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The effect of position on the lumbar intervertebral disc

Lyndsay Ann Alexander

**A thesis submitted in partial fulfilment of the requirements of Robert
Gordon University for the degree of Doctor of Philosophy**

January 2014

The effect of position on the lumbar intervertebral disc

Lyndsay Ann Alexander

A thesis presented for the Degree of Doctor of Philosophy

Abstract

This thesis comprises three phases with a combined aim which was to investigate the effect of position on the lumbar intervertebral disc (IVD).

The effect of position on the lumbar IVD in asymptomatic subjects and subjects with discogenic low back pain (DLBP) was explored using positional Magnetic Resonance Imaging (pMRI). Convenience samples of 11 asymptomatic and 34 DLBP subjects were recruited to have sagittal and axial pMRI scans performed in sitting (Neutral, Flexed and Extended), standing and lying (Supine and Prone extension) positions.

The sagittal plane migration of the nucleus pulposus (NP) of each lumbar IVD in each position was measured from the sagittal and axial pMRI scans.

Within and between group inferential analysis was performed using non-parametric tests. Both the asymptomatic and DLBP subjects' demonstrated that position had statistically significant effects on the sagittal plane NP migration. Both groups demonstrated significantly greater posterior sagittal plane NP migration in Neutral and Flexed sitting positions compared to the other positions. However, between group comparisons identified that the asymptomatic subjects also demonstrated significantly greater posterior sagittal plane NP migration than the DLBP subjects. This pattern was more common in the upper lumbar IVDs (L1/2 and L2/3) between positions and less common in the lower IVDs (L4/5 and L5/S1) between positions.

New knowledge regarding the behaviour of the lumbar IVD emerged from this research. The differences detected between the asymptomatic and DLBP subjects suggest that some current theories regarding DLBP may be incorrect. The results also support imaging of DLBP subjects in sitting positions as opposed to current supine positions. Although the limitations of the study reduce

generalisation of the results, the implications for clinical practice, imaging and suggestions for further research from this work are important to improve understanding and conservative management of DLBP.

Keywords: Intervertebral disc, Discogenic low back pain, Nucleus pulposus, positional Magnetic Resonance Imaging

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List of abbreviations

LBP: Low back pain

NSLBP: Non-specific low back pain

DLBP: Discogenic low back pain

IVD: Intervertebral disc

AF: Annulus fibrosis

oAF: Outer annulus fibrosis

iAF: Inner annulus fibrosis

NP: Nucleus pulposus

HNP: Herniated nucleus pulposus

IDD: Internal disc disruption

DDD: Degenerative disc disease

NHS: National Health Service

GP: General Practitioner

USA: United States of America

CSP: Chartered Society of Physiotherapy

MRI: Magnetic resonance imaging

CT: Computed tomography

pMRI: Positional magnetic resonance imaging

rMRI: Recumbent magnetic resonance imaging

kMRI: Kinetic magnetic resonance imaging

T: Tesla

T1: Longitudinal relaxation time

T2: Transverse relaxation time

W: Weighted

T1W: T1 weighted

T2W: T2 weighted

HIZ: High intensity zone
MC: Modic changes
FOV: Field of view
FSE: Fast spin echo
NEX: number of excitations
RF: Radiofrequency
SE: Spin echo
TE: Time of echo
TR: Repetition time
NRS: Numerical rating scale
ROM: Range of Movement
SLR: Straight leg raise
N: number of subjects
ICC: Intra-class correlation coefficient
SPSS: Statistical package for the Social Sciences
SD: Standard deviation
SEM: standard error of the mean

Chapter 1: Introduction

This thesis aims to improve the understanding of the sagittal plane lumbar intervertebral disc (IVD) macroscopic behaviour in loaded and unloaded positions such as sitting, standing and lying. Current understanding of lumbar IVD behaviour relies primarily upon laboratory and animal studies which, while providing valuable information, do not reflect the *in vivo* upright loaded human lumbar IVD. Clinicians treating low back pain (LBP) due to the lumbar IVD (discogenic low back pain), base clinical assessment and treatment on assumptions of lumbar IVD behaviour that come from these laboratory and animal studies. Therefore there is a need to establish the *in vivo* upright loaded behaviour of the human lumbar IVD. The overall hypothesis is that improved understanding of lumbar IVD behaviour will lead to enhanced diagnosis, classification, and assessment of discogenic low back pain (DLBP). It is hoped this enhancement will ultimately lead to improved conservative clinical management of DLBP which can then be demonstrated and evaluated by future research using specific and appropriate tools such as magnetic resonance imaging (MRI). MRI is currently regarded as the most appropriate tool available for investigation of the IVD in clinical and research settings.

This chapter will therefore introduce the topic and cover the background surrounding the IVD, DLBP, and the investigation of DLBP via MRI. The structure of this thesis will then be presented, followed by the aims and objectives of the research.

The results from the series of studies presented in this thesis will provide an exploratory objective analysis of the behaviour of the lumbar IVD in asymptomatic and DLBP populations. These results will add to the information surrounding IVD behaviour in healthy individuals and those with DLBP which can enhance the conservative clinical management of this condition.

Invasive investigation and surgical management of DLBP is out with the scope of this thesis and therefore will not be considered.

1.1: The lumbar intervertebral disc

The key structures involved in DLBP are the five lumbar IVDs. The individual IVD consists of an outer annulus fibrosis (AF) and an inner gelatinous nucleus pulposus (NP) lying between two vertebral end plates (VEP). The IVD is attached via the superior VEP to the vertebral body (VB) above and via the inferior VEP to the VB below (Hughes et al 2012).

The AF consists of concentric lamellae rings of cartilage that are obliquely orientated with alternate fibre direction between each lamellae (Bogduk 2005). The primary role of the AF is to resist load bearing/compression as well as resisting tensile forces such as shear, rotation and distraction (Philips & Laurysen 2010).

The VEPs are thin cartilaginous end-plates covering the majority of the adjacent VB which rely on the adjacent NP hydrostatic pressure to hold them in place (Adams et al 2006). Their role is to assist equal loading across the VB as well as preventing NP migration into the adjacent VBs.

The NP consists of a gel like substance that mainly contains water (70-85%) as well as proteoglycans and collagen. The proteoglycan gel can attract and retain large quantities of water which provides the IVD with its hydrodynamic properties (Adams et al 2006). Under loading the NP works in tandem with the AF. The NP under compression forces spreads radially which is in turn resisted by the AF. This NP expansion also causes internal bracing of the AF that then resists internal lamellar buckling (Adams et al 2006). Therefore, the main role of the IVD is in weight-bearing where it resists and transfers compressive loads while still enabling small movements (Inoue& Espinoza Orias 2011, Gregory et al 2012).

The IVD has been recognised as playing a key role in the development of non-specific low back pain (NSLBP) and DLBP (Schafer et al 2009, Miyagi et al 2012). The IVD has been shown to be a cause of DLBP via mechanical compression of nerve roots or chemical irritation/inflammatory mediators (Leinonen 2004). This in turn can cause pain, and neurological symptoms such as numbness, motor weakness, and altered tendon reflexes and in severe cases even cauda equina syndrome (symptoms can include bladder and bowel dysfunction, saddle

anaesthesia, leg weakness and absence of ankle reflexes)(Leinonen 2004). However, the full pathophysiological mechanisms involved in these processes have still to be fully understood and demonstrated within the literature (Olmaker et al 2002, Takahashi et al 2008). There is a need for research to investigate these mechanisms as demonstrated nerve root compression, as well as pathological and degenerative changes in the IVD on imaging, does not always result in pain and clinical symptoms (An et al 2004, Kjaer et al 2005, Veres et al 2008, Phillips & Laurysen 2010, Hughes et al 2012).

Degenerative changes in the IVD are a normal part of ageing and can result in a variety of pathological changes such as IVD hydration loss; reduced IVD height; increased AF lamellar disorganisation; and reduced cell density including proteoglycan content (Setton & Chen 2004, Adams et al 2006). These changes in IVD structure then lead onto alteration of the IVD mechanics and behaviour as the IVD loses its hydrostatic properties (Setton & Chen 2004, Adams et al 2006).

Investigation of lumbar IVD behaviour is largely based upon laboratory studies using cadavers or animal specimens. Acknowledged limitations of these studies are that while of interest they do not replicate the upright loaded human IVD. There is a lack of literature reporting the *invivo* behaviour of the human IVD in healthy subjects and those with IVD pathology or DLBP; however this limitation is partly due to the lack of non-invasive tools available to perform the task. Additional investigation of the IVD has focused upon the effects of IVD degeneration and whilst of importance, there still remains the need for basic understanding of IVD behaviour in the normal healthy state as well as in pathology with or without degeneration. This thesis will therefore add to the current understanding concerning the IVD by investigating the *invivo* behaviour of the lumbar IVD in normal asymptomatic and symptomatic participants.

1.2: Discogenic low back pain

Low back pain (LBP) is a universal problem within western society in terms of cost and effectiveness of management and over 85% of patients cannot be diagnosed with a specific cause for their LBP. For these patients, they are

defined as having non-specific low back pain (NSLBP) (Koes et al 2006).

Current literature however supports the sub-classification of LBP into specific sub-groups that can then receive targeted management that will lead to improved and cost-effective outcomes (Fersum et al 2010).

Discogenic low back pain (DLBP) is thought to be one of the main sub-groups of NSLBP accounting for 25-57% of LBP cases (Zhou & Abdi, 2006, Konstantinou & Dunn 2008, Schafer et al 2009). This is back pain that is due to the lumbar intervertebral disc (IVD) (Koes et al 2007). In comparison to LBP, people with DLBP are thought to be younger, suffer more persistent and severe pain with longer disability, and have a poorer outcome and higher consumption of available health resources (Awad & Moskovich 2006, Konstantinou & Dunn 2008, Casey 2011, Hill et al 2011, Ong et al 2011). Therefore, there is a need to explore this important LBP sub-group in terms of establishing the optimal assessment and cost-effective management strategies for both clinicians and patients.

DLBP is known by a range of terms in the literature, such as sciatica, radiculopathy, radicular pain, nerve root pain, nerve root entrapment, and lumbosacral radicular syndrome (Konstantinou and Dunn 2008). Table 1.2.1 displays some of these terms and reflects the variation shown in the literature of the definitions attributed to each term. Historically, sciatica is commonly used in the literature but this term reflects a symptom of DLBP whereas other terms such as radiculopathy and nerve root pain reflect the cause of DLBP more accurately. The International Association for the Study of Pain (IASP 2013) have called for the use of sciatica as a term to be abandoned as it relates to an earlier era when pain in general was poorly understood. Although radiculopathy and nerve root pain are more specific terms, they can also be attributed to structures other than the lumbar IVD such as spinal stenosis or vascular issues. The variation in terminology surrounding the lumbar IVD and DLBP is further demonstrated by the IASP's Classification of Chronic Pain (IASP 2013) where there are five terms of DLBP listed with similar definitions (Lumbar discogenic pain, Internal disc disruption, Sprain of the Annulus Fibrosis, Prolapsed IVD and lumbar discitis). All five terms can only be confirmed via invasive procedures such as discography, local anaesthetic injections or needle biopsy. There are no

reliable or valid non-invasive clinical tests currently available that can diagnose each term.

For the purposes of this thesis and to aid readability, the term DLBP will be used throughout. The term "DLBP" within this thesis will encompass all the DLBP terms discussed previously, including the IASP terms, to reflect pain originating from within the IVD (such as internal disc disruption) and from outwith the IVD (such as mechanical effects or chemical mediators). It is acknowledged that this term may not be the optimal choice but in light of a lack of an available internationally recognised definition, it will provide consistency throughout the thesis. The range of terms available to describe DLBP highlights the need for international agreement to be reached in this area. By reaching a consensus, future research can then focus on homogenous groups of DLBP rather than on the varied inclusion criteria and definitions currently in use that include other structures or processes causing LBP with or without referred leg pain.

Table 1.2.1: Definitions of terms for Discogenic low back pain

Term	Definition	Symptoms
Sciatica	<p>"Pain in a distribution area of a lumbar nerve root, often accompanied by sensory and motor deficits" (Leinonen 2004).</p> <p>"symptoms of pain, tingling, and numbness which arise from nerve root compression or irritation in the lumbosacral spine and are felt in the distribution of the nerve root" (Koes et al 2007).</p> <p>"low back pain with pain radiating into the leg" (van der Windt et al 2010)</p> <p>"low back pain radiating to the leg" (Tubach et al 2004)</p> <p>"pain radiating to the leg, normally below the knee and into the foot and toes" (Konstantinou and Dunn 2008).</p> <p>Pain in the distribution of the sciatic nerve due to pathology of the nerve itself (Stafford et al 2007)</p>	<p>Typically extend to below the knee — from the buttocks, across the back of the thigh, to the outer calf, and often to the foot and toes (Koes et al 2007).</p> <p>"tends to approximate the dermatomal distribution of the nerve root affected (most often L5/S1) and is often associated with numbness or pins and needles in the same distribution...muscle weakness and reflex changes may also be present" (Konstantinou and Dunn 2008).</p>
Radiculopathy	<p>"loss of sensation, myotomal strength or muscle stretch reflex" (Leininger et al 2011)</p> <p>"spinal nerve root dysfunction causing dermatomal pain and parasthesia, myotomal weakness and/or impaired deep tendon reflexes" (Casey 2011)</p>	
Radicular pain	<p>"pain in the normal distribution of a spine nerve" (Leininger et al 2011)</p> <p>Pain perceived as arising in a limb or the trunk caused by ectopic activation of nociceptive afferent fibres in a spinal nerve or its roots or other neuropathic mechanisms (Stafford et al 2007).</p> <p>"spinal nerve root dysfunction causing dermatomal pain and parasthesia, myotomal weakness and/or impaired deep tendon reflexes" (Casey 2011)</p>	

1.3: Physiotherapy management

People with LBP and DLBP are routinely assessed and managed by physiotherapists in the UK and physiotherapy internationally accounts for the greatest proportion of direct costs for LBP (Foster et al 1999, Casserley-Feeney et al 2008, Dagenais et al 2008, Dagenais et al 2009). In Scotland, there are around 3000 referrals per month to NHS Physiotherapy out-patient departments for LBP (NHS QIS 2008). The initial physiotherapy assessment for LBP and DLBP patients consists of a subjective history from the patient and an objective assessment (Koes et al 2007, van der Windt et al 2010). At present, there are no individual clinical tests available that can accurately and reliably identify patients with DLBP. There is therefore a need for research to be targeted at this key sub-group in order to establish accurate assessments that can reliably identify patients with this condition. From this, further research can then be structured to evaluate and identify appropriate cost-effective management strategies.

1.4: Investigation of discogenic back pain

Current UK LBP guidelines state that imaging should not be used unless serious spinal pathology is suspected (such as cauda equina) or surgical intervention is planned (NICE 2009). Despite this guidance, within the literature, there is some debate around imaging for DLBP patients whose symptoms are not improving after 6 weeks.

Despite the advice against routine imaging, diagnostic imaging of LBP and DLBP is a common clinical investigation and MRI is recognised as an ideal tool for investigation of DLBP (Morishita et al 2008, Beric 2010, Roudsari & Jarvik 2010, Hancock et al 2011). MRI has been shown to be highly accurate for demonstrating abnormalities of the IVD and VEP (Alyas et al 2008, O'Neill et al 2008, Carrino et al 2009, Cheung et al 2009, Roudsari & Jarvik 2010). MRI can provide images with high quality resolution; it is non-ionising, and suitable for claustrophobic individuals (Jarvik and Deyo 2002, Westbrook and Kaut 2002). MRI is also ideally placed as the only non-invasive modality capable of imaging

the NP in terms of physiology, morphology and positional change which can infer the overall IVD behaviour (Fazey 2011).

Despite MRI providing highly detailed images, these images themselves may not provide a definitive answer or identify a specific structural cause of LBP or DLBP (Jarvik et al 2001, Chou et al 2009, Beric 2010, Roudsari & Jarvik 2010). Indeed, a high prevalence of IVD abnormalities has been demonstrated in asymptomatic individuals (Jarvik et al 2001, Takatalo et al 2009). However, it is recognised that there are no other diagnostic investigation tools currently available that can provide superior imaging for DLBP. Until such a tool is developed, MRI will continue to be acknowledged as the best diagnostic imaging tool for LBP.

Currently, routine MRI scans within the UK National Health Service (NHS) are performed with the patient in a supine lying position for all LBP MRI scans. This unloaded position has been suggested to contribute to the false positive and false negative rates reported for stenosis and IVD herniation (Alyas et al 2008). It has been noted that scanning patients in clinically significant positions (such as upright sitting/standing) would be of benefit in the overall assessment and management of patients (An et al 2004, Beric 2010).

1.5: Positional MRI

There have been many different developments in MRI scanning techniques and methods and one such development has been the introduction of positional "Upright" MRI scanning where patients can be scanned in sitting, lying and standing positions. The positional MRI (pMRI) (Upright MRI, Fonar Corporation, Melville, NY, USA) consists of a 0.6T field which is generated between 2 large magnets. A moveable bed/table lies between these magnets and can be positioned at any angle from the horizontal to vertical planes, enabling supine and standing positions. An MRI compatible seat can be attached to the bed/table allowing seated images to also be taken (Hirasawa et al 2007).

The great benefit of this type of system is that patients can be imaged in clinically significant positions. pMRI has been employed by researchers to demonstrate and investigate:

- the effect of diurnal variation on the IVD
- the effect of surgical interventions on the spine
- the effect of different postures on the spine
- to demonstrate findings not visible on conventional MR images such as reduced IVD height, disc bulging/herniation and spondylolisthesis (Weishaupt et al 2000, Bashir et al 2003, Muthukumar et al 2004, Siddiqui et al 2005, Karadimas et al 2006, Siddiqui et al 2006a, 2006b, Beastall et al 2007, Hirasawa et al 2007, Alyas et al 2008, Morishita et al 2008, Zou et al 2008, Kumar et al 2008, Beric 2010).

However, at the time of conducting this study, pMRI was only available within the UK at two centres and to the author's knowledge was only used for research and private patients. The author acknowledges that subsequent pMRI centres have now been established in England.

As yet, there are no studies that have reported the accuracy of pMRI for LBP, DLBP or changes in the IVD. The majority of support for pMRI in the literature is via pictorial reports, case studies, conference abstracts or retrospective studies. The results from these studies are limited due to small numbers, inclusion criteria variation, selection bias and interpretation bias. Therefore, despite the theoretical benefit and trend towards support for pMRI in the investigation of IVD pathology and DLBP, there is a need for more research to be focused on the use of pMRI for IVD imaging, as well as adequately powered diagnostic accuracy studies for DLBP.

Despite published articles on the spine using pMRI, there is minimal literature available that specifically investigates NP behaviour. As pMRI is ideally placed to enable visualisation and investigation of AF and NP behaviour in functional positions, there is a need for further research in this area to inform IVD behaviour awareness, DLBP understanding and development of further conservative management strategies. Therefore, this project will use pMRI to investigate the macroscopic behaviour of the lumbar IVD in asymptomatic and symptomatic DLBP subjects' in functional positions.

1.6: Structure of thesis

This chapter has introduced the proposed research project along with the background that supports it. The following section presents the research question, hypotheses, aims and objectives for this project. Thereafter, a detailed review of the current literature surrounding the IVD, DLBP and the investigation of DLBP via MRI and pMRI will be presented in Chapter 2. Chapter 3 will discuss the methods, study design and ethics of this project. Each phase of this project will then be presented as a separate chapter where the asymptomatic subjects (phase 1) will be Chapter 4, 3SPACE Fastrak™ (Phase 2) will be presented in Chapter 5 and the DLBP subjects (Phase 3) will be presented in Chapter 6. Chapter 7 will follow on from this to discuss the overall project, including limitations, and the implications for clinical practice. Chapter 8 will then present the conclusions of this thesis including key findings along with suggestions for further research.

This thesis is presented as a series of studies in order to answer the research question: How does the lumbar IVD behave in functional positions?

In this thesis it is hypothesised that:

- The lumbar NP will migrate posteriorly in flexed positions and anteriorly in extended positions in the sagittal plane.
- This pattern of NP migration will be demonstrated in asymptomatic subjects and those with DLBP.
- There is a relationship between the pattern of NP migration between different positions and three-dimensional spinal movement.

In contrast, the Null hypotheses would suggest that:

- The lumbar NP does not behave in a predictable pattern (i.e. migrate posteriorly in flexed positions and anteriorly in extended positions).
- This pattern of NP migration is not demonstrated in asymptomatic or DLBP subjects.
- There is no relationship between the pattern of NP migration between different positions and three-dimensional spinal movement.

1.7: Aims of research

The aim of the thesis was to explore the sagittal plane macroscopic behaviour of the lumbar IVD in functional positions such as standing, sitting and lying.

1.8: The objectives of this project were

1. To establish the intra-tester reliability of the Osiris software system in measuring the position of the five lumbar intervertebral discs' nucleus pulposus from sagittal and axial pMRI scans.
2. To establish the intra-tester reliability of the 3SPACE Fastrak™ system in measuring 3-dimensional movement of the lumbar spine in flexion, extension, bilateral side flexion in standing and sitting; and bilateral rotation in sitting.
3. To establish a database of the extent of migration of the Nucleus Pulposus of the five lumbar intervertebral discs in healthy asymptomatic subjects during different functional positions from pMRI.
4. To establish a database of the 3-dimensional magnitude of movement of the lumbar spine in healthy asymptomatic subjects performing functional movements using the 3SPACE Fastrak™ system.
5. To investigate if there is any relationship between 3-dimensional movement of the lumbar spine (3SPACE Fastrak™ system) and all sagittal plane lumbar NP migrations (pMRI) during functional movements and positions in healthy asymptomatic subjects.
6. To establish a database of the extent of sagittal plane migration of the NP of the five lumbar vertebrae in DLBP subjects during different functional positions from pMRI.
7. To compare the extent of sagittal plane migration of the NPs' of the five lumbar intervertebral discs of asymptomatic and DLBP subjects during different functional positions via pMRI scans.

Chapter 2: Literature review

2.1: Introduction

This thesis is focused on a specific sub-group of nonspecific low back pain (NSLBP) with a discogenic presentation as stated in Section 1.2 (pp. 4). For the purposes of this thesis the term DLBP will be used throughout. This chapter will consider the literature in regard to the lumbar IVD anatomy, mechanics and pathology. Subsequent sections will consider the literature in terms of LBP briefly and will then focus on the sub-group of DLBP. Conservative physiotherapy management of DLBP will be briefly considered for background information but surgical management of DLBP will not be considered as this is out with the scope of this thesis. Final sections will consider the literature in terms of the investigation of DLBP via MRI.

2.2: The lumbar intervertebral disc

As the aim of this thesis is to investigate lumbar IVD behaviour it is necessary to review the literature and background around the IVD. Therefore this section will review the literature on lumbar IVD morphology (including innervation, blood supply and nutrition), biomechanics, and consider the effect of degeneration on the IVD as well as pathological effects such as bulging, herniation and internal disc disruption. As this thesis is concerned with the macroscopic behaviour of the IVD, literature concerning cellular background is out with the scope and will only be considered briefly as required in order to set the scene.

The lumbar spine consists of five vertebrae with five IVDs in between. The lumbar vertebra are noted in the literature as L1, L2, L3, L4 and L5 (numbered from superior to inferior) and the IVD between each are noted as L1/2 (the IVD in-between L1 and L2), L2/3 (the IVD in-between L2 and L3), L3/4 (the IVD in-between L3 and L4), L4/5 (the IVD in-between L4 and L5), and L5/S1 (the IVD in-between L5 and the sacrum) (Adams et al 2006). This notation will be used throughout to refer to the relevant vertebral levels and IVD.

2.2.1: Intervertebral disc morphology

The IVD consists of two structural regions, the outer annulus fibrosis (AF) and the inner nucleus pulposus (NP) which are sandwiched between two vertebral end plates (VEP) (Adams et al 2006, Hughes et al 2012). The mean size of the lumbar IVDs have been reported to be 18.16cm² (L3/4), 20.14cm² (L4/5) and 18.23cm² (L5/S1) (Seidel et al 2008).

The AF consists of 10-25 layers of concentric lamellae which are rich in type I and type II collagen fibres (~80%) although type III, V, VI, IX and XI are also present (Adams et al 2006, Mwale et al 2008). The AF consists of approximately 50% water, proteoglycans (10% dry weight) and collagen (up to 70% dry weight) (Phillips and Laurysen 2010). The type I fibres tend to concentrate around the AF periphery with the type II fibres concentrating around the inner AF and NP (Adams et al 2006). The collagen fibre orientation alternates between lamellae but remains obliquely orientated (around 65° from the vertical plane) and parallel throughout the AF (Bogduk 2005). The alternate fibre direction arrangement between each lamellae (one layer slopes to the left, the next layer to the right and so on), creates a containment that prevents the NP seeping or bursting through (Adams et al 2006). This is a necessary and critical requirement to ensure the security of the IVD. The layers of the lamellae are well attached to one another via the inter-lamellar bridging matrix which provides strength and resistance to delamination (Schollum et al 2008, 2009, Gregory et al 2012).

This lamellar arrangement enables the IVD to sustain considerable compression loads and tension (such as sliding, twisting and distraction) in a range of directions (Adams et al 2006). The variety of collagen types and distributions throughout the IVD has been theorised by Adams et al (2006) to reflect their different mechanical functions. The outer AF functions as a strong ligament to resist excessive bending and twisting of adjacent VBs. The middle to inner lamellae behave like a fluid in young IVD but become more solid and fibrous with aging (around the age of 35 years) and so then resist compressive loading (Gregory et al 2012). In tension, the anterior AF is softer and weaker than the posterior and the inner AF is weaker again (Adams et al 2006).

The IVD is attached to the vertebral bodies via the superior and inferior VEPs. These are thin cartilaginous endplates covering the superior and inferior IVD surfaces (Adams et al 2006). The mean VEP areas have been reported for L3 to L5 to range from 15.06cm² to 17.49cm² (Seidel et al 2008). The VEP concavity is symmetrical in the coronal plane but demonstrates considerable variation in the sagittal plane (Lakshmanan et al 2012). Lakshmanan et al (2012) aimed to identify common morphological VEP shapes between L3 to S1 in 174 lumbar MRI scans from a digital archive of patients (aged under 60 years with Pfirrmann (2001) grade 1 & 2 only) (Section 2.2.9, page 27, discusses degenerative grading of IVDs). Their results demonstrated that the majority of lumbar VEPs are concave whilst the majority of sacral VEPs (84.5%) are flat. Oblong (uniform concavity) and ex-centric (concavity started after less curved or flat portion with an ex-centric apex) shapes were also defined. The ex-centric shape was more commonly seen in the lower lumbar levels.

Although similar to articular cartilage near its osseous junctions, the VEP is only loosely attached to the underlying bone. It relies on the hydrostatic pressure from the NP to hold it in place (Adams et al 2006). The VEP covers the majority of the corresponding vertebral body (VB) with only a narrow rim of bone, the ring apophysis, around the perimeter left free (Adams et al 2006). As a consequence, the outer AF (oAF) fibres (also called the ligamentous portion of the AF) attach directly onto the bone, and the inner AF (iAF) fibres attach onto the VEP (Phillips and Laurysen 2010). From this, the iAF fibres and the VEP therefore create a continuous "envelope" around the NP and as such the iAF has been referred to as the capsular portion of the AF (Adams et al 2006). The function of the VEP is to help to equalise the loading of the VB as well as to prevent NP migration into the VBs. A further function of the VEP is to act as a barrier to rapid fluid loss from the NP during sustained loading and so indirectly aids internal pressurisation of the IVD (Adams et al 2006).

The central NP consists of a rich semi-fluid proteoglycan (PG) gel and is 70-85% water, proteoglycans (50% dry weight) and collagen (less than 20% dry weight) (Adams et al 2006). This PG gel is able to attract and hold onto large quantities of water which "endows the NP with its hydrodynamic properties" (Adams et al 2006). These large PG molecules which hold onto the water in the NP also hinder the flow of other molecules through the matrix such as glucose and

water. Therefore there is a very slow fluid flow within the NP in reaction to mechanical loading (Adams et al 2006). The exact water content of the NP depends on factors including age, and loading history and it has a profound effect on the internal mechanics of the IVD. Any increase in water content increases the internal NP pressure which in turn resists IVD bulging, increases IVD height, and increases the IVD's resistance to bending (Adams et al 2006).

Compression of the NP causes the PG gel to spread out in a radial fashion. This is resisted by the surrounding AF but conversely, the NP expansion causes internal bracing of the AF that resists internal buckling of the lamellae (Adams et al 2006). Therefore the AF and NP work together to maintain the IVD stiffness against compressive loading, but they are still able to permit movement between vertebrae (Inoue & Espinoza Orias 2011). If the NP loses its PGs it can no longer hold water, and therefore the NP is unable to properly brace the AF. As a consequence of this, the IVD can no longer resist compressive loads and so becomes progressively compressed and narrowed under daily loading forces (Adams et al 2006). The water content in the NP enables it to deform easily and equalise any stresses applied to it. When rapid loading is applied, some parts of the NP can behave more like a viscoelastic solid and resist considerable shear stresses (Adams et al 2006). However, the tensile strength of the NP has never been reported in the literature to date. Under compression the AF is subject to high tensile stresses from the NP. Michalek et al (2012) have reported from bovine experiments that even without external loads there remain large circumferential residual stresses within the AF.

The NP has been considered in the literature to be a separate structure from the rest of the IVD components and defining the boundary between the NP, AF and VEP has been recognised as a challenge (Wade et al 2012). Wade et al (2011) demonstrated via novel VEP-NP-VEP loading experiments in ovine spines that the separate NP concept is incorrect. In fact, the NP has significant structural integration with the VEP and contains a coherent arrangement of collagen fibres that sit between the VEPs that reveal a load bearing ability (Wade et al 2011). In a recent study Wade et al (2012) have gone on to repeat the 2011 study methods in ovine IVDs, but with the aim of investigating the iAF-NP boundary. Their experimental results have identified that there is a subtle "structural gradation" between the iAF and NP rather than a distinct separation that infers a

tethered mobility to the NP. This in turn enables the NP the ability to support transverse loading which can be mechanically demonstrated as well as supporting physiological functions. The authors propose a structural model where the NP fibres “sweep in and align with the fibrosity ” of the iAF layers much like the mechanism reported by Pezowicz et al (2006) for the interlamellar layers within the AF. The subtle demarcation between the AF and NP also becomes increasingly difficult to identify with increasing age (Wade et al 2012).

The function of each IVD is to resist and transfer compressive loading while still allowing small movements between VBs such as bending as well as twisting and sliding (Gregory et al 2012). The movements are limited by the resulting tension that develops in the AF collagen fibres in the direction of the movement (Adams et al 2006). For example, flexion (in vivo and in vitro) has been shown to cause stretching of the posterior AF by 50% or greater (Adams and Hutton 1982). Each IVD is around 10mm in height and so collectively, the lumbar IVDs provide around 5cm to the length of the spine (Adams et al 2006). Due to diurnal effects (where during the day due to weight-bearing and the effect of gravity, IVDs loose water, but over night the IVD re-absorb water), individuals height increases by approximately 2cm overnight (Matsumura et al 2009).

During the day, upright postures, gravity and physical activity cause the volume and height of the IVD to reduce by approximately 20% (Adams et al 2006). During the night when the spine is unloaded by lying down, the IVD’s elevated internal swelling pressure soaks up water until it reaches equilibrium with external forces. This diurnal variation has been investigated by previous authors using different methods and will be discussed later in this thesis (see section 2.4.5.3, page 68).

The IVD has been shown to respond and adapt to loading and stretching as the NP cells proliferate and produce more collagen (Adams et al 2006). However, although IVDs can strengthen (PG content increases in proportion to subchondral bone thickness), it occurs more slowly than in bones. In addition, the IVD has demonstrated only a limited ability to heal after injury therefore this poses a challenge to clinicians treating DLBP (Adams et al 2006).

Investigation of IVD behaviour and function is challenging as cadaveric and animal experiments do not reflect accurately the functionally loaded IVD.

Seminal work by Nachemson and Morris (1964) aimed to address this by inserting pressure sensors into the L3/4 IVD of conscious volunteers in an effort to examine spinal compression. However, as the sensor remained insitu via a needle, this did not encourage normal or rapid movement behaviour in the volunteers. Adams et al (2006) in a summary of more recent research, suggests that current methods to estimate spinal loading may underestimate true loading by nearly a third.

Sustained loading of the IVD such as upright postures causes a gradual reduction in height (diurnal variation) which is caused by “creep” in the collagenous tissues (Roberts and Urban 2011). Creep occurs as a result of a sustained constant force that is applied to collagenous structures causing further slight movement to occur over time (McKenzie and May 2003). Creep causes elongation and rearrangement of collagen fibres and PGs with a loss of water from the tissue at the same time. Once the force applied to the tissue is released, the tissue begins to recover but at a slower rate than the initial deformation. The rate at which recovery occurs between the force application and removal is called hysteresis (McKenzie and May 2003).

IVD creep due to sustained loading over time is characterised by IVD deformation and fluid loss (Roberts and Urban 2011). Spinal creep has been associated with changes in visco-elastic tissue such as acute inflammation, microdamage and increased stretch (Solomonow et al 2003). The majority of creep is due to water loss, but approximately 25% is thought to be due to AF deformation, although this may be a secondary effect due to NP water loss (Adams et al 2006). In sustained flexed postures, spinal creep has been shown to increase the flexion angle by around 10% within 20 minutes (McKenzie and May 2003).

IVD creep has been used as an indirect method to quantify spinal loading, however comparisons between subjects is difficult because IVD creep rate depends upon numerous factors such as age, loading history, IVD hydration, degree of IVD degeneration, IVD area, and posture (Adams et al 2006, O’Connell et al 2011). However, even by acknowledging these factors, spinal compression does provide a measure of spinal loading over time. A general rule of thumb is that full recovery of the IVD occurs when the unloaded recovery

time is far longer than the loading time (O'Connell et al 2011). O'Connell et al (2011) used cadaveric upper lumbar spines (L1/2 & L2/3) to investigate the creep and recovery response to axial compression. Their results demonstrated that with short duration gradual loading (approximately 30 minutes) the IVD immediately recovered 70% of the displacement and recovered full stiffness and IVD height within eight hours. With rapid load applied over four hours the IVD recovered only 20% of the creep displacement and full recovery was predicted to take approximately 40 hours.

By applying these principles to DLBP patients, clinicians can advise patients regarding spinal loading and management of symptoms that are aggravated by sustained postures. However, there is a need to clarify this via further research into functionally loaded human *in vivo* IVDs.

2.2.2: Intervertebral disc innervation

There are a number of sources of innervation to each lumbar IVD and it has been recognised as an ongoing challenge to clearly identify the sensory and pain pathways in the IVD (Edgar 2007). The AF is supplied anteriorly and laterally by a fine network of nerves derived from the sympathetic trunks and its grey rami communicantes (Phillips and Laurysen 2010). Posteriorly, the AF is supplied via a network derived from the sinuvertebral nerves from the dorsal root ganglion (DRG) segmentally innervating each IVD as well as direct branches from the ventral ramus (Lotz & Ulrich 2006, Edgar 2007). Takahashi et al (2008) have demonstrated in rats however that the L5/S1 IVD can be innervated by the L2 DRG neuron. Other authors have also noted that there could be multi-level innervation of the lumbar IVDs (Prithvi Raj 2008, Takahashi et al 2008).

The outer third (especially the ligamentous portion) of the AF is richly innervated but this reduces until the inner third of the AF and NP are completely absent of nerve fibres (Edgar 2007, Dimitroulias et al 2010). The majority of AF nerve endings are free nerve endings which are thought to provide a nociceptive function. There are also encapsulated and complex unencapsulated nerve endings in the lateral superficial AF which are thought to play a proprioceptive role (Adams et al 2006, Edgar 2007). Nerve endings have also been

demonstrated in the sub-chondral bone of the VEPs and although their function is unknown it is thought they could have a nociceptive role (Adams et al 2006). Lotz & Ulrich (2006) have suggested that as the density of the VEP innervation is similar to that in the peripheral AF it is therefore an important source of DLBP.

2.2.3: Intervertebral disc blood supply

The lumbar IVD has no direct blood supply and is known as the “largest avascular structure in the human body” (Urban et al 2004, Arun et al 2009, Motaghinasab et al 2012). The blood supply is limited to tiny vessels from arteries that supply the adjacent VBs and a sparse capillary supply to the external AF surface (Palmgren et al 1999, Grunhagen et al 2006). The blood supply and therefore nutritional state of the IVD is inherently dependent upon the capillary bed design, porosity of the sub-chondral bone and optimisation of the blood vessel lumens (Benneker et al 2005, Grunhagen et al 2006).

2.2.4: Nutrition of the intervertebral disc

Lacking a direct blood supply, the main source of nutrition for the IVD is via diffusion (pumping effect/convective transport or concentration gradients) of solutes across the VEP and the AF periphery (Rajasekaran et al 2007, Hughes et al 2012). Solute of glucose and oxygen are transported into the IVD in this manner and waste products such as lactic acid and carbon are transported out in the same way. However, this process is slow and influenced by a number of factors such as PG density within the IVD, VEP permeability, IVD size, and solute molecular weight (Adams et al 2006, Motaghinasab et al 2012). IVD nutrition is aided by movement as this causes bulk flow of water and nutrients into and out of the IVD (Hadjipavlou et al 2008). Mechanical loading of the IVD can have contrasting effects on nutrition where the reduction in IVD height facilitates nutrient transport from the VEP to the centre of the IVD but the reduction in tissue fluid content affects metabolic rates and solute diffusion (Grunhagen et al 2006, Motaghinasab et al 2012).

Conditions due to pathology or aging affect the IVD blood supply and nutrition such as VEP calcification/sclerosis, arterial atherosclerosis and loss of density in the capillary network (Rajasekaran et al 2004, Benneker et al 2005, Grunhagen

et al 2006). Clinicians assessing DLBP patients will have information regarding this from their subjective history covering previous medical history and current medical history as well as current medications. Clinicians can then build up an informed background of the IVD initial health from their assessment as well as the overall patient health.

Urban et al (2004) carried out a review of IVD nutrition especially in regard to IVD degeneration. The authors reported that nutrients to the IVD centre would need to diffuse up to 7-8mm in an adult IVD. As a result there are wide variations in concentration of oxygen, glucose and lactic acid across the IVD, with the NP centre having the lowest concentration of oxygen and glucose but the greatest concentration of lactic acid. The concentration levels depend upon a balance between cellular demand and diffusion which can be affected by VEP calcification or increases in nutritional demand. The review concluded that poor nutritional supply can lead to IVD degeneration via cell death, matrix production loss and increased matrix degradation.

Arun et al (2009) demonstrated the *in vivo* effect of loading on diffusion in human IVDs. Forty normal IVDs in eight healthy volunteers had serial post-contrast 3.0T supine MRI performed in two phases (supine unloaded and loaded) over successive time points. The results demonstrated that sustained supine loading (to mimic erect spinal loading) for 4.5 hours reduced small solute transport into the centre of the IVD that required 3 hours of recovery positioning for the loaded IVD diffusion rate to catch up to the unloaded IVD. The authors also noted that there were regional differences in diffusion between the outer and inner IVD as well as in loaded and unloaded conditions. The authors concluded that sustained mechanical loading may impair nutrient and metabolite transport into and out of the IVD, possibly pre-disposing to degeneration.

2.2.5: Intervertebral disc mechanics

When discussing compression within the spine, the definition of Adams et al (2006) will be applied throughout: "it is conventional to speak of the compressive force as being that force which acts down the long axis of the spine, at 90° to the mid-plane of the intervertebral discs". Stress profiling has

clearly revealed the internal mechanics of the IVD via *in vivo* and *in vitro* methods (Adams et al 2006). Pressure transducers inserted through the AF into the IVD along its mid-line have been shown to be accurate other than at the outer 2-4mm of the AF (as it behaves as a fibrous solid therefore preventing reliable recordings to be obtained) (Adams et al 2006).

Direct axial compression causes increased NP pressure which then causes increased tensile stress on the AF (Barbir et al 2011). This "hoop" stress in the AF reduces from the inner to outer lamellae. The AF also directly resists compression which causes it to bulge outwards with a corresponding reduction in height. This in turn causes the VEP to come closer together but this is limited by the fluid filled NP lying in-between. Therefore the central VEP areas bulge into the corresponding VBs. It has been demonstrated in the literature that increased NP pressure will cause VEP failure before any macroscopic AF damage is observed (Veres et al 2008).

Veres et al (2008) investigated the effect of increased NP hydrostatic pressure on AF disruption in a small sample of 12 motion segments from four ovine lumbar spines. Despite the small numbers and the use of sheep spines which limited generalisation, the results demonstrated that the posterior AF wall is the most susceptible to high levels of NP pressure. In addition they reported the posterior oAF lamellae to have a weaker interlamellar adhesion than the mid-AF lamellae.

Some of the compression effects on the IVD have been demonstrated using cadavers. Around 2kN of compression stretches the surface collagen fibres by <2% and causes the IVD to bulge by ~0.4-1.0mm. Bulging varies around the IVD with the greatest observed in the anterior or posterolateral AF. Compared to a preload of 250N, a compressive force of 4.5kN reduces the height of a motion segment by 0.9mm, but the NP height loss is only 50% of this, so each end plate must bulge into its VB by ~0.25mm. VEP bulging has been reported to reach 0.8mm before failure (Adams et al 2006). Compression response by an IVD depends upon its precise height and shape: IVDs with a higher ratio of height/area will exhibit higher tensile stresses in the oAF, and more radial bulging, for the same applied compressive force. This makes it difficult to

extrapolate mechanisms of IVD structural mechanical failure from one spinal level to another, or from human to animal IVDs (Adams et al 2006).

