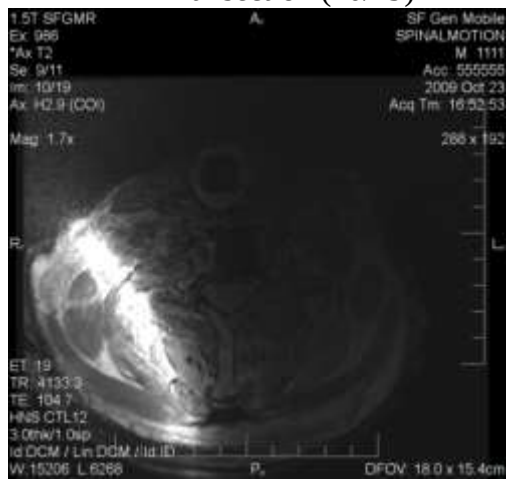
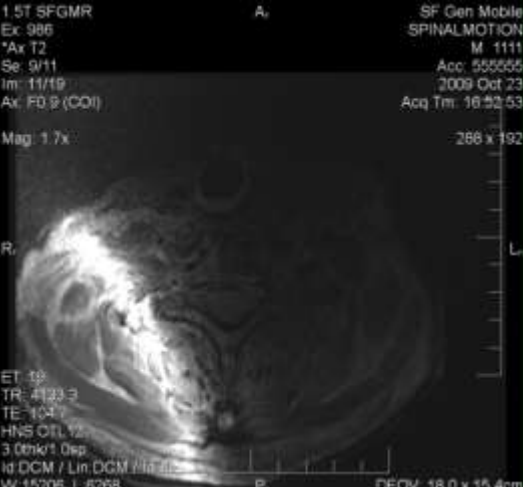


Figure 71: T2 weighted sagittal image 8 of 14, 5.2x magnification. Largest artefact found on image series, 9mm anterior, 11mm posterior and 19mm distance between extents.

Table 30: T2 weighted sagittal section, image 4 to 14

Magnetic Resonance Images (MRI)	
T2 Sagittal section (4/14)	T2 Sagittal section (5/14)
T2 Sagittal section (6/14)	T2 Sagittal section (7/14)
T2 Sagittal section (8/14)	T2 Sagittal section (9/14)
T2 Sagittal section (10/14)	T2 Sagittal section (11/14)

Table 31: T2 weighted axial section, images 7 to 12

Magnetic Resonance Images (MR)	
T2 Axial section (7/19) 	T2 Axial section (8/19) 
T2 Axial section (9/19) 	T2 Axial section (10/19) 
T2 Axial section (11/19) 	T2 Axial section (12/19) 