Flexion of an IVD occurs around a centre of rotation close to the NP with a corresponding compression of the anterior AF and stretching and thinning of the posterior AF. Posterior AF tension increases the NP hydrostatic pressure (Adams et al 2006). Adams et al (2006) have summarised the effect of flexion on the IVD as follows:

- Anterior AF height reduces by 25-35%
- Anterior AF bulges outwards by around 0.1mm/degree movement
- Compressive stress concentrations can appear or grow in anterior AF matrix
- Posterior AF flattens and stretches by 50-90% in full flexion
- Crimped collagen fibres can be stretched by 10-15% before failure
- Direct measurement of IVD surface strain indicates fibre strains of only 0.7% per degree of flexion

These high vertical deformations of the AF can be achieved only by removal of the radial bulge, and by reorientation of some of the fibres within each lamella. The elastin network of the IVD may help return collagen fibres to their original orientation (Adams et al 2006). During short periods of flexion, the fluid content and volume of the posterior AF must remain constant therefore the increased stretch is balanced by a thinning of the radial bulge. Degenerate IVDs with their reduced water content and increased stiffness cannot spread load evenly between adjacent VBs during flexion and extension. Therefore, a high compressive strain develops in the AF anteriorly during flexion and posteriorly during extension (Adams et al 2006). It is thought that similar mechanisms also operate when the IVD is bent sideways in lateral flexion. In rotation, tension is created in half the AF collagen fibres while the other half slacken and inter-laminar shear forces are created in the AF (Barbir et al 2011). In theory, it is thought that only 3° of rotation occurs in the lumbar IVDs but this doesn't account for the AF radial bulge and the collagen fibre crimp (Adams et al 2006). Rotation of cadaveric IVDs by 6° by a 15Nm torque stretches surface collagen fibres by 7% and annular bulge is reduced by 0.2mm. Torsion raises NP

pressure due to the tension within the oblique collagen fibres causing simultaneous compression. (Adams et al 2006).

The VEP is the weakest area of the lumbar spine and when compressive forces reach their maximum it is usually the VEP that displays the first signs of damage (Adams et al 2006). It has been suggested however, that the VEP requires to be thin/weak in order to enable the diffusion of nutrients into the IVD (Adams et al 2006). Failure of the VEP causes bulging of the adjacent NP into the VB that is best viewed on MRI (Takahashi et al 1995, Alyas et al 2008, Carrino et al 2009). Intra-osseous herniations of the NP into the VB are called Schmorl's nodes whereas Modic changes (MCs) refer to biological reactions to VEP fractures (Adams et al 2006). Damage to the VEP can also threaten the adjacent IVDs in that healing of the damaged bone can block the pathways essential for nutrient transport/diffusion (Adams et al 2006).

2.2.6: Posture and the intervertebral disc

Small postural changes have been shown to cause changes in compressive stress within the AF. In a neutral posture (i.e. no flexion), the IVD has a fairly constant compressive stress throughout apart from a small peak in the posterior AF (Adams et al 2006). In erect standing (2° extension for a motion segment); this peak increases whereas flexed postures usually distribute the stresses uniformly across the IVD (Adams et al 2006). In full flexion stress peaks appear in the anterior AF but they are rarely as high as those in the posterior AF in extension unless the IVD displays severe degeneration and narrowing (Adams et al 2006).

The NP is also affected by posture. During a compressive force of 500N, the NP pressure is 40% less in 4° extension than in a neutral posture. Adams et al (1994) suggest this is due to the neural arches from adjacent vertebrae approximating and so resisting more of the force. However, in full flexion, NP pressure increases by 100% due to stretching of the neural arch ligaments causing a compression of the IVD (Adams et al 2006). A young, healthy, well hydrated IVD behaves like a "bag of fluid" and is therefore less affected by posture changes. However, degenerated IVDs are less able to distribute

compressive forces evenly and so the effects of posture become magnified where minimal bending can greatly increase forces (Adams et al 2006).

With loading in different positions (such as flexion), the NP will normally migrate/deform away from the compressed area (Adams et al 2000, Fazey et al 2006, Kolber and Hanney 2009). In the literature there has been some contradiction to this however, with some authors reporting that NP migration/deformity is in the opposite direction (Fennell et al 1996, Edmondston et al 2000). These results have to be viewed with caution due to a lack of methods available to carry this out in humans in different positions reflecting normal function. Full discussion of sagittal IVD behaviour will be presented in the MRI section that follows (Section 2.4.5, page 65).

As lateral flexion is not a prime functional movement in the lumbar spine like flexion or extension, it has less research investigating it. However, as the side to side diameter of the IVD is around 50% greater than the sagittal diameter, it is important to appreciate that lateral flexion will then cause 50% more vertical deformation of the AF than in the sagittal plane (Adams et al 2006).

Posture has been shown to have an effect on IVD transport of metabolites in both diffusion and fluid flow (Adams et al 2006). Flexion causes the anterior AF to compress by 35% and the posterior AF to stretch by 60% (Adams and Hutton 1982, Pearcy & Tibrewal 1984). In order to keep a constant tissue volume, the thickness of the anterior and posterior AF must increase and decrease respectively. Therefore flexion enhances metabolite diffusion into the posterior inner AF as well as stretching the posterior AF so that a larger amount of metabolites can diffuse into the inner posterior AF (Adams & Hutton 1986). Correspondingly, flexion causes reduced diffusion into the anterior AF but studies have shown that this area is the last area of the IVD to demonstrate degenerative changes (Adams & Hutton 1986, Adams et al 2006).

Posture also affects fluid flow across the IVD. Cadaveric experiments have demonstrated that fluid flow into and within the IVD is maximised when alternating between flexion and extension (Ferguson et al 2004, Adams et al 2006). This is in accordance with current NSLBP guidelines that advocate keeping active as a management strategy for patients. For DLBP patients, it can be theorised from the literature that movement and changing postures can

benefit the IVD in terms of improving diffusion which will maximise healing and nutrition. However, due to the effects of creep and compressive loading, the time spent in different postures and moving about as well as being upright requires clarification via further research.

A recent study by Passias et al (2011) investigated segmental ROM in 10 subjects with clinically and radiographically confirmed L4/5 and L5/S1 DLBP. Their results demonstrated that the L3/4 segment demonstrated the greatest ROM suggesting that the adjacent segment develops hypermobility as a compensation or result of the changes in those segments.

2.2.7: Classification of intervertebral disc pathology

Due to the widespread variations in terminology and definitions around the IVD, there have been efforts made over the years to develop detailed IVD pathological definitions that can be adopted internationally. Fardon and Milette (2001) reported the work of a joint American task force (North American Spine Society (NASS), American Society of Neuroradiology and American Society of Spine Radiology) to develop diagnostic definitions for imaging studies for IVD pathology that clarified earlier work by NASS in 1995. For the purpose of this thesis, the definitions described in this article will be adopted throughout. Table 2.2.1 displays some of the key definitions applicable for this thesis, which has been adapted from Fardon & Milette (2001).

Table 2.2.1: Intervertebral disc definitions (adapted from Fardon and Milette 2001).

Terminology	Definition
Annular tear/fissure	"Separations between annular fibres, avulsion of fibres from their VB insertions, or breaks through fibres that extend radially, transversely or concentrically, involving one or many layers of the annular lamellae"
Degeneration	"may include any or all of real or apparent desiccation, fibrosis, narrowing of the IVD space, diffuse bulging of the annulus beyond the IVD space, extensive fissuring, and mucinous degeneration of the annulus, defects and sclerosis of the VEPs and osteophytes at the vertebral apophyses"
Herniation (can also exist as protrusion, extrusion, sequestration and intravertebral/Schmorl's node)	"Localised displacement of IVD material beyond the limits of the IVD space. The material may be nucleus, cartilage, fragmented apophyseal bone, annular tissue, or any combination thereof. The IVD space is defined craniad, and caudad by the VEPs and peripherally by the ring apophyses, exclusive of osteophytic formations."
Bulging	"refers to an apparent generalised extension of IVD tissue beyond the edges of the apophyses".

2.2.8: The intervertebral disc as a pain source

The IVD has been recognised as playing a key role in the development of non-specific low back pain and DLBP (Schaffer et al 2009, Miyagi et al 2012).

However, the pathophysiologic mechanisms behind this have still to be fully understood and demonstrated in the literature (Olmaker et al 2002, Takahashi et al 2008).

It is thought that the IVD can contribute to DLBP via two main routes: chemically mediated inflammation or by mechanical nerve root (NR) compression (Olmaker et al 2002, Leinonen 2004, Stafford et al 2007). Degenerative changes, and internal disc disruption (IDD), can lead to the formation of AF fissures enabling inflammatory mediators to travel through the IVD and cause excitation of the nociceptive nerve fibres in the outer third of the

AF with subsequent DLBP felt (Schaffer et al 2009). NP prolapse or herniation through the AF fissures also cause inflammation of the nerve roots and subsequent pain (Schaffer et al 2009). Mechanical NR compression can be caused by many structures but a common one is prolapsed or herniated IVDs (Schaffer et al 2009). The mechanical compression causes a restriction in the neural blood flow, increased neural pressure and nerve fibre deformation which is in turn thought to lead to pain (Schaffer et al 2009). Although it has been shown that compression of nerves does not always result in pain (Kjaer et al 2005), it has been suggested that sudden onset, such as an acute prolapsed IVD, can trigger this effect (Schaffer et al 2009).

It has been shown that a key event in the development of DLBP is the release of biochemical substances from the NP that causes the inflammation and an autoimmune response especially due to IVD herniation (Karppinen et al 2001, Ahn et al 2002, Geiss et al 2007).

It is thought that in-growth of nerve fibres through radial tears into the inner IVD may be a cause of DLBP (Hyodo et al 2005, Edgar 2007, Takahashi et al 2008) but it has only been observed in painful IVDs. A recent PhD study (Stefanakis 2011) reported that in-growth of nerve fibres and blood vessels occurred as a result of high stress gradients causing progressive AF disruption and fissures in the IVD. The author went on to suggest that the most likely site of DLBP occurred in the middle to oAF due to concentrations of nerves and blood vessels and DLBP was related to attempted healing by the IVD rather than degenerative changes in the NP. While these findings are of interest, they must be viewed conservatively as the study involved stress profilometry of cadaveric IVDs.

As a response to nerve injury or inflammation, it has been suggested that peripheral or central sensitisation could also be involved in the generation of DLBP (Brisby 2006, Edgar 2007). This is where nuclear material that escapes the AF confinement irritates the nerve root and nerve endings which in turn cause an amplified response by the nerve endings and nerve roots to normally innocuous stimuli.

Previous research of injury models involving the IVD has used animal studies (such as rats, mice and rabbits) to replicate human IVDs. Although animal

studies can investigate the IVD, a key limitation of this method is the lack of compression force that is inherent in upright human spines (due to weight-bearing/body weight and gravity). There have also been discrepancies reported between animal and human IVD studies where inflammatory mediators settle to pre-injury levels in animal studies yet can continue to cause pain in human studies (Burke et al 2002, Miyagi et al 2011). Miyagi et al (2012) have suggested that long lasting inflammation can be a cause of DLBP in humans. A recent study by Miyagi et al (2012) has aimed to address previous limitations by investigating IVD injury and compression in rats over an eight week period. Their results demonstrated that IVD injury alone caused a transient increase in IVD inflammatory mediators with a long-lasting increase in dorsal root ganglion (DRG) neuropeptides. IVD injury and compression however, caused long-lasting increases after an initial delay in both inflammatory mediators and neuropeptides. In addition, the IVD dynamic compression induced on-going nerve injury with regeneration of the IVD afferent fibres. The authors went on to suggest that the long-lasting increase in inflammatory mediators can lead on to neuropathic pain pathogenesis and so DLBP may well be a mix of inflammatory and neuropathic pain.

2.2.9: Intervertebral disc degeneration

IVD degenerative changes are a normal part of aging but the factors instigating this and aiding the progression of the changes are still unclear (An et al 2004, Hadjipavlou et al 2008). Even though IVD degeneration is thought to precede or be associated with DLBP, it is unclear how much the degenerative process contributes as a pain source as degenerative changes can commonly be present without pain (An et al 2004, Battie et al 2004, Veres et al 2008, Phillips & Laurysen 2010, Hughes et al 2012). It is recognised that the IVD degenerative cascade has a multifactorial aetiology (Hadjipavlou et al 2008). Columbini et al (2008) have defined IVD degeneration as "an abnormal cell-mediated response to progressive structural failure". Factors involved in this process are thought to be age, mechanical loading, biochemical issues, smoking, genetic factors, aortic atherosclerosis and ethnicity (Battie et al 2004, Stokes & Iatridis 2004, Hadjipavlou et al 2008, Veres et al 2008, Kauppila 2009, Siemionow et al 2011).

It has been suggested that degeneration at the lower two lumbar IVD levels is more common and severe (Hammer 2002, Hadjipavlou et al 2008) and a recent review of 1712 IVDs has demonstrated a significantly faster rate of degeneration at the L5/S1 level, especially in those under 40 years of age (Siemionow et al 2011). This has been postulated as occurring due to the high compressive and shear forces acting at the lumbosacral junction.

Battie et al (2004) have suggested that heredity can explain over 70% of the variance in IVD degeneration. Boos et al (2002) in a large histologic study using cadaveric and surgical specimens have demonstrated that a diminished blood supply to the VEP leads to tissue breakdown that begins in the NP as early as the second decade. Their results also supported the concept of a nutrition related initiation of IVD degeneration which has been demonstrated in the literature (Benneker et al 2005). Brisby (2006) agrees with a nutritional initiation factor as well as suggesting IVD mechanical injury as an additional initiating factor.

IVD degeneration is associated with pathologic and macroscopic changes in both the biochemistry and structure of the extracellular matrix; loss of IVD hydration; reduced IVD height; increased AF lamellar disorganisation/delamination; reduced cell density; loss of PG content and changes in PG structure; osteophyte formation; irregular IVD contour; and VEP erosion (Setton & Chen 2004, Brisby 2006).

Degenerative changes in the IVD biochemical balance (structural and composition changes in matrix, elastin and PGs) lead to considerable biomechanical and kinematic effects which are characterised by reduced NP osmotic pressure, changes in ROM, reduced neutral zone as well as altered creep behaviour (Tanaka et al 2001, Setton and Chen 2004, Little et al 2007, Barbir et al 2011, O'Connell et al 2011). However, the alteration in creep behaviour has not yet been fully established in the literature.

A single internationally accepted IVD degeneration definition has not yet been established in the literature due to inconsistencies in measurements, their attributed grades and reliability (Adams et al 2006, Battie & Videman 2006, Hadjipavlou et al 2008, Phillips & Laurysen 2010). The preferred method for degeneration evaluation in the literature is via MRI (Battie & Videman 2006).

Researchers and clinicians have a variety of scales/methods available via MRI to categorise degeneration such as the Thompson scale (1990) which grades IVD degeneration based on gross morphology on a five point scale (Grade 1 indicates a completely healthy IVD and Grade 5 indicates the most severely degenerated IVD) or the Pfirrmann scale (2001) which also uses a five point scale (Grade I indicates a homogenous bright white IVD with clear distinction of the AF and NP and Grade V indicates an inhomogenous black IVD with lost distinction of the AF and NP) on axial T2 weighted MRI scans. The Pfirrmann scale is presented in Table 2.2.2.

Table 2.2.2: Pfirrmann scale for magnetic resonance imaging scans (from Pfirrmann et al 2001).

Grade	Structure	Distinction of NP and AF	Signal intensity	Height of IVD
I	Homogenous, bright white	Clear	Hyperintense, isointense to CSF	Normal
II	Inhomogenous ± horizontal bands	Clear	Hyperintense, isointense to CSF	Normal
III	Inhomogenous, gray	Unclear	Intermediate	Normal to slightly decreased
IV	Inhomogenous, gray to black	Lost	Intermediate to hypointense	Normal to moderately decreased
V	Inhomogenous, black	Lost	Hypointense	Collapsed IVD space

Key: NP = Nucleus Pulposus, AF = Annulus Fibrosus, IVD = intervertebral disc, CSF = cerebrospinal fluid

Adams and colleagues (2006) have reported stress profiles for IVDs of all levels of degeneration:

- Grade 1 IVDs are young and healthy and display approximately equal vertical and horizontal compressive stresses that do not vary with position across the IVD.
- Grade 2 IVDs are mature (typical of non-degenerate IVDs over 35 years) which is reflected in the hydrostatic central region shrinking in area to

that of the NP. Small stress concentrations can be observed in the AF usually posterior to the NP.

- Grade 3 IVDs are usually moderately degenerated, which is reflected in an irregular stress profile indicating variable resistance to compression from a disrupted fibrous matrix where the central hydrostatic region is small or absent.
- Grade 4 IVDs are severely degenerated and characterised by highly irregular and variable stress profiles and an overall reduction in compressive stress. This suggests they are shielded from compressive loading by adjacent structures such as the neural arch or osteophytes.

The majority of the age-related changes in the IVD occur within the NP and VEP (Adams et al 2006). With increasing age, the PG and water content of the IVD decrease, especially within the NP (Adams et al 2006, Inoue & Espinoza Orias 2011) as well as increasing collagen content with the iAF type II fibres replaced by type I. Within the VEP, similar changes occur causing calcification of the cartilage which can compromise the nutritional supply (Benneker et al 2005, Adams et al 2006). The VEP changes include local and generalised changes such as Schmorl's nodes, modic changes, irregularity and sclerosis (Fazey 2011). Modic changes (MC) are classified into three levels which reflect the progressive nature of the bone marrow changes (Modic & Ross 2007).

The water and biochemical changes that occur with aging are the main reason for the changing appearance of IVDs on MRI. These biochemical changes with aging also cause functional changes where the NP becomes dry and stiff, (losing pliancy, volume and hydrostatic capability) and the inner AF which exhibits hydrostatic pressure is reduced so that increased compressive load-bearing is taken up by the AF (especially the posterior elements) (Adams et al 2006, Fazey 2011, Inoue & Espinoza Orias 2011). Due to these changes in load mechanics in the initial stages of degeneration, the IVD becomes unstable (in which a motion segment exhibits an abnormal magnitude or direction of movement when subjected to a normal load, Adams et al 2006) although other authors have contradicted this effect (Inoue & Espinoza Orias 2011, Kettler et al 2011). A possible reason for these conflicting results is that there has been a lack of tools

available in which to study this phenomenon accurately. With progressive degeneration, the IVD stabilises again (Kirkcaldy-Willis & Farfan 1982). IVD instability has been suggested as a “transitional” stage in degeneration (Adams et al 2006) where initial changes lead to instability but subsequent degenerative changes (such as osteophyte formation and IVD resorption) can cause reduced spinal movement. From the literature, all attempts to investigate IVD instability have involved cadaveric or laboratory based studies. There is still a need to establish this phenomenon *in vivo* using appropriate tools.

The AF tensile properties are slightly affected with age, yet it has been shown that IVD height does not generally decrease. However, this is dependent on the part of the IVD measured. Overall, it is the AF height that determines the pedicle loading and degenerative changes can cause gross collapse of the AF (Adams et al 2006). Adams et al (2006) have stated that flexion and extension both decrease by approximately 20% between 20-55 years of age, although extension has a tendency to be lost in the older ages.

Iatridis et al (2007) have reported variations in the PG content across different planes in mild to moderately degenerated IVDs. Their results indicated that sagittal and coronal variations of PG content were different and there was no uniform PG content within the NP. The largest content of PG was found in the NP and the lowest in the oAF with posterior areas demonstrating greater concentrations than anterior. In the axial plane, the greatest PG content was shown to be in the central region. However, only nine older L2/3 and L3/4 IVDs were dissected from cadavers and analysed therefore results cannot be generalised to reflect the entire lumbar spine IVDs.

In an effort to identify age related changes of the extracellular matrix (ECM) in the AF & NP, Singh et al (2008) examined forty-six normal IVDs. These samples were obtained from T11-L5 of human donors aged 32-80 years. All IVDs were classified as normal if graded as 1 or 2 on the Thompson scale (Thompson et al 1990) on sagittal MRI scans prior to undergoing chemical assay. In total only 24 of the 46 IVDs were analysed. No information was provided as to which IVD level was included or any previous medical history for inclusion purposes. Analysis separated the IVD into the outer AF (oAF), inner AF (iAF) and the NP as the authors felt that it was increasingly apparent that the IVD must be analysed

as three separate compartments. The results demonstrated total PG and collagen contents in both the AF and NP consistently decreased with ageing. However there was variation in the concentrations of small PGs. In the oAF decorin levels decreased (it was thought that decorin is part of the repair process following tissue damage and so its loss may trigger age-related tissue degeneration), but biglycan (unknown role in the regulation of the ECM) and fibromodulin (implicated as a factor in the degenerative cascade where fragmentation and release of this small PG elicits an inflammatory response) levels increased with age. In the iAF and NP, biglycan increased significantly with age. The functional significance of these changes is still to be demonstrated however.

A recent biomechanical study investigating the VEP strength in degeneration (Hou & Yuan 2012) used 120 VEPs from 12 cadavers (mean age 73.8 years). The authors reported a statistically significant difference ($p < 0.05$) in that the periphery of the VEP is stronger than the centre, especially the posterolateral areas in front of the pedicles. They also reported a negative correlation between disc degeneration and failure loads of the VEP ($p < 0.01$). With increasing IVD degeneration, there was an overall loss of VEP strength demonstrated although the periphery was still the strongest. A limitation of this study was the lack of prior power analysis and also the use of radiographs (X-rays) to establish IVD health at inclusion. It has been shown that x-rays are not the optimum choice for investigation of IVDs and so perhaps the use of MRI to categorise IVD health would have been a better option.

A common feature of IVD degeneration is the formation of clefts between AF lamellae which have been suggested to indicate local delamination and a break down in the complex inter-lamellar bridging matrix (Schollum et al 2008, Inoue & Espinoza Orias 2011). On the whole the tensile strength and elastic response of the AF reduces with increasing age and degeneration (Adams et al 2006, Inoue & Espinoza Orias 2011). A recent study by Gregory et al (2012) has investigated the mechanical properties of the inter-lamellar matrix of the AF in 17 human IVDs using a 180° Peel test. The superficial AF lamellae were shown to be statistically stronger (33%) than the deeper layers and the authors suggested that delamination and herniation may progress more easily in the deeper layers.

In degenerative and painful IVDs nerve fibres have been shown to extend farther into the AF by as much as a third (rather than the 3mm expected in healthy IVDs) in around 50% of subjects (Edgar 2007). This occurrence has been suggested to be as a result of granulation tissue growing into the degenerated IVD (Brisby 2006, Edgar 2007). However, Nerlich et al (2007) have demonstrated that vascular in-growth deeper into the AF does not occur in degeneration.

During aging, cellular senescence can compromise the normal turnover of matrix components, leading to "progressive tissue deterioration" (Columbini et al 2008). IVDs demonstrate degenerative changes relatively early in life. Cellular senescence has been linked to degenerative changes in other connective tissues such as OA. Roberts et al (2006) investigated the degree of cell senescence in different regions of IVD from patients with herniated IVDs (n=25), DLBP (n=25), spondylolisthesis (n=2), scoliosis (n=6) and cadaveric samples (n=4). There were significantly more cell senescence markers in herniated IVDs than the others. There was more senescence of cells in the NP compared to the AF and in herniated IVDs a higher proportion of cells in cell clusters. The authors concluded that the study demonstrated an increased degree of cell senescence in herniated discs, particularly in the NP where cell clusters occur.

2.2.10: Internal disc disruption

Internal disc disruption (IDD) is considered by some to be the pathological basis for DLBP (Adams et al 2006). IDD is characterised by internal architectural disruption with radial fissures forming from the NP to the oAF while the outer IVD perimeter remains intact (Fardon and Milette 2001, Adams et al 2006, Veres et al 2008). It is thought that the further the fissures extend it is more likely that the IVD will be painful (Adams et al 2006). IDD can be diagnosed via Computed Tomography-discography (positive discography and radial tears on CT) and the presence of high intensity zones in the posterior AF on magnetic resonance imaging (Adams et al 2006). A high intensity zone is a radial fissure that has circumferentially extended between the outer AF laminae (Adams et al 2006). It is thought to be highly predictive of the affected IVD to be painful and is thought to account for 30-50% of patients with chronic LBP (April & Bogduk

1992, Ito et al 1998, Veres et al 2008). Although IDD can be detected, there is debate around the cause with VEP fracture, an inflammatory reaction or alteration of the NP pH causing NP matrix degradation with its associated reduction in load-bearing (Adams et al 2006). The radial fissures are then thought to develop due to IVD mechanical stress or peripheral extension of the NP degradation. The IVD becomes painful as inflammation is present around the peripheral end of the radial fissure and there is increased pressure on the remaining intact lamellae of the outer AF (Adams et al 2006). Adams et al (2006) have postulated that "IDD is an acquired lesion most likely due to fatigue failure of the VEP".

2.2.11: Intervertebral disc prolapse/herniation

In contrast to IDD, where the AF remains intact, does not bulge outwards and no nuclear material extends beyond the IVD perimeter, prolapse of the IVD involves annular and nuclear material extending beyond the IVD perimeter (Adams et al 2006). The NP can extend through radial fissures in the AF. The prolapse is said to be contained if a layer of AF or the posterior longitudinal ligament still cover it (Adams et al 2006). It is called an extrusion if it breaches the covering layer and if the prolapsed material loses contact with the material still contained within the IVD it is called a sequestered fragment (Adams et al 2006, Veres et al 2009). Protrusions can occur with or without nuclear involvement. Herniation routes commonly occur in the central posterior, paracentral posterior and posterolateral annulus and may track superiorly, inferiorly or at mid-disc height. Herniated IVD material can include the NP, AF and VEP, alone or in combination (Veres et al 2009).

In the herniated or extruded IVD, the NP has gone through the ruptured AF. IVD herniation can cause mechanical compression of the nerve roots and chemical irritation mainly by activation of inflammatory processes (Leinonen 2004). Tumour necrosis factor-alpha and several other cytokines appear to be clearly associated with the inflammatory process in sciatica (Leinonen 2004, Phillips and Laurysen 2010).

Veres et al (2009) investigated the effect of flexion on the AF's ability to resist rupture during hydrostatic loading. The authors acknowledge that a flexed position has a drastic effect on IVD rupture due to hydrostatic overloading. Forty two ovine motion segments were each flexed to 7° or 10° while each NP was gradually injected with a gel until failure occurred. Subsequent microcomputed tomography and microscopy identified that flexion promoted radial rupture, limited circumferential disruption, and made the VEP junction vulnerable to failure. The authors also suggested that flexion played a developmental role in central posterior radial ruptures

The natural course of the herniated NP is to have spontaneous resorption. This is thought to occur via an inflammatory reaction in the outer most layers of herniation, with macrophages as the predominating cellular population. Recently, the molecular mechanisms of this phagocytic process have been clarified. Rim enhancement around the herniated disc in contrast-enhanced MRI is thought to represent a neovascularised zone with macrophage infiltration, which has an essential role in phagocytosis and herniation regression (Autio et al 2006).

2.2.12: Summary

This section has presented a review of the IVD and its role in DLBP. It has also demonstrated that the majority of research on the healthy, degenerate and pathological IVDs relies on laboratory, animal and cadaveric studies. While these studies are of interest and add to the body of knowledge, there remains a need to investigate the healthy and pathologic IVD using appropriate tools that can reflect normal function and loading of the spine. This project will address this by investigating macroscopic IVD behaviour in healthy subjects and those with discogenic LBP in normal loaded positions such as standing, sitting and lying.

2.3: Discogenic Low Back Pain

2.3.1: Low Back Pain - the size of the problem

Low back pain (LBP) is a problem in society and has been noted in literature from earliest times. In Greece, Hippocrates and colleagues were some of the first authors to document the existence and treatment of LBP but it has also been noted in early texts from other Western nations (Chedid & Chedid 2003, Karampelas et al 2004).

Low back pain has been defined as "pain, muscle tension or stiffness localised below the costal margin and above the inferior gluteal folds, with or without leg pain (sciatica)" (van Tulder et al 2002, Manek & MacGregor 2005, Koes et al 2006).

Low back pain is a common condition in developed nations with up to 80% of society experiencing back pain at some point in their lives (Andersson 1999, Maniadakis & Gray 2000, Manek & MacGregor 2005, Koes et al 2006). The yearly prevalence for LBP has been reported to be between 15-45% in adults (Andersson 1999) and around 36-37% of the population in the UK (Maniadakis & Gray 2000). Prevalence has been defined as measuring the "proportion of the population that experiences LBP at any specified point or in a past period such as one month, one year or a lifetime" (Manek & MacGregor 2005). Prevalence of LBP has been shown to increase with age up to around 65 years with men and women equally affected (Maniadakis & Gray 2000, ARMA 2004, Mortimer et al 2006, NHS QIS 2009). The most common age for LBP has been reported as between 35 to 55 years of age (Andersson 1999) although more recently in Scotland this has been reported as slightly older, between 41 to 64 years of age (NHS QIS 2009). There has also been increasing recognition of LBP affecting children and adolescents in recent years (Manek & MacGregor 2005). Watson et al (2003) sampled 1446 schoolchildren (aged 11-14 years) and reported a one month LBP prevalence of 24% which increased with age. Due to the frequency of LBP symptoms in childhood the authors hypothesised this could have implications for LBP in adulthood. Hestbaek et al (2006) have also demonstrated that LBP in children has demonstrated a significant correlation with LBP in adulthood in an eight year study of 6,540 Danish twins.

LBP affects around 17.3 million people (approximately one third of the population) in the UK with 3.1 million adults experiencing pain throughout the entire year (Maniadakis & Gray 2000). As a result of this LBP is considered to be a major health problem in society imposing a greater financial burden to the National Health Service (NHS) (£1067 million in 1998) than other conditions such as coronary heart disease, Alzheimer's disease, stroke, arthritis, diabetes, epilepsy, depression, multiple sclerosis and chest infections (Maniadakis & Gray 2000). LBP also causes a major negative impact upon the overall economy of the UK due to the financial costs of lost productivity and informal care which has been estimated at £10668 million (Maniadakis & Gray 2000). In a systematic review of the cost of LBP in the USA and internationally, Dagenais et al (2008) included 27 studies which varied widely in methodology for direct and indirect costs. However, the authors stated that despite this LBP had to be considered to be a major burden across the globe.

In summary, LBP is an ongoing, common global and costly problem. In order to effectively manage the condition an accurate assessment is a vital initial component for clinicians to undertake.

2.3.2: Low Back Pain – assessment and classification

LBP is routinely classified via diagnostic triage into

1. specific/serious spinal pathology,
2. nerve root/radicular pain or
3. non-specific LBP (Airaksinen et al 2006, van Tulder et al 2006).

Specific/serious LBP is deemed to be caused by symptoms attributable to a specific pathology such as fracture, cancer, infection or cauda equina syndrome (Manek & MacGregor 2005, Ferguson et al 2010b). These pathologies can be identified with routine investigation and can then be appropriately managed. Nerve root pain is identified via pain distribution and physical examination. The

IVD has been identified as a cause of nerve root pain but is not the only structure or mechanism involved (Airaksinen et al 2006, van Tulder et al 2006).

For the majority of individuals with LBP (approximately 85-90%), a specific patho-anatomic cause cannot be identified and these people are classified as having "non-specific LBP" (Atlas & Deyo 2001, Hoeijenbos et al 2005, Koes et al 2006). Non-specific LBP (NSLBP) has been defined as "LBP not attributable to a recognisable pathology such as osteoporosis, fracture, tumour or infection" (Koes et al 2006).

The term NSLBP encompasses many diagnostic labels such as back ache, lumbar pain, strain, lumbago, facet joint pain, sacroiliac problems, somatic dysfunction, ligamentous strain, myofascial syndrome, motor control dysfunction, simple back pain, mechanical back pain, discogenic pain, slipped disc, and sciatica (Atlas & Deyo 2001, O'Sullivan 2000, ARMA 2004). Currently, no reliable and valid definition or classification system exists for the majority of individuals with NSLBP although many have been proposed (Manek & MacGregor 2005, van Tulder & Waddell 2005, Rossignol et al 2009).

It has been proposed that treatment for LBP could be targeted more effectively and specifically if individuals with NSLBP could be sub-divided into more homogenous sub-groups (Petersen et al 2004, O'Sullivan 2005, Brennan et al 2006, Dankaerts et al 2006, 2007, Fersum et al 2010), and this has been identified as a research priority requiring adequately powered randomised controlled trials as well as reliability and cohort studies (Bogduk 2000, Maluf et al 2000, May 2006). Indeed, a recent update of primary care research priorities in LBP rated identification and treatment of clinical subgroups as the top priority (da Cunha Menezes Costa et al 2013). Many NSLBP classifications have been published worldwide in the literature (McKenzie and May 2003, Petersen et al 2004, Dankaerts et al 2007, Schafer et al 2009) but no single classification approach has been universally adopted. Appropriate patient classification is a necessary preliminary step in the assessment and management of clinical problems but controversy still surrounds the reliability and validity of these various approaches (van Dillen et al 1998, Fritz & George 2000, Billis et al 2007). Indeed, in recent clinical guidelines classification of NSLBP patients has not been recommended due to the lack of available evidence (Foster et al 2011).

In a cross country review of NSLBP classification systems Billis et al (2007), identified nine countries with classification systems that followed one of the following three paradigms:

1. Biomedical (based on pathoanatomic &/or clinical features),
2. Psychosocial (based on psychological and social/work elements) and
3. Biopsychosocial (based on mixed biomedical and psychosocial elements).

The results of this review recommended that a biopsychosocial approach should be adopted for NSLBP classification and existing systems could be improved by including dimensions from other high quality classification studies alongside cultural elements for specific ethnic populations. This conclusion is also reflected in the results from Kanayannis, Jull and Hodges's (2012) review of movement based classification systems. They concluded that movement based classification systems predominantly assessed biomechanical aspects whilst psychosocial aspects and neurophysiological pain states had minimal consideration.

Therefore, despite a growing body of literature on classification systems for NSLBP, there is still more high quality research required in terms of:

1. Adopting a statistical approach to classification development rather than a judgemental one by professionals;
2. More appropriately powered reliability studies to support/refute individual classification systems and their content validity;
3. Development and/or merging of robust classification systems to cover the entire biopsychosocial paradigm;
4. Cost effectiveness evaluations to identify direct and indirect costs of each system to justify their use clinically.

Symptom duration:

NSLBP is routinely further classified into categories according to length of time from onset of symptoms: acute; sub-acute and chronic (Weiser & Rossignol 2006, Negrini et al 2008). Acute NSLBP has been defined as NSLBP up to 6 weeks duration; sub-acute is NSLBP between 7-12 weeks and chronic refers to

NSLBP of more than 12 weeks duration (Atlas & Deyo 2001, Heijmans et al 2003, Carragee 2005, Koes et al 2006, Van Tulder et al 2006). Evidence, however, would suggest that this classification is inaccurate as LBP is not a short term problem, but rather a multifactorial, episodic condition that varies in intensity with acute attacks often occurring as a flare up of long standing symptoms (van Tulder et al 2002, Enthoven, Skargren and Oberg 2004, Cassidy et al 2005, O'Sullivan 2005, Hestbaek et al 2006, NHS QIS 2009). Manchikanti (2000) in a review of LBP epidemiology summarised a recurrence rate of chronic LBP at three, six and 12 months to range from 35-79%.

2.3.3: Acute Low Back Pain

For acute LBP, it has been shown that 75-90% of people will improve within one month, although recurrences and episodic phases are common and can affect up to 25-50% of individuals over the next year (Andersson 1999, Atlas & Deyo 2001, Koes et al 2001, Pengel et al 2003). Recovery after 12 weeks has been shown to be slow and unpredictable (Andersson 1999).

Pengel et al (2003) in a systematic review of acute LBP, found as many as 73% of patients had a recurrence of LBP within a year and there was an 84% risk of recurrence after three years. Within a month, the authors reported that improvements in pain (58%), disability (58%) and return to work (82%) were typically seen and gradually continued to improve up to three months after onset of the symptoms.

Bekkering and colleagues (2005) in a study of 500 LBP patients referred for physiotherapy found pain, sick leave and functioning improved in the first three months but only small improvements were gained up to 12 months and a substantial proportion of patients still had pain and disability one year later.

Jones et al (2006) found in study of 974 patients, 39% (363) of patients who consulted their General Practitioner (GP) with LBP still had LBP three months later. This result may be an over estimation as there is no information available between the time points assessed and the authors may have identified recurrent LBP rather than continual LBP.

Croft et al (1998) found in patients consulting their GP due to LBP, only a minority had recovered three months later. Their results also highlighted the recurrent nature of LBP and that GP consultations were not a direct measure of pain and disability as patients did not tend to return to their GP about their LBP. The authors found only 25% of patients consulting with LBP had fully recovered one year later and most patients had some degree of pain and disability but would not consult their GP about it.

A range of prognostic factors have been suggested in the literature that may lead to acute LBP continuing beyond the acute (0-6week) phase. These factors can be grouped into three key factors: psychological (fear avoidance behaviour, pre-existing psychological disorders); occupational (low job satisfaction, compensation issues, job dissatisfaction, failure to return to work after 3 months); and physical (leg pain, duration of current episode, other types of chronic pain) (Croft et al 1998; Andersson 1999; Pengel et al 2003; Bekkering et al 2005; Carragee 2005).

2.3.4: Chronic Low Back Pain

It has been estimated that around 6-10% of people with acute LBP will go on to develop chronic LBP (CLBP) (Andersson 1999, Ekman et al 2005), whereas other authors have stated this percentage may be as high as 33-40% (O'Sullivan 2005, Steenstra et al 2005). Although LBP has a high financial cost in terms of healthcare utilisation and lost productivity, it has been demonstrated that not all people with LBP create this economic drain.

Maetzel & Li (2002) carried out a review of the economic burden of LBP between 1996 and 2001 and reported a small percentage of patients with CLBP accounted for a large proportion of the financial costs.

Van Tulder et al (2002) stated it was important to identify the small proportion of NSLBP patients that were at risk of developing long term disability and work absenteeism. They carried out a comprehensive review of the literature on LBP and found factors such as distress, depression, somatisation, job dissatisfaction, low education level and high levels of pain and disability were associated with

CLBP. Fear avoidance has also been shown to be a factor in developing long term LBP (Manek & MacGregor 2005).

Over 45 years of age, smoking, neurological signs, psychosocial factors and distress were also reported by Grotle et al (2005) to be prognostic factors for non-recovery after three months in a group of 123 Norwegian patients presenting with an episode of LBP of less than three weeks duration.

In a Canadian population, Kopec et al (2004) found an increased risk in CLBP for men aged 45-64 years, low health status, increased height, heavy physical employment, stress and lack of work around the home or gardening. The authors also identified risk factors for CLBP in women were linked to restrictions in activity, arthritis, stress, and any history of psychological trauma.

Enthoven et al (2006) aimed to identify potential predictive factors for disability at one and five year follow-ups for LBP in 148 Swedish LBP patients. Their results suggested that factors such as being female, longer duration of current episode, low exercise levels prior to this episode and higher pain frequency were predictive for disability at a five year follow-up. These results were advised to be viewed with caution due to wide confidence intervals in the results.

It has been recognised that patients with long term/CLBP often report other symptoms (Hagen et al 2006). In a study of 457 patients, Hagen and colleagues recorded additional significant symptoms such as other musculoskeletal pain (neck, upper back, foot); headache/migraine; sleep problems; flushes/heat sensations; anxiety and sadness/depression. It has been shown that CLBP significantly affects the quality of sleep in people and in a survey of 268 CLBP patients, Marin, Cyhan and Miklos (2006) reported a significant relationship between pain and sleep disturbance.

In summary, it has been acknowledged in the literature that improved assessment of LBP would occur via sub-classification of patients into specific groups. However, as demonstrated here, there are many options for sub-classification but yet no system has yet been shown to be better than any other. Further research is required within the sub-classification of LBP to identify clinically useful systems that are reliable and valid.

2.3.5: Discogenic Low Back Pain

Individuals suffering from LBP can also report symptoms that extend from the back down across the buttocks and into the legs. This has been suggested to represent around 25-57% of LBP cases (Zhou & Abdi 2006, Schafer et al 2009). In around 90% of patients with these symptoms, it can often be attributed to pain/problems arising from the IVD (Koes et al 2007).

Discogenic LBP (DLBP) has been generally defined clinically as pain radiating from the back into the buttock and leg, normally beyond the knee and most commonly caused by prolapse of the intervertebral disc. The term is also used to refer to pain anywhere along the course of the sciatic nerve as well as being associated with neurological changes (such as sensation, muscle strength and reflexes) (Konstantinou & Dunn 2008). Adams et al (2006) interpret DLBP to mean "pain arising as a result of stimulation of nociceptive nerve endings in the IVD". They use this definition to refer to pathological processes limited to the IVD that result in the stimulation of its nociceptive nerve endings such as IDD and discitis. This means that the exterior of the IVD remains essentially intact and "normal" macroscopically whereas the interior contains the pathology. However, in a clinical assessment it is not possible to identify this without the use of invasive procedures. Additionally, there is debate in the literature as to the correct definition to be used when discussing DLBP (Fairbank 2007, Koes et al 2007, Genevay et al 2010, Sweetman 2011b) such as sciatica, radicular pain, radiculopathy, lumbosacral radicular syndrome, and referred pain.

Therefore, for the purposes of this thesis, the term DLBP will be used to refer to the definition stated by Konstantinou and Dunn (2008) as this can be used clinically without the need or use of invasive procedures.

As stated previously, the intervertebral disc (IVD) has been attributed to be a causative factor in both nerve root and NSLBP groups when classified via diagnostic triage which demonstrates the limitation of this classification system for DLBP. Therefore, for the purposes of this review the NSLBP and nerve root groups will be combined under the umbrella of NSLBP.

Sciatica, like LBP has been recognised in early European texts and discogenic pain began to emerge as the dominant reason for LBP during the second half of

the last century (Lutz, Butzlaff and Scultz-Venrath 2003, McKenzie and May 2003, Sweetman 2011a). The theory of the IVD gaining credence as a causative factor for LBP was introduced around the 1930's with the introduction of radiographs/X Ray technology, the ability to visualise and surgically treat the IVD, and the publication of journal articles relating to the effect of the IVD (Chedid & Chedid 2003, Lutz, Butzlaff and Scultz-Venrath 2003, Karampelas et al 2004).

It has been reported that the IVD is one of the most common causes of NSLBP accounting for up to 45% of chronic LBP cases (Bogduk 1995, Luoma et al 2000, Awad & Moskovich 2006, Konstantinou & Dunn 2008). In a review of 1092 cases of sciatica in a Moroccan population, Bejia et al (2004) reported 58% of discogenic pain was due to IVD herniation.

L5 is thought to be the most commonly affected nerve root in DLBP (Bejia et al 2004), although 98% of sciatica/radicular pain has been shown to involve both the L5 (L4/5 IVD) and S1 (L5/S1 IVD) nerve roots (Atlas & Deyo 2001, Awad & Moskovich 2006, Stafford et al 2007).

In contrast to LBP, discogenic pain has been reported by authors as more commonly observed in younger patients, with a peak between the 20's and 40's (Atlas & Deyo 2001, Bejia et al 2004, Awad & Moskovich 2006, Casey 2011). Discogenic pain due to degenerative spinal stenosis is more commonly observed in the older patient (Atlas & Deyo 2001, Pahl et al 2006).

2.3.6: Discogenic Low Back Pain prevalence

In a study by Vroomen et al (2002) 67% of patients referred by GPs into a study investigating LBP had DLBP. Tubach and colleagues (2004) have reported a 19.5% prevalence of sciatica in a French population which was similar to a previously reported UK prevalence of 17.6%. Luoma et al (2000) reported a 12 month and four year prevalence of 29.9% and 39% respectively for DLBP in a group of 164 Finnish men. In contrast, Miranda et al (2002) reported a one year sciatica prevalence of 9% in a cohort of 2077 asymptomatic Finnish forestry industry workers. Bogduk (2009) has suggested that the prevalence rates reported in the literature are unreliable as studies have not followed clear

definitions for sciatica/DLBP. He goes on to suggest that following the IASP strict definitions, the prevalence should be around 12% or less for herniated IVDs.

In a recent review of sciatica prevalence, Konstantinou & Dunn (2008) included 23 studies and reported that prevalence varied from 1.6% - 43%. Lifetime prevalence was reported from 5 studies as 12.2% - 43%, and annual prevalence from 9 studies as 2.2% - 34%. The reasons for these variations were thought to be due to differences in sciatica definition, different data collection methods and differences in the populations studied.

2.3.7: Discogenic Low Back Pain prognosis

The prognosis for discogenic pain (other than due to cancer or infection) is generally good (Vroomen et al 2002, Bejia et al 2004, Tubach et al 2004, Peul et al 2008) with the majority of cases resolving naturally within eight weeks. Spontaneous recovery is thought to occur in 80% of DLBP patients within 8 weeks and 95% within a year (Legrand et al 2007). However, it has also been suggested that the prognosis is not as favourable as previous studies might suggest and certainly not as good as the prognosis for acute NSLBP (Vroomen et al 2000, Tubach et al 2004).

DLBP patients have been reported as having a less favourable outcome compared to those with NSLBP, utilising more health resources, and having more intense and longer lasting pain with longer absences from work and prolonged disability (Konstantinou & Dunn 2008, Hill et al 2011, Ong et al 2011). Up to 30% of DLBP patients are thought to have continual pain for longer than one year (Jacobs et al 2011). Additionally, Hill et al (2011) have reported that at 6 months, less than half of their participants with pain radiating below the knee reported any overall improvement and their disability scores were double those participants with no leg pain.

Vroomen et al (2002) reported around one third of LBP patients recovered in the first two weeks and around three quarters recovered after 12 weeks. Reported recovery rates for discogenic pain in the literature vary between 46-60% of patients and Grotle et al (2005) found a slower recovery rate for patients with

neurological signs than for those without in a study of 123 Norwegian patients. Bejia and colleagues (2004) found a six month success rate for conservative treatment of LBP of 77%.

Tubach et al (2004) evaluated the natural history of discogenic pain in 622 French workers reporting sciatica over a four year period. They found that over 50% of people still had symptoms two and four years later and of those that had recovered from sciatica, 61% still had LBP and 27% had long term LBP.

Andersson (1999) has also noted that patients with discogenic pain take longer to recover than those patients with only LBP. Miranda et al (2002) reported 53% of people suffering from discogenic pain at baseline still had severe pain one year later.

2.3.8: Discogenic Low Back Pain risk factors

Risk factors for the onset of discogenic pain have been suggested as mental stress, age, smoking, genetic pre-disposition and physical workload factors and in contrast to NSLBP guidelines walking has demonstrated a positive association with DLBP (Miranda et al 2002, Stafford et al 2007, Spiker et al 2009).

A systematic review of cardiovascular and lifestyle risk factors in DLBP (Shiri et al 2007) reviewed 19 articles and concluded that weight (being overweight or obese), smoking (long history), high levels of physical inactivity and inflammatory mediators were associated with DLBP. However, the authors did highlight the need for further studies to clarify these associations.

Kaaria et al (2011) carried out a recent large longitudinal study (N = 5261) of middle aged employees' (aged 40-60 years at baseline) risk factors for sciatica. Their results demonstrated that occupational class (especially manual); unhealthy health behaviours (smoking, being overweight & physically inactive) and previous neck and back pain were the main risk factors for sciatica over the 7 year period. However, 80% of the sample was female and data was analysed for gender differences therefore not all the results for the male group were statistically significant due to their small numbers.

Prognostic factors favouring poor outcomes in recovery from discogenic pain have been suggested to be:

1. Individual (obesity, female gender, older age, sciatica lasting longer than six months, sciatica lasting more than 30 days, intensity of back and leg pain, increased pain on sitting, pain on coughing, sneezing or straining, a positive straight leg raise (SLR) test and positive reverse SLR test, history of previous LBP or sciatica, sciatica symptoms the year before study inclusion, little or moderate leisure time physical activity);
2. Psychosocial (substance abuse, low socioeconomic status, depression, worrying and health anxiety, or other psychological problems);
3. Occupational (heavy manual work, compensation claims, work dissatisfaction, carrying heavy loads at work, machine drivers exposed to whole body vibration, driving more than two hours a day, prolonged constrained sitting)

These factors are also related to persistence of symptoms (Carragee & Kim 1997, Luoma et al 2000, Atlas & Deyo 2001, Miranda et al 2002, Vroomen et al 2002, Bejia et al 2004, Tubach et al 2004, Peul et al 2008, Jensen et al 2010, Casey 2011).

A systematic review of prognostic factors for LBP (Hayden et al 2009) identified 17 reviews of varying methodological design and conduct. Despite many prognostic factors identified with LBP, the authors could only identify a small number of important prognostic factors that were consistently reported, and one of which was the presence of sciatica.

A recent systematic review of prognostic factors for DLBP (Ashworth, Konstantinou and Dunn 2011), identified seven medium to high quality studies but again did not reach a firm conclusion on prognostic factors. The authors of the review concluded that heterogeneity of the included studies prevented firm conclusions being reached. They also went on to call for further research of high methodological quality, using a consistent definition for DLBP to investigate psychological factors as well as clinical and radiological findings for DLBP.

2.3.9: Clinical assessment of Discogenic Low Back Pain

Many people suffering from LBP (including DLBP) are seen by physiotherapists for assessment and treatment of their condition with physiotherapy playing a key role in their management (Foster et al 1999, Casserley-Feeney et al 2008, Dagenais et al 2008). In a study of care seeking behaviour for LBP in Sweden, Vingard et al (2002) reported around 5% of the study population sought treatment over a three year period. This is similar to the Scottish figure of 6% of the population visiting their GP in any one year (Lochlainn et al 2008).

Dagenais et al (2008, 2009) has reported in two systematic reviews that the greatest proportion of direct costs for LBP internationally is due to physiotherapy. In the UK, LBP accounts for 35-50% of the workload of physiotherapists (Foster et al 1999, Waddell 2005, Byrne et al 2006, Ferguson et al 2010a). Annually, it has been estimated that 1.6 million patients are treated by NHS physiotherapists with an economic cost to the NHS of £251 million (Maniadakis & Gray 2000).

In Scotland, it has been reported that there are around 3000 LBP referrals per month to NHS Scotland physiotherapy departments (NHS QIS 2008). Over 55,000 people were referred with back pain in 2007 to NHS Scotland Physiotherapy departments with the majority of referrals via the GP (63%, includes GPs advising patient to refer themselves) (NHS QIS 2009). Nearly 96% (N = 2,074) of these LBP patients were managed initially via diagnostic triage.

The main reasons people suffering from LBP & DLBP consult a GP or physiotherapist are due to the symptoms of pain, stiffness and disability that restrict their quality of life (Foster et al 1999, Mortimer and Ahlberg 2003, Koes et al 2007, Ferreira et al 2009). Common complaints from DLBP patients include worsening symptoms due to prolonged weight-bearing and increased pain due to sitting or flexion/bending movements (McKenzie and May 2003, Zhou and Abdi 2006, Passias et al 2011). Suri et al (2010) in a study of 154 patients with MRI confirmed IVD herniation were unable to identify a specific inciting event in the majority of patients.

Due to the economic (time off work and healthcare costs) and personal burden of LBP & DLBP, effective and efficient treatment of these conditions is a priority

for patients and clinicians. The physiotherapy clinical assessment of LBP and DLBP consists of a clinical history and physical examination that informs the subsequent management plan (Koes et al 2007, Dagenais et al 2010, van der Windt et al 2010). A common element of a physical examination is the assessment of lumbar spine range of movement (ROM) which can also be used to monitor ROM changes over time (Ha et al 2012).

The Scottish National Physiotherapy Low Back Pain Audit (NPLBPA) (NHS QIS 2009) presented a demographic picture of a subset of patients (N = 2,147) included in the full audit. The interesting factor in this group was that over half of the patients (54%, N = 1,161) initially presented with LBP and leg pain (22.4% LBP referred to knee and 31.6% LBP referred to below the knee) which is often a clinical symptom of DLBP (these figures are displayed alongside the 25-57% incidence reported in the literature (from Section 2.3.5) in figure 2.3.1). However, the results of the audit identified that documentation of a full neurological assessment (including reflexes, myotomes, dermatomes and passive Straight Leg Raise) for patients with nerve root pain (defined as pain from lumbar spine to below the knee) was evident in less than 60% of clinical notes. This improved after feedback to around 75%, but the audit recommendations highlighted the need for full neurological assessments to be carried out and recorded for patients with LBP referred into the leg. Caution should be used however, as the demographic data was not available for the complete 55,000+ patients. We cannot assume therefore, that this demographic picture reflects the true status of DLBP patients attending for NHS Scotland physiotherapy management but it does however provide an informative snap shot of a large group of patients attending NHS physiotherapy in Scotland.

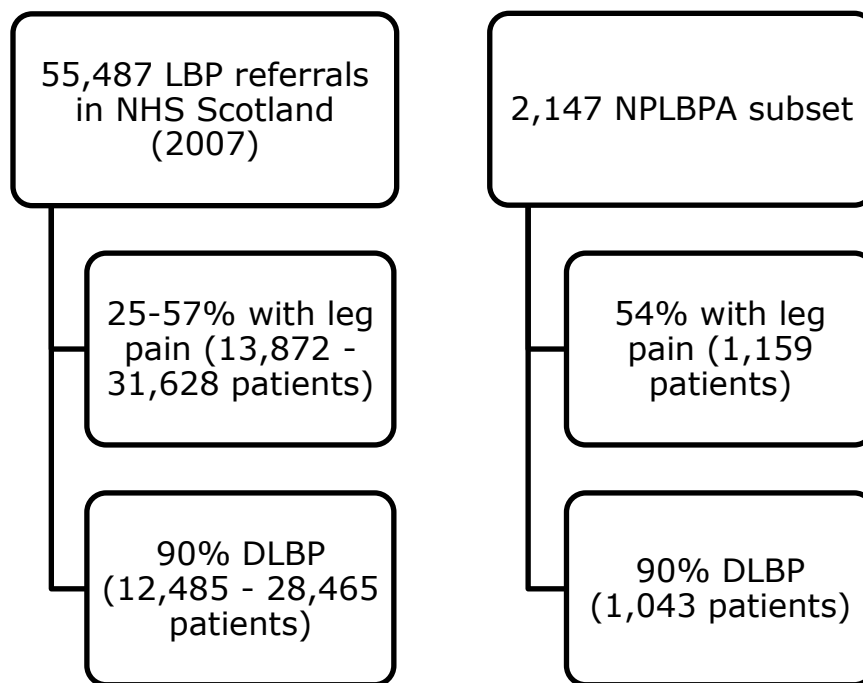


Figure 2.3.1: Potential Scottish DLBP population from NPLBPA

The specific assessment and management of DLBP presents an even greater challenge than LBP as no reliable and valid clinical assessment has been identified for this condition (Wetzel & Donelson 2003). Indeed, as the internationally recognised initial clinical assessment (diagnostic triage) cannot allocate DLBP to one specific classification (nerve root or NSLBP) there is an inherent lack of reliability around this classification system. However, this is still the assessment of choice for Scottish physiotherapists as demonstrated in the NPLBPA (NHS QIS 2009). There is a need for international consensus to agree and establish a global definition of DLBP which can then guide more high quality research investigating the assessment of the IVD as a source of back pain. This would ultimately lead to the identification of robust methods to assess/classify and guide the appropriate conservative management of DLBP.

In a recent systematic review, van der Windt et al (2010) updated and combined two earlier reviews to investigate the physical examination for lumbar radiculopathy due to IVD herniation. Sixteen cohort studies and three case control studies were included but only one study was performed in a primary care population. The authors reported that although the performance of most diagnostic tests was poor (see Table 2.3.1), it should be recognised that this

finding was limited by the fact the majority of studies covered surgical populations. Additionally, it was also noted that in practice, a combination of information (such as clinical history and physical examination) is used by clinicians to inform diagnostic decisions rather than individual tests. The authors recommended that future studies should investigate multiple diagnostic assessment criteria (such as history, physical examination and imaging) in primary care cohorts in order to optimise the clinical diagnosis.

Table 2.3.1: Diagnostic accuracy of clinical tests for herniated intervertebral disc (Amended from van der Windt et al 2010)

Test	Sensitivity	Specificity
SLR or Lasegues test	0.37 – 0.81 ^a 0.79 – 0.98 ^b	0.37 – 1.00 ^a 0.10 – 0.82 ^b
Crossed SLR or crossed Lasegues test	0.23 – 0.43	0.83 – 1.00
Paresis or muscle weakness	0.27 – 0.62	0.47 – 0.93
Muscle wasting	0.15 – 0.38 ^b	0.50 – 0.94 ^b
Impaired reflexes (TA)	0.14 – 0.61	0.60 – 0.93
Sensory deficits	0.28 – 0.67	0.42 – 0.69
Forward flexion	0.45 – 0.90	0.16 – 0.74
Slump test	0.44 – 0.84	0.58 – 0.83

Key: ^a – imaging as reference standard; ^b – surgery as reference standard; SLR – straight leg raise; TA – Achilles tendon reflex

A limitation of this review and indeed in the area of DLBP research is that there is still confusion over the definition of DLBP, sciatica, radicular pain or radiculopathy despite work by authors and groups such as IASP (Bogduk 2009). Therefore, the literature has to be viewed in a conservative light as elements of DLBP are investigated with heterogeneous populations which have a knock on effect on the strength of published results and the subsequent identification of appropriate treatment (Luijsterburg et al 2007a).

Common physiotherapy assessment strategies in DLBP involve the investigation of loading and movement effects on symptoms (Delitto, Erhard and Bowling 1995, Sahrman 2002, Petersen et al 2003, McKenzie and May 2003, O'Sullivan 2005).

One of the most commonly used classification systems in the physiotherapy assessment and management of LBP is the Mechanical Diagnosis and Therapy (MDT) system (Foster et al 1999, Gracey, McDonough and Baxter 2002, McKenzie and May 2003, Byrne, Doody and Hurley 2006). The MDT system consists of a mechanical assessment of patient's pain patterns using repeated end-range movements with or without static loading (McKenzie and May 2003). Key indicators are investigated during the assessment such as directional preference or centralisation (pain moves from distal to proximal in response to loading strategies) that will indicate the mechanical sub-group classification (derangement, dysfunction, posture or other syndromes) to guide subsequent treatment (McKenzie and May pp.134, 295). The conceptual model for the derangement syndrome identifies the IVD as the primary structure involved in symptom generation (McKenzie and May, Chapter 9). The derangement syndrome is also the most commonly classified syndrome by clinicians (Hefford 2008) and the phenomena of directional preference and centralisation are demonstrated only within this syndrome (McKenzie and May 2003, chapter 9). The symptom of centralisation has been shown to have excellent reliability in assessment of LBP patients with kappa scores of 0.79 – 1.0 (Fritz et al 2000, Clare, Adams and Maher 2005).

Aina, May and Clare (2004) conducted a systematic review of centralisation of spinal syndromes. The authors reported that centralisation was a commonly found LBP subgroup with a prevalence of 70% in acute/subacute LBP patients and 52% in CLBP patients. Aina, May and Clare (2004) concluded that the presence of centralisation was associated with positive outcomes for patients. A recent study by Wernecke et al (2011) determined the baseline prevalence of directional preference and centralisation in 584 LBP patients. Overall there was a prevalence of 60% directional preference and 41% centralisation in the LBP patients. Long, May and Fung (2008) also conducted a secondary analysis of a previous randomised controlled trial and concluded that patients with directional preference/centralisation who received matched treatment were around 8 times more likely to have a good functional outcome.

Donelson et al (1997) demonstrated that the centralisation phenomenon (a symptom of the derangement syndrome) was a predictor of AF competence and an indicator of DLBP in a group of 63 CLBP patients who had a MDT assessment

and discography. The authors concluded that patients with pain that centralised or peripheralised had a 72% chance that the pain was due to DLBP.

A lateral shift deformity (where the upper body is visibly shifted to one side) in patients is also considered to relate to IVD pathology (McKenzie and May 2003, pp. 94, 296).

The centralisation phenomenon is not solely demonstrated in the MDT system. Other movement based classification systems also use loading strategies to elicit centralisation in their assessment (Delitto, Erhard and Bowling 1995, Petersen et al 2003). Although centralisation has demonstrated excellent reliability in the assessment process there is still further research required to demonstrate that this phenomenon, and other clinical tests used together, provides the optimal assessment for DLBP patients.

A recent publication has investigated the cost-effectiveness (indirect and direct costs) of the treatment-based classification (TBC) (Delitto, Erhard and Bowling 1995) in sub-acute and chronic LBP with a one year follow-up (Apeldoorn et al 2012). The TBC approach consists of three levels based on the patient's subjective history, symptom behaviour and clinical signs (Delitto, Erhard and Bowling 1995). Previously two randomised controlled trials (Fritz et al 2003, Brennan et al 2006) had reported slightly more positive results with the TBC system than usual care and a trend towards reduced direct medical costs. Although Apeldoorn et al (2012) modified the TBC system for application in a Dutch population (n=156), the results demonstrated statistically significant differences between the groups in terms of recovery (as measured by global perceived effect) in favour of the classification approach. Although there was a trend towards reduced direct health care costs for the classification group; total costs (direct and indirect) were greater for this group. The authors concluded that based on a "societal cost perspective", they could not recommend this system.

2.3.10: Clinical management of discogenic low back pain

As patients with DLBP are often referred to physiotherapy for assessment and treatment, Luijsterburg et al (2007b) carried out a Dutch cost-effectiveness

investigation for GP and Physiotherapy care against GP care alone for patients with acute lumbosacral radicular syndrome. After one year, there was a significant difference favouring physiotherapy care in terms of global perceived recovery, however, the addition of physiotherapy was not shown to be more cost-effective than GP care alone. The results from this study highlight again the need for a global consensus on DLBP terminology so that specific populations can be included and reliable and accurate clinical assessments can identify appropriate subjects for inclusion.

LBP management encompasses many treatment options yet the optimal assessment and treatment package to provide pain relief and functional improvement remains largely enigmatic (Fritz & George 2000, Dankaerts et al 2007, Luijsterburg et al 2007a). The wide variety of treatments and modalities used by physiotherapists in the management of LBP has been reported in the literature to involve the combinations of four elements, namely, advice, manual therapy, exercise and electrotherapy (Foster et al 1999, Gracey et al 2002).

A recent systematic review to determine the efficacy of conservative treatment for lumbar IVD herniation with associated radiculopathy (Hahne et al 2010) identified 18 trials (7 of high quality) which included 1,671 subjects. Their conclusions reported that advice was equally effective as surgery (microdiscectomy) in the long term; moderate evidence favoured stabilisation exercises above no treatment, manipulation over sham manipulation and the inclusion of mechanical traction to medication and electrotherapy.

In another recent systematic review, Dahm and colleagues (Dahm et al 2010) combined and updated two previous reviews regarding advice to remain active versus bed rest for people with acute LBP with or without sciatica. They included ten randomised controlled trials (N = 1,923) and concluded that for individuals with sciatica there was little to no difference between staying active or resting in bed (moderate quality evidence). They also reported low quality evidence suggested there was little or no difference in pain relief or function between those who received advice to remain active, exercises or physiotherapy.

A new single blind, randomised, clinical controlled trial has provided interesting results to support active conservative therapy for patients with severe sciatica

rather than surgery (Albert & Manniche 2012). One hundred and eighty one consecutive patients with radicular pain below the knee were randomised into two treatment groups. One group received symptom guided exercises (derived from a symptom guided algorithm), advice to stay active and information and the other group received sham exercises (general exercises to improve circulation), advice to stay active and information. Patients were examined at baseline, eight weeks and one year after treatment by the same examiner. Despite the sham exercise group having a greater expectation of treatment, the symptom guided exercise group demonstrated significantly more improvement in most outcomes. The results of this study can be viewed in a positive light as a sample size calculation was initially carried out to inform group numbers and outcomes were linked to clinically important changes. In addition, treatments were based on common physiotherapy practice and carried out by qualified staff that did not require specialist training. There was also a small dropout rate that was clearly explained. The results of this study suggest that even patients with severe sciatica that would qualify for surgical intervention can be managed successfully with conservative care. The authors also pointed out that active conservative treatment enables patients to return to work sooner, the treatment is cheap in comparison to surgery, has no side effects, is straight forward to implement and has high satisfaction levels reported by patients.

From the literature presented here it is clear that DLBP is a common condition, yet due to the way LBP is assessed clinically this condition is not always assessed nor managed effectively. There needs to be a consensus, agreed internationally, that defines DLBP and also a shift in research reporting that clearly encompasses this condition and the optimal treatment choice. There is support in the literature for the conservative management of DLBP but it has not been clearly reported nor adopted in policy or by clinicians. Efficacy trials such as Albert & Manniche (2012) go some way to clear the way but there are many more required to be carried out in order to definitively clarify this condition and its optimal management.

Current UK guidelines for the management of LBP (NICE 2009) recommend that imaging should not be used routinely unless surgical intervention is planned or serious pathology suspected. Magnetic resonance imaging is an ideal tool for non-invasive imaging of the IVD providing excellent resolution of the IVD and

surrounding structures. For patients suffering from DLBP there is some debate in the literature regarding imaging with some recommending imaging if symptoms do not appear to be settling after 6 weeks (Lateef and Patel 2009, Graves et al 2012). Physiotherapists managing patients with DLBP need to be aware and understand the guidelines for imaging and onward referral for patients demonstrating any red flag signs and symptoms, who are worsening or have not responded to conservative management. Indeed, guidelines and recent Scottish Government policy documents have highlighted the fact that physiotherapists are now working in new ways and extended roles such as referring patients for and acting on diagnostic tests such as MRI (NHS QIS 2009, Joint Effects 2011).

2.3.11: Summary

This section has identified the size and cost of LBP in the literature. In summary, LBP is a huge problem in society and calls in the literature to identify more specific sub-groups of NSLBP has been suggested as a way forward in improving the overall conservative management of this problem. This study is focused on a sub-group of NSLBP due to the lumbar intervertebral disc (DLBP), often referred to as sciatica or radiculopathy. DLBP is one of the main causes of NSLBP, yet this review has demonstrated the lack of consensus in the literature around the definition of this condition. There is a need to achieve an internationally recognised consensus on a definition so subsequent research can include homogenous populations.

This review has also demonstrated the need for research to identify reliable and valid clinical assessments that in turn will lead onto effective management.

The following section in this chapter will consider the literature in regard to imaging of DLBP using MRI and pMRI.

2.4: Imaging of discogenic low back pain:

2.4.1: Imaging of the intervertebral disc

Diagnostic imaging of the IVD is a common clinical procedure with multiple tools available to carry it out such as magnetic resonance imaging (MRI), computed tomography (CT), and discography. This thesis concerns the use of positional MRI; therefore MRI and positional MRI (pMRI) will be considered in the following section but all other methods of IVD diagnostic imaging are outwith the scope of this thesis and will not be reviewed. The following section will consider and review the literature on what MRI is, the use and value of MRI in discogenic LBP (DLBP), as well as pMRI and its use and value in the diagnostic assessment and investigation of DLBP.

2.4.2: What is Magnetic Resonance Imaging?

MRI is a non-invasive diagnostic imaging tool that provides anatomical imaging in any plane with no ionising radiation risk to the patient. The underlying mechanisms, physics and technology involved in MRI are complex and are outwith the terms of this literature review, but a working knowledge of MRI is required to ensure effective use of this tool practically. Therefore, an overview of MRI will be presented here.

MRI scanners consist of a large magnet which has coils wrapped around it through which an electrical current is passed, thus creating a high strength magnetic field. The body is composed of around 70% water and it is the hydrogen nuclei contained within the water that is important. Hydrogen is the most abundantly found atom in the body, being found in both water and fat. When a patient is within the MRI magnetic field (normally lying flat on a bed) low energy hydrogen nuclei align their magnetic moments parallel to the direction of the magnetic field (spin up nuclei) and high energy hydrogen nuclei align in anti-parallel direction (spin down). There is a small difference in number in each direction which causes a net magnetisation vector. A radiofrequency pulse is then applied (excitation) causing resonance of the nuclei. The corresponding energy absorption causes an increase in the number of spin down nuclei. This results in magnetisation in the transverse phase that is "in phase".

When a receiver coil is placed in the area of the moving magnetic field a voltage is induced in the coil (this is the magnetic signal) and this is subsequently processed by a computer to produce images. The nuclei in different biological tissues return to their original alignment at different rates. Therefore, by adjusting MRI scanner settings, image contrast can be created between different biological tissues (Westbrook & Kaut 2002, Gould & Edmonds 2010). Figure 2.4.1 demonstrates the steps of the MRI process.

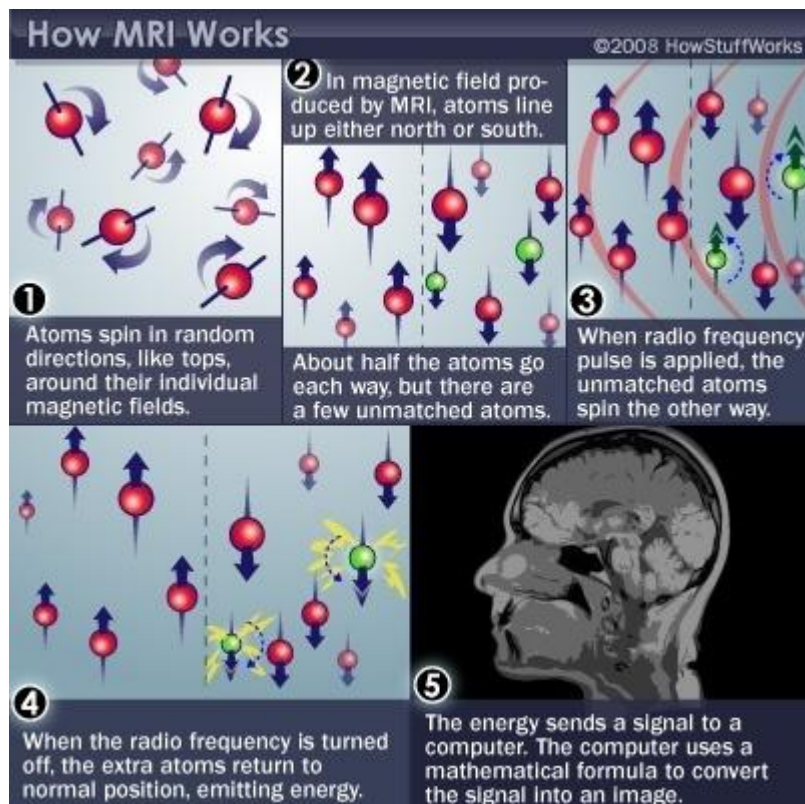


Figure 2.4.1: The steps of a Magnetic Resonance Imaging process (Image from © 2008 HowStuffWorks.com, Gould & Edmonds 2010. Reprinted courtesy of HowStuffWorks.com. All rights reserved.)

2.4.2.1: Advantages of Magnetic Resonance Imaging

MRI has been shown to be ideal for imaging of soft tissues of the body such as brain, nerves and the intervertebral disc (IVD) enabling the identification of pathology with great sensitivity (Modic et al 1988, Morishita et al 2008, Beric

2010, Roudsari & Jarvik 2010, Hancock et al 2011). MRI of the lumbar spine is clinically one of the most frequently requested MRI examinations and allows the comprehensive assessment of spinal structures (Gedroyc 2008, Alomari et al 2010). MRI is often part of the diagnostic investigation where large IVD herniations and nerve root compression are most commonly considered to be the anatomical structures indicative of sciatica and DLBP (Jensen et al 2007). Additionally, there is no ionising radiation used to perform MRI scans (Jarvik & Deyo 2002) therefore it can be used frequently without posing an accumulative radiation risk to patients.

As already stated, MRI provides a high degree of contrast resolution enabling the ability to distinguish differences between similar but not identical tissues. For example, in T1 weighted(T1W) MRI scans tissues containing water and fluid appear dark and tissues containing fat appear bright; whereas, on T2 weighted (T2W) MRI scans, water and fluid filled tissues are bright and tissues containing fat are dark (Westbrook & Kaut 2002). It is acknowledged that T2W MRI scans provide better discrimination of IVDs from other structures than T1W scans (Alomari et al 2010). Additionally, T2 relaxation time sensitivity to water and proteoglycan content and the collagen structure can be inferred between healthy and degenerated IVDs. For example, high T2 values for the NP have been shown in healthy IVDs; whereas the T2 value decreases with the associated reduction in water and proteoglycan levels with disc degeneration (Haughton 2006, Trattinig et al 2010). It has been suggested that the NP signal in T2W scans are probably the most sensitive indication of IVD degeneration (An et al 2004).

2.4.2.2: Disadvantages of Magnetic Resonance Imaging

Like all tools, MRI has acknowledged disadvantages which include: the high costs associated with it; the image production time requiring patients to remain still for long periods; and claustrophobic patients can find the narrow tunnel unpleasant. Although MRI can diagnose vertebral abnormalities CT can often be used in addition as it provides clearer bone imaging (Alomari et al 2010). In addition, the excellent visualisation of spinal pathology by MRI may not provide definitive answers, explain patient's clinical symptoms or improve patient

outcomes (Jarvik et al 2001, Chou et al 2009, Beric 2010, Roudsari & Jarvik 2010).

A MRI scan is a relatively safe procedure for the majority of patients, but like any procedure there are a range of relative and absolute contraindications (relating to the magnetic field) which include: ferromagnetic objects within the body; medical implants; pregnancy in the first trimester; and external metal objects. Therefore, all patients having a MRI scan are screened carefully prior to the procedure as well as changing into gowns and storing personal belongings (watch/purse/jewellery) (personal communication with MRI staff).

2.4.3: The use of Magnetic Resonance Imaging in the diagnosis of discogenic low back pain

MRI is a useful non-invasive tool for evaluating abnormalities of IVDs and the vertebral end-plates (Alyas et al 2008, Carrino et al 2009). This includes IVD contour abnormalities (such as bulge, herniation, extrusion, protrusion), degenerative changes, high intensity zones, modic changes, nerve root impingement, spinal instability, and spinal stenosis (Aprill & Bogduk 1992, Leone et al 2007, Rahme & Moussa 2008, Carrino et al 2009, Moon et al 2009, Sakamaki et al 2009). T2W images can demonstrate good contrast between the outer (more fibrous) annulus fibrosus (AF) and the inner AF and nucleus pulposus (NP) which contains a higher water and proteoglycan content (Roudsari & Jarvik 2010). The bony vertebral end-plate signal intensity is normally very low, as it contains minimal water content (Autio 2006).

2.4.3.1: Accuracy of Magnetic Resonance Imaging

MRI has been reported to be highly accurate in detecting changes in the IVD such as:

1. Degeneration
2. Bulges and herniations (accuracy 76-96%; sensitivity 60-100%; specificity 43-100%; positive likelihood ratio 1.1-33 and negative likelihood ratio 0-0.93);
3. Stenosis (sensitivity 77-90%; specificity 72-100%)

4. Annular tears (accuracy 31-43%)

(Jarvik et al 2001, Jarvik & Deyo 2002, Autio 2006, O'Neill et al 2008, Cheung et al 2009, Roudsari & Jarvik 2010).

Jensen et al (2007) have reported 90% accuracy in detecting the symptomatic disc level from MRI findings in a group of 154 patients with sciatica.

Weiner & Patel (2008) reported the accuracy of MRI in detecting lumbar IVD containment in a sample of 50 consecutive patients undergoing discectomy. Overall, sensitivity was 72%; specificity was 68% and accuracy 70% for MRI detecting contained herniated lumbar IVDs against surgery as the reference standard (where visualisation by surgeon was noted).

2.4.3.2: High intensity zone

Aprill & Bogduk (1992) first indicated that T2W scans could also demonstrate radial and circumferential tears in the posterior AF as high intensity signals and termed the phrase High Intensity Zone (HIZ). The HIZ is identified as a high intensity signal within the AF that is clearly dissociated from the NP on T2W MRI scans (Aprill & Bogduk 1992). The reported accuracy of a HIZ in detecting IVD tears has been reported as having sensitivity 26% - 81%, specificity 79% - 95.6%, positive predictive value 60% - 89%, and negative predictive value 47% - 97% (Schellehas et al 1996, Saifuddin et al 1998, Ito et al 1998, Lam et al 2000).

It has been postulated that the presence of HIZ on images represents an area of inflammation in the AF, vascularised granulation tissue, an annular tear/fissure, internal disc disruption (IDD) or IVD degeneration (Aprill & Bogduk 1992, Lam et al 2000, Narvani et al 2003, Rankine 2004, Peng et al 2006). IDD is represented by radial fissures that extend into the AF (Narvani et al 2003).

Although HIZ has been reported in symptomatic LBP and DLBP populations, Carragee et al (2000) reported a 24% prevalence rate in a group of 54 asymptomatic subjects. The author concluded that presence of a HIZ on T2W images could not be seen to be a reliable indicator of IDD as this MRI finding was common in subjects without LBP. This is echoed by Kang et al (2009) who

reported HIZ alone was not helpful in indentifying a disc with concordant pain (sensitivity 56.8%, specificity 83.6% and positive predictive value 53.2%). However, they suggested that presence of a disc protrusion with HIZ on T2W images could predict a positive discography in patients (sensitivity 45.5%, specificity 97.8% and positive predictive value 87%). Carrino and colleagues (2009) indicated that MRI findings of HIZ and degenerative marrow changes could be useful diagnostic indicators although more research is required in this area.

2.4.3.3: Modic changes

Modic changes (MC) are characterised by a change in the signal intensity within the bone marrow adjacent to the vertebral end-plate (Modic et al 1988). It is thought MCs are a normal consequence of the ageing and degenerative process of the spine and these changes increase with increasing age (Jensen et al 2008). In a systematic review of MC prevalence, Jensen and colleagues (2008) reported a median prevalence for MC in non-specific LBP as 43% and 6% in asymptomatic subjects. The presence of MC in degenerative disc disease is thought to be between 19-59% whereas it is less common in subjects without degenerative disc disease (3-10%) (Rahme & Moussa 2008). The relationship between MC and DLBP is still debateable. Several studies have reported high specificity (87-98%) and positive predictive value (88-91.3%) but a low sensitivity (14-48%) for MC as predictors of DLBP using provocation discography as the reference standard (Braithwaite et al 1998, Weishaupt et al 2001, Maus 2010). Prior studies investigating this relationship are limited due to small sample size and conflicting results.

The studies of MRI accuracy discussed above have used discography or surgical findings as the reference standard to compare against. However, there is no gold standard for reference and discography has been acknowledged as having limitations (lack of specificity and high false-positive rate) which may affect the overall accuracy of MRI findings (Wills et al 2007, Chou et al 2009, Maus 2010).

O'Neill et al (2008) investigated MRI accuracy for the diagnosis of DLBP in 143 patients. Five MRI characteristics were defined (HIZ, nuclear signal, disc height,

disc contour and bone marrow intensity change) and correlated with each other and discography findings. The results indicated moderate nuclear signal loss and IVD bulge had a sensitivity of 79.8 and specificity 79.3%. The addition of moderate IVD height loss had sensitivity 82% and specificity 73.6%, while the addition of a grade II HIZ had sensitivity 54.7% and specificity 92.6%. The authors concluded that MRI accuracy improved with the combination of MRI parameters, but this was only in the presence of moderate nuclear signal loss.

A systematic review of the diagnostic accuracy of tests to identify the IVD as a source of LBP included 28 studies (Hancock et al 2007). HIZ, vertebral end-plate changes and IVD degeneration observed on MRI increased the probability of the IVD as the source of LBP (+LR 1.5-5.9, 1.6-4, 0.6-5.9 respectively). However, heterogeneity of the data prevented pooled analysis so further research is required to clarify the accuracy of these diagnostic tests.

A more recent study by Hancock et al (2011) compared rates of MRI findings between 30 acute LBP (thought to be likely DLBP) patients and 30 pain free controls to identify if IVD pathology was more common in the LBP group. Two blind assessors reviewed the MR images and concluded that findings including IVD degeneration, MC, and herniation were more likely in the LBP group but no single MRI finding was more important than any other. More research was recommended however to investigate the value of MRI findings as prognostic factors. One limitation of this study were the small numbers in the control group when split into 15 people with no LBP history and 15 people with 1-2 previous episodes for secondary analysis.

Jensen et al (2007) investigated the possible prognostic value of disc related MRI findings in relation to recovery in patients with sciatica who participated in a RCT of conservative treatment. Broad based protrusions and extrusions at baseline were strongly associated with a positive outcome. Nerve root compromise and location of disc herniation were not associated with definitive recovery which is in contrast to previous reports that these findings predict recovery from sciatica at 12 weeks (Vroomen, Wilminck and De 2002). These differences were explained by the authors to be due to different analyses. Men had a higher prevalence of herniations and were more likely to recover from sciatica than women. In conclusion the authors suggested that it is possible to

predict the clinical outcome for men on the basis of MRI findings (broad based protrusions, extrusions and male sex predictive).

It is worth noting that imaging of the natural course of IVD herniations has demonstrated natural resolution in 65-100% of cases and large herniations are more likely to resolve (Maus 2010).

In summary, the literature presented here demonstrates that although there is no gold standard tool available for diagnostic imaging of DLBP, MRI currently provides the most accurate imaging of the morphological structure of the IVD both clinically and for research purposes. However, further research is required to fully establish MRI as a gold standard.

2.4.3.4: Intervertebral disc ageing and degeneration

Like all tissues, the IVD changes with advancing age and this causes changes in the MR images produced (Autio 2006). MRI has been suggested as the “modality of choice” for imaging IVD degeneration (An et al 2004). In young, healthy IVDs the distinction between the NP and the AF on T2W images is relatively sharp and well defined. The NP has high water content and is seen on T2W MRI as a high signal intensity that is surrounded by the AF with a low signal intensity. As the NP ages, there is a corresponding reduction in the water content and the proteoglycans become desiccated which in turn causes it to resemble the inner structure of the AF (Buckwalter 1995). Therefore as the IVD degenerates, there is a loss/reduction in signal from the NP and the demarcation between the high intensity NP and low intensity AF becomes indistinct (Maus 2010). A strong linear correlation has been reported between AF and NP water content and T2W signal intensity where increasing water content causes a brighter signal intensity (Weidenbaum et al 1992, Marinelli et al 2009).

Quint & Wilke (2008) investigated the relationship between degeneration and function using 18 cadaveric lumbar spines and MRI. They found that although T2W images with low signal intensity reflected IVD degeneration, they were less certain whether this finding was a reliable indicator of “structural degenerative changes”. They concluded by stating MRI could only identify advanced stages of IVD.

Masui et al (2005) followed 21 conservatively treated patients (mean age 49 years) with lumbar IVD herniation over 7 years and used MRI to assess them at baseline, 2 years and final stage. The authors reported that MRI demonstrated a significant reduction in the herniation at 2 years and final stage but also progression of IVD degeneration over the 7 year period.

Several classifications have been proposed to grade the degenerative changes in the IVD based on T2W signal loss and one of the most commonly used classifications grades IVD degeneration into five categories (Pfirrmann et al 2001). Loss of T2W signal due to degeneration has had reported sensitivity of 90-98% and specificity 39-77% for DLBP against provocation discography (O'Neill et al 2008, Maus 2010). Loss of IVD height due to IVD degeneration has also had reported sensitivity 87% & 73% and specificity 69% & 81% using provocation discography (O'Neill et al 2008, Maus 2010).

As well as a clinical tool, MRI has been used extensively as a research tool to investigate the IVD and DLBP (Masui et al 2005; Quint & Wilke 2008; Trattinig et al 2010). A key limitation of MRI in previous research is the heterogeneous inclusion criteria of LBP rather than DLBP subjects but this is an inherent problem as no gold standard currently exists for the clinical diagnosis of DLBP (Hancock et al 2011). Additionally, traditional MRI scans are performed in supine and this has been acknowledged as a limitation in studies as the loading effects of gravity, body weight and postural muscle activity are negated.

2.4.4: Asymptomatic intervertebral disc pathology & Magnetic Resonance Imaging

One of the most commonly recognised limitations of MRI findings is the high prevalence of IVD pathology/abnormalities in asymptomatic subjects (Jarvik et al 2001, Takatalo et al 2009). They are thought to occur in around one third of adults under 40 years and virtually all adults aged 60-80 years (O'Neill et al 2008).

The prevalence of IVD pathologies varies in asymptomatic subjects as follows:

1. Degenerative IVDs (46-93%)

2. IVD bulging (20-81%)
3. IVD protrusions (18-33%), extrusions (0-18%), and herniation (9-76%)
4. HIZ (6-33%)
5. Annular tears (20-56%)
6. Central canal stenosis (1-21%)
7. Vertebral end-plate/modic changes (2-7%)

(Jensen et al 1994, Jensen et al 2008, Lurie et al 2008a, Takatalo et al 2009, Maus 2010, Hancock et al 2011).

The methods used in previous research have inherent issues that affect MRI findings thus explaining the wide ranges reported (Hancock et al 2011). For instance, there has been no control factor for previous LBP history in pain free populations (MRI findings may represent old or episodic pathology); and the effect of ageing and the inclusion of older subjects with the increased potential for degenerative changes have not been factored in either. Many previous studies have also focused on degenerative IVDs or herniation, rather than the range of IVD pathologies that MRI can demonstrate.

2.4.5: Positional Magnetic Resonance Imaging and its role in the investigation of discogenic low back pain

Current UK guidelines only recommend the use of imaging for LBP when surgical interventions are being considered or there is a specific cause of LBP suspected (such as cauda equina syndrome) (NICE 2009). These guidelines are based upon MRI studies carried out in conventional supine/flat-bed MRI scanners where it has been recognised that there may be nothing remarkable to observe on the MRI scans. This may be because patients can report their symptoms to have a positional effect where they are more uncomfortable in upright (sitting and standing) loaded positions but gain relief from pain by lying down (Gedroyc 2008). Additionally, the supine position has been identified as a reason behind the high false positive and false negative rates for stenosis and disc herniation (Alyas et al 2008). Ideally, scanning patients in a clinically significant position (such as upright MRI) would be of benefit in the overall assessment and

management of a patient where findings may be demonstrated that were not apparent on conventional supine imaging (An et al 2004, Beric 2010).

Supine MRI with axial loading has been used to simulate upright loaded spinal positions, but it has been acknowledged that this method is limited in that it does not truly represent the upright/loaded, erect spine (Saifuddin et al 2003, Alyas et al 2008, Beric 2010).

There have been many different developments in MRI scanning techniques and methods and one such development has been the introduction of positional "Upright" MRI scanning where patients can be scanned in sitting, lying and standing positions. The positional MRI (pMRI) (Upright MRI, Fonar Corporation, Melville, NY, USA) consists of a 0.6T field which is generated between 2 large magnets and has been available for around the last 12 years. A moveable bed/table lies between these magnets and can be positioned at any angle from -20 to 90° (vertical), enabling supine and standing positions. An MRI compatible seat can be attached to the bed in the upright position allowing seated images to also be taken (Hirasawa et al 2007).

2.4.5.1: Advantages of positional Magnetic Resonance Imaging

The greatest advantage of pMRI is that patients can be imaged in positions reflecting their clinical symptoms (Jinkins et al 2002, Smith & Pope 2003, Beric 2010). The low magnetic field strength (0.6T) minimises image artefact production due to chemical shift and metal (therefore preferred for imaging of post-operative spines that may contain metal) and may reflect neural structures more clearly (Jinkins et al 2002, Alyas et al 2008, Beric 2010). Claustrophobic patients can be imaged comfortably as they are able to see out at all times during the scan and patients who are unable to lie in a supine position (due to cardiac or respiratory pathology) can also be scanned (Jinkins et al 2002, Alyas et al 2008).

2.4.5.2: Disadvantages of positional Magnetic Resonance Imaging

A limitation of pMRI is that the range of flexion and extension achieved within the scanner is limited by the chair size and the position that patients can maintain without movement for the duration of the scan. Ensuring patients adopt a position they can maintain without movement for the scan is important as the MR images can be subject to motion artefact if patients are unable to remain still (Alyas et al 2008). Images acquired in the standing position are most likely prone to degradation from movement artefact depending on scan time. As subjects must remain motionless in standing during the scan, the length of time required to maintain this can lead to the threat of a vasovagal episode (if longer than 10 minutes) as well as the risk of increasing pain levels (Alyas et al 2008).

Some authors use the term kinetic or kinematic MRI (kMRI) to represent upright pMRI (Zou et al 2008, Morishita et al 2008, Zou et al 2009, Do et al 2011). However, this terminology infers a dynamic, motion element to the MRI procedure which is not the case. All kMRI and pMRI scans require subjects to remain still for a specific period while the images are acquired and produced, therefore for the purposes of this thesis, all upright positional and kinematic MRI scans will be referred to as pMRI.

As pMRI enables images to be performed in the clinically significant position, it is acknowledged that this can provoke pain; therefore patients may require pain relief prior to a pMRI scan in order that they can remain comfortably still (Morishita et al 2008).

Instead of lying within a cylindrical tube as per routine recumbent MRI scans, patients having pMRI scans can be in functional positions. The pMRI system differs to the traditional recumbent MRI scans in that patients need to wear a coil around the area of interest rather than be within a tube. The coil width (different coils available dependent on patient girth) enables patients to adopt functional positions within the pMRI. However, this limits the field of view to that only within the coil range (field of view). However, in terms of lumbar spine imaging this is not a restriction as the entire lumbar spine can be viewed.

2.4.5.3: Investigation of the intervertebral disc via positional Magnetic Resonance Imaging

pMRI has been employed by researchers to demonstrate and investigate:

1. The effect of diurnal variation on the IVD (Matsumura et al (2009), Ludescher et al (2008))
2. The effect of surgical interventions
3. The effect of different postures on the spine
4. Findings not visible on conventional MR images such as reduced IVD height, disc bulging/herniation and spondylolisthesis

(Weishaupt et al 2000, Bashir et al 2003, Muthukumar et al 2004, Siddiqui et al 2005, Karadimas et al 2006, Siddiqui et al 2006a, 2006b, Beastall et al 2007, Hirasawa et al 2007, Alyas et al 2008, Morishita et al 2008, Zou et al 2008, Kumar et al 2008, Beric 2010).

In a review of the ability of upright MRI to identify changes in the spine that were undetected in supine MRI, Elsig & Kaech (2006) presented illustrative evidence to support a positional effect on posterior disc protrusions, central canal and foraminal stenosis and mobile spinal instability (spondylolisthesis) where supine MRIs have been unremarkable. They concluded that upright MRI offered better correlation between patient symptoms and imaging reports.

In a pictorial review Alyas et al (2008) presented symptomatic and non-symptomatic lumbar spine pMRI images. They reported that in a normal IVD there is a small but insignificant increase in posterior IVD bulge from supine to upright pMRI. They do acknowledge however, that some authors have presented conflicting results using objective measurements (Lee et al 2003 found small increase in kneeling but Schmid et al 1999 found no significant change in sitting).

Previous radiological methods have only been able to identify indirect (segmental degenerative changes) or direct (vertebral body malalignment) instability signs, whereas pMRI can demonstrate positional changes in the spinal segment that correlate to clinical symptoms (Alyas et al 2008, Beric 2010, Niggemann et al 2011).

As yet, there are no studies that have reported the accuracy of pMRI for LBP, DLBP or changes in the IVD. Ferreiro Perez et al (2007) investigated the differences between traditional recumbent MRI (rMRI) and pMRI findings in cervical and lumbar spine pain. The project included 45 LBP patients and 44 patients with cervical spine pain (+/- radiculopathy), aged 20-60 years with ten asymptomatic volunteers for comparison. The authors concluded that pMRI was superior in identifying posterior herniation (58%) and anterior spondylolisthesis for both cervical and lumbar spine pain. Interestingly, rMRI was reported to be superior to pMRI in 11 subjects which was thought to be due to mobile posterior spondylolisthesis which may become more visible in a supine position.

Zou et al (2008) investigated whether the use of pMRI (flexion & extension) is beneficial in the diagnosis of IVD herniation. The study included 553 LBP patients (+/- radiculopathy) referred for pMRI and consisted of 319 females and 234 males with a mean age 46.2 years (range 18-76). The authors assessed the degree of IVD bulge from L1/2 to L5/S1 using MR analyser software. They reported a significant increase in the degree of herniation between flexion and extension compared to neutral. An increase in IVD herniation was seen in 16.49% of extension images and 12.04% of flexion images.

Skelly et al (2007) conducted a health technology assessment of pMRI and its ability to detect clinically important findings, its impact on clinical decision making (and on treatment and pertinent treatment outcomes), the economic and cost-related effects, and to identify gaps in current research and recommend research priorities. The authors conducted a systematic review of pMRI in degenerative spondylolisthesis, spinal or foraminal stenosis, radicular pain, NSLBP and extra-spinal pain and functional loss. The gold standard for this assessment was upright myelogram in combination with CT-myelogram for the spinal studies. The overall conclusion from this assessment was that there is limited data on the accuracy and diagnostic utility of pMRI and there is no evidence available from well designed clinical trials to support pMRI accuracy or effectiveness for specific spinal conditions or patient populations.

The majority of support for pMRI is presented as pictorial reports that provide visual comparison between supine and positional images, case studies,

conference abstracts or retrospective reports based on patients referred for pMRI scans (see table 2.4.1). The findings of these articles are limited in generalisability due to small samples sizes and selection and interpretation bias. There is a need to establish the accuracy of pMRI compared to rMRI in terms of sensitivity, specificity, predictive values and likelihood ratios for LBP, DLBP and the IVD as this has not yet been reported in literature. In addition, there is a need for further studies of DLBP in patient populations as well as investigating the healthy asymptomatic IVD to establish normative behaviour using pMRI.

Table 2.4.1: Intervertebral disc parameters investigated via positional Magnetic Resonance Imaging

Study	Subjects	IVD parameter	Position scanned	Outcome measure	Results	Comments
Alanay et al (2007)	300 consecutive back pain & 20 asymp 128 F: 172 M 10 F: 10M	Segmental ROM in healthy and degenerated IVDs	Dynamic MRI: N.Sit, F.Sit (40°) & E.Sit (10°)	IVD degeneration: Phirrmann classification Global & segmental sag angulational ROM	Global lumbar ROM decreases with increased degenerated segments Reduced motion is not compensated for by increased motion of healthy adjacent segment	Conference abstract
Alyas et al (2010)	2 male CLBP patients 43 & 32 years	Case report to demonstrate positional changes in signal intensity and morphology of HIZ	pMRI: N.Sit, F.Sit, E.Sit (sag & axial T2W FSE images)	Observational review by 2 radiologists	Change in morphology and signal of HIZ between positions may increase sensitivity of HIZ findings	Case study but demonstrates positional effects on HIZ
Bashir et al (2003)	15 asymp volunteers	Diurnal height variation	Standing & supine pMRI	IVD height L1/2 - L5/S1: $(a+p)/2$ & $(a+m+p)/3$	Mean % loss height: Supine = 7.70 -7.09mm Standing = 7.29 -7.52mm	Conference abstract - minimal detail
Basher et al (2006)	20 asymp volunteers	Investigated IVD water content positional changes to determine optimal seating position	pMRI supine & diff seated positions with 8 tubes for water calibration tapes to their back	Pixel intensity in phantoms & IVD measured in every position	L4/5 & L5/S1 water content decreased significantly in flexed sitting. 135° sitting better than 90 in terms of in-vivo water content	Conference abstract
Bashir et al (2006b)	22 asymp	To define optimal seating position via pMRI	pMRI in sitting	Lumbar lordosis angle IVD height NP translation	135° thigh trunk angle was optimal seating position. NP showed limited ROM without overall area change in normal IVD	Conference abstract
Cargill et al (2007)	2 pain free male subjects Aged 30 & 33	pMRI & rMRI to develop novel method of accurately determining lumbar vertebral position invivo.	pMRI NSit, FSit, ESit & St		Lengthy processing but produced 3D data representing anatomy & movement of specific subject	Case reports
Do et al (2011)	410 consecutive LBP patients referred for kMRI	Used kMRI (0.6T pMRI) to investigate association btn facet	T2W mid-sag & axial images in N.Sit, F.sit & E.Sit	L3/4, L4/5 & L5/S1 measured IVD bulge (mm) from	Results suggest severe facet tropism is associated with increased IVD bulge at	Lack of controls to compare

	140 F:270M Mean 40.7years (range 16-80)	tropism & IVD bulge related to age		mid-sag via MRI analyser V 3 Facet angle	L4/5 in older subset but may be due to biomechanical factors.	findings to. Retrospective, & broad inclusion criteria
Ferreiro Perez et al (2007)	45 patients with LBP (+/- radiculopathy) 44 patients with cervical spine pain (+/- radiculopathy) Aged 20-60 years 10 asymptomatic volunteers for comparison	Project investigating differences between rMRI & pMRI in Cx & Lx spine pain	pMRI: T1 & T2W sag FSE images, axial T2W FSE images in supine, N.Sit & N.Sit after 10 min sitting or standing	Area & linear dimensions of posterior IVD herniation & area of residual patent central spinal canal compared between positions and % degree of change calculated	76% (68/89) patients had spinal pathology. Focal posterior IVD herniation in 24/45 (53%) with 2 only seen on upright position; reduction in posterior IVD herniation seen in 4 on upright position; anterior & posterior spondylolisthesis seen in 13/45 (29%) in LBP patients. Overall combined rMRI miss rate for above pathologies = 10/68 (15%). Overall combined rMRI underestimation rate for both pathologies = 42/68 (62%). pMRI superior in 52 patients (58%) in posterior herniation & anterior spondylolisthesis (both Cx & Lx). rMRI superior to pMRI in 11 (12%) thought to be due to mobile posterior spondylolisthesis	Unable to reproduce method from details provided. Descriptive analysis. Pt motion artefact inhibited accurate measurement in 20% images. Retrospective.
Fryer et al (2010)	6 asymp volunteers But only 4 for pMRI part: 2F: 2M Mean age 29.2 years (range 20-35)	Feasibility of pMRI & stadiometry to measure changes after sitting	pMRI: T2W FSE images in sitting	Osiris to measure: Mid-sag area between VB (proxy IVD fullness), vertical height and lordotic angle	pMRI is capable of detecting changes in spine morphology such as spine height and lordotic curve	No sitting instructions, therefore error for testing between measures Only 4 completed pMRI section

Gilbert et al (2008)	35 yr old male LBP + sciatica	Case study to illustrate the potential usefulness of repeat pMRI in diagnosis of LBP	pMRI in sitting	Neural foramen diameter Spondylolisthesis measurement	Neural foramen and spondylolisthesis both increased and pMRI identified findings consistent with patient's radiculopathy	Case study only but demonstrates potential of pMRI
Gilbert et al (2011)	997 pMRI scans of symptomatic patients	Determine rate of lumbar stenosis detected on rMRI and pMRI		Stenosis, central stenosis, lateral recess stenosis & foraminal stenosis	Stenosis rate varied between 38.5% versus 56.7% (rMRI v pMRI respectively). Further work required to investigate if pMRI better for stenosis investigation	Retrospective
Hirasawa et al (2003)	17 asymp volunteers	Postural changes in IV foramen	pMRI: ly, St, N.Sitt, F.Sitt, E.Sitt	Sag image: width, height, CSA of IV foramina @ pedicle level (L1/2-L5/S1) Mid-sag image: IVD height L1/2 - L5/S1, lordosis (L1-S1 angle)	Sig diff in foraminal dimensions due to position.	Conference abstract – minimal detail but more than the studies above. Only reported results for L3/4 & L4/5.
Hong et al (2007)	510 LBP (+/- radiculopathy) patients 186 F: 324 M Mean age 42.2 years (range 16-85)	To evaluate how many missed spondylolisthesis on rMRI can be identified on dynamic MRI	Dynamic MRI: N.Sit, F.Sit (40°), E.Sit (10°)	Translation from L1/2 - L5/S1 via Meyerding's method Missed spondylolisthesis counted where N.Sit normal but F.Sit or E.sit showed >3-4mm	Missed spondylolisthesis in neutral MRI but found in F.Sit MRI is 18.1%, where translation >3mm. More common in flexion than extension due to greater anterior translation	Conference abstract
Karadimas et al (2006)	30 LBP (+/- leg pain) patients on surgical waiting list 16 female: 14 male Mean age 44.5 years (range 25-61)	Positional change effect on segmental degeneration, end-plate angles and IVD height	Conventional supine MRI followed by pMRI N.Sit (pMRI: sag & axial FSE T2W images)	IVD degeneration (via Woodend classification) L1/S1 angle IVD height (a, m, p) End-plate angles	pMRI interobs error pMRI: End-plate angles = 0.997, L1/S1 angle = 0.995, IVD height = 0.968-0.988 Results analysed according to grouping of degeneration. Results showed changes in lumbar kinematics with degenerative changes. Concluded pMRI useful tool	Osiris image analysis software used. Inclusion bias – surgical patients

					to quantify reduced lumbar ROM & IVD height.	
Keorochana et al (2011)	430 consecutive LBP patients (+/- leg pain) 189 F: 241M Mean 42.98 years (range 16-85)	Retrospective analysis of effect of lordosis on spinal kinematics & IVD degeneration	pMRI: T1 & T2W FSE sag images N.Sit, F.Sit & E.Sit	L1/2 - L5/S1 measured T12-S1 lordosis angle via Cobb method & classified into 3 alignments (straight, normal, hyperlordotic) Segmental translational & angular motion at each level in F.Sit & E.Sit IVD degeneration via Pfirrmann scale	Segmental mobility increased in mild to moderate degeneration whereas reduced in severe degeneration & corresponds to previous work Showed statistically significant relationship between degeneration degree & posture. pMRI was able to demonstrate relationship between sag lordosis, IVD degeneration & segmental mobility	No control data
Magnusson et al (2003)	10 male asymp, aged 23-30	IVD height changes after 10Kg loading and hyperextension	Hyperextension pMRI Stadiometer	Spine length T11/12 - L5/S1	Sitting demonstrated loss of height and hyperextension demonstrated height recovery (mean gain 2.1mm, SD +/-1.57mm)	Conference abstract - minimal detail
Meakin et al (2008)	24 male volunteers (pain free) Median 26 years (range 20-55)	Active shape model created from pMRI images	T2W pMRI images in St	L1-S1 active shape model & lordosis via end-plate angles	Active shape model more accurate than lordosis via end-plate angles (as they can have error of ~10degrees)	
Morishita et al (2008)	587 symptomatic back pain patients 459 cervical patients	Review article of previous work Of spinal kinematics using pMRI/kMRI	T2W & T1W FSE sag images in NSit, FSit & ESit	Vert height, spondy, IVD height, IVD bulge/herniation, SC AP diameter, sag segmental motion, global & segmental lordosis (Cobb), Lx gravity line, global height & IVD degeneration	Results conclude that kMRI is effective in diagnosing IVD herniations that are often missed on rMRI. The degree of bulge increased significantly in flex & ext compared to neutral positions	Review of previous work - method issues (inclusion, controls, retrospective work etc..)
Muthukumar et al (2004)	116 LBP (+/- sciatica) patients 45 female: 71	Value of seated pMRI	pMRI: supine, N.sit, F.Sit, E.Sit	IVD height (a & p) IVD behaviour	Demonstrated positional behaviour of IVD prolapsed Identified 21 cases of grade	Conference abstract

	male Mean age 44 years (range 35-71)				1 spondylolisthesis in sitting Concluded pMRI advantageous for imaging spondylolisthesis and positionally dependent IVD prolapse	
Naxera et al (2008)	40 year old patient with positionally motion dependent pain on left side	Demonstration of possibilities of pMRI of spine	pMRI in upright positions	Visual examination and diagnosis	Evident pMRI findings correlated with patient's symptoms despite unremarkable rMRI	Case study
Niggemann et al (2009)	53 year old male with long standing LBP	First documented evidence of posterior instability in a patient with spondylolisthesis	pMRI: sag t2W images in supine, N.Sit, F.Sit & E.Sit; axial T2W images in N.Sit	Observational diagnosis	Posterior instability due to spondylolitic defect. pMRI is the only device available to demonstrate this phenomena	Case study
Niggemann et al (2011)	4 patients	Case reports of 4 patients to demonstrate pMRI role in TCS			pMRI can identify or rule out TCS and also identify area of tethering from flex & ext images	Case reports
Smith et al (2003)	63 consecutive LBP & sciatica patients referred for MRI 20 female: 43 male Mean 42 years (range 35-67)	Value of IVD imaging in sitting	pMRI: supine & N.Sit, F.Sit & E.Sit (sag & transverse T1 & T2 images)	IVD signal loss on T2W images IVD height IVD prolapsed Spinal instability	No difference in IVD height between healthy IVDs in seated or supine MRI IVD with signal loss had 1- 3mm reduction IVD height 56 cases had prolapsed IVD that changed btn sitting positions 6 cases demonstrated previously unseen spinal instability.	Conference abstract
Wei et al (2007)	461 LBP patients 169 F: 192 M Aged 15-85 years	The effect of position on central SC	Dynamic MRI: N.Sit, F.Sit (40°), E.Sit (10°)	Degeneration grade via T2W image signal change Change ratios of SC diameter between position calculated	Statistically sig diff between N.Sit & F.Sit and N.Sit & E.Sit SC diameter. Dynamic MRI shown to be accurate in demonstrating the amount of change in CSA in SC.	Conference abstract

					SC widest in flex and narrowest in ext	
Wei et al (2010)	491 patients 181F: 310 M aged 16-85 years	pMRI study to examine correlation b/n lumbar SC diameter change & angular motion	pMRI FSit, NSit & ESit positions	Measured SC diameter & segmental angle at each level in mid-sag plane in each position	pMRI demonstrated amount SC diameter change was statistically correlated with segmental angular motion of spine during flex & ext	
Weishaupt et al (2000)	30 CLBP patients 13 F: 17 M Mean age 38 years (range 20-50)	To evaluate if pMRI can demonstrate NR compromise not visible on rMRI	rMRI pMRI: F.Sit & E.Sit (T2W FSE images)	CSA dural sac Qualitative grading: IVD abnormalities, NR compromise, foraminal size (as per Wildermuth et al) VAS score for pain by patient for pMRI positions L2/3 - L5/S1 assessed	Results support previous findings that dural sac & neural foramina dimensions are position dependent. Concluded pMRI demonstrates minor forms of neural compromise than rMRI	Limited on objective analysis. Narrow spectrum of pts recruited after positive MRI. 6 pts excluded due to pain on pMRI. Retrospective.
Wildermuth et al (1998)	30 consecutive patients referred for lumbar Myelography 17 F: 13 M Mean 58 years (range 27-84)	Investigate the positional effect on dural sac and IV foramina	pMRI: supine, F.Sit, E.Sit lumbar myelography	Sag AP diameter of dural sac (L1/2 - L5/S1) Qualitative scoring of foraminal size Interobserver reliability.	Small but statistically sig positional effect on dural sac diameter was shown in lower lumbar spine. Sag diameter of dural sac can be reliably measured with pMRI (r = 0.81 - 0.97) Methodological issues prevented objective testing for a positional effect on foraminal size	Pts recruited after results obtained from Myelography (reference standard).
Zamani et al (1998)	25 pts (back pain, radicular pain & claudication) 5 asymp volunteers Age range 22-79 67% male	0.5T open MRI To determine feasibility of obtaining, and the findings, of lumbar MRI in lying and sitting	pMRI: FSit, ESit & NSit rMRI: supine (15 subjects only)	Both performed 2 days apart Qualitative/visual estimate of change in posterior IVD bulge, foraminal & central canal size	No appreciable change in post IVD bulge between supine and NSit. Increased post bulge noted in 27% (24/90 IVDs) with extension	Small sample size. No clear demarcation of results b/n asymp & sympt. Retrospective.
Zou et al (2008)	553 LBP patients (+/-)	To determine if addition of flexion &	kMRI; NSit, FSit & ESit positions	Assessed degree of IVD bulge from L1/2 -	Significant increase in degree of herniation via	Retrospective

	radiculopathy) referred for kMRI 319F: 234 M Mean 46.2 years (range 18-76)	extension MRI is beneficial in IVD herniation diagnosis	T1W & T2W images	L5/S1 with MR analyser software V3	flexion & extension compared to neutral. Increased IVD herniation seen in 16.49% in extension & 12.04% in flexion. Missed IVD herniation ranged from 9.09 – 19.46% in extension & 4.55 – 15.29% in flexion	
Zou et al (2009)	513 patients with back pain & referred for kMRI 298 F: 215 M Mean 42.6 years (Range 19-74)	pMRI used to describe degenerate IVD bulge in different positions	pMRI T1 & T2W FSE images in N.Sit, F.Sit & E.Sit	L1/2 – L5/S1 levels investigated IVD degeneration classified via Pfirrmann scale Disc migration via MRI analyser version 3 software	IVD bulge increases with IVD degeneration severity Increased bulging at L4/5 & L5/S1 All grade I NPs migrated ant in extension & post in flexion. But less predictable in grade II-V and this study showed paradoxical response but results were not statistically significant	Minimal description of IVD migration method & IVD bulge

Key: pMRI= positional MRI; T2W= T2 weighted, NSit = Neutral sitting; FSit = Flexed sitting; ESit = Extended sitting; St = Standing; flex = flexion; ext = extension; F = female; M = Male; asymp = asymptomatic; sympt = symptomatic; sig diff = significant difference; IV = intervertebral; VB = vertebral body; NR = nerve root; CSA = cross sectional area; ROM = range of movement; NP = nucleus pulposus; T1W = T1 weighted; FSE = fast spin echo; rMRI = recumbent MRI; kMRI = kinetic MRI; Cx = cervical; Lx = lumbar; VAS = visual analogue scale; a = anterior; p= posterior; m = middle; AP = antero-posterior; sag = sagittal; LBP = low back pain; IVD = intervertebral disc; TCS =tethered cord syndrome; vert = vertebral; SC = spinal cord; Spondy = spondylolisthesis; interob = interobserver

2.4.5.4: Investigation of lumbar nucleus pulposus behaviour

There are many *in vitro* and *in vivo* studies investigating the behaviour of the IVD as well as theoretical assumptions and there are also a growing number of reports investigating the IVD in loaded, upright positions. Despite the disadvantages already discussed, pMRI is currently an ideal tool for the investigation of the IVD in upright, loaded positions.

Clinical studies using MRI mainly focus on the outer IVD, namely the AF for diagnosis of tears or herniation in order to guide clinical management. The NP is only included when there is annular disruption and NP containment failure (Fazey 2011). MRI is ideally placed as the only non-invasive modality that can image the NP in terms of physiology, morphology and positional change which can then infer the overall behaviour of the IVD (Fazey 2011).

In a search of the literature to identify articles using MRI to investigate NP behaviour, only 13 peer-reviewed articles were found. These studies are displayed in Table 2.4.2.

T2W sagittal, axial and coronal MRI images have been used to investigate the unloaded effect of position on the NP using different measurement techniques (Beattie et al 1994, Fennell et al 1996, Brault et al 1997, Edmondston et al 2000, Fazey et al 2006, Fazey et al 2010, Takasaki et al 2010) whereas others have used pMRI to investigate loaded effects on the IVD and NP (Zou et al 2009, Nazari et al 2012). Other authors have investigated the IVD and NP via geometric modelling and 3D volume reconstruction in subjects with scoliosis and spondylolisthesis (Perie et al 2001, Perie et al 2003, Violas et al 2007, Perie & Curnier 2010) but these pathologies are outwith the scope of this thesis so will only be included in Table 2.4.2 for information, but will not be commented on within this thesis.

Previous studies investigating the NP response to flexion and extension in the sagittal plane (Beattie et al 1994, Fennell et al 1996, Brault et al 1997, Edmondston et al 2000) have been restricted to conventional supine MRI. Beattie et al (1994) & Fennell et al (1996) visually identified both anterior IVD margins and NP boundaries but did not report ICCs. Beattie and colleagues

Table 2.4.2: Nucleus Pulposus parameters investigated via Magnetic Resonance Imaging

Study	Sample	Investigation	Outcome measure	Results	Comment
Beattie et al (1994)	20 healthy asymptomatic women Mean 23.8 years (+/- 2.6)	The effect of flex & ext on NP position in 1.5T rMRI (T2W sag images)	Supine rMRI in flex & ext (using cushions and knee/hip flex) Lumbar flex via Schober & ext via reverse Schober Lumbar spine angle via Cobb NP Ant & post distance for L3/4 to L5/S1 measured in each position	Mean angle flex 36.6 degrees & ext 48.8 Significant differences in post distance of NP at each level between flex & ext but no significant differences in anterior distances. Abnormal NPs may not move in same manner as normal NPs	Small sample, measurements reliant on observation of NP boundaries, therefore requires good resolution of images and minimal degenerative changes
Brault et al (1997)	10 male asymp subjects 21-38 years	Quantify pattern of MRI pixel intensity variation in IVD & monitor NP displacement in sag plane	rMRI 1.5T with lumbar spine supported in flex & ext with pads mid-sag images PPI. segmental ROM via Cobb method	Peak intensity shifted post during flex & ant during ext. Mean AP diam IVD 35.28mm in flex and 35.92mm in ext	First time PPI method reported. Small sample and unloaded positions
Edmondston et al (2000)	10 asymptomatic subjects Mean 30 +/- 5.8 years 6F:4M	Evaluated effect of sag plane positions on IVD height & NP displacement	1.0T T2W sag images L1-S1 in supine flex & supine ext. IVD height, NP position via PPI from ant IVD boundary. IVD degen (Thompson scale) ROM (Cobb angle)	From flex to ext, signif increase in ant IVD height & ant displacement of NP (p<0.0001). 30% IVDs had post shift. Degen changes in 26% IVDs. ICC 0.71 for NP mmt.	Small sample, unloaded positions. Although trend in IVD/NP behaviour, need further investigation to explain 30% IVDs having opposite behaviour.
Fazey et al (2006)	3 asymp females Mean age 27 years	1.0T MRI - T2W images (sag & axial): supine extension, left trunk rotation in supine extension, supine flexion and left rotation in supine flexion	Pixel profile technique Cobb angle for L1/S1 change between flexion & extension position. Zygapophyseal joint angles. IVD degeneration Mid axial slices at L1/2 & L4/5 had pixel	5 out of 6 IVDs, NP deformed ant in extension & post in flexion. Left rot caused right migration in 9 out of 12 IVDs Intra-rater reliability of peak pixel intensity was 3.9% (CVs)	Small sample, unloaded effects. Pixel intensity profiling presented for first time in axial scans

			intensity profiles derived using ImageJ	demonstrating reliable method to determine profile of signal maps within IVD	
Fazey et al (2010)	21 healthy volunteers. 11 F: 10M Mean 24.8 years (range 20-34 years)	NP deformation response to lumbar lateral flexion	Axial T2W & coronal T1W images from L1-S1 in neutral & left lateral flexion in 0.2T open MRI Intersegmental range of lat flex & axial rot evaluated Magnitude & displacement of NP using previous pixel profile technique (Fazey et al 2006)	NP displaced away from direction of lat flex in 100/105 IVDs (p<0.001). Extent of displacement assoc strongly with lat flex at L2/3 (p<0.01). Reliability of lat flex angle measurement, ICC = 0.99 btn 2 testers.	First invivo report of NP response to lat flex 2 assistants held lat flex position during scans. Authors acknowledge limitations: measurement error with small ranges, pre-existing scoliosis effect & only studied healthy young subjects
Fennell et al (1996)	3 volunteers (1F:2M, aged 18, 25 & 46 years)	rMRI in NLSly, FLSly, ELSly with cushions to measure migration of NP during flex & ext segmental angles	1.5T rMRI L5/S1 excluded as unable to visualise. Ant & post margins of NP determined in each position	Results mimic cadaveric studies and extent of migration correlates to flex/ext angle. 2 subjects had anterior migration of NP in flex	Small sample and variable subjects (previous pain, age range) Reliant on observation of NP boundaries.
Nazari et al (2012)	25 asymptomatic male volunteers Mean age 26.8 (SD 5.6) (range 20-38 years)	Compared effect of different postures on IVD & NP using pMRI	pMRI: sitting, supine and Standing from L1-S1 imaged. All IVDs graded III or more (Pfirschmann) excluded. IVD height via Dabbs Lordosis (L1/S1 angle) via Cobb NP & IVD length, Ant & post distance of NP using Osiris software	RME reported for measurements. Lordosis: st = 58.4°; sit = 26°; supine = 59.1° Sig diff in ant IVD height btn supine & upright; post IVD height in sit @ L4/5 & L5/S1; st @ L3/4 & L4/5. Sig increase IVD & NP length at all levels in upright postures (sit>st). 8/25 (32%) had at	No post-hoc testing carried out (multiple comparisons) Only L3/4 to L5/S1 reported. Claimed NP longer & thinner in diff postures but didn't evaluate NP height. Only males included. Only assessed sagittal plane.

				least 1 degenerate level. NP length increase more than IVD in upright postures	
Perie et al (2001)	14 children with scoliosis	Developed new geometric model of IVD via MRI & quantified NP migration in scoliotic IVDs	Sag & coronal T2W images of entire spine in 1.5T MRI. Displacement of NZ centroid in relation to adjacent VB centroid represented NZ migration	NZ migration & wedge angle quantified. Signif correlation ($p < 0.0001$) btn NZ migration & wedge angle in coronal plane. Results in agreement with theory of IVD behaviour – NP migrates into curvature away from narrowing	Method limited to non-degenerate IVDs. Small sample of scoliotic children
Perie et al (2003)	11 scoliotic girls (mean age 12.5 +/- 2years)	Correlate scoliotic NZ migration & VB behaviour	1.5T T2W sag & coronal images CT images also Used previous method to calculate NZ migration & mechanical migration (Perie et al 2001)	NZ migration occurred in convexity of curvature	Limited study and only investigated scoliotic girls. Due to radiation from CT and processing time, not suitable for clinical use
Perie & Curnier (2010)	29 patients 14 spondylolisthesis (mean age 14.7 +/- 2.9 years) 15 scoliosis (mean age 13.6 +/- 2.7 years) 9F: 6M	To propose parameters of NP signal intensity distribution & quantify changes in spondylolisthesis or scoliosis	1.5T T2W sag MR images. Quantified distribution btn signal intensity centre & geometric centre. T12/L1 to L5/S1 classified via Thompson scale HIZ of NP semi-automatically detected via MatLab software	Significant differences in NP signal intensity due to pathology and its severity. Suggests this technique may be useful for early diagnosis IVD pathology as highlights abnormal MR signals.	Retrospective study. No L5/S1 included for spondylolisthesis assessment due to degenerative changes. Still reliant on manual identification of NP zone on MR image. Authors acknowledge conditions have 3D complexities and so require 3D analysis.
Takasaki et al (2010)	34 year old female with derangement syndrome (right sided pain)	Comparison of NP profiles from MRI pre & post MDT treatment. Supine sag, axial &	L4/5 IVD MRI 1 month apart measured using pixel intensity method used previously by	The pixel intensity method demonstrated an initial shift of pixels to the left whereas 1	Case study Limitation acknowledged that authors assumption of

		coronal T1 & T2W images from 0.2T open MRI	Fazey et al (2006)	month later they were equally balanced between right and left	NP relocation was based on MDT treatment but more work needed to establish this
Violas et al (2007)	28 patients with idiopathic scoliosis 26 F: 2M Mean age 14 years 8 months (range 11 - 19)	3D reconstruction from MRI of volume properties of IVD pre and post surgery 1.5T T2W images	Cobb angle for curvature Contours of AF & NP segmented semi automatically and volumes reconstructed using custom-made image processing software.	Pre-op data most relevant: IVD volume ranged between 7300 - 10,000mm ³ , NP volume between 3500-4600mm ³ and standard deviations ~30% for both. Volume occupied by the NP was 50%	Although limited findings as investigated scoliotic IVDs. Good method for volume investigation but no full method given.
Zou et al (2009)	513 patients with back pain & referred for kMRI 298 F: 215 M Mean 42.6 years (Range 19-74)	pMRI used to describe degenerate IVD bulge in different positions	pMRI T1 & T2W FSE images in N.Sit, F.Sit & E.Sit L1/2 - L5/S1 levels investigated IVD degeneration classified via Pfirrmann scale Disc migration via MRI analyser version 3 software	IVD bulge increases with IVD degeneration severity Increased bulging at L4/5 & L5/S1 All grade I NPs migrated ant in extension & post in flexion. But less predictable in grade II-V and this study showed paradoxical response but results were not statistically significant	Minimal description of IVD migration method & IVD bulge. Retrospective

KEY: ant = anterior; post = posterior; PPI = peak pixel intensity; HIZ = high intensity zone; N.Sit = upright neutral sitting; F.Sit = flexed sitting; E.Sit = extended sitting; sit = sitting; st = standing; NLSly = neutral left side lying; FLSly = flexed left side lying; ELSly = extended left side lying; mmt = measurement; signif = significant; asymp = asymptomatic; AP = antero-posterior; diam = diameter; T1W = T1 weighted; T2W = T2 Weighted; F = female; M = male; sag = sagittal; VB = vertebral body; IVD = intervertebral disc; NP = nucleus pulposus; AF = annulus fibrosus; post = posterior; ext = extension; flex = flexion; rot = rotation; ant = anterior; CV = coefficient of variation; btn = between; MDT = mechanical diagnosis and therapy; assoc = associated; rMRI = recumbent MRI; NZ = neutral zone; degen = degenerative

(1994) reported an average difference between measurements of anterior and posterior measurements as 0.1mm for both. Edmondston et al (2000) employed a peak pixel intensity method to identify/infer the NP centre and reported an intra-class correlation ($ICC_{1,1}$) of 0.71. These studies were limited due to small sample sizes, varying inclusion criteria, they employed different techniques for analysis of the NP response and overall, results were mixed.

Beattie et al (1994) measured the distances from the L3/4, L4/5 & L5/S1 NPs to the anterior and posterior IVD boundaries in flexion and extension in 20 asymptomatic females with a mean age 23.8 years (range 20-30 years, SD +/- 2.6 years). Flexion and extension positions were maintained during the rMRI scans with foam pads and a lumbar roll. The authors demonstrated significant differences in the posterior NP distance at each level between flexion and extension but no significant difference in the anterior distance. The authors acknowledged the difficulty in identifying the demarcation between the AF & NP in IVDs due to decreased NP signal and that 8 subjects (20%) had at least one IVD with a reduced NP signal.

Fennell et al (1996) investigated the NP response to position in three volunteers. They identified the positions of the anterior and posterior margins of the NP for neutral, flexed and extended positions via visual tracings. The results supported theory where flexion caused posterior NP migration and extension caused anterior NP migration. However, the authors also noted that in two subjects, the anterior border of L4/5 migrated anteriorly in flexion. This anomaly was explained by the history of the subjects both having had previous back pain and possibly degenerative changes although no classification was used to grade degenerative changes in this study.

Brault et al (1997) investigated the NP response to flexion and extension via a more objective method using pixel intensities along the mid-sagittal slice. Ten asymptomatic men with no history of back pain aged 21-38 years had extension and flexion rMRI scans performed. The flexion and extension positions were maintained using pads for support. The pixel intensity graphs produced had the distances converted from millimetres to percentages (0% =

anterior border & 100% = posterior) to allow comparison within and between subjects. The peak pixel intensity was selected as representing the peak hydration of the NP and the shift in this peak was calculated between positions as a percentage of the IVD diameter for all IVDs (L1/2 – L5/S1). The AP diameter of healthy IVDs was reported as 35.28mm in flexion and 35.92mm in extension. The greatest NP migration was demonstrated in the upper lumbar IVDs (L1/2, L2/3) with the least migration demonstrated in L4/5 which was significant at the $p < 0.05$ level. Although this study was limited in terms of sample size and only recumbent scans performed it did present for the first time a quantitative method of NP migration analysis via mathematical modelling. The authors also recognised that the pixel profiles presented a relative hydration pattern which was dependent on the signal intensity. Of the nine abnormal IVDs in this study, the authors also reported that the pixel intensity distribution was variable and did not fit the curve developed for the normal healthy IVDs. Overall, the authors concluded that in flexion the peak pixel intensity moves posteriorly and in extension the peak moves anteriorly.

Edmondston et al (2000) investigated the effect of flexion and extension on IVD height and NP displacement in 10 asymptomatic subjects (mean age 30 +/- 5.8 years). Both scans were performed in supine with pillows, wedges and towels used to hold the flexion and extension positions during scans. NP displacement was calculated between the two positions via identification of the peak pixel intensity on sagittal T2W scans. The distance from the anterior boundary of the IVD to this peak signal intensity was measured and then expressed as a percentage of the total IVD antero-posterior diameter. The reliability of this measurement was stated as $ICC_{1,1}$ 0.71, with a standard error of measurement = 4.3%. The authors reported that in moving from flexion to extension, there was a significant increase in anterior IVD height and anterior displacement of NP (6.7%; $p < 0.0001$). However, 30% of all IVDs did not follow this trend and demonstrated a posterior displacement. Degenerative changes were reported in 26% of all IVDs assessed. The authors recommended caution in applying a stereotypical behaviour to IVDs and that further research should be conducted to clarify these results.

Fazey et al (2006) reported a study investigating the torsional effect on the IVD using a conventional MRI scanner. This study included an asymptomatic sample of 3 females (mean age 27 years) and analysed the axial scans to investigate the IVD response/deformation. Three parallel pixel intensity profiles were derived from mid axial slices using Image J (NIH Image-J, Bethesda, USA) image analysis software at L1/2 & L4/5 levels. The raw pixel profile data were then normalised to 100 points using Labview software (National Instruments, Austin, USA) and then averaged. The authors reported a reliability of 3.9% (coefficient of variation) for intra-rater reliability for peak pixel intensity. In five of the six IVDs assessed, the peak pixel intensity reflected theoretical assumptions of NP and IVD behaviour in that the intensity shifted anteriorly in extension and posteriorly in flexion.

In a more recent study, Fazey et al (2010) investigated the NP deformation in response to side flexion in 21 healthy volunteers (mean age 24.8 years; range 20-34 years) in a 0.2T horizontally open MRI. Subjects were manually held in place for the duration of the side flexion scan. Image J (NIH Image-J, Bethesda, USA) image analysis software was again used on T2W neutral & laterally flexed axial images from L1/2 to L5/S1. The previous method of peak pixel intensity profiling (Fazey et al 2006) was used to determine the direction, extent and pattern of hydration for neutral and side flexed images. There was a significant difference at all IVD levels for the NP peak pixel position between neutral and side flexion positions ($P < 0.001$). The results demonstrated a strong association between NP deformation and side flexion direction, where 95% (100/105) NPs deformed away from the direction of side flexion. Acknowledged limitations in this study were the small sample of young healthy volunteers, potential measurement errors due to the small ranges investigated and the effect of subjects having unknown pre-existing scoliosis.

Although pMRI has been involved in the assessment of LBP, there has been minimal literature published specifically investigating the NP. Zou et al (2009) used pMRI to investigate the degenerate IVD bulge in different positions. The sample included 513 patients with back pain that were referred for pMRI (298 females: 215 males; mean age 42.6 years; range 19-74 years). pMRI images were taken in neutral, flexed and extended sitting

positions and L1/2 – L5/S1 levels were evaluated for IVD degeneration (Pfirrmann et al 2001) and IVD migration. The authors reported that the IVD bulge increases with IVD degeneration severity. All grade I NPs migrated anteriorly in extension and posteriorly in flexion. This behaviour was less predictable in degenerative IVDs with grade II-V. Although this study included a large sample size, this was a retrospective project and so subject to inclusion bias as well as having a large age range. Another limitation of this study was the lack of description provided regarding the IVD migration method for measurement.

Nazari et al (2012) recently investigated the effect of different postures on the lumbar IVD & NP using pMRI. They recruited 25 asymptomatic male volunteers (mean age 26.8 years, range 20-38 years) to have pMRI scans performed in sitting, supine and standing. L1 to S1 were imaged and all IVDs graded for degenerative changes (Pfirrmann et al 2001). All IVDs with grade III or above changes were excluded from analysis. The remaining IVDs had measurements of IVD height, lordosis (L1/S1 angle), IVD & NP length and NP anterior and posterior distance in each position recorded. Significant differences were reported in anterior IVD height between supine and upright postures; and posterior IVD height in sitting at L4/5 & L5/S1 and standing at L3/4 & L4/5. A significant increase in IVD & NP length was reported at all IVD levels in upright postures (sitting greater than standing). At least one degenerative IVD (Grade III or above) was reported in 8/25 subjects (32%). The authors concluded that the NP length increases more than the IVD length in upright postures. Acknowledged limitations of this study included a small single sex sample (male only) and only sagittal plane effects were assessed. However, additional limitations include limited analysis (no post-hoc tests included due to the multiple comparisons evaluated); L1/2 to L5/S1 were imaged but only L3/4 to L5/S1 were reported; and the authors claimed the NP is longer and thinner in different postures but failed to evaluate or report the NP height between postures to support this claim.

From the above literature investigating the NP behaviour it is apparent that more research is required to establish a definitive behaviour pattern/range

for the lumbar NP including asymptomatic healthy populations, degenerative changes and clinical populations with DLBP. pMRI is ideally placed as a tool to investigate all three areas in the sagittal, axial and coronal planes.

2.4.6: Summary

This section has reviewed the literature relevant to MR imaging of the IVD and DLBP including: advantages, disadvantages, the use, accuracy, and asymptomatic MRI findings as well as pMRI and its role in the investigation of DLBP and the behaviour of the IVD.

This review has highlighted the lack of imaging studies related to IVD behaviour. Clearly, there are advantages and disadvantages to MRI and pMRI, but despite this, pMRI is ideally placed to enable the current investigation of non-invasive IVD behaviour via the NP response. Previous research has investigated the NP response to flexion, extension, torsion and side flexion but very few have investigated the NP response in loaded, weight-bearing positions. There is a need to establish the NP response to loaded positions using objective methods that can add to the knowledge base and then inform the assessment and conservative management of DLBP. Therefore this study will investigate the lumbar IVD behaviour in different positions (sitting, standing and lying) via the NP response using pMRI in asymptomatic and DLBP participants.

Chapter 3: Methods

3.1: Study design

The purpose of the following study was to carry out the previously stated objectives in the lumbar IVD in people with DLBP and without back pain using pMRI and 3SPACE Fastrak, to identify the IVD behaviour in both groups as well as any differences between the two groups.

Therefore, the study design was an analytic observational study (Centre for Evidence Based Medicine 2009) where the principle investigator attempted to quantify the effect of position on the lumbar IVDs using non-probability sampling (Trochim 2006). Non-probability sampling uses convenience samples that fit the purpose of the study in question (Ross 2012). The advantages of this type of study are that it has a relatively small time and financial cost requirement to carry out compared to probability sampling techniques that require randomisation and large numbers. Convenience sampling has a more focused approach than other types of sampling with specific pre-defined groups (asymptomatic healthy subjects and DLBP subjects for this study) and is useful when it is important to reach a target sample quickly. The disadvantage of using convenience sampling is that there is a risk of over or under-recruiting particular groups within the population, and that there is an inherent bias as the sample was not chosen at random therefore it may be unlikely to be representative of the population being studied (Trochim 2006, Lund & Lund 2010). However, LBP is a very common condition in society, so the chances of under-recruiting the required sample were expected to be low.

3.2: Ethics

In accordance with the Declaration of Helsinki (World Medical association 2008) it is important to consider and justify the ethical and moral basis of the proposed research project. Within the NHS, ethical approval for research is given from the National Research Ethics Service (NRES) which has core aims of "protecting the rights, safety, dignity and well-being of research participants" while "facilitating and promoting ethical research that is of potential benefit to participants, science and society" (NRES 2013).

As this project required subjects to adopt and maintain positions (sitting and standing) that could be potentially provocative to those with discogenic pain it was important to fully consider this. The position order selected for pMRI scanning was chosen so that the theoretically provocative positions were adopted first followed by positions used in routine clinical practice for treatment of back pain (extended and lying down positions). This scan order would then theoretically minimise any potential discomfort or pain provocation. All subjects were provided with an information sheet detailing their proposed participation, as well as the author discussing any queries with them, prior to them giving written informed consent before their pMRI scans.

Ethical approval for this study was granted by the North of Scotland Research Ethics Service (REC number: 06/S0802/40, Appendix 1) and the School Research Review Group (SRRG), School of Health Sciences, Robert Gordon University (SRRG reference number: SHS10/04, Appendix 1). Approval for a significant amendment to the study for phase 3 (DLBP subjects) was granted by the North of Scotland Research Ethics Service (Amendment number: AM01, Appendix 1).

Chapter 4: Asymptomatic subjects (Phase 1)

As the study planned to identify the sagittal plane NP migration in the pMRI scans, it was necessary to establish if the author could reliably identify the NP on pMRI scans. Phase 1¹ was designed to establish the reliability of the author in the identification of the lumbar NP from sagittal and axial pMRI scans. Secondary aims of this phase were to identify the optimum positions for testing in the pMRI scanner as this had not been performed before and some of the positions could have a potentially provocative effect for LBP/DLBP subjects. In addition, the effect of position on the NP sagittal plane migration required to be investigated as this has not been attempted using pMRI before and this would also enable the author to perform sample size and power calculations on the results to inform the sample size for Phase 3 (the DLBP subjects).

The aim of phase 1 was:

- To establish the within day intra-tester reliability of tester 1 in the identification of the lumbar NP in pMRI scans
- To identify the optimal positions to examine the lumbar IVD using pMRI
- To establish the effect of position on the sagittal migration of the lumbar NP

The author, who had been trained in the use of the Osiris image analysis software for pMRI scans, was responsible for carrying out all the pMRI measurements in this study.

4.1: Sample

A convenience sample of 11 healthy volunteers (4 male: 7 female) was recruited by response to a general notice and word of mouth among School of Health Science staff, family and friends.

¹ The results from phase 1 have been published in Spine - (Alexander et al 2007, Appendix 5)

Participants attended the Positional MRI Centre, Woodend Hospital, Aberdeen for the pMRI assessment on one occasion. Data collection for phase 1 was conducted over a 4 month period.

Inclusion criteria for this phase were:

- No present history of LBP
- No previous history of LBP that required medical treatment
- No cognitive, mental or communication impairment that would prevent informed consent.
- Aged 18 – 65 years
- Male or female

It was important that this group had no current history of LBP so that they could be compared as a control group to the group of interest in this study. However, as LBP is very frequent in society (Maniadakis & Gray 2000), it would be challenging to recruit enough people to the study from the convenience population if the study only included people who had never had LBP. Therefore, people may have had some LBP in the past but were only included if it did not require treatment from a medical professional.

Participants also needed to have no prior cognitive, mental or communication issues that would prevent informed consent. This is because this study was largely unfunded, so there was no financial provision available to provide the measures required to enable informed consent from any potential participant that had any of these issues (e.g. communication – no interpreter available for potential participants that did not have English as their first language).

The age and gender criteria justification were that LBP affects male and female equally and most commonly in the working age such as 18-65 years (Maniadakis and Gray 2000, NHS QIS 2009), therefore the same criteria were employed for the DLBP & asymptomatic group to enable comparison between both groups.

Exclusion criteria included:

- Any contraindications to a MRI procedure
- Hip/shoulder width greater than 45cm (width of pMRI).

The exclusion criteria were related to the pMRI scanner. Everyone who undergoes a MRI scan has to be screened by the MRI radiographer first to identify any contraindications to the procedure (Appendix 4). In addition, the width between the pMRI magnets is 45cm; therefore anyone with a hip or shoulder width greater than this was excluded from the project as they would not fit in to the scanner.

4.2: Protocol

A 0.6 Tesla, positional "Upright" MRI (Fonar Corp., Melville, NY) was used to carry out the scans. This scanner can image the spine in supine, erect (weight-bearing), and seated positions in both neutral and other (e.g. flexed/extended) postures (37,38). Sagittal (TR-3848, TE-120) and axial (TR-890, TE-140) T2 weighted images through the 5 lumbar IVDs were taken: field of view = 30cm, slice thickness = 4.5mm, slice interval = 5mm, acquisition matrix = 180 x 256/3NEX, imaging time = 4 to 5 minutes per sequence. The same radiographer carried out each scan at the same time each day to minimise diurnal effects (Swinkels & Dolan 2000), in the same order: Standing, Sitting (Neutral, Flexed and in Extension), Supine and Prone extension (see figure 4.2.1). Initial work revealed that this sequence minimised subject discomfort, as the most provocative positions were used first with positions that are used in physiotherapeutic management introduced later. The initial work also revealed that standing flexion and extension, held for around five minutes, were not feasible positions to assess due to the healthy volunteer being unable to remain stationary. Flexed standing caused some postural hypotension and discomfort in the calf muscles and standing extension caused lower back discomfort. As a result both these positions were deemed unfeasible and unethical to investigate via

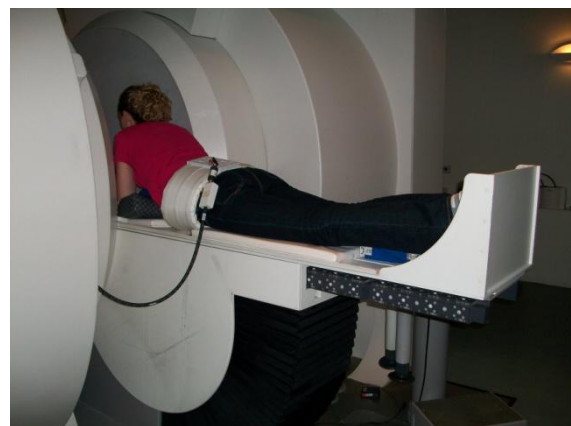
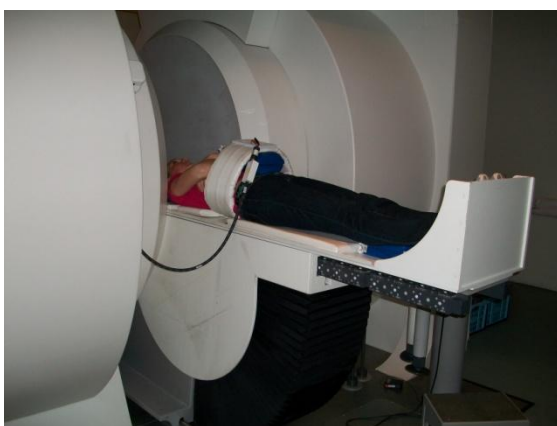


Figure 4.2.1: positional Magnetic Resonance Imaging scan positions (from left to right: Top - Flexed sitting, Standing; Middle - Neutral sitting, Extended sitting; Bottom - Supine and Prone extension).

pMRI and in a population with DLBP and will not be included in the rest of this project.

Extended sitting and Prone extension were maintained passively using foam rolls and wedges. Subjects were required to maintain each position for approximately 20 minutes per scan (sagittal and axial views) and there were 6 scans performed. Due to the time required to acquire each scan, each subject was instructed to adopt each position at the point where they felt they could maintain it for the duration of the scan (i.e. no end range positions were adopted).

Unlike a standard supine MRI scanner used clinically, the pMRI scanner can require subjects to wear a coil around the region of interest whilst in the scanner. In this study subjects had a coil around the lower back area (see figure 4.2.1: supine and prone extension images) but it did not restrict movement or positioning in the scanner. Examples of the images produced in each position are shown in Figure 4.2.2.

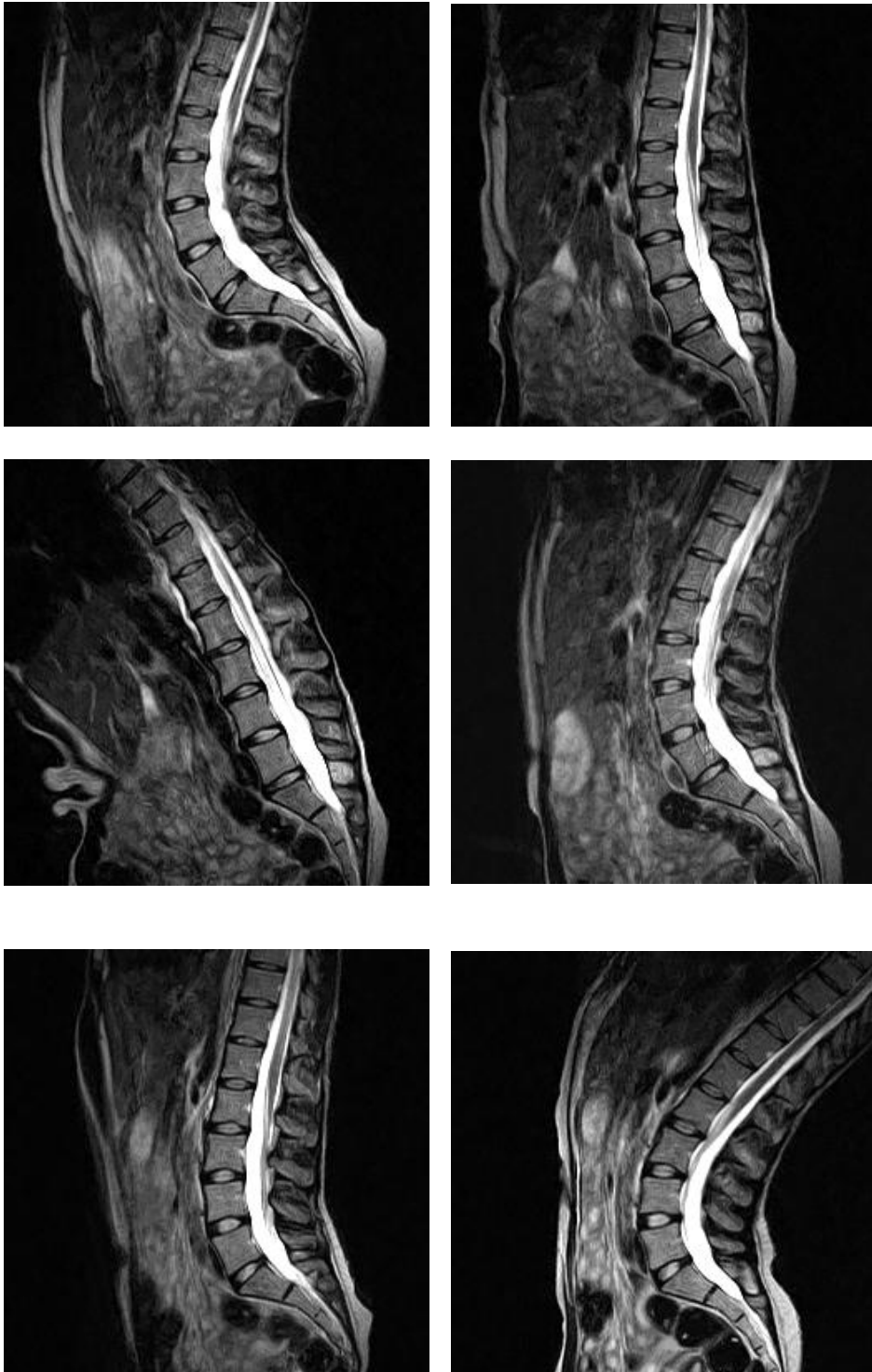


Figure 4.2.2: Examples of positional Magnetic Resonance Imaging sagittal scans (From left to right: Top - Standing, Neutral sitting; Middle - Flexed sitting, Extended sitting; Bottom - Supine and Prone extension)

4.3: Analysis

All images were transferred to CD ROM, and subsequent measurements were performed using the Osiris 4.19 software program (University of Geneva, Geneva, Switzerland) by the author. In addition, all images were examined and reported by a consultant radiologist using standard radiology reporting methods.

The Osiris software comprises general medical image manipulation and analysis software with basic tools available such as contrast/intensity adjustment, region of interest management, and angle and distance measurements as well as more complex tools. This software has been used previously in spinal research involving pMRI and has had high levels of reliability reported (Siddiqui et al 2005, Karadimas et al 2006, Siddiqui et al 2006a, Siddiqui et al 2006b, Beastall et al 2007, Kumar et al 2008). The reported reliability however has only been established for IVD height and endplate angles; there still remains a need to establish the reliability for NP migration within the IVD.

4.3.1: Sagittal scan measurement protocol

The mid-sagittal slice image was identified for each subject, in each position. The author then located the centre of the lumbar NP in each image using the peak pixel intensity method of Brault et al (1997). This is where the mid-disc line and the point of peak pixel intensity on that line are identified (Figure 4.3.1 demonstrates an example of this). The distance from the anterior disc boundary to this point was then recorded in millimetres and defined as the extent of sagittal migration of the NP; therefore, greater values represented greater posterior migration of the NP.



Figure 4.3.1: An example of the measurement of sagittal Nucleus Pulposus migration from sagittal positional Magnetic Resonance Imaging

4.3.2: Axial scan measurement protocol

IVD measurements from axial MRI scans are less common in the literature than sagittal scans. Therefore the author initially had minimal guidance from the literature to inform the measurement method for the axial scans.

For this study, the mid-disc axial T2W images had three parallel pixel profile intensity lines equidistant apart (5mm), placed from anterior to posterior across each IVD from left to right in the coronal plane (see figure 4.3.2). The distances from the anterior IVD boundary to the peak pixel intensity on each line was measured (mm) three times and then the mean was calculated from the three values. As for the sagittal scans, greater values inferred greater posterior migration of the NP.

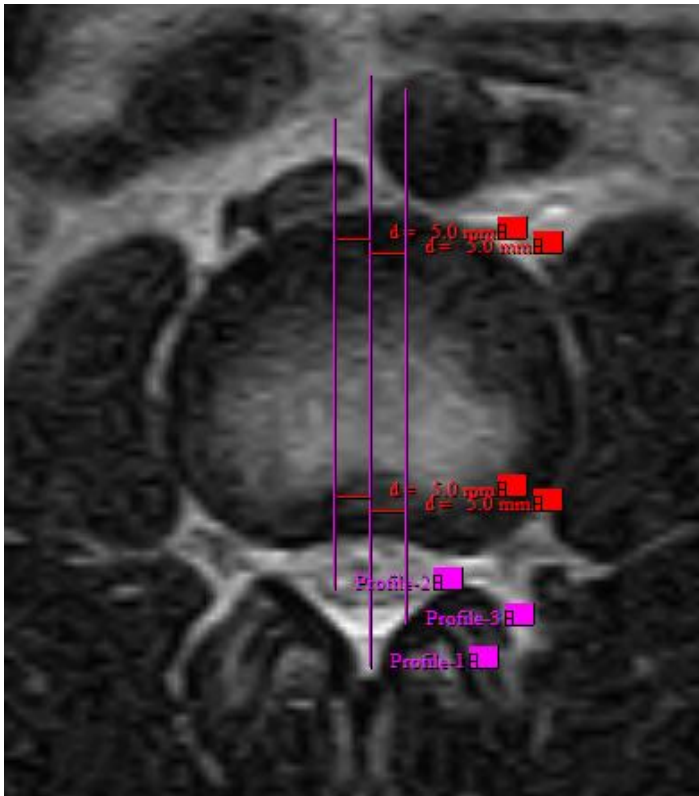


Figure 4.3.2: An example of the measurement of sagittal Nucleus Pulposus migration from axial positional Magnetic Resonance Imaging

It has been demonstrated that the mean data from three line samples is considered more representative of hydration profiles than a single line sample in axial MRI images (Fazey et al 2006). Axial images have also been considered to represent the broad distribution of the NP hydration signal better than sagittal images (Fazey 2011). This axial measurement method has been used previously by Fazey et al (Fazey et al 2006; Fazey et al 2010; Takasaki et al 2010; Fazey 2011), although they normalised the raw pixel intensity data to 100 points and averaged them using a Labview software routine (National Instruments, Austin, Texas, USA). By measuring the distance in the axial T2W scans and calculating the mean distance at each level in each position in this study, it can enable a comparison to be made between the axial and sagittal images in this study.

Previous authors investigating the lumbar spine using pMRI have used OSIRIS image analysis software whereas other IVD researchers have used

Image J (NIH Image-J, Bethesda, USA) image analysis software. Both types of software are equally adept for the requirements of this project, but as the author has previously used and is experienced with OSIRIS, this software was identified for use in this project. It has been reported in literature related to Image J that this software also has a steep learning curve, and therefore would require extra time in the overall project to get the author proficient in its use. In addition, the pMRI images produced are not compatible with Image J software unless further conversion to DICOM (Digital Image Communication in Medicine) is carried out prior to using Image J.

Neither previous publications by Fazey et al (2006 & 2010) nor discussion with Peter Fazey (personal communication) have clarified the optimal distance to be chosen between the three parallel lines (Lim 2010). For the purpose of this study, the distance between the lines was set at 5mm which creates 3 pixel intensity profile lines covering approximately 1/3 of the IVD diameter. A 5mm distance between the three pixel intensity lines was determined based on the calculations of the IVD and NP diameters. From a group of asymptomatic individuals (N = 7, previously collected data), axial T2W images in upright neutral sitting were evaluated to determine the NP diameter. Table 4.3.1 displays the measurements obtained and corresponding mean values (and standard deviations) for each IVD level.

There is a lack of dimensions reported in the literature for the IVD but a small Turkish study (N= 25) has demonstrated a mean anterior IVD height of 0.88cm – 1.20cm and an IVD volume of 16.23 – 22.16 with no differences between gender (Gocmen-Mas et al 2010). A recent Australian PhD thesis has also reported the average width and height dimensions for the IVD to be 56mm and 11mm respectively (Fazey 2011).

Table 4.3.1: Axial mid slice Nucleus Pulposus width (mm) in Neutral sitting (only non-degenerate intervertebral discs)

IVD level	S1	S2	S3	S4	S5	S6	S7		Mean	SD
L1/2	30	32	Degen	Fuzzy	Fuzzy	26	Fuzzy		29.33	3.06
L2/3	33	31	44	38	32	36	28		34.57	5.29
L3/4	35	43	38	Degen	29	35	31		35.17	5.0
L4/5	Degen	35	Degen	Degen	31	31	37		33.5	3.0
L5/S1	23	Degen	Degen	27	Degen	26	29		26.25	2.5

KEY: S = Subject, Degen = degenerated IVD, Fuzzy = poor visualisation/resolution and therefore unable to identify NP boundary, SD = standard deviation

Scans were opened in Osiris and magnified to 400% as per previous image analysis protocols (Siddiqui et al 2005, Karadimas et al 2006). The mid disc slice was then viewed and the widest point (horizontally) of the NP boundary was then identified visually and measured in mm (See figure 4.3.3).

Any IVD level demonstrating degenerative changes was not included as the NP boundary becomes indistinguishable from the AF with degeneration.

Additionally, any image that the resolution was insufficient to allow identification of the NP boundary was also excluded from analysis.

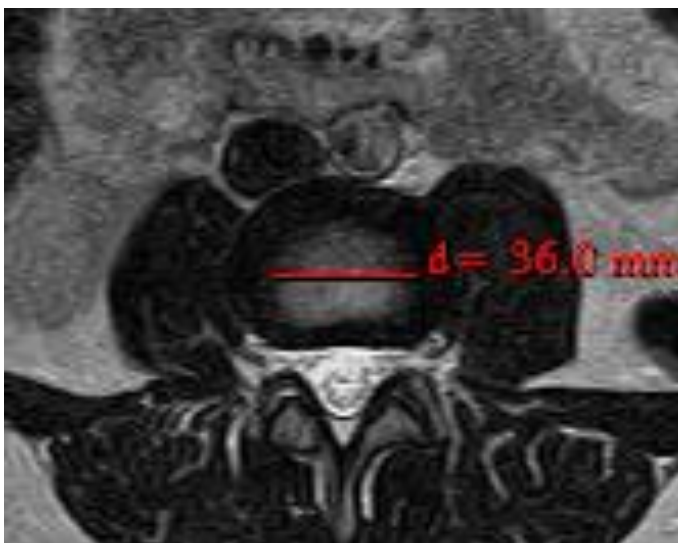


Figure 4.3.3: Measurement of L2/3 Nucleus Pulposus width

There were seven subjects included in the analysis of NP width (5 female: 2 male; mean age 37 years \pm 11 years). The mean NP diameter ranged from 26.25mm – 35.17mm, however every intervertebral level apart from L2/3 demonstrated degenerative IVDs or images with poor resolution thus reducing the overall sample for analysis.

The 5mm distance between the three pixel intensity profile lines amounts to a 10mm wide area within the approximate centre of the NP that can then reflect approximately the central third of the NP. It is advantageous to examine the central third of the NP as the outer thirds may have more variable pixel profiles as the NP and iAF approximate at more than the anterior and posterior NP boundaries (indeed, in some subjects the outer third would incorporate the AF which will affect the overall hydration profile and resultant data). By focusing on the central NP area, the anterior and posterior AF/NP boundaries should be clearly demarcated for analysis. As this method of analysis has never been carried out before, it is therefore based upon modification of the previously reported studies and logical discussion.

4.3.3: Reliability

Before analysing the effect of position on lumbar NP migration, the intra-tester reliability of locating the NP centre was assessed by measuring each midsagittal scan, for each subject, at each level in neutral sitting, 3 times on a blind basis. Neutral sitting was chosen as this position would have the spine in a neutral alignment to allow measurements to be performed in the anatomical position. The measurements were repeated three times as per recommendations by Bruton et al (2000). This process was repeated for both the sagittal and axial pMRI scans.

Separate intraclass correlation coefficients (ICC 2,1), for each IVD level (L1/2 to L5/S1), in upright sitting, were calculated to quantify the intra-tester reliability of location of the NP centre from the sagittal and axial images. The ICC (2, 1) was chosen as it would allow generalisation of the results for comparison to previous studies (Rankin & Stokes 1998). A two-way random effects model for absolute agreement was then chosen in SPSS Version 17.0,

to reflect the (2,1) Shrout and Fleiss model (Shrout and Fleiss 1979). In addition to the ICC (2,1), the standard error of the mean (SEM) and 95% confidence intervals were also calculated to present the magnitude of the measurement error as it has been acknowledged that no single test provides a complete measure of reliability (Eliasziw et al 1994, Bruton et al 2000).

4.3.4: The effect of position

All sagittal NP migration measurements were inputted into Excel and then exported to SPSS™ version 17.0 for subsequent analysis.

Before carrying out any inferential tests, it was important to establish if the assumptions for the use of parametric tests with this data were satisfied.

The main requirements for this are that:

1. The sample distribution is normally distributed
2. There is homogeneity of variance – variances should be the same throughout the data
3. The data should be in the form of interval or ratio data
4. Independence – where the behaviour of one participant did not affect or influence the behaviour of another (Field 2009).

The third and fourth elements of these requirements were met in that the data collected was in the form of the measurement of the NP migration (mm) in the sagittal and axial planes (ratio data), and data collection occurred where participants did not have the opportunity to confer or meet during their participation in this study. In order to satisfy the requirements of the first two elements, the data was explored visually via probability-probability plots and histograms and quantified via skewness and kurtosis as well as testing for normality using the Shapiro-Wilk test as the sample size was small ($n < 50$) (Field 2009).

The results of the Shapiro-Wilk test indicated that there were significant differences in the data at six levels (20% of the data) – L1/2 in Neutral sitting and Flexed sitting ($p = 0.018$ and 0.044 respectively), L2/3 in

Extended sitting ($p = 0.026$), L4/5 in Flexed sitting ($p = 0.011$), and L5/S1 in Flexed sitting and Prone extension ($p = 0.011$ and 0.046 respectively). As the requirements for parametric testing could not be met, non-parametric testing (Friedman's ANOVA) was used for inferential analysis (Field 2009). To determine which positions were significantly different a post-hoc Wilcoxon signed rank test was performed. With Bonferroni correction (15 tests in total), statistical significance was determined at $p < 0.003$ (Bland & Altman 1995).

Although some of the data failed to meet all the underlying assumptions for a parametric analysis, the comparison of groups using a paired t-test allowed an assessment of level of response and the difference effects with the significance levels now being approximate. The more robust Wilcoxon tests had already established where the significant differences existed.

The effect of position on the axial migration of the lumbar NP was also investigated using Friedman's ANOVA after 10% of the data was found to fall outwith the levels considered for normality (L1/2 in Neutral and Extended sitting and L2/3 in Prone extension). Statistical significance was set at $p < 0.05$. Post-hoc differences were also explored using the Wilcoxon signed rank test and paired t-test. With Bonferroni correction (15 tests in total), statistical significance was also determined at $p < 0.003$ (Bland & Altman 1995).

4.4: Results

All except one participant was employed at the time of this study. The group consisted of 7 females and 4 males with a mean (\pm SD) age of 36 (± 9 years); height 1.72 (± 0.08 m); and weight 72.09 (± 14.25 Kg).

4.4.1: Reliability

A high level of intra-tester reliability was found for the lumbar NP migration measurements (performed with the Osiris 4.19 software program) with ICCs for each position ranging from 0.71 to 0.97 (mean \pm SD, 0.89 ± 0.06). These results are displayed in table 4.4.1. While the consultant radiologist did

identify degenerative changes in 6 subjects, these were deemed to be indicative of normal, age-appropriate “wear and tear” in a healthy spine.

Table 4.4.1: Intra-class correlation (2,1), 95% confidence intervals and standard error of the mean results (mm) for sagittal and axial pMRI scan lumbar nucleus pulposus migration reliability results in Neutral sitting

Level	Sagittal			Axial		
	ICC	CI	SEM	ICC	CI	SEM
L1/2	0.973	0.929 – 0.992	1.77	0.750	0.15 – 0.99	0.44
L2/3	0.890	0.73 – 0.966	1.61	0.816	0.24 – 0.995	0.61
L3/4	0.706	0.394 – 0.9	1.04	0.962	0.72 – 0.999	1.11
L4/5	0.818	0.585 – 0.942	0.94	0.954	0.645 – 0.999	1.49
L5/S1	0.912	0.78 – 0.973	1.28	0.955	0.579 – 0.999	0.79

Key: ICC = Intra-class correlation, CI = confidence interval, SEM = standard error of the mean

4.4.2: Sagittal behaviour of the intervertebral disc

Initial descriptive analysis of the data is presented in table 4.4.2 and 4.4.3, where it can be seen that the mean NP migration ranged from 4.06mm to 9.49mm. The sitting positions all demonstrated the greatest posterior NP migration whereas the lying positions demonstrated the least amount of posterior NP migration.

Table 4.4.2: Mean (\pm standard deviation) sagittal plane Nucleus Pulposus migration (mm) in each position from sagittal positional Magnetic Resonance Scans

Position	L1/2	L2/3	L3/4	L4/5	L5/S1
Standing	19.42 (4.57)	20.06 (5.04)	17.43 (5.15)	15.58 (6.27)	15.55 (4.39)
Neutral sitting	20.94 (5.88)	21.61 (5.36)	20.30 (3.46)	21.30 (3.12)	22.46 (4.25)
Flexed sitting	21.42 (4.63)	22.73 (4.14)	19.94 (3.39)	21.70 (5.19)	20.06 (4.88)
Extended sitting	18.88 (4.32)	19.61 (4.49)	16.40 (4.24)	16.61 (5.17)	20.18 (6.22)
Supine	19.49 (5.44)	21.52 (3.76)	16.82 (2.88)	16.06 (4.7)	12.97 (5.33)
Prone extension	17.33 (4.87)	18.67 (3.67)	15.64 (3.85)	14.97 (4.01)	13.79 (5.53)
Overall migration range	4.09	4.06	4.66	6.73	9.49

Table 4.4.3: Descriptive statistics for sagittal positional Magnetic Resonance Imaging scan measurements of sagittal plane Nucleus Pulposus migration (mm)

Position	N	Mean	Standard deviation	Median	Minimum	Maximum
Standing	55	17.61	5.29	17.33	7.00	27.00
Neutral sitting	55	21.32	4.43	22.00	9.67	29.33
Flexed sitting	55	21.12	4.45	22.00	8.00	28.67
Extended sitting	55	18.33	5.01	20.00	5.67	29.67
Supine	55	17.37	5.27	17.00	4.67	26.67
Prone extension	55	16.08	4.62	15.67	7.00	27.67

The results of the Friedman's ANOVA analysis revealed that at all levels position exerted a statistically significant effect on the sagittal migration of the lumbar NP, $X^2(5) = 93.648$, $p < 0.001$. To determine between which positions the differences lay, post-hoc analysis was performed using the Wilcoxon signed rank test and the results are presented in table 4.4.4.

Table 4.4.4: Results of the post-hoc Wilcoxon signed rank test for sagittal plane Nucleus Pulposus migration from sagittal positional Magnetic Resonance Imaging scans

	T value	Asymptotic significance (2-tailed)
Neutral sitting – standing	1323.00	0.001*
Flexed sitting – Standing	1229.50	0.001*
Extended sitting - Standing	865.00	0.426
Supine – Standing	759.50	0.930
Prone extension – standing	432.50	0.008
Flexed sitting – Neutral sitting	795.00	0.834
Extended sitting – Neutral sitting	147.00	0.001*
Supine – Neutral sitting	137.50	0.001*
Prone extension – Neutral sitting	30.00	0.001*
Extended sitting – Flexed sitting	230.50	0.001*
Supine – Flexed sitting	149.50	0.001*
Prone extension – Flexed sitting	64.00	0.001*
Supine – Extended sitting	610.00	0.350
Prone extension – Extended sitting	369.00	0.001*
Prone extension – Supine	395.50	0.005

Key:* = significant at $p < 0.003$ level

From table 4.4.4 it can be seen that for Flexed sitting (Median = 22.00mm) there was a significantly greater amount of posterior sagittal plane NP migration compared to Standing (Median = 17.33mm), $T = 1229.50$,

$p < 0.001$; Extended sitting (Median = 20.00mm), $T = 230.50$, $p < 0.001$; Supine (Median = 17.00mm), $T = 149.50$, $p < 0.001$; and Prone extension (Median = 15.67mm), $T = 64.00$, $p < 0.001$.

Neutral sitting also demonstrated significantly greater posterior sagittal plane NP migration compared to Standing (Median = 17.33mm), $T = 1323.00$, $p < 0.001$; Extended sitting (Median = 20.00mm), $T = 147.00$, $p < 0.001$; Supine (Median = 17.00mm), $T = 137.50$, $p < 0.001$; and Prone extension (Median = 15.67mm), $T = 30.00$, $p < 0.001$.

Extended sitting (Median = 20.00mm) also demonstrated greater posterior sagittal plane NP migration compared to Prone extension (Median = 15.67mm), $T = 369.00$, $p < 0.001$.

Further results and histograms demonstrating the paired differences between positions are provided in Appendix 15.

4.4.3: Axial behavior of the intervertebral disc

Of the 11 subjects included in phase 1 of this study, nine had T2W axial scans performed that were of sufficient resolution (i.e. the anterior IVD border could be identified) to be included for measurement and analysis. Initial descriptive analysis of the data is displayed in Table 4.4.5 and 4.4.6 where it can be seen that the NP migration ranged from 4.7mm to 7.53mm between positions.

Table 4.4.5: Mean (\pm standard deviation) sagittal plane Nucleus Pulposus migration (mm) in each position from axial positional Magnetic Resonance Imaging scans

Position	L1/2	L2/3	L3/4	L4/5	L5/S1
Standing	23.04 (2.69)	24.58 (3.66)	22.07 (3.78)	21.18 (3.84)	23.08 (3.22)
Neutral sitting	25.00 (6.00)	24.96 (4.41)	25.63 (2.47)	25.25 (3.68)	26.09 (5.02)
Flexed sitting	28.73 (5.56)	27.72 (4.46)	24.08 (5.90)	27.48 (2.89)	27.19 (5.05)
Extended sitting	27.07 (9.17)	22.59 (3.85)	20.93 (2.59)	26.18 (4.83)	25.46 (4.16)
Supine	25.17 (3.53)	25.92 (3.32)	21.46 (2.68)	20.87 (6.16)	23.79 (5.61)
Prone extension	22.52 (4.9)	23.58 (3.08)	22.88 (3.86)	19.95 (2.96)	20.81 (5.37)
Overall NP migration range	6.21	5.13	4.7	7.53	6.38

Table 4.4.6: Descriptive statistics for axial positional Magnetic Resonance Imaging scan measurements of sagittal plane Nucleus Pulposus migration

	N	Mean	Standard Deviation	Median	Minimum	Maximum
Standing	42	22.74	3.51	22.00	12.00	32.67
Neutral sitting	37	25.41	4.09	26.67	16.33	32.67
Flexed sitting	33	26.83	4.86	26.33	10.00	38.00
Extended sitting	40	24.16	5.13	22.67	16.33	43.33
Supine	38	23.35	4.73	23.00	12.33	35.00
Prone extension	36	22.07	4.12	22.33	12.67	31.33

The results of the Friedman’s ANOVA test indicated a significant effect of position on the sagittal NP migration from the axial pMRI scans, $X^2(5) = 20.834$, $p < 0.001$. The results of the post-hoc analysis using Wilcoxon signed rank test are presented in Table 4.4.7. From the table it can be seen that for Flexed sitting (Median = 26.33mm) there was a significantly greater amount of posterior sagittal NP migration compared to Standing (Median = 22mm), $T = 78.5$, $p < 0.002$; Extended sitting (Median = 22.67mm), $T = 77.5$, $p < 0.001$; Supine (Median = 23mm), $T = 54$, $p < 0.002$; and Prone extension (Median = 22.33mm), $T = 26$, $p < 0.001$. In addition, Neutral sitting (Median = 26.67mm) demonstrated significantly greater posterior sagittal NP migration compared to Standing (Median = 22mm), $T = 111.5$, $p < 0.001$ and Prone extension (Median = 22.33mm), $T = 88$, $p < 0.001$.

Table 4.4.7: Results of the post-hoc Wilcoxon signed rank test for sagittal plane Nucleus Pulposus migration from axial positional Magnetic Resonance Imaging scans.

	T value	Asymptotic Significance (2-tailed)
Neutral sitting – Standing	111.5	0.001*
Flexed sitting – Standing	78.5	0.002*
extended sitting - Standing	305.5	0.487
Supine – Standing	260	0.367
Prone extension - Standing	233.5	0.401
Flexed sitting – Neutral sitting	107	0.135
extended sitting – Neutral sitting	152	0.022
Supine – Neutral sitting	151.5	0.007
Prone extension – Neutral sitting	88	0.001*
extended sitting – Flexed sitting	77.5	0.001*
Supine – Flexed sitting	54	0.002*
Prone extension – Flexed sitting	26	0.001*
Supine – Extended sitting	267.5	0.608
Prone extension - extended sitting	161.5	0.144
Prone extension – Supine	183	0.031

Key: * = significant at $p < 0.003$

Further results and histograms demonstrating the paired differences between positions are provided in Appendix 16.

4.5: Discussion

The first phase of this study involved an asymptomatic group of subjects. The study objectives relating to this group were:

- To establish the intra-tester reliability of the Osiris software system in measuring the position of the five lumbar intervertebral discs' nucleus pulposus from sagittal and axial pMRI scans.
- To establish a database of the extent of migration of the nucleus pulposus of the five lumbar intervertebral discs in healthy asymptomatic subjects during different functional positions from pMRI.

While it is difficult to guarantee a sample comprised of individuals with completely asymptomatic spines and no pathology, the sample did meet the specified inclusion criteria (see Section 4.1) and all scans were classified as within normal limits by a Consultant Radiologist.

4.5.1: Reliability

Objective 1 (section 1.8) aimed to establish the intra-tester reliability of the Osiris software system in measuring the sagittal plane migration of the five lumbar NP from sagittal and axial pMRI scans. The first phase of this study addressed this objective (see Section 4.4.1) and demonstrated ICCs (2,1) for sagittal and axial scans ranging from 0.706 to 0.973 and 0.750 to 0.962 respectively (Table 4.4.1).

Previous authors (Beattie, Brooks & Rothstein 1994; Fennel, Jones & Hukins 1996) have used different methods to visually identify both the anterior IVD margin and NP boundary from sagittal MRI scans but due to less rigorous reporting methods, they did not report ICCs. The peak pixel intensity method (Brault et al 1997) was used in this study to identify the lumbar NP center. This yielded a mean sagittal and axial ICC of 0.86 and 0.89 respectively. An earlier study using the same technique as the present study (Edmondston et al 2000) reported a sagittal ICC of 0.71.

By applying the definitions of Landis & Koch (1977) (where ICC values of 0-0.2 = *slight* reliability; 0.21-0.4 = *fair* reliability; 0.41-0.6 = *moderate* reliability; 0.61-0.8 = *substantial* reliability and 0.81-1.0 = *perfect* reliability) the sagittal and axial ICC values for the asymptomatic subjects can be classed as:

- *Substantial* reliability – sagittal L3/4 and axial L1/2
- *Perfect* – all other levels (both sagittal and axial pMRI scans)

As reported in the literature (Eliasziw et al 1994, Bruton et al 2000), reliability should not be based solely on the ICC results. Other information should be included to complement the results such as confidence intervals (CI) and the standard error of the measurement (SEM). The CI can support reliability estimates by providing a range of values that span the true sample value (Eliasziw et al 1994). The asymptomatic subject's CIs in the present study demonstrate a wide variation for sagittal scan L3/4 and L4/5 (0.394 – 0.9 and 0.585 – 0.942 respectively) and axial scan L1/2, L2/3 and L5/S1 (0.145 – 0.992, 0.243 – 0.995 and 0.579 – 0.999 respectively) measurements.

The SEM represents the inherent variability in the author's measurements (Eliasziw et al 1994). The SEM is interpreted as: "The smaller the SEM the greater the reliability" (Bruton et al 2000). The range of SEM values reported for the asymptomatic subjects was 0.94mm – 1.77mm for the sagittal pMRI scans and 0.44mm – 1.49mm for the axial pMRI scans.

Therefore, although the ICC results would indicate that the author has substantial to perfect reliability in measuring the lumbar NP position in sagittal and axial pMRI scans, the CI and SEM results would suggest a more conservative assumption of reliability. Although previous authors using this measurement approach have reported ICC values for sagittal pMRI scan measurements, there have been no axial data reported or SEM or CI results. It is acknowledged that there are factors that can affect results and ultimately the reliability of the results. One factor that may have influenced the results was observer variability where measurements were performed manually by this author using image analysis software. However, strategies to address this in the study included development of a standardised measurement protocol which was followed for both sagittal and axial scans (see sections 3.2.3.1 and 3.2.3.2, page 95-100) and the author was trained and experienced in the use of Osiris image analysis software prior to this study. Another factor that will have influenced the results is inherent subject variability. The use of inclusion and exclusion criteria throughout this study

aimed to ensure that the subjects minimised this variability, as much as possible, as a homogenous group.

From these results, it can be concluded that the author is reliable in the measurement of NP migration from pMRI scans using Osiris image analysis software. This conclusion infers confidence that the results obtained for the asymptomatic and DLBP subjects were determined from a reliable tool.

4.5.2: Feasibility of pMRI positions

During initial pMRI scanning protocol development (in which verbal report from a volunteer and quality of pMRI scans were obtained) it was identified that two positions were neither ethical nor feasible to carry out with the equipment at the time of this study. It had been initially intended to evaluate dynamic lumbar movement and the underlying behavior of the IVD using pMRI and 3-SPACE Fastrak. However, it was established following early trials that although some authors have referred to pMRI as “dynamic” (Jinkins & Dworkin 2002, Jinkins et al 2002), this was incorrect as pMRI images could only be produced from statically held positions. Standing flexion and extension were initially chosen for their functional impact on the spine but as this study had not been undertaken before, the physiological effect of maintaining these positions for 20 minutes per scan had not previously been established. As these problems were identified in a healthy asymptomatic volunteer (the author), it was decided that these positions were potentially very provocative to people with LBP and so were removed from the scan position order for subsequent pMRI scans in this series of studies. Morishita et al (2008) have previously acknowledged that upright MRI positions can be provocative to subjects with a DLBP presentation when sustained for longer than 30 minutes.

Future pMRI developments with faster image acquisition will enable the standing flexion and extension positions to be investigated in asymptomatic and DLBP populations.

4.5.3: Behavior of the intervertebral disc from sagittal pMRI scans

Initial inferential analysis of the sagittal pMRI scans demonstrated that position had a significant effect on sagittal plane NP migration at all IVD

levels ($p < 0.001$). Post-hoc analysis revealed that Neutral and Flexed sitting demonstrated significantly greater posterior NP sagittal plane migration compared to Standing, Extended sitting, Supine and Prone extension ($p = 0.001$).

The results of this study for sagittal plane NP behavior from sagittal pMRI scan in asymptomatic subjects is similar to previously published research in that flexed postures cause posterior migration of the NP in the sagittal plane (Fennel, Jones & Hukins 1996; Edmondston et al 2000). The results also support the findings of Nazari et al (2012) where the authors reported sitting postures induced the NP (L3/4, L4/5 and L5/S1) to move closer to the spinal canal whilst standing caused the NP to move in the opposite direction. This suggests that standing may well be preferable, in terms of reduced risk of posterior derangement than sitting postures (Neutral and Flexed).

Interestingly, Extended sitting, which is generally accepted as a "better" sitting posture, did not differ significantly from Standing, which would suggest that, for asymptomatic subjects, both Standing and Extended sitting are preferable. It has been demonstrated that standing causes a lordotic effect on the lumbar spine and so can reflect an extended sitting alignment (McKenzie and May 2003).

Prone extension, a position commonly used as a treatment technique in physiotherapy, (McKenzie & May 2003) induced the least amount of posterior NP migration. Interestingly, Supine lying also showed less posterior NP migration than any of the 3 sitting positions, yet this is not a position commonly advocated by physiotherapists for treatment.

These results from the current study support previously published literature that has reported a posterior migration of the IVD in flexion and an anterior migration in extension in asymptomatic subjects from rMRI images (Beattie et al 1994, Fennell et al 1996, Brault et al 1997, Edmondston et al 2000).

The results from the current study also support this behavior in studies of asymptomatic subjects in upright/open MRI images (Fredericson et al 2001, Nazari et al 2012).

Nazari et al (2012) reported that in sitting there was a significant reduction in anterior IVD height at all levels (except L4/5 which had a significant increase) and a significant increase in posterior IVD height at all levels compared to

supine. It can be concluded from Nazari et al (2012) that the NP will migrate away from the anterior compressive load posteriorly as has been suggested by previous authors investigating torsion and lateral flexion effects on the IVD (Fazey et al 2006, 2010).

Although Nazari et al's (2012) results reflect the results demonstrated in the current study in that position had a significant effect on the IVD, their study has some limitations which affect the confidence in their results. The authors measured the NP length relying on identification of the NP/iAF boundary from pMRI scans (grade I and II IVDs only from Pfirrmann scale). As has been demonstrated by Wade et al (2012) this boundary is a subtle gradation rather than a distinct border, therefore the measurement of exact NP length is not a precise measurement. Nazari et al (2012) have also gone on to suggest that NP migration does not exist and it is rather NP length deformation that occurs in response to different positions in the sagittal plane. Despite Nazari et al's (2012) limitations, it would be of benefit to repeat the current study's measurements as well as those of Nazari et al (2012) to identify optimal measurements (reliable and valid) that fully reflect the behavior of the NP and IVD as a whole from pMRI.

4.5.4: Behaviour of the intervertebral disc from axial pMRI scans

From the results it was demonstrated that there was also a significant effect of position on the sagittal plane lumbar NP migration in the axial pMRI scans ($p=0.001$). Post-hoc analysis identified that there was significantly greater posterior sagittal plane NP migration for Flexed sitting compared to Standing ($p<0.002$), Extended sitting ($p<0.001$), Supine ($p<0.002$) and Prone extension ($p<0.001$). Neutral sitting also demonstrated significantly greater posterior sagittal plane NP migration compared to Standing ($p<0.001$) and Prone extension ($p<0.001$). These differences are presented in table 4.5.1.

Table 4.5.1: Statistically significant differences ($p < 0.003$) in Nucleus Pulposus migration from axial positional Magnetic Resonance Imaging scans in asymptomatic subjects

Position	Greater posterior NP migration than
Flexed sitting	Standing Extended sitting Supine Prone extension
Neutral sitting	Standing Prone extension

The results of the axial pMRI scan measurements reflect the sagittal pMRI scan results although there is some variation between the two pMRI scan planes.

In contrast to published sagittal MRI analysis of NP behaviour (loaded and unloaded), there is very little literature available on axial MRI (rMRI and pMRI) analysis of NP behaviour in healthy asymptomatic subjects. The only research published in this area has been by Fazey et al (2006) in a study of NP behaviour in three asymptomatic female volunteers (mean age 27 years). The authors investigated the L1/2 and L4/5 IVDs using a pixel profile technique discussed in section 3.2.3.1 (page 95). The results of this study demonstrated that in five out of the six IVDs analysed, in the sagittal plane, the peak pixel intensity migrated anteriorly in extension and posteriorly in flexion. There was a mean 9% (range 1-15%) change in sagittal IVD diameter with greater migration evident at L4/5 (mean 11% change) in comparison to L1/2 (mean 4% change). These results support the findings of this current study in that the flexed positions created a significantly greater posterior sagittal plane migration of the NP than extended positions. However, caution must be taken with the results from Fazey et al (2006) as there were a very small number of IVDs analysed (six from three asymptomatic volunteers) and the measurements were taken from unloaded rMRI scans.

In conclusion, although the axial pMRI scans results mirrored the sagittal pMRI results, further research is required to investigate the sagittal plane NP behaviour in different positions via axial pMRI scans.

4.5.5: Asymptomatic nucleus pulposus sagittal migration database

The first phase of this study also achieved objective 3 (section 1.8) in that a database of the extent of sagittal plane lumbar NP migration was established for healthy asymptomatic subjects from sagittal and axial lumbar pMRI scans. Although this database is small (N=11) and consisted of more females than males (7:4) it can be increased over time as additional subjects are scanned. This will then enable future retrospective IVD analysis of a large sample of asymptomatic individuals and also comparisons for samples of subjects with LBP. This is an area that has not been reported in the literature to date.

4.6: Conclusion

This chapter has presented the first phase of this study where the effect of functional positions has been investigated in asymptomatic normal subjects. From this phase it has been demonstrated for the first time using pMRI that there is a predictable pattern of effect on the NP in different functional positions. In addition, the author was found to be reliable in the measurement of NP migration. As the objectives for this phase of the study had been achieved, the second phase of this study could progress.

Chapter 5: 3SPACE Fastrak™ (Phase 2)

As this study initially planned to use the 3SPACE Fastrak™ (FT) motion analysis system to measure functional spinal range of movement in asymptomatic and DLBP subjects, it was necessary to establish if the device was a reliable measurement tool. Therefore, the second phase of this study was designed with the following aims:

1. To establish the within day intra-tester reliability of the 3SPACE Fastrak™ system in the measurement of lumbar spine range of movement.
2. To establish a database of the 3-dimensional movement of the lumbar spine using the 3SPACE Fastrak™ system.

The author, who was trained and experienced in the use of the FT system and related software, was responsible for carrying out the FT measurements in phase 2.

5.1: Sample

A convenience sample of 20 healthy volunteers was aimed to be recruited from staff and students of the School of Health Sciences, Robert Gordon University. Fourteen people expressed an interest following posters and email flyers but two were excluded (LBP at the time and previous LBP injury) and two had to cancel the booked sessions at the last minute (due to illness and work commitments).

Location:

The University's Human Performance Laboratory. Data collection for phase 2 was conducted over a four month period. All participants read the information sheet (Appendix 6) and provided written informed consent (Appendix 7) prior to their inclusion in this phase of the study.

Inclusion criteria for this phase were:

- Aged 18-65
- Free of LBP at the time of the study
- Able to perform spinal movements

As for the asymptomatic subjects, the age range for this group was again across the working age and participants had to be free from LBP at the time of this study. As this phase was investigating spinal movement, it was important that all subjects were able to perform these movements. This was initially stated by verbal report from the subject and then verified by the author during the practice movements.

Exclusion criteria included:

- Significant LBP within the previous year (requiring time off work and/or consultation with a healthcare professional)
- Previous spinal surgery
- Other medical or orthopaedic conditions that would affect spinal motion (e.g. Rheumatoid arthritis, hemiplegia, recent fractures, pregnancy).

This study, like the asymptomatic subjects, also included people with a prior history of LBP as long as it had not required time off work or treatment from a healthcare professional. Previous spinal surgery and any medical and orthopaedic conditions known to affect/alter spinal mechanics and motion or the ability to stand or move were also excluded from this group.

The 3SPACE Fastrak™ (Polhemus Navigation; Colchester, VT, USA) is a non-invasive, portable electromagnetic device (see figure 5.1.1 and 5.1.2) that has been used extensively in biomechanics research and more recently as the gold standard by which other systems are compared to for spinal motion studies (Saber-Sheikh et al 2010, Straker et al 2010, Ribeiro et al 2011, Ha et al 2012). The system consists of up to four sensors that can detect an electromagnetic field produced by a source at a sampling rate of 120Hz (Ha et al 2012).

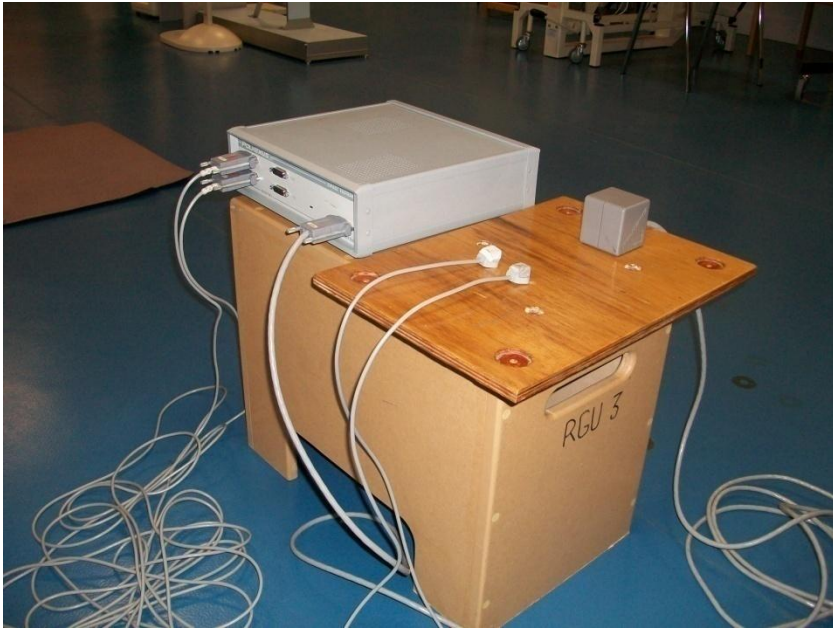


Figure 5.1.1: The 3SPACE Fastrak™ motion analysis system



Figure 5.1.2: Spinal attachment of 3SPACE Fastrak™ system

The FT system has been reported as a reliable and valid system for 3-dimensional motion analysis of the lumbar spine with a reported total Root Mean Square (RMS) error for rotations of less than 0.2° (Pearcy & Hindle 1989). Less than 2% errors for lumbar spine movements have been reported when measured within 60-70cm of the electromagnetic source (An et al 1988). Manufacturer data indicates that the system has a static accuracy of 0.8mm RMS for sensor position and 1.5° for sensor orientation within 76.2cm of the source (Saber-Sheikh et al 2010, Ha et al 2012). Burnett et al (2008) have reported standard error of measurement (SEM) values between 0.7° and 2.4° for axial rotation reliability measurements.

Despite the common use of this system in spinal motion analysis, there are recognised disadvantages to it. The effect of metal within the electromagnetic operating environment has been previously reported; the measurement accuracy is increasingly affected with increasing distance between the sensor and transmitter; and gimbal lock and quadrant errors can occur (Mannion & Troke 1999, Burnett et al 2008, Hagemeister et al 2008, Ng et al 2009, Saber-Sheikh et al 2010, Straker et al 2010, Ribeiro et al 2011). Skin slippage error for skin mounted sensors has also been acknowledged to affect measurements (Ha et al 2012) and Yang et al (2008) have reported a 5° error and a 7.7° absolute error for gross spinal motion. Even though these instrumental and real errors exist with the FT system, they are not insurmountable and steps can be taken to address and minimise them (indeed no measurement systems exist that are free of error). Therefore the system is considered to be an appropriate "gold standard" system for spinal measurement (Mannion & Troke 1999, Straker et al 2010) and therefore a suitable tool for this phase.

5.2: Protocol

In order to minimise the effect of diurnal variation (Mannion & Troke 1999, Swinkels & Dolan 2000, Lee 2002, Burnett et al 2004) testing sessions for each individual was booked for similar times at least 3 hours after rising.

Prior to each testing session an interference test was carried out to ensure that the FT system was free of any electromagnetic interference at the time of testing. In accordance with operating recommendations, the FT and subject testing area was set up with no metal objects within the recommended operating distance (at least twice the distance from transmitter as the sensor) (Day et al 2000).

Each subject was given a visual demonstration of each movement and was instructed to only move as far as was comfortable or able. With sensors in situ, subjects performed practice movements through each plane to control for learning effects (Jordan et al 2000). This also served as a warm-up for participants. Before recording movements in each plane FT was boresighted to 0, 0, 0° in relaxed standing or upright neutral sitting. To control for order effects sagittal plane movements were always performed first followed by frontal and transverse plane movements (Jordan et al 2000).

The FT source and sensor placement are described in Appendix 8. Each subject performed a total of 36 lumbar spine movements– flexion, extension, left side flexion, right side flexion, left rotation and right rotation repeated three times in standing and sitting (See Appendix 8 for descriptions of each movement). Subjects were given a rest period of approximately two minutes between each movement. For analysis, the mean of the three repetitions for each movement was used (Ha et al 2012). Each movement began from the upright standing or sitting positions and returned to this position (i.e. neutral standing to flexion and back to neutral standing rather than neutral standing to flexion then through extension and return to neutral standing). The neutral position in standing and sitting is detailed in Appendix 8.

5.3: Analysis

All data was collected as text pad files then exported into excel using previously custom designed software for this purpose. Graphs were inspected for data quality and errors such as gimbal lock. The relative angles between the two sensors were calculated for each movement at a sampling rate of 60Hz for each sensor. Descriptive analysis (mean, maximum,

minimum and standard deviation) was performed on all standing and sitting movements using SPSS v17.0 (IBM Corporation, USA). As per phase 1 (asymptomatic subjects pMRI measurements), separate intraclass correlation coefficients (ICC 2, 1), SEM and 95% confidence intervals for each movement were calculated to quantify the intra-tester reliability of the FT system.

5.4: Results

There were 10 subjects recruited for this project (5 male: 5 female) and the mean age was 42 years (± 9 years).

The mean distance of the source to the sensors in standing and sitting were 75.8cm and 81.9cm respectively.

The overall within day reliability/ICC results for each movement recorded by the 3SPACE Fastrak system is displayed in Table 5.4.1.

Table 5.4.1: Results of Intra-class correlation (2, 1), 95% confidence intervals and standard error of measurement ($^{\circ}$) within day results for 3SPACE Fastrak™

Movement	ICC(2,1)	95% CI	SEM
EIS	0.40	-0.23 – 0.804	1.40
FIS	0.173	-0.325 – 0.645	3.76
LR	0.687	0.119 – 0.896	0.84
LSF	0.334	-0.232 – 0.734	1.04
RR	0.602	0.022 – 0.888	0.69
RSF	0.542	-0.061 – 0.861	1.06
SITE	0.805	0.425 – 0.948	1.37
SITF	0.261	-0.838 – 0.424	1.56
SITLR	0.547	-0.049 – 0.849	0.96
SITLSF	0.476	-0.138 – 0.829	0.96
SITRR	0.789	0.380 – 0.948	1.15
SITRSF	0.647	0.040 – 0.876	1.93

Key: EIS = extension in standing; FIS = flexion in standing; LR = left rotation in standing; LSF = left side flexion in standing; RR = right rotation; RSF = right side flexion in standing; SITE = extension in sitting; SITF = flexion in sitting; SITLR = left rotation in sitting; SITLSF = left side flexion in sitting; SITRR = right rotation in sitting; SITRSF = right side flexion in sitting; SEM = Standard error of measurement; CI = confidence interval; ICC = intra-class correlation

The mean range of movement (ROM) for each movement in sitting and standing is presented in table 5.4.2 with table 5.4.3 presenting the mean ranges alongside other published data from the literature.

Table 5.4.2: Sitting and standing mean range of movements (degrees)

Subject	1	2	3	4	5	6	7	8	9	10	MEAN	SD
EIS	17.4	12.1	15.8	6.8	4.1	11	21.6	22	4.2	10.2	12.5	6.6
FIS	24.3	58.6	55.5	24.6	38.6	33.2	29.7	42.1	13	37.3	35.7	14.1
LR	13.5	5.1	12	4.7	5.9	10.9	8.6	10.1	5.9	12.2	8.9	3.3
LSF	11.1	21.1	19.4	14.9	17.7	20.3	11.7	17.9	7	23.2	16.4	5.1
RR	7.9	4.9	8	7.9	7	17.5	6.6	10.6	7	10.5	8.8	3.5
RSF	12	21.2	15.5	16.5	17.7	18.7	9.3	21.5	7.8	22	16.2	5.1
SITE	5.2	16.6	5.2	4.1	13.8	12.2	6.3	20.6	3.9	11.9	10.0	5.9
SITF	24.2	35.6	36.3	23.6	26.9	29.6	37.8	34.9	26.2	28.8	30.4	5.3
SITLR	4.7	8.2	10.9	6.7	4.9	12.8	9.5	14.6	8.8	11.6	9.3	3.3
SITLSF	16.3	19.2	19.5	15.4	20.1	17.5	10.8	24.7	12.2	21	17.7	4.2
SITRR	7.8	16.2	10.9	4.5	8.2	12.1	9.4	17.4	13	6.8	10.6	4.1
SITRSF	15	17	14.2	13.8	23.1	18.5	8	16.3	10.3	23.4	16.0	4.9

Key: EIS = extension in standing; FIS = flexion in standing; LR = left rotation in standing; LSF = left side flexion in standing; RR = right rotation; RSF = right side flexion in standing; SITE = extension in sitting; SITF = flexion in sitting; SITLR = left rotation in sitting; SITLSF = left side flexion in sitting; SITRR = right rotation in sitting; SITRSF = right side flexion in sitting; SD = standard deviation; ICC = intra-class correlation coefficient

Table 5.4.3: Comparison of mean values of range of movement in lumbar spine

Range of movement (°)	Flexion	Flexion in sitting	Extension	LSF	RSF	LR	RR	Subject numbers (male:female)	Location of measurement
This study	35.7	30.4	12.5	16.4	16.2	8.9	8.8	10 (5:5)	L1 - S2
Ha et al (2012)	56.9		26.7	25.8	26.1	15.5	14.8	26 (12:14)	L1 - sacrum
Lee & Wong (2002)	58.1		15.6	21.3	19.9	7.6	9.8	20 (20 male)	L1 - sacrum
Mannion & Troke (1999)	56.4	55.5	19.7	53.4*		34.0*		11 (5:6)	L1 - S1
Lee et al (2011)	46.7		20.4					10 (7:3)	T12 - S1
Yang et al (2008)	62.8							17 (17 male)	L1 - S1

Key: LSF = left side flexion; RSF = right side flexion; LR = left rotation; RR = right rotation; * = combined data for left and right

5.5: Discussion

This phase of the study aimed to establish the intra-tester reliability of the FT system for lumbar spine range of movement measurement and create a database of lumbar spine three-dimensional movement. By completing this phase, objectives 2 and 4 were achieved (see section 1.8).

5.5.1: Reliability

As for the asymptomatic subjects, this phase calculated intraclass correlation coefficients (ICC 2, 1), CI and SEM for each movement in standing and sitting to quantify the intra-tester measurement reliability. By applying the definitions of Landis & Koch (1977) (where ICC values of 0-0.2 = *slight* reliability; 0.21-0.4 = *fair* reliability; 0.41-0.6 = *moderate* reliability; 0.61-0.8 = *substantial* reliability and 0.81-1.0 = *perfect* reliability) the ICC values for this phase can be classed as:

- *Slight* reliability – flexion in standing
- *Fair* reliability – Extension in standing, left side flexion and flexion in sitting
- *Moderate* reliability – right side flexion, left rotation in sitting and left side flexion in sitting
- *Substantial* reliability – left rotation, right rotation, right rotation in sitting, right side flexion in sitting
- *Perfect* reliability – extension in sitting

Table 5.5.1 demonstrates ICC (2, 1) values produced by this phase and previous values reported in the literature for the FT system. Of the eight studies presented, seven reported *substantial to perfect* reliability whereas only five of the 12 movements performed in this study achieved this.

Sagittal plane movements are the main movements assessed in a clinical examination of LBP therefore it is disappointing that flexion and extension in standing demonstrated only *slight to fair* reliability (0.17 & 0.4 respectively) in this study.

Table 5.5.1: Intra-class correlation (2,1) reliability results for lumbar spine range of movement using 3-SPACE Fastrak™ (unless indicated otherwise)

Author	ICC (2,1) range
This study	0.26 – 0.81
Barrett et al (1999)	0.79 – 0.92
Swinkels & Dolan (2004)	0.06 – 0.91
Swinkels & Dolan (2004b)	0.88 – 0.91*
Swinkels & Dolan (1998)	0.61 – 0.70
Mannion & Troke (1999)	0.82 – 0.99
Lin et al (2005)	0.78 – 0.99 ¹
Jordan et al (2000)	0.54 – 0.82 ² ; 0.62 – 0.81 ¹
Amiri, Connell and Saifuddin (2003)	0.85 – 0.95

KEY: * = in ankylosing spondylitis patients; ¹ = for shoulder; ² = for cervical spine; ICC = Intra-class correlation

Sources of error affecting these results can be attributed to skin slippage, accuracy in spinal palpation, a small sample size, and the distance from the source to the sensors (Billis, Foster & Wright 2003, Matsui, Shimada & Andrew 2006, Harlick, Milosavljevic & Milburn 2007, Robinson et al 2009). The use of skin mounted sensors has been acknowledged to carry inherent error (Yang et al 2008, Ha et al 2012), and some authors have proposed alternative methods of sensor attachment to address this (Abdoli-E & Stevenson 2008, Burnett et al 2008, Ha et al 2012). However, the method employed here is the same as that employed in other projects (Maffey-Ward Jull and Wellington 1996, Swinkels and Dolan 1998, Swinkels & Dolan 2000), and conducted by an experienced manual therapist, but perhaps a more secure attachment may have improved results.

The FT manufacturer recommends a distance of 76cm between the source and sensors for data collection. In this group the mean distances were 75.8cm and 81.9cm (standing and sitting respectively), but as the source was located behind the subject, movement into flexion would have increased this distance and therefore could have decreased the accuracy (Ribeiro et al 2011). This may provide some explanation for the lower ICC values for standing and sitting flexion.

As three repetitions of each movement were performed (36 in total) it is not possible to ensure that the same ROM was performed each time, although repeated measurements are accepted common practice in motion analysis. In addition, the data collection involved long periods standing and sitting still while the FT bore-sighted prior to data collection including data file set-up. The combination of these factors as well as participant fatigue, motivation, and creep may also have affected the results (Ha et al 2012).

Further investigation and testing of the FT system used in the current study as well as refinement of the user interface would address some of the reliability and long data collection periods experienced in the current study.

5.5.2: Lumbar spine 3-dimensional movement

From the results and table 5.4.2 and 5.4.3 it can be seen that objective 4 (section 1.8) was achieved in that there was a database of lumbar ROM created in standing and sitting. As this study is concerned with the sagittal plane behaviour of the lumbar IVD, the sagittal plane ROM from the FT system is of interest. The mean standing flexion and extension ROM in this study (35.7° and 12.5° respectively) are both less than the mean ROM reported by previous authors ($46.7^\circ - 62.8^\circ$ and $15.6^\circ - 26.7^\circ$ respectively) (Mannion and Troke 1999, Yang et al 2008, Lee et al 2011, Ha et al 2012). In addition, the mean ROM for flexion in sitting (30.4°) is less than that reported by Mannion and Troke (1999) (55.5°).

The ROMs recorded here were consistently less than previously reported values for all movements other than left rotation. Yang et al (2008) reported that the measurement of lumbar ROM using FT was generally underestimated by around 5° in comparison to bony marker measurement but this does not fully explain these lower values. In a study of lumbar ROM using X-ray Pearcy et al (1984) reported ROM to be: flexion $35-52^\circ$; extension $15-29^\circ$; side flexion $16-25^\circ$; and rotation $5-16^\circ$. The present results all fall within these ranges except for extension, however the results would infer greater confidence if they had been within the ranges reported for the other studies using FT.

Therefore, despite achieving objective 4 in creating a database of lumbar ROM, the database itself is of less value as the ROMs recorded were lower

than normal. By addressing the reliability issues stated above, a new data base can be established in future research projects.

5.5.3: The relationship between lumbar range of movement and functional position

In order to begin to evaluate whether there was any relationship between lumbar ROM and behaviour of the lumbar IVD the results of the asymptomatic subject's NP migration and the FT ROM results were compared to identify common areas (Objective 5, section 1.8). Immediately it was apparent that both systems were incompatible as the FT system assesses motion in real time and not the IVD specifically; whereas the pMRI scans were achieved through static maintenance of functional positions with specific visualisation of each lumbar IVD. Even though it was possible to measure ROM in both systems, the FT system was a real-time measurement potentially to end of range, whereas the pMRI could measure range but not full active range. The calculation of ROM also differed as the FT system calculated this 3-dimensionally using 6 degrees of freedom electronically whereas the pMRI ROM is calculated 2-dimensionally by hand using a modified Cobb angle process (Vrtovec, Pernus and Likar 2009). It was therefore decided that although the FT system has been previously used in spinal research, it is neither compatible nor an appropriate tool at this time for the investigation of IVD behaviour.

5.6: Conclusion

In conclusion, the FT system is a reliable motion analysis system for lumbar spine motion analysis as demonstrated in previous research. However in this study low levels of reported reliability, especially in the sagittal plane, via ICCs as well as low values for ROM indicate that further work is required on the data collection protocols and current set up to establish this specific system as a reliable tool for lumbar spine analysis. The final phase of this study therefore focused only upon the use of pMRI to investigate IVD behaviour in DLBP subjects.

Chapter 6: Discogenic low back pain subjects (Phase 3)

The final phase in this study was the recruitment of DLBP subjects to have pMRI scans. The same measurement software and protocols from the asymptomatic group were employed in the analysis for this phase.

Due to 2 suspensions of studies the North of Scotland Research Ethics Service (NoSRES) agreed to extend this project until 30 June 2010. However, a substantial amendment was submitted to NoSRES to extend this date to the end of August 2010 for data collection purposes and to allow a wider recruitment pool via private physiotherapy practices in and around Aberdeen as well as amending the inclusion criteria. NoSRES granted ethical approval for these amendments on 4/2/10 (Appendix 1).

Inclusion criteria for this project were:

- Aged 18-65 years
- Male or female
- Non-specific low back pain (with or without leg pain)
- +/- Positive straight leg raise
- +/- altered neurological tests (myotomes, reflexes or sensation)

As per the earlier phases of this study, age and gender justification reflected the male, female and working age population for LBP. NSLBP was also included as this is the largest group of LBP sufferers (>85%) (Koes et al 2006) and is a commonly used classification within physiotherapy assessment. NSLBP is where a specific cause for the pain is unidentified, however this classification can also include DLBP (Konstantinou and Dunn 2008, Schafer et al 2009), and therefore the group of interest for this study could be assumed to be represented here. With or without leg pain was included as not all DLBP patients have pain extending into the leg (McKenzie and May 2003), although pain below the knee has been acknowledged as perhaps being indicative of sciatica (Van der Windt et al 2010). As there is no specific clinical test to identify discogenic LBP, the straight leg raise test and altered neurological tests were included as they have been shown in the literature to aid clinical identification of discogenic LBP (Vroomen et al 2002).

Exclusion criteria included:

- Any contraindications to a MRI procedure
- Any previous spinal surgery

Again, like the asymptomatic group, the exclusion criteria for this group included any contraindication to a MRI procedure, which was screened using the MRI screening form (Appendix 4) by both the author during recruitment and the MRI radiographer immediately before the pMRI scans. Also, any previous spinal surgery was excluded as this would alter spinal mechanics and therefore affect any measurements recorded.

The reliability for the author in the use of the Osiris image analysis software was established in the asymptomatic subjects and found to be *good to perfect* (0.706-0.973; Landis & Koch 1977).

6.1: Sample size

From the results of the asymptomatic subjects (the effect of position on sagittal plane NP migration), sample size calculations using Minitab identified that 34 NSLBP patients were required to detect a 5mm difference in NP migration at 80% power.

6.2: Sample

A convenience sample of 34 NSLBP patients was aimed to be recruited from NHS Grampian Physiotherapy Out-patient departments and private physiotherapy practices in and around Aberdeen. This decision was based on practical reasons: the positional MRI is based within Aberdeen and as the pMRI scans took around 1.5 hours to perform, it was aimed to have as little time spent in provocative positions for NSLBP subjects (such as long car journeys to and from the pMRI Centre).

Convenience sampling was employed in all three phases of this study. The limitations of this sampling strategy have been acknowledged (previously discussed in section 3.1): under-representation of target population, potential for bias, and inability to generalise results due to small sample sizes (Bowling 2009, Ross 2012, p 101). However, this strategy was useful in each phase of this study as access to the target populations and recruitment/data collection time was limited: the NSLBP subject recruitment was initiated via the treating physiotherapist. In addition, convenience sampling was considered to be an adequate choice here. It was not identified as a significant limitation as each phase of this study was of an exploratory nature. The results from each phase were likely to result in the need for further research to be carried out; therefore future research would consider alternative sampling strategies.

Following letters to private practitioners, a presentation to NHS Grampian Out-patient physiotherapy staff, telephone calls and face to face conversations, NHS Grampian physiotherapists and private physiotherapy practitioners volunteered to participate in subject recruitment. As discussed in Section 2.3.5 and 2.3.9, there is no internationally recognised definition of DLBP and there is no reliable and valid clinical assessment to identify DLBP. Therefore, the author of this study spent time in the initial stages with clinicians to clarify the study aims and objectives in order to enhance the recruitment of a homogenous group. All recruiting clinicians were also encouraged to contact the author to discuss any potential subjects prior to clinicians distributing recruitment packs to them. These steps and the use of professionally qualified physiotherapists in the recruitment process was hoped to eliminate mass recruitment pack distribution for patients in order to gain quick access for a MRI scan.

A reminder of the inclusion and exclusion criteria was sent to each participating department and practice along with recruitment packs. Each recruitment pack contained a letter of invitation with a tear-off opt-in slip (Appendix 9 and 10), an information sheet (Appendix 11 and 12) and a freepost return envelope addressed to the author. Physiotherapists identified potential subjects and then issued them with recruitment packs. The potential subjects who were interested in taking part in the study then

completed the tear-off slip on the letter of invitation (Appendix 9 and 10) and returned it to the author in the freepost envelope provided.

Figure 6.2 summarises the recruitment process. It can be seen that during the recruitment and data collection period there were 38 potential subjects interested in taking part in the study.

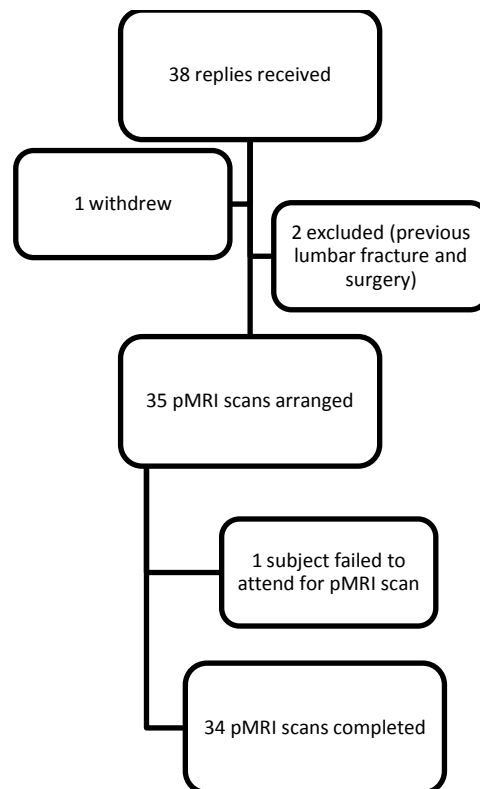


Figure 6.2: Recruitment summary for DLBP subjects

6.3: Consent

All subjects had time to read the study information sheet (Appendix 11 and 12) prior to deciding whether to take part in the study or not. After contacting the subject, the pMRI sessions were arranged at least 48hours later, giving the subject time to change their mind and withdraw if they wished. All subjects provided written informed consent (Appendix 13) for this study prior to having their pMRI scan. At the time of giving their consent, all subjects were reminded that some of the pMRI scan positions

could be provocative to their pain and that they could stop at any time or withdraw from the study at any point.

6.4: Location

Participants attended the Positional MRI Centre, Woodend Hospital, Aberdeen for a pMRI scan on one occasion. Data collection for this study was conducted over a five month period.

6.5: Protocol

The same 0.6 Tesla, Positional "Upright" MRI (Fonar Corp., Melville, NY) that was used to carry out the scans in the asymptomatic subjects was used for the DLBP subjects. Figure 6.5 displays the data collection process. Each stage will be described and justified.

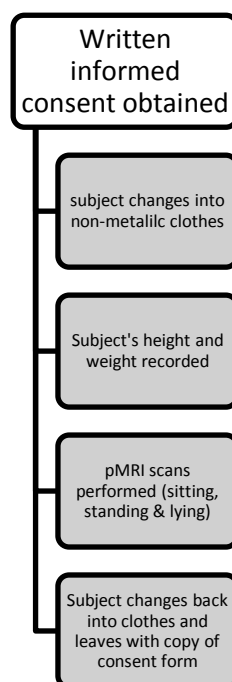


Figure 6.5: Flowchart of data collection process for DLBP subjects

6.6: Ethical considerations

All participants attended the pMRI Centre at a prearranged time and date for their scan. On arrival, participants were asked to provide written informed consent (Appendix 13) after having any questions they may have had answered. Participants also completed a data collection form (Appendix 14) in which they provided their contact details (in order to send them the project summary report at the end of the project), their GP details (in order to send the pMRI Consultant Radiologist report to their GP), their date of birth (to provide an age range for the group) as well as job title and a yes/no tick box for them to state whether they were off work at the time of the study or not. Subjects also had to complete the MRI screening form (Appendix 4).

6.7: Clothing

After completing the paperwork, subjects changed into non-metallic clothing before having the pMRI scan. MRI scans use very strong magnets therefore no clothing with zips or eyelets can be allowed within the Scanning room. In addition to this being a risk factor metal can also cause artefacts on scan images which can affect subsequent measurement (personal communication with the Senior pMRI Radiographer).

6.8: Subject measurements

The following measurements were recorded prior to the subject having the pMRI scan: height (cm) was recorded using a measuring tape and weight (Kg) using electronic scales. Height and weight were necessary to provide background demographic details about the sample group. Weight is also required to be inputted to the pMRI scanner for each individual prior to their scan by the pMRI radiographer.

6.9: Positional Magnetic Resonance Imaging scans

Sagittal (TR-1734, TE-140) weighted images through the 5 lumbar IVDs in all 6 positions were taken: field of view = 36cm, slice thickness = 4.5mm,

acquisition matrix = 256x156/2NEX. Axial (TR – 1245, TE-120) weighted images were also taken through the five lumbar IVDs in all six positions: field of view = 25cm, slice thickness = 4.5mm, acquisition matrix = 220x220/2NEX.

The order of scans were altered from the asymptomatic subjects in that the sitting scans were performed before the standing scans which were then followed by supine and prone extension as before. The reason for this was due to health and safety/risk assessment: the pMRI staff had identified that standing could be related to fainting more than any other position, therefore to try and maximise imaging to get some upright positions it was decided to scan in the sitting positions first then move onto standing. Personal communication with the Senior pMRI Radiographer identified that in approximately 9000 scans over a 10 year period, they had had around 20 patients fainting in the scanner in the standing position, with no faints recorded in any other position. The order of the scans in this study was therefore: Neutral sitting, Flexed sitting, Extended sitting, Standing, Supine and Prone extension. Extended sitting and Prone extension were again maintained passively using foam rolls and wedges. Subjects were again required to maintain each position for around 20 minutes per scan (sagittal and axial views). Again, each subject was instructed to adopt the position at the point that they felt they could maintain it for the duration of the scan (i.e. no end range positions were adopted).

Not all participants were able to maintain all six scan positions due to discomfort. Subject 14 fainted during the Extended sitting scan due to pain; and so the remainder of this session was cancelled. It was noted during data collection up to this point that Extended sitting was reported as uncomfortable by other subjects (N = 2) and the scan in this position had to be halted. As a precaution, all participants after subject 14 were instructed to stand up and walk about between the Flexed sitting and Extended sitting scans while the scanner bed was re-adjusted (approximately 1 minute), in an attempt to reduce any induced discomfort. Subject 29 did not have the lying down positions (Supine & Prone extension) scanned as the pMRI bed broke down and would not move into the position required.

6.10: Positional Magnetic Resonance Imaging coil comparison

In phase 1 of this study (asymptomatic subjects), all of the pMRI scans were performed using the circular coil (solenoid receiver coil – see Supine and Prone extension positions in figure 4.2.1) as per standard pMRI practice at that time. Subsequent developments in pMRI practice since then had led to the development of new coils becoming available such as the quadrature (quad planar) coil and the scoliosis coil. Standard practice for pMRI scans had therefore also moved forward and so the quad planar coil was now used as the standard coil for lumbar spine imaging. This coil is reported to have reduced signal to noise ratio and therefore produces higher quality/resolution images (personal communication with Senior pMRI Radiographer). A literature search and search of the Fonar website by the author was unable to identify any literature to support this claim. Therefore the author underwent two pMRI scans in Neutral sitting using both coils to allow a visual comparison. Both scans are shown in figure 6.10.1 & 6.10.2.

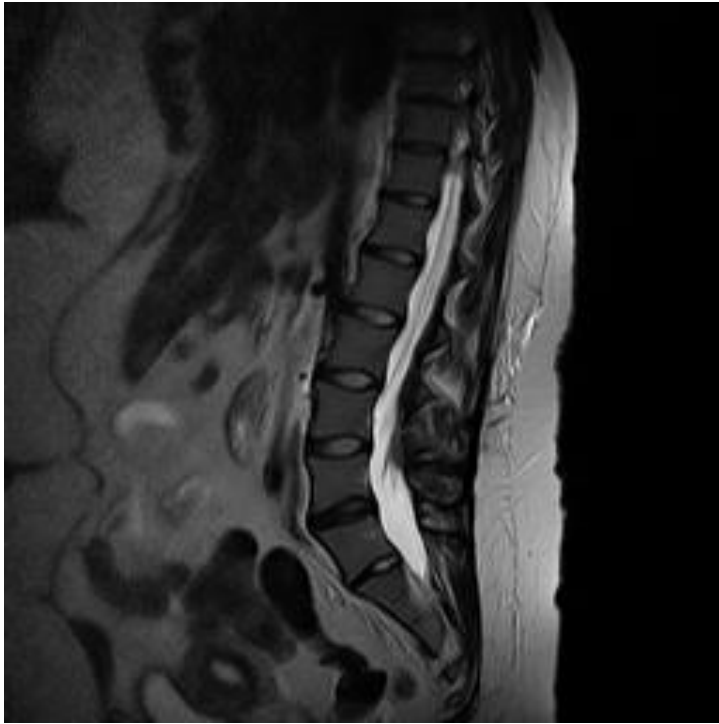


Figure 6.10.1: Neutral sitting positional Magnetic Resonance Imaging scan using flat planar thoracic-lumbar coil (used for upright positions in DLBP subjects)

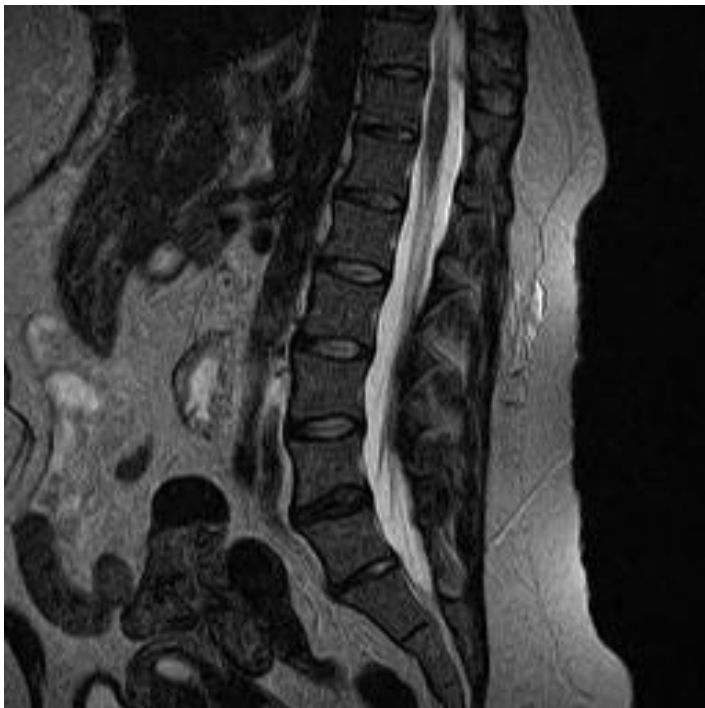


Figure 6.10.2: Neutral sitting positional Magnetic Resonance Imaging scan using solenoid receiver circular coil (used for all asymptomatic subjects and lying positions in DLBP subjects)

The scans were sagittal T2W pMRI scans taken in Neutral sitting (approximately four minutes each) with both the circular coil and the flat quad planar coil. The two scans were performed within the pMRI Centre, Woodend Hospital, Aberdeen on one occasion. Osiris image analysis software was used to measure sagittal migration of the nucleus pulposus using each coil and the data was analysed via a non-parametric Wilcoxon test using SPSS v.17.0 to identify significant differences. The reliability of the author in using Osiris software for this task has previously been established as 0.7 and above (section 3.2.4.1, page ?).

6.10.1: Results

From visual inspection of figure 3.4.3 and 3.4.4 it can be seen that figure 3.4.3 using the new coil provides an image with superior resolution for measurement and diagnostic purposes. This observation was supported by the results of the Wilcoxon test as no significant differences were identified at any level between L1/2 and L5/S1 between the two coils ($p>0.05$).

Therefore, in order to maximise resolution for the final phase of this study, the quad planar coil was used for the sitting and standing scans (sagittal and axial). The circular coil was used for the lying scans as the prone extension position using the quad planar coil had poor scan quality as the lumbar spine was on the edge of the field of view (i.e. the lumbar spine was furthest away from the coil when lying prone on the coil).

6.11: Data management and analysis

As for the asymptomatic subjects, all DLBP subject scans were saved onto CD with subsequent measurements performed using the Osiris 4.19 software program (University of Geneva, Geneva, Switzerland) and all images were examined and reported by a consultant radiologist using standard radiology reporting methods. A copy of the radiologist report was then sent to each subject's GP and physiotherapist.

Sagittal and axial scan measurements were performed as per the asymptomatic subjects for each lumbar IVD in each position. All

measurements were inputted into SPSS v17.0 for subsequent descriptive and inferential analysis. Age, weight and height measurements from this sample were tested for normality using the Shapiro-Wilk test.

6.11.1: Nucleus Pulposus migration from sagittal pMRI scans

All sagittal NP migration measurements were inputted into Excel and then exported to SPSS™ version 17.0 for subsequent analysis. Before carrying out any inferential tests, it was important to establish if the assumptions for the use of parametric tests with this data were satisfied. This was carried out in the same way as for the asymptomatic subjects' data (see section 3.2.3.4, page 101).

The results of the Shapiro-Wilk test indicated that the data was not significantly different from normal except for Flexed sitting L4/5 ($p < 0.026$), Extended sitting L3/4 ($p < 0.01$) and Supine L5/S1 ($p < 0.034$). As there are many values in this data set, you would expect that around 5% would not fall within normal values. However, in this group 9% of the data fell outwith normal values therefore the data was considered to be non-normally distributed. Due to this the requirements of parametric testing could not be met and therefore non-parametric testing (Freidman's ANOVA test) was used for inferential analysis (Field 2009).

Statistical significance was initially set at $p < 0.05$, and post-hoc testing of significant differences was carried out (Wilcoxon signed rank test) of all possible comparisons between positions. Following Bonferroni correction statistical significance was lowered to a more conservative $p < 0.003$.

Although some of the data failed to meet the all the underlying assumptions for parametric analysis, the comparison of groups using a paired t-test allowed an assessment of level of response and the difference effects with the significance levels now being approximate. The more robust nonparametric Wilcoxon tests had already established where the significant differences existed.

6.11.2: Nucleus Pulposus migration from axial pMRI scans

In order to establish if the assumptions for the use of parametric tests with this data were satisfied, the data was explored in the same way as for the sagittal pMRI scan analysis. The data was explored visually via probability-probability plots and histograms and quantified via skewness and kurtosis as well as testing for normality using the Shapiro-Wilk test ($n < 50$) (Field 2009).

The results of the normality test (Shapiro-Wilk test) demonstrated that all values were greater than 0.05 indicating that they were not significantly different from normal except for neutral and extended sitting ($p < 0.044$ & 0.019 respectively) and prone extension ($p < 0.036$). As for the sagittal data, this data set also had a large amount of values but 10% fell outwith normal values therefore the data was considered to be non-normal. In keeping with the sagittal data analysis in section 3.4.11.1 (page 150), non-parametric testing (Friedman's ANOVA test) was used for inferential analysis (Field 2009).

Statistical significance was set initially at $p < 0.05$, and post-hoc testing of significant differences was carried out (Wilcoxon signed rank test) of all possible comparisons between positions. Following Bonferroni correction (15 comparisons) statistical significance was set at $p < 0.003$.

Although some of the data failed to meet all the underlying assumptions for parametric analysis, the comparison of positions using a paired t-test allowed an assessment of level of response and the difference effects with the significance levels now being approximate. The more robust nonparametric Wilcoxon tests had already established where the significant differences existed.

6.11.3: Between group analysis for asymptomatic and DLBP subjects from sagittal positional magnetic resonance scans

Following normality testing using Shapiro-Wilk test ($N < 50$), it was demonstrated that 3 out of the 33 (9%) sets of data were non-normally distributed (Flexed sitting at L4/5; Extended sitting at L3/4 and Supine at L5/S1). Therefore inferential statistics were applied to the data to identify differences between the asymptomatic subjects and the DLBP subjects at

each level and in each position via the independent t test and Mann Whitney test (Field 2009).

Levene's test (Field 2009) was used to identify variance between both groups and all levels in each position were non-significant ($p > 0.05$) and so roughly equal variances were assumed except for neutral sitting at L4/5 and L5/S1. For these two, equal variances were not assumed and the test statistics for this were read and recorded for the corresponding modified t-test.

The two-tailed probability for the independent t test identified significant differences between normal and DLBP sagittal posterior migration in five out of the six positions tested.

6.11.4: Between group analysis for asymptomatic and DLBP subjects from axial positional magnetic resonance scans

Following normality testing with the Shapiro-Wilk test as before ($n < 50$), it was demonstrated that three items in the data set (10%) were non-normally distributed (Neutral and extended sitting at L1/2 and prone extension at L2/3). Therefore parametric and non-parametric inferential statistics were applied to the data to identify between group differences at each level for each position using the independent t-test and the Mann Whitney U test, respectively (Field 2009). Levene's test (Field 2009) was used to identify variance between both groups and all levels in each position were non-significant ($p < 0.05$) and so roughly equal variances were assumed except for flexed sitting at L4/5. For this, equal variances were not assumed and the test statistics for this were read and recorded for the corresponding modified t-test.

6.12: Results

6.12.1: Sample descriptives

Thirty seven subjects were recruited for the main study via the NHS or private physiotherapy. When contacted by the researcher to check the inclusion/exclusion criteria, pMRI patient safety form and organise the pMRI scan one subject declined to participate. A second subject was excluded from the project as they had had previous spinal surgery, and a third subject failed to attend for the arranged pMRI scan.

One subject did not respond after being contacted and asking for the study information to be emailed to them. Two subjects were excluded as one had suffered L1 & L4 burst fractures one year previously and the other had undergone previous lumbar spine surgery. Of the 35 pMRI sessions arranged, 34 took place with 1 subject failing to attend for their session. The final sample of 34 subjects comprised 24 subjects (11 male & 13 female) recruited from NHS Grampian with the other 10 from private practice (6 male & 4 female).

Therefore 34 subjects gave written informed consent and were included in the project. Each subject had T2W sagittal and axial pMRI scans performed in six positions: upright sitting, flexed sitting, extended sitting, standing, supine, and extended prone lying. It was acknowledged prior to data collection that these positions can be provocative to people with back pain/discogenic pain. Twenty five subjects completed all six scan positions, eight were restricted due to pain, and one was restricted due to the pMRI gantry breaking down. Table 6.12.1 demonstrates the positions scanned for each subject.

Table 6.12.1: Positional Magnetic Resonance Imaging scans performed

ID No.	Upright sitting		Flexed sitting		Extended sitting		Standing		Supine		Prone extension		Full data (yes/no)
	Sag	Axial	Sag	Axial	Sag	Axial	Sag	Axial	Sag	Axial	Sag	Axial	
1	✓	✓	✓	✓	✓	✓			✓	✓			No
2	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Yes
3	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Yes
4	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Yes
5	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Yes
6	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Yes
7	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Yes
8	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Yes
9	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Yes
10	✓	✓	✓	✓					✓	✓	✓	✓	No
11	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Yes
12	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Yes
13	✓	✓	✓	✓					✓	✓	✓	✓	No
14	✓	✓	✓	✓									No
15	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Yes
16	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Yes
17	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Yes
18	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Yes
19	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Yes
20	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	No
21	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Yes
22	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Yes
23	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	✓	No
24	✓	✓	✓	✓	✓		✓	✓	✓	✓	✓	✓	No
25	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Yes
26	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Yes
27	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Yes
28	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Yes
29	✓	✓	✓	✓	✓	✓	✓	✓					No
30	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	No
31	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Yes
32	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Yes
33	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Yes
34	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	Yes
Total	34	34	34	33	30	29	30	30	32	32	31	31	25

Key: ID No. = Subject ID number, Sag = sagittal

Equal numbers of males and females were included in the project (17 male & female) and subjects were recruited from two main sources – NHS Grampian physiotherapy out-patient departments and Physiotherapy private practices. Twenty four subjects (11 male: 13 female) were recruited from NHS Grampian with the other 10 from private practice (6 male: 4 female).

Two subjects were unemployed at the time of the project and the remaining 32 were employed in a variety of areas. Eight subjects were signed off and

one person was on maternity leave at the time of the study. One person had started back to work on a rehabilitation scheme.

All scans were reviewed by a consultant radiologist and three subjects had scans judged to be within normal limits. The other subjects all demonstrated IVD changes across the five IVD levels with L5/S1 having the greatest number of IVD bulges, prolapses and herniations. Eleven subjects (32%) demonstrated impingement of at least one nerve root or the conus medullaris. Table 6.12.2 demonstrates the range of pathology and IVD changes reported by the Consultant Radiologist. In addition to the reported changes, nine subjects (27%) were recommended for surgical opinion by the Consultant Radiologist based on their pMRI scans.

Table 6.12.2: Intervertebral disc pathology as reported by Consultant Radiologist

IVD level	Findings (number if greater than 1)
L1/2	Massive central prolapse
L2/3	Herniation into VEP L3, annular tears, loss signal, Grade 1 facet, scoliosis centred at L2/3, minor facet degeneration, muscular atrophy, spinal instability
L3/4	Narrowing, annular tears, left prolapse, minor facet degeneration, loss signal, spinal instability
L4/5	Posterior bulge, narrowing (2), degeneration inc. Loss of signal (5), minor facet degeneration, herniation into VEP L5, large right prolapse, Schmorl's node, inflammatory VEP changes, spinal instability (2)
L5/S1	Very small tear, small/mild posterior/central bulge (4), right prolapse (3, inc 2 large), left prolapse (4), herniation left & right, degeneration inc. Signal loss & narrowing (4), grade 1 facet

Key: IVD – intervertebral disc; VEP – vertebral end plate; inc – including

6.12.2: Sagittal behaviour of the intervertebral disc

The sagittal NP migration data for the asymptomatic and the DLBP subjects are presented in table 6.12.3. Table 6.12.4 presents the results of the Shapiro-Wilk test.

Table 6.12.3: Mean (\pm standard deviation) sagittal migration of each lumbar Nucleus Pulposus in each position for asymptomatic and DLBP subjects from sagittal positional Magnetic Resonance Imaging scans

		Asymptomatic subjects (n = 11)	DLBP subjects (n = 34)
Gender (M:F)		4:7	17:17
Age (years)		36.27 (8.98)	39.44 (9.84)
Height (m)		1.72 (0.08)	1.72 (0.97)
Weight (Kg)		78.09 (14.25)	79.2 (14.56)
N.Sit:	L1/2	20.94 (5.88)	16.8 (4.72)
	L2/3	21.61 (5.36)	17.69 (5.22)
	L3/4	20.3 (3.46)	17.78 (4.74)
	L4/5	21.3 (3.12)	18.09 (5.79)
	L5/S1	22.46 (4.25)	18.47 (6.77)
F.Sit:	L1/2	21.42 (4.63)	19.27 (4.6)
	L2/3	22.73 (4.14)	18.63 (4.37)
	L3/4	19.94 (3.39)	18.05 (4.63)
	L4/5	21.7 (5.19)	18.45 (6.12)
	L5/S1	20.06 (4.88)	19.14 (6.99)
E.Sit:	L1/2	18.88 (4.32)	15.26 (5.08)
	L2/3	19.61 (4.49)	14.7 (5.04)
	L3/4	16.4 (4.24)	15 (4.49)
	L4/5	16.61 (5.17)	15.58 (6.18)
	L5/S1	20.18 (6.22)	16.77 (6.17)
St:	L1/2	19.42 (4.57)	16.05 (4.38)
	L2/3	20.06 (5.04)	15.07 (5.25)
	L3/4	17.43 (5.15)	15.48 (4.99)
	L4/5	15.58 (6.27)	17.17 (4.87)
	L5/S1	15.55 (4.39)	13.44 (5.86)
Supine:	L1/2	19.49 (5.44)	15.21 (4.57)
	L2/3	21.52 (3.76)	15.45 (5.01)
	L3/4	16.82 (2.88)	15.91 (4.78)
	L4/5	16.06 (4.7)	15.43 (6.23)
	L5/S1	12.97 (5.33)	13.24 (7.7)
EIL:	L1/2	17.33 (4.87)	15.29 (3.99)
	L2/3	18.67 (3.67)	16.13 (4.49)
	L3/4	15.64 (3.85)	13.17 (4.71)
	L4/5	14.97 (4.02)	14.13 (5.59)
	L5/S1	13.79 (5.53)	14.12 (7)

Key: M:F = male: female ratio; N.Sit = neutral sitting; F.Sit = flexed sitting; E.Sit = extended sitting; St = standing; EIL = prone extension

Table 6.12.4: Shapiro-Wilk results for normality of sagittal data for asymptomatic and DLBP subjects

	df	Sig.
Subject age	26	.077
Subject height	26	.312
Subject Weight	26	.301
Neutral sit L1/2	26	.296
Neutral sit L2/3	26	.158
Neutral sit L3/4	26	.878
Neutral sit L4/5	26	.628
Neutral sit L5/S1	26	.692
Flex.Sit L1/2	26	.441
Flex.Sit L2/3	26	.245
Flex.Sit L3/4	26	.282
Flex.Sit L4/5	26	.026
Flex.Sit L5/S1	26	.083
Ext.Sit L1/2	26	.263
Ext.Sit L2/3	26	.427
Ext.Sit L3/4	26	.010
Ext.Sit L4/5	26	.125
Ext.Sit L5/S1	26	.937
Stand L1/2	26	.297
Stand L2/3	26	.612
Stand L3/4	26	.723
Stand L4/5	26	.493
Stand L5/S1	26	.326
Supine L1/2	26	.876
Supine L2/3	26	.120
Supine L3/4	26	.266
Supine L4/5	26	.588
Supine L5/S1	26	.034
EIL L1/2	26	.424
EIL L2/3	26	.801
EIL L3/4	26	.073
EIL L4/5	26	.591
EIL L5/S1	26	.217

The results of the Friedman’s ANOVA test indicated a significant effect of position on the NP position, $X^2(29) = 119.987$, $p < 0.001$. Combining the NP results by position, the Friedman’s test on the six positions was highly significant, $X^2(5) = 152.145$, $p < 0.001$, indicating at least one significant difference among the positions. The results of the post-hoc test are shown in table 6.12.5.

Table 6.12.5: Results of post-hoc Wilcoxon signed rank test

Comparison	T value	Asymptotic significance (2 tailed)
Flexed sitting – Neutral sitting	7849	0.004
Extended sitting – Neutral sitting	2639.5	0.001*
Standing – Neutral sitting	2898.5	0.001*
Supine – Neutral sitting	2818.0	0.001*
Prone extension – Neutral sitting	2311.0	0.001*
Extended sitting – Flexed sitting	1854.5	0.001*
Standing – Flexed sitting	1804.5	0.001*
Supine – Flexed sitting	1779.0	0.001*
Prone extension – Flexed sitting	1540.5	0.001*
Standing – Extended sitting	4846.5	0.914
Supine – Extended sitting	4649.5	0.650
Prone extension – Extended sitting	3926.0	0.145
Supine – Standing	4294.5	0.230
Prone extension – Standing	3771.0	0.072
Prone extension – supine	5014.5	0.583

Key: * = significant at $p < 0.003$ level

Further results (table of effects with means and difference effects) and histograms demonstrating the paired differences between positions are provided in Appendix 17.

6.12.3: Axial behaviour of the intervertebral disc

The mean axial migration for the NP from the asymptomatic subjects and the DLBP subjects are presented in table 6.12.6.

Table 6.12.6: Mean (\pm standard deviation) sagittal plane Nucleus Pulposus migration in each position for the asymptomatic and the DLBP subjects from axial pMRI scans

		Asymptomatic subjects (N = 9)	DLBP subjects (N = 33)
N.Sit:	L1/2	25 (6.01)	20.26 (3.71)
	L2/3	24.96 (4.41)	20.71 (4.2)
	L3/4	25.63 (2.47)	20.42 (4.36)
	L4/5	25.25 (3.68)	21.66 (6.01)
	L5/S1	26.09 (5.02)	20.93 (6.49)
F.Sit:	L1/2	28.73 (5.56)	20.03 (3.77)
	L2/3	27.72 (4.46)	21.30 (5.31)
	L3/4	24.08 (5.9)	21.34 (4.65)
	L4/5	27.48 (2.89)	21.63 (4.99)
	L5/S1	27.19 (5.05)	20.96 (6.21)
E.Sit:	L1/2	27.07 (9.17)	18.17 (4.34)
	L2/3	22.59 (3.85)	17.75 (5.0)
	L3/4	20.93 (2.59)	18.77 (3.82)
	L4/5	26.18 (4.83)	20.98 (5.25)
	L5/S1	25.46 (4.16)	21.37 (6.86)
St:	L1/2	23.04 (2.69)	20.04 (4.18)
	L2/3	24.58 (3.66)	20.18 (5.0)
	L3/4	22.07 (3.78)	19.59 (4.7)
	L4/5	21.18 (3.84)	20.24 (5.36)
	L5/S1	23.08 (3.22)	18.81 (5.86)
Supine:	L1/2	25.17 (3.53)	19.64 (3.61)
	L2/3	25.92 (3.32)	18.86 (3.32)
	L3/4	21.46 (2.68)	18.01 (3.7)
	L4/5	20.87 (6.16)	19.47 (4.93)
	L5/S1	23.79 (5.61)	18.17 (5.28)
EIL:	L1/2	22.52 (4.9)	17.68 (3.53)
	L2/3	23.58 (3.08)	18.23 (3.87)
	L3/4	22.88 (3.86)	17.73 (3.39)
	L4/5	19.95 (2.96)	18.05 (4.04)
	L5/S1	20.81 (5.37)	18.03 (5.0)

Key: N.Sit = Neutral sitting; F.Sit = Flexed sitting; E.Sit = Extended sitting; St = Standing; EIL = Prone extension

The results of the Shapiro-Wilk test are presented in table 6.12.7.

Table 6.12.7: Shapiro-Wilk test results for normality of axial pMRI scan data

	Statistic	df	Sig.
Standing L1/2	.977	23	.855
Standing L2/3	.935	23	.141
Standing L3/4	.959	23	.434
Standing L4/5	.947	23	.253
Standing L5/S1	.947	23	.255
Neutral Sitting L1/2	.911	23	.044
Neutral Sitting L2/3	.928	23	.101
Neutral Sitting L3/4	.965	23	.582
Neutral Sitting L4/5	.954	23	.353
Neutral Sitting L5/S1	.976	23	.836
Flexed Sitting L1/2	.944	23	.223
Flexed Sitting L2/3	.950	23	.293
Flexed Sitting L3/4	.977	23	.855
Flexed Sitting L4/5	.966	23	.599
Flexed Sitting L5/S1	.952	23	.323
Extended Sitting L1/2	.894	23	.019
Extended Sitting L2/3	.976	23	.831
Extended Sitting L3/4	.945	23	.235
Extended Sitting L4/5	.968	23	.635
Extended Sitting L5/S1	.980	23	.909
Supine L1/2	.963	23	.519
Supine L2/3	.970	23	.696
Supine L3/4	.959	23	.441
Supine L4/5	.947	23	.248
Supine L5/S1	.950	23	.289
Prone Extension L1/2	.966	23	.585
Prone Extension L2/3	.907	23	.036
Prone Extension L3/4	.974	23	.788
Prone Extension L4/5	.963	23	.522
Prone Extension L5/S1	.960	23	.471

Key: df = degrees of freedom, sig = significance level

The results of the Friedman's ANOVA test indicated a significant effect of position on the NP position in the axial plane, $\chi^2(29) = 100.353$, $p < 0.001$. In order to identify which positions demonstrated this effect a post-hoc Wilcoxon signed rank test was performed with correction for the number of tests carried out. The results of the post-hoc test are shown in table 6.12.8.

From table 6.12.8 it is apparent that the NP position was significantly different to Neutral and Flexed sitting and Prone extension. Neutral sitting NP position was significantly different to Standing, Extended sitting, Supine and Prone extension. Flexed sitting was significantly different to Standing, Extended sitting, Supine and Prone extension. Extended sitting was significantly different to Neutral sitting, Flexed sitting, and Prone extension. Standing was significantly different to Neutral and Flexed sitting and Prone extension. Supine was significantly different to Neutral and Flexed sitting. Prone extension was significantly different to Standing, Neutral, Flexed and Extended sitting. Prone extension and Supine were approaching significance for differences in the NP migration between the two positions ($p < 0.005$).

Table 6.12.8: Results of axial pMRI data post-hoc Wilcoxon signed rank test.

	T value	Asymptotic significance (2 tailed)
Neutral sitting – Standing	5876.50	0.001*
Flexed sitting – Standing	5744.50	0.001*
Extended sitting – Standing	3418.50	0.482
Supine – Standing	3187.00	0.193
Prone extension – Standing	1903.00	0.001*
Flexed sitting – Neutral sitting	5453.50	0.641
Extended sitting – Neutral sitting	1925.00	0.001*
Supine – Neutral sitting	2582.00	0.001*
Prone extension – Neutral sitting	1643.50	0.001*
Extended sitting – Flexed sitting	1946.50	0.001*
Supine – Flexed sitting	2839.50	0.001*
Prone extension – Flexed sitting	1799.00	0.001*
Supine – Extended sitting	3533.00	0.577
Prone extension – Extended sitting	2321.00	0.003*
Prone extension – Supine	3005.00	0.005

Key: *Significant at $p < 0.003$ level

Further results (table of effects with means and difference effects) and histograms demonstrating the paired differences between positions are provided in Appendix 18.

6.12.4: Between sample differences in sagittal intervertebral disc behaviour for asymptomatic subjects and discogenic low back pain subjects from sagittal positional MRI scans

Initial analysis of the data for sagittal migration of the IVD in asymptomatic “normal” and DLBP subjects demonstrated that at all levels and in each position there was greater posterior migration of the NP in the asymptomatic subjects than the DLBP subjects except at L4/5 in standing and L5/S1 in prone lying.

The relative mean posterior NP migrations for the two groups are displayed in figure 6.12.1 – 6.12.6 for each position, with significant differences being highlighted in the footnotes.

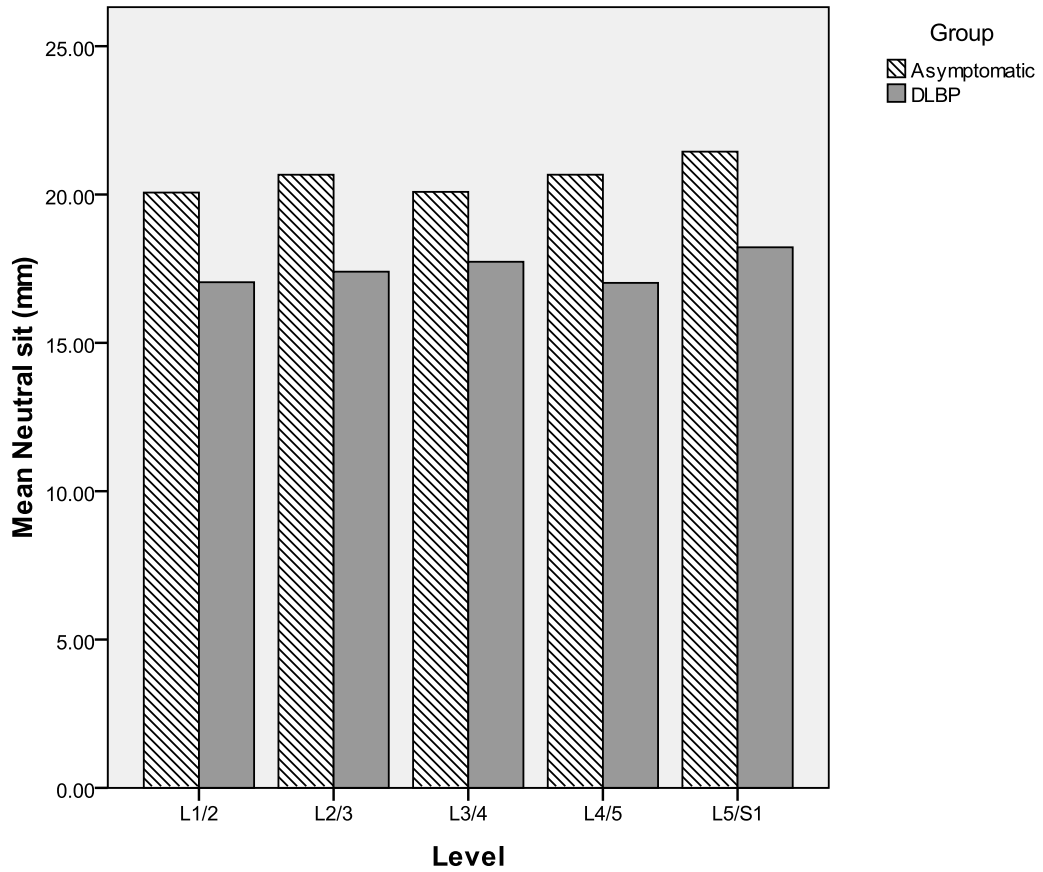


Figure 6.12.1: Mean Nucleus Pulposus migration (mm) at each level in Neutral sitting for asymptomatic and DLBP subjects from sagittal pMRI scans

Note: Main study results are generally lower. The differences are significant at 5% level for L2/3, L4/5 and L5/S1.

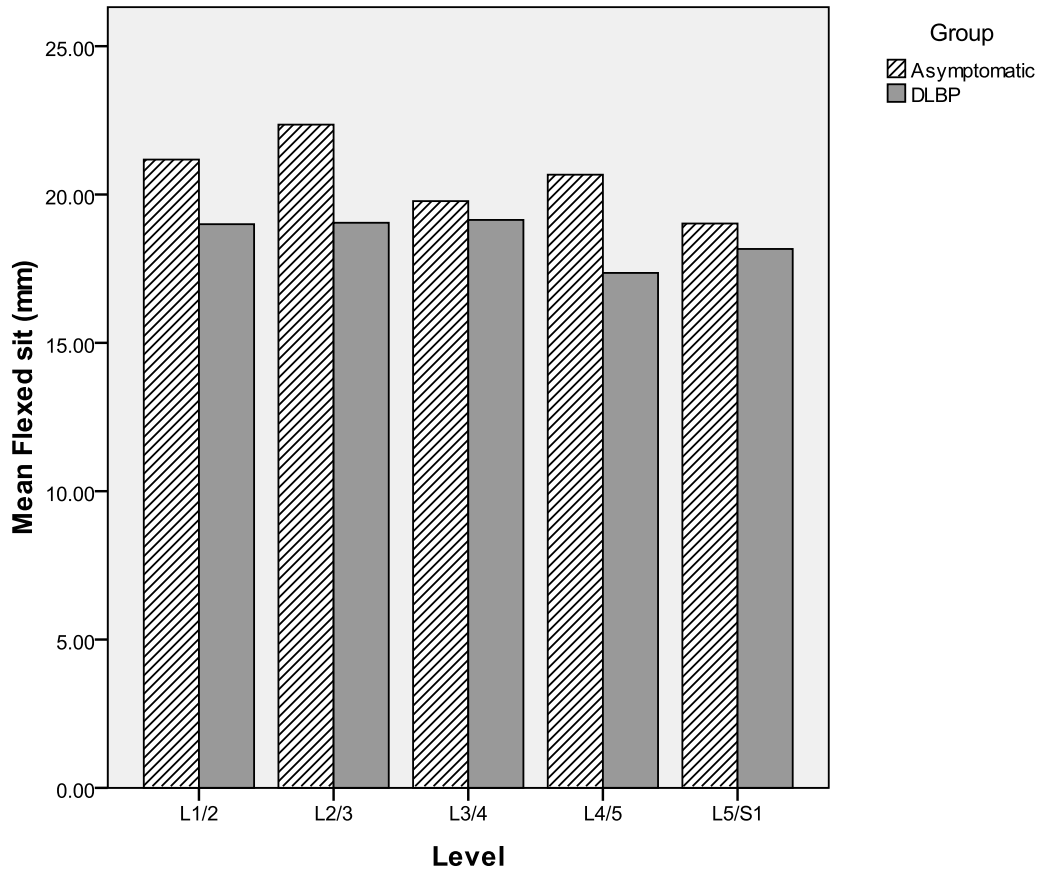


Figure 6.12.2: Mean Nucleus Pulposus migration (mm) at each level in Flexed sitting for asymptomatic and DLBP subjects from sagittal pMRI scans

Note: Main study results are generally lower. The differences are significant at 5% level for L2/3 and L4/5.

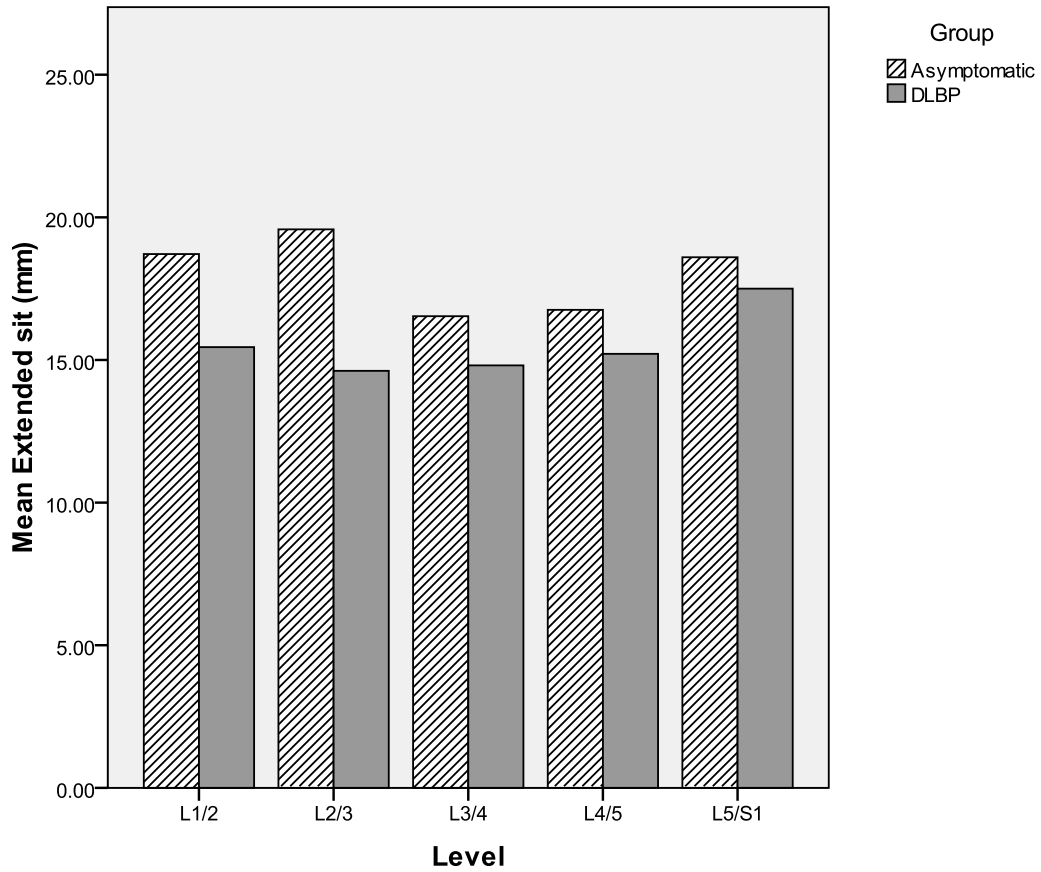


Figure 6.12.3: Mean Nucleus Pulposus migration (mm) at each level in Extended sitting for asymptomatic and DLBP subjects from sagittal pMRI scans

Note: Main study results are generally lower. The differences are significant at 5% level for L1/2 and L2/3.

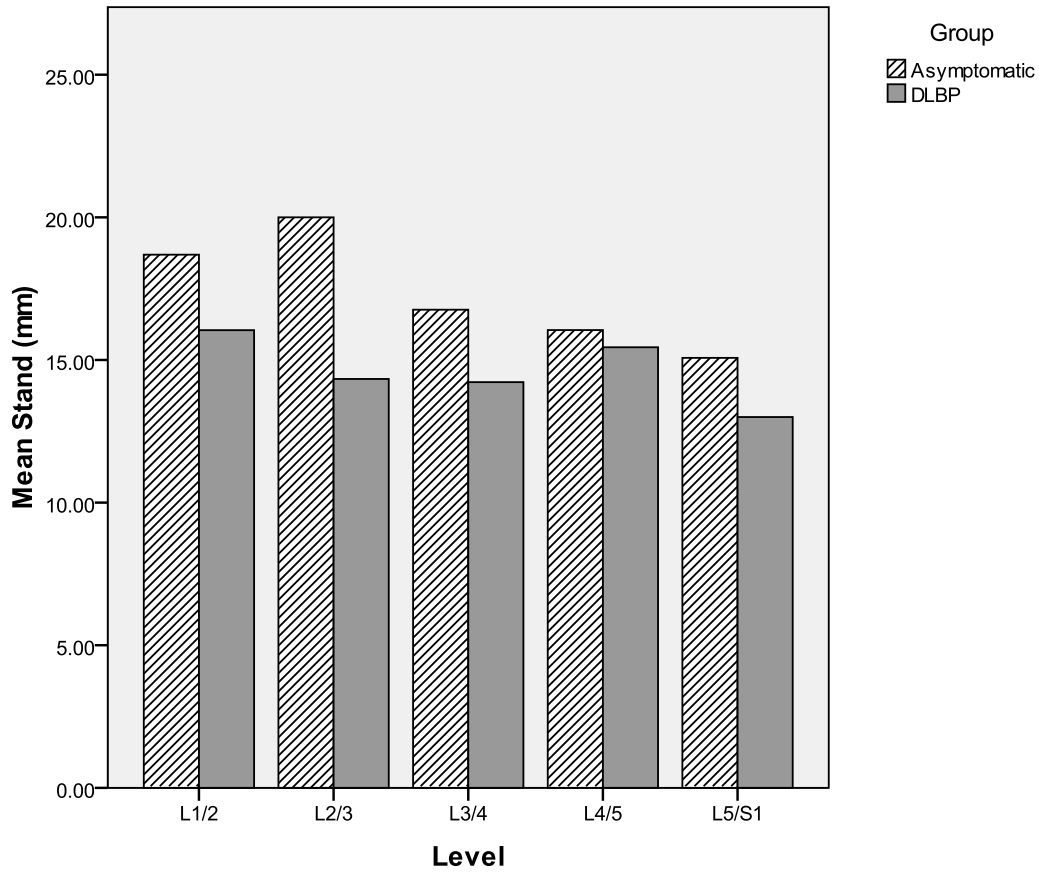


Figure 6.12.4: Mean Nucleus Pulposus migration (mm) at each level in Standing for asymptomatic and DLBP subjects from sagittal pMRI scans

Note: Main study results are generally lower. The differences are significant at 5% level for L1/2 and L2/3.

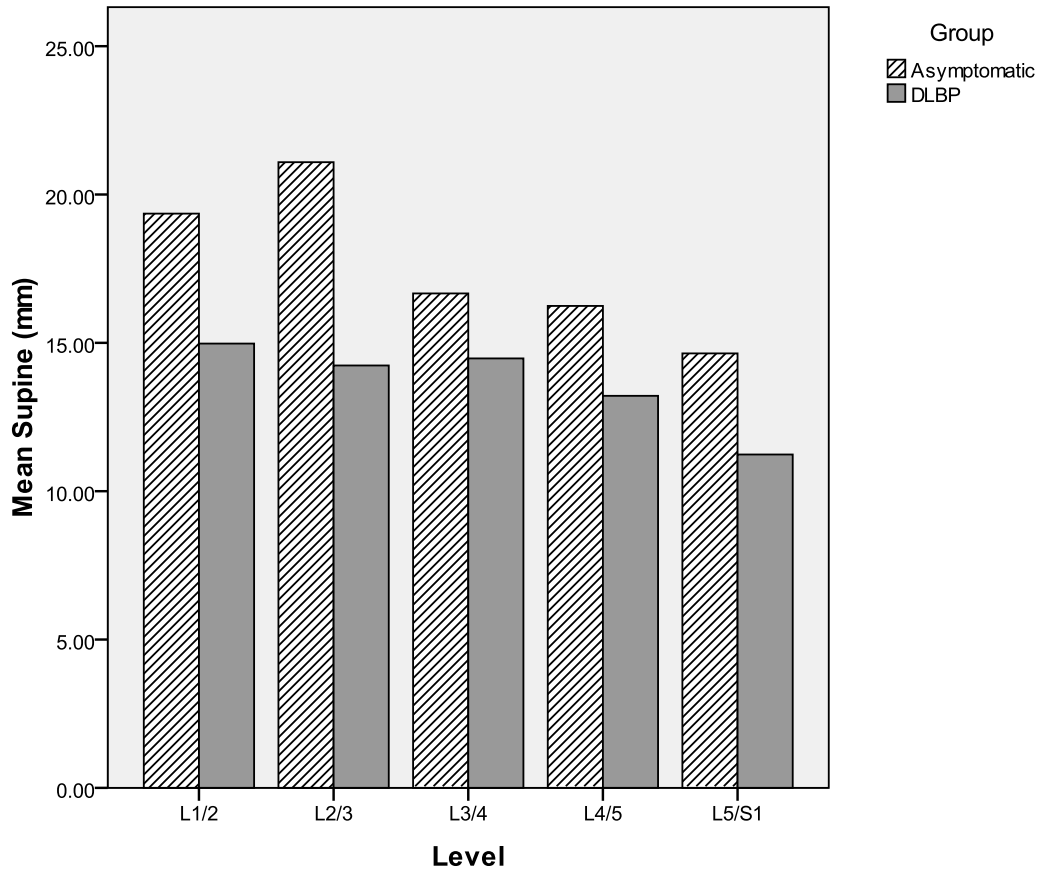


Figure 6.12.5: Mean Nucleus Pulposus migration (mm) at each level in Supine for asymptomatic and DLBP subjects from sagittal pMRI scans

Note: Main study results are generally lower. The differences are significant at 5% level for L1/2 and L2/3.

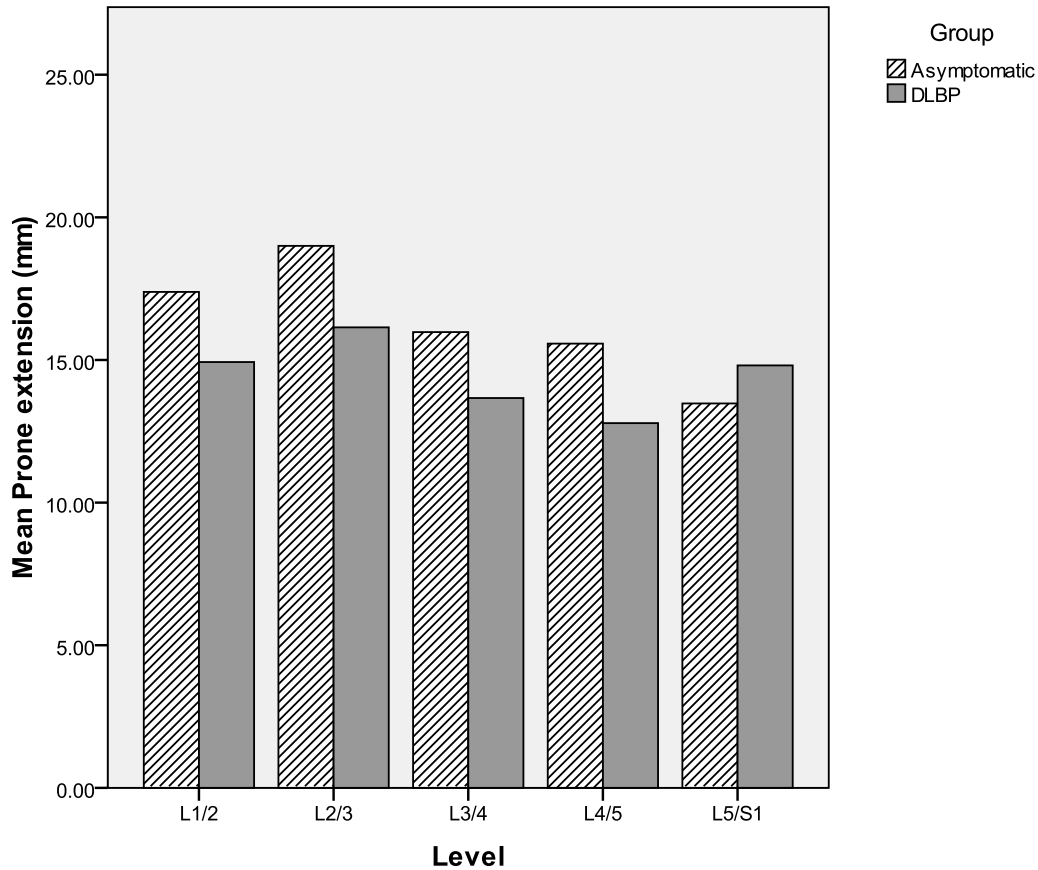


Figure 6.12.6: Mean Nucleus Pulposus migration (mm) at each level in Prone extension for asymptomatic and DLBP subjects from sagittal pMRI scans.

Note: Main study results are generally lower, but not significantly different at any level.

Table 6.12.9 displays the group statistics for the normally distributed data.

From table 6.12.9 it can be seen that significant differences between the two groups were seen at L1/2 (in extended sitting, standing and supine), L2/3 (neutral sitting, flexed sitting, extended sitting, standing and supine), L4/5 (neutral sitting) and L5/S1 (neutral sitting). There were no significant differences identified between the two groups at any level for prone extension.

Table 6.12.9: Group statistics for asymptomatic and DLBP subjects

	Group	N	Mean	SD	SEM	t-value	Sig value	Mean difference (effect size)
Neutral sit L1/2	Asymp	11	20.94	5.88	1.77393	2.377	.22	4.13465
	DLBP	34	16.80	4.72	.80945			
Neutral sit L2/3	Asymp	11	21.61	5.36	1.61532	2.152	.037*	3.92078
	DLBP	34	17.69	5.22	.89545			
Neutral sit L3/4	Asymp	11	20.30	3.46	1.04218	1.622	.112	2.51890
	DLBP	34	17.78	4.74	.81327			
Neutral sit L4/5	Asymp	11	21.30	3.12	.93924	2.352	.025*	3.21570
	DLBP	34	18.09	5.79	.99363			
Neutral sit L5/S1	Asymp	11	22.46	4.25	1.28140	2.305	.029*	3.98516
	DLBP	34	18.47	6.77	1.16103			
Flex.Sit L1/2	Asymp	11	21.42	4.63	1.39466	1.341	.187	2.15091
	DLBP	33	19.27	4.60	.80130			
Flex.Sit L2/3	Asymp	11	22.73	4.14	1.24723	2.728	.009*	4.10061
	DLBP	33	18.63	4.37	.76101			
Flex.Sit L3/4	Asymp	11	19.94	3.39	1.02151	1.242	.221	1.88788
	DLBP	33	18.05	4.63	.80596			
Flex.Sit L5/S1	Asymp	11	20.06	4.88	1.47242	0.404	.688	0.92030

	DLBP	33	19.14	6.99	1.21633			
Ext.Sit L1/2	Asymp	11	18.88	4.32	1.30168	2.101	.042*	3.62342
	DLBP	30	15.26	5.08	.92698			
Ext.Sit L2/3	Asymp	11	19.61	4.49	1.35372	2.839	.007*	4.90670
	DLBP	30	14.70	5.04	.91990			
Ext.Sit L4/5	Asymp	11	16.61	5.17	1.55725	0.492	.626	1.02894
	DLBP	30	15.58	6.18	1.12884			
Ext.Sit L5/S1	Asymp	11	20.18	6.22	1.87483	1.567	.125	3.41515
	DLBP	30	16.77	6.17	1.12710			
Stand L1/2	Asymp	11	19.42	4.57	1.37761	2.164	.037*	3.37864
	DLBP	30	16.05	4.38	.79995			
Stand L2/3	Asymp	11	20.06	5.04	1.51844	2.727	.01*	4.99458
	DLBP	30	15.07	5.25	.95834			
Stand L3/4	Asymp	11	17.43	5.15	1.55143	1.098	.279	1.94655
	DLBP	30	15.48	4.99	.91048			
Stand L4/5	Asymp	11	15.58	6.27	1.89113	-0.857	.397	-1.59030
	DLBP	30	17.17	4.87	.88860			
Stand L5/S1	Asymp	11	15.55	4.39	1.32396	1.080	.287	2.10203
	DLBP	30	13.44	5.86	1.06989			
Supine L1/2	Asymp	11	19.49	5.44	1.63874	2.553	.014*	4.27702
	DLBP	32	15.21	4.57	.80724			

Supine L2/3	Asymp	11	21.52	3.76	1.13417	3.666	.001*	6.06827
	DLBP	32	15.45	5.01	.88553			
Supine L3/4	Asymp	11	16.82	2.88	.86726	0.593	.557	0.91102
	DLBP	32	15.91	4.79	.84585			
Supine L4/5	Asymp	11	16.06	4.70	1.41711	0.307	.760	0.63341
	DLBP	32	15.43	6.23	1.10186			
EIL L1/2	Asymp	11	17.33	4.87	1.46758	1.370	.179	2.04430
	DLBP	30	15.29	3.99	.72885			
EIL L2/3	Asymp	11	18.67	3.67	1.10592	1.683	.1	2.53733
	DLBP	31	16.13	4.49	.80589			
EIL L3/4	Asymp	11	15.64	3.85	1.16063	1.558	.127	2.46507
	DLBP	31	13.17	4.71	.84570			
EIL L4/5	Asymp	11	14.97	4.01	1.21034	0.458	.650	0.84188
	DLBP	31	14.13	5.59	1.00445			
EIL L5/S1	Asymp	11	13.79	5.53	1.66754	-0.141	.888	-0.33047
	DLBP	31	14.12	7.00	1.25784			

Key: * = significant difference between Asymptomatic and DLBP subjects ($p < .05$), SD = standard deviation, SEM = standard error of the mean, sig value = significance value, Asymp = Asymptomatic subjects, DLBP = Discogenic low back pain subjects, flex sit = flexed sitting, ext sit = extended sitting, EIL = prone extension

The remaining non-parametric data was analysed using the Mann Whitney test and the results are displayed in Table 6.12.10.

Table 6.12.10: Results of Mann Whitney test

	Group	N	Mean Rank	Sum of Ranks	Exact sig. (2-tailed)
Flex.Sit L4/5	Asymp	11	29.05	319.50	0.050*
	DLBP	33	20.32	670.50	
Ext.Sit L3/4	Asymp	11	23.45	258.00	0.436
	DLBP	30	20.10	603.00	
Supine L5/S1	Asymp	11	22.91	252.00	0.789
	DLBP	32	21.69	694.00	

Key: * = significant difference between groups ($p < .05$), flex sit = Flexed sitting, ext sit = Extended sitting, Asymp = Asymptomatic subjects, DLBP = Discogenic low back pain subjects

The Mann Whitney test was non-significant (two-tailed) for the sagittal NP posterior migration in extended sitting at L3/4 and supine at L5/S1. This indicates that there were comparable levels of posterior migration for asymptomatic subjects and those with DLBP in these two positions at those two levels.

However, there was a significant difference in posterior NP migration at L4/5 in the flexed sitting position ($p < 0.05$). The value of the mean rankings indicates that the asymptomatic subjects had significantly greater posterior migration than the DLBP subjects.

From table 6.12.9 and 6.12.10 it can be seen that there was a greater mean or mean ranking for posterior migration of the NP in all the asymptomatic subjects at each level and position except Standing at L4/5 and Prone extension at L5/S1.

6.12.5: Between sample differences in sagittal intervertebral disc behaviour for asymptomatic subjects and discogenic low back pain subjects from axial positional MRI scans

Initial analysis of the data for axial pMRI scans for the asymptomatic and DLBP subjects demonstrated that at all levels and in each position there was greater posterior migration of the NP in the asymptomatic subjects than the DLBP subjects (see table 6.12.6). The relative mean posterior NP migration for the two groups are displayed in figures 6.12.7 – 6.12.12 for each position, with significant differences highlighted in the footnotes.

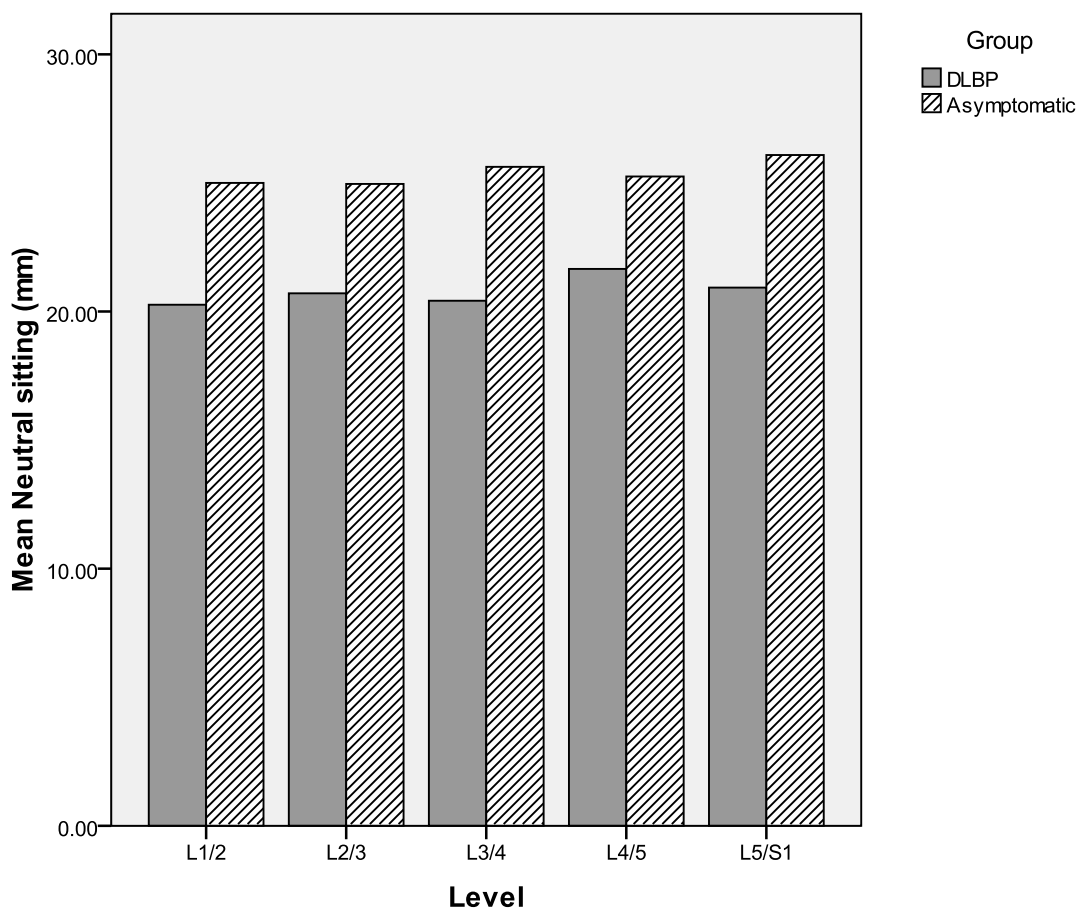


Figure 6.12.7: Mean posterior NP migration (mm) for each level in Neutral sitting for asymptomatic and DLBP subjects from axial pMRI scans.

Note: Main study results are generally lower. The differences are significant at 5% level for L2/3, L3/4 and L5/S1

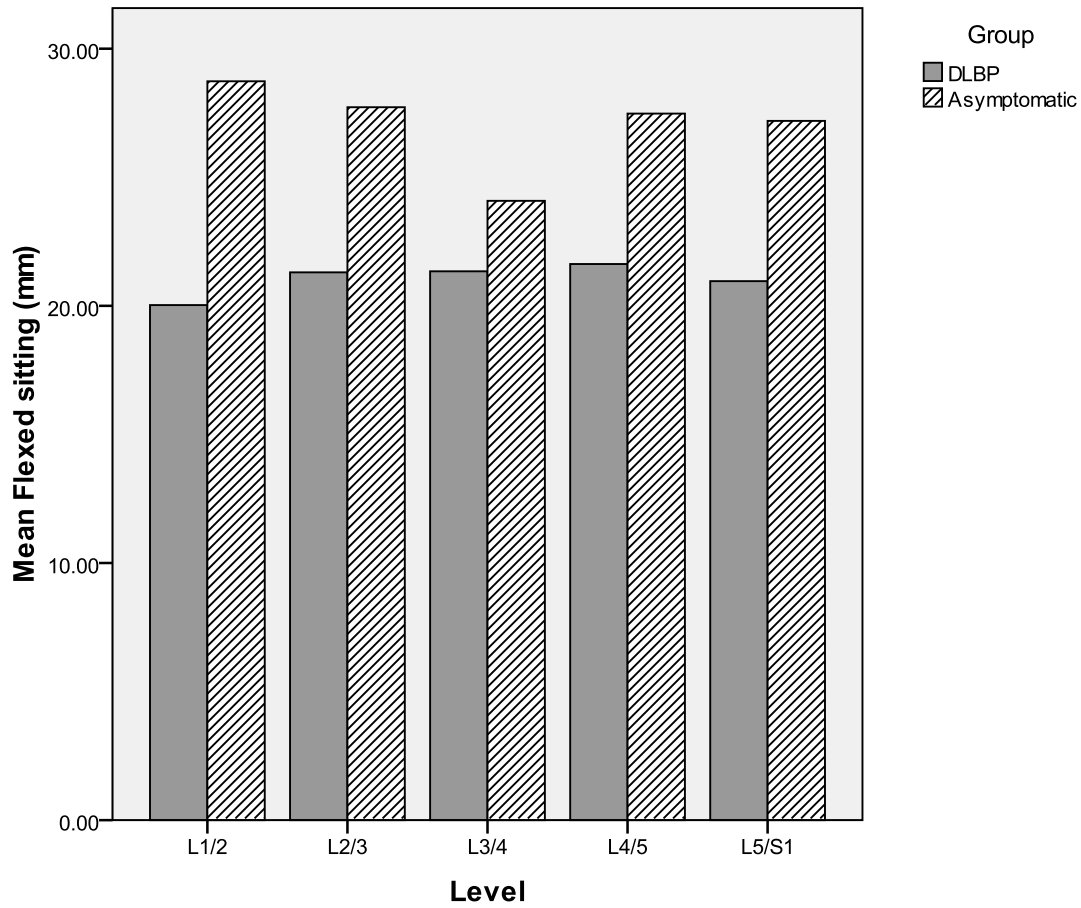


Figure 6.12.8: Mean posterior NP migration (mm) for each level in Flexed sitting for asymptomatic and DLBP subjects from axial pMRI scans

Note: Main study results are generally lower. The differences are significant at 5% level for L1/2, L2/3, L4/5 and L5/S1

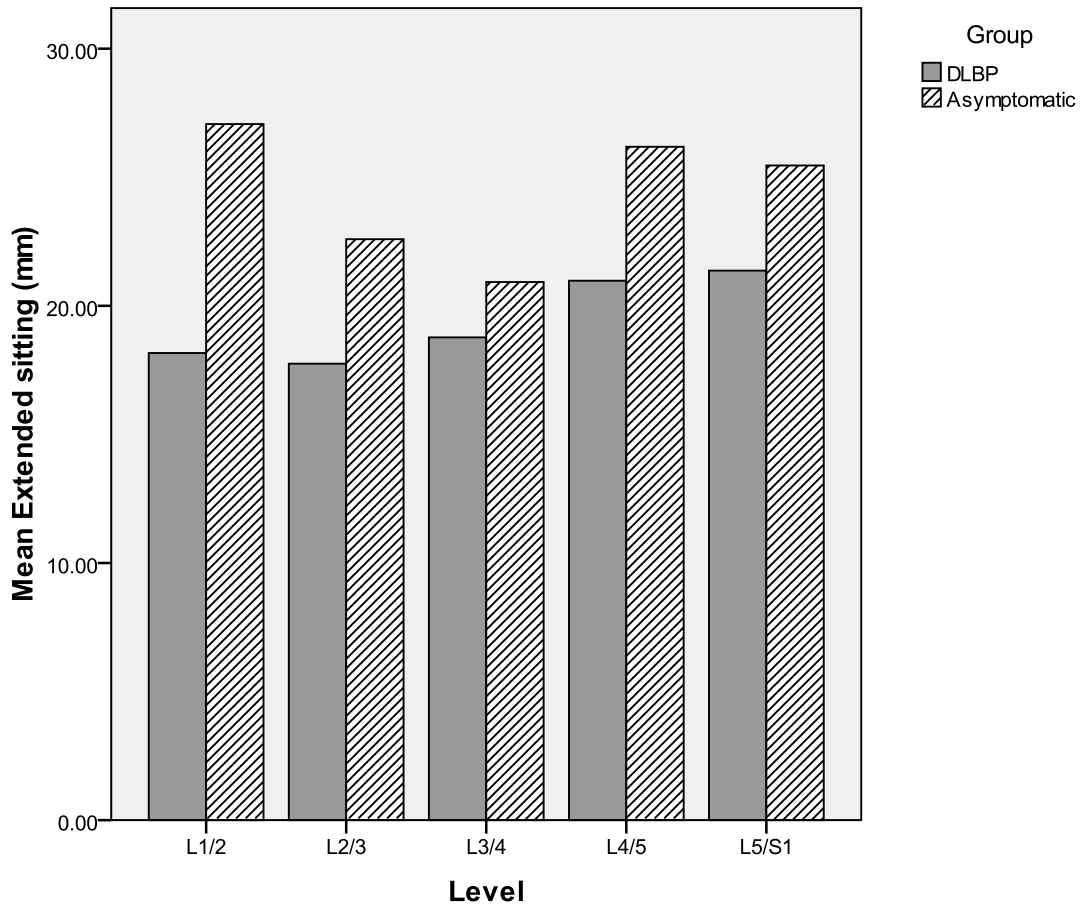


Figure 6.12.9: Mean posterior NP migration (mm) for each level in Extended sitting for asymptomatic and DLBP subjects from axial pMRI scans.

Note: Main study results are generally lower. The differences are significant at 5% level for L1/2, L2/3 and L4/5.

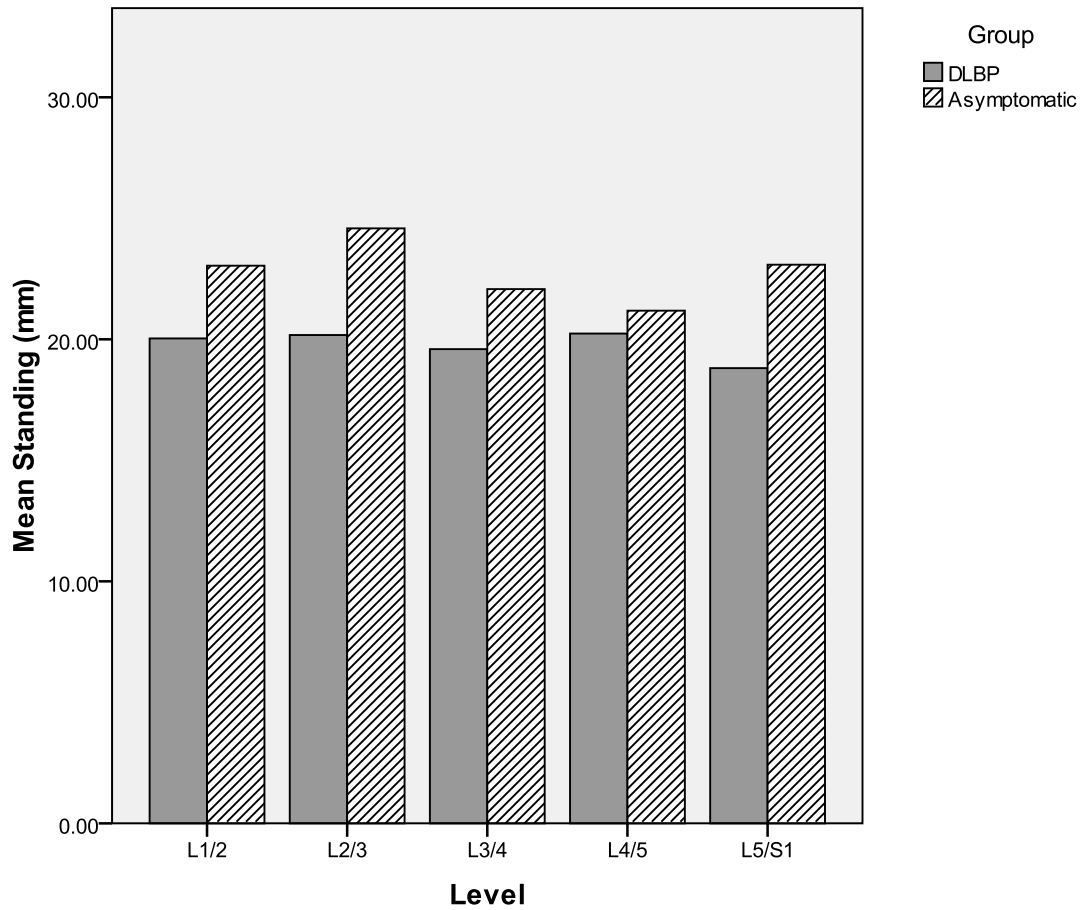


Figure 6.12.10: Mean posterior NP migration (mm) for each level in Standing for asymptomatic and DLBP subjects from axial pMRI scans.

Note: Main study results are generally lower. The differences are significant at 5% level for L2/3.

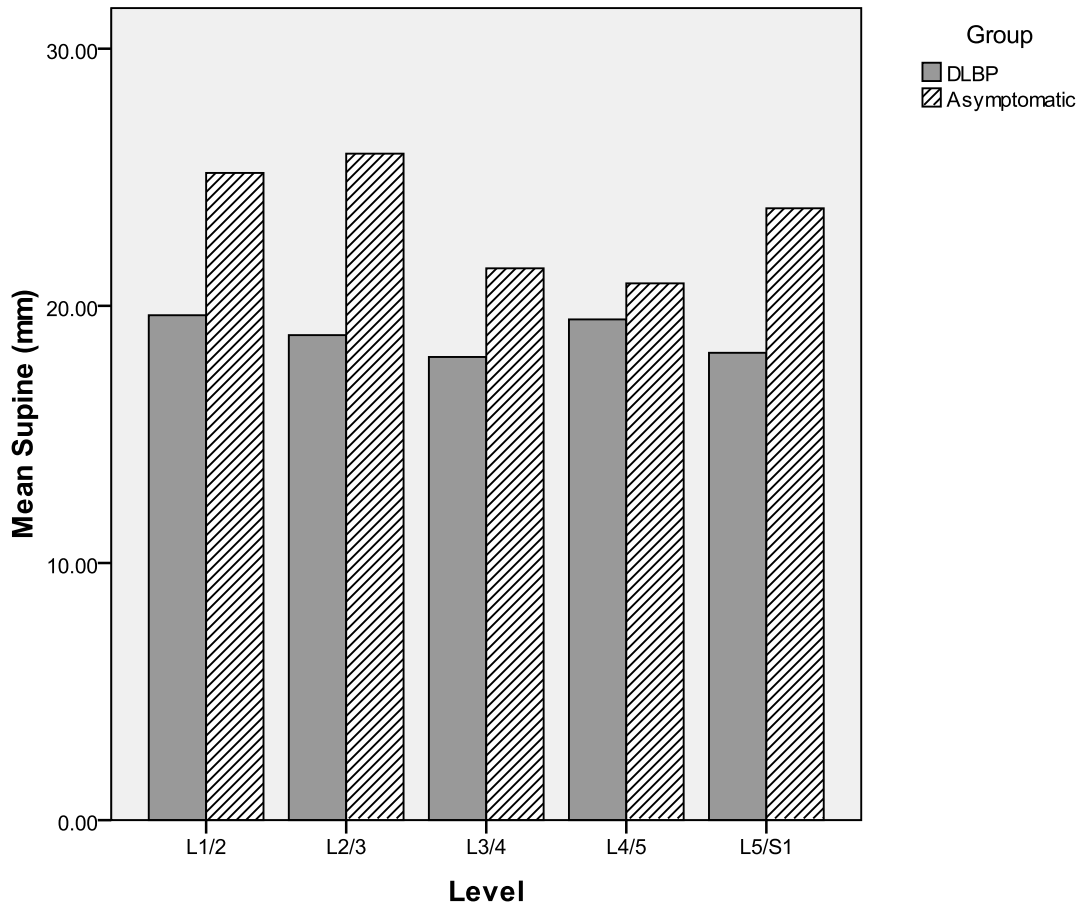


Figure 6.12.11: Mean posterior NP migration (mm) for each level in Supine for asymptomatic and DLBP subjects from axial pMRI scans.

Note: Main study results are generally lower. The differences are significant at 5% level for L1/2, L2/3, L3/4 and L5/S1.

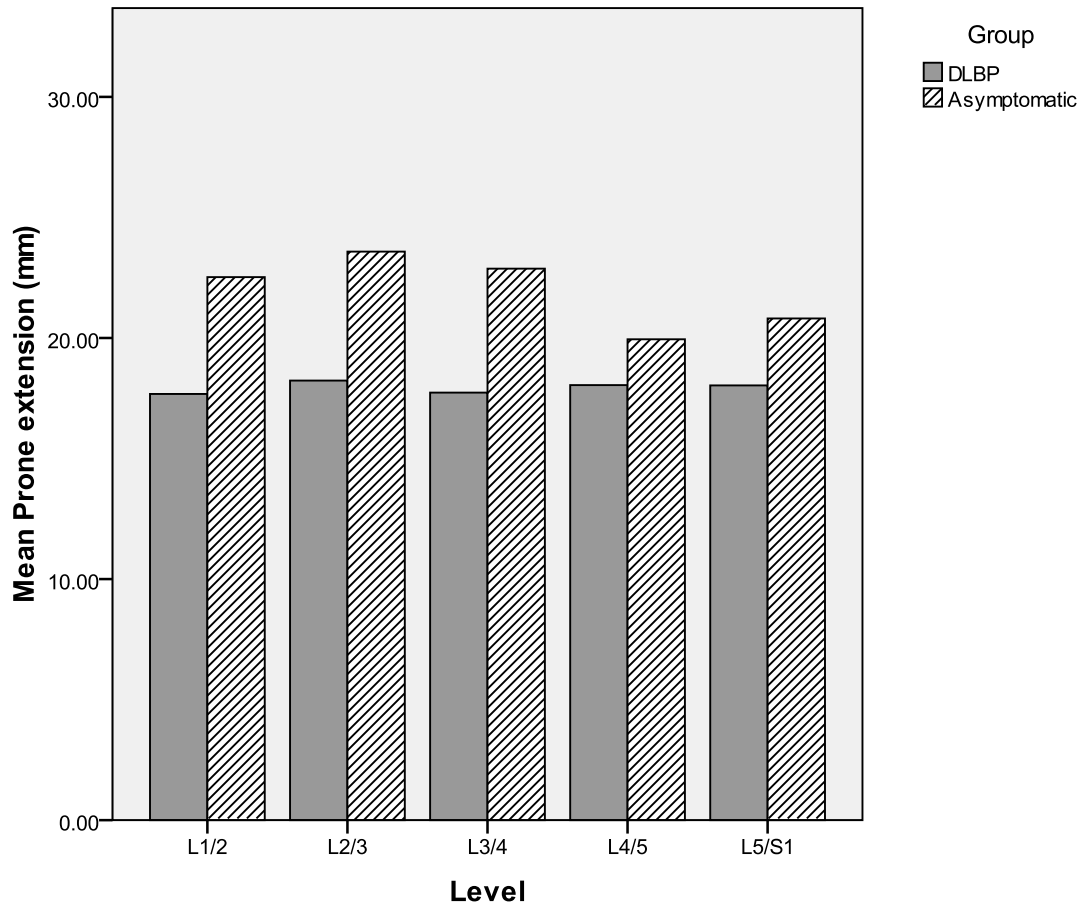


Figure 6.12.12: Mean posterior NP migration (mm) for each level in Prone extension for asymptomatic and DLBP subjects from axial pMRI scans.

Note: Main study results are generally lower. The differences are significant at 5% level for L1/2, L2/3 and L3/4.

The results of the normality test (Shapiro-Wilk) for the data is presented in table 6.12.11.

Table 6.12.11: Shapiro-Wilk test results for testing normality of the axial pMRI scan data

	Statistic	df	Sig.
Standing L5/S1	.961	24	.464
Neutral Sit L1/2	.908	24	.032
Neutral Sit L2/3	.951	24	.284
Neutral Sit L3/4	.965	24	.545
Neutral Sit L4/5	.957	24	.382
Standing L2/3	.922	24	.065
Standing L3/4	.953	24	.312
Standing L1/2	.976	24	.809
Standing L4/5	.948	24	.245
Neutral Sit L5/S1	.973	24	.730
Flexed Sit L1/2	.928	24	.088
Flexed Sit L2/3	.973	24	.741
Flexed Sit L3/4	.978	24	.849
Flexed Sit L4/5	.967	24	.587
Flexed Sit L5/S1	.954	24	.330
Extended Sit L1/2	.892	24	.015
Extended Sit L2/3	.972	24	.711
Extended Sit L3/4	.952	24	.293
Extended Sit L4/5	.966	24	.579
Extended Sit L5/S1	.979	24	.886
Supine L1/2	.974	24	.756
Supine L2/3	.945	24	.210
Supine L3/4	.967	24	.586
Supine L4/5	.950	24	.268
Supine L5/S1	.951	24	.281
Prone Extension L1/2	.968	24	.620
Prone Extension L2/3	.916	24	.047
Prone Extension L3/4	.972	24	.706
Prone Extension L4/5	.961	24	.469
Prone Extension L5/S1	.967	24	.595

Key: df = degrees of freedom, sig = significance level

The two-tailed probability for the independent t-test identified significant differences between the asymptomatic and DLBP subject's axial pMRI scan posterior NP migration in all six positions tested. Table 6.12.12 displays the group statistics for the normally distributed data.

From table 6.12.12 it can be seen that the significant differences between the two groups were seen at all levels - L1/2 (in neutral sitting, flexed sitting, supine and prone extension), L2/3 (in neutral sitting, flexed sitting, extended sitting, and standing), L3/4 (in supine and prone extension), L4/5 (in flexed sitting and prone extension) and L5/S1 (in neutral sitting, flexed sitting and supine).

Table 6.12.12: Axial pMRI scan group statistics for asymptomatic and DLBP subjects

	group	N	Mean	Std. Deviation	Std. Error Mean	t value	Sig value	Mean difference (effect size)
Standing L1/2	DLBP	28	20.04	4.19	.79175	-1.908	0.065	-3.00482
	Asymptomatic	8	23.04	2.69	.95029			
Standing L2/3	DLBP	28	20.18	5.00	.94535	-2.310	0.027*	-4.40625
	Asymptomatic	8	24.58	3.66	1.29405			
Standing L3/4	DLBP	28	19.59	4.70	.88779	-1.437	0.160	-2.48016
	Asymptomatic	9	22.07	3.78	1.25949			
Standing L4/5	DLBP	28	20.24	5.36	1.01363	-0.488	0.629	-0.94476
	Asymptomatic	9	21.18	3.84	1.28129			
Standing L5/S1	DLBP	28	18.81	5.86	1.10682	-1.967	0.057	-4.27286
	Asymptomatic	8	23.08	3.22	1.13689			
Neutral Sit L2/3	DLBP	33	20.71	4.20	.73117	-2.546	0.015*	-4.25303
	Asymptomatic	8	24.96	4.41	1.56022			
Neutral Sit L3/4	DLBP	33	20.42	4.36	.75841	-3.236	0.002*	-5.20652
	Asymptomatic	8	25.63	2.47	.87146			
Neutral Sit L4/5	DLBP	33	21.66	6.01	1.04647	-1.610	0.115	-3.59445
	Asymptomatic	8	25.25	3.68	1.29928			
Neutral Sit L5/S1	DLBP	33	20.93	6.49	1.12921	-2.093	0.043*	-5.15530

	Asymptomatic	8	26.09	5.02	1.77621			
Flexed Sit L1/2	DLBP	33	20.03	3.77	.65648	-4.523	0.001*	-8.70230
	Asymptomatic	5	28.73	5.56	2.48492			
Flexed Sit L2/3	DLBP	33	21.30	5.32	.92519	-2.778	0.009*	-6.42091
	Asymptomatic	6	27.72	4.46	1.82205			
Flexed Sit L3/4	DLBP	33	21.34	4.65	.80911	-1.420	0.164	-2.73917
	Asymptomatic	8	24.08	5.90	2.08412			
Flexed Sit L4/5	DLBP	33	21.63	4.99	.86893	-4.195	0.001*	-5.84996
	Asymptomatic	7	27.48	2.89	1.09088			
Flexed Sit L5/S1	DLBP	33	20.96	6.21	1.08058	-2.480	0.018*	-6.23143
	Asymptomatic	7	27.19	5.05	1.90823			
Extended Sit L2/3	DLBP	28	17.75	5.00	.94474	-2.654	0.012*	-4.84075
	Asymptomatic	9	22.59	3.85	1.28207			
Extended Sit L3/4	DLBP	28	18.77	3.82	.72147	-1.571	0.125	-2.15234
	Asymptomatic	9	20.93	2.59	.86436			
Extended Sit L4/5	DLBP	28	20.98	5.25	.99213	-2.636	0.012*	-5.20766
	Asymptomatic	9	26.18	4.83	1.60911			
Extended Sit L5/S1	DLBP	28	21.37	6.86	1.29558	-1.595	0.120	-4.08821
	Asymptomatic	8	25.46	4.16	1.47199			
Supine L1/2	DLBP	31	19.64	3.61	.64902	-3.445	0.002*	-5.53382
	Asymptomatic	6	25.17	3.53	1.44193			
Supine L2/3	DLBP	31	18.86	3.32	.59579	-5.362	0.001*	-7.05685

	Asymptomatic	8	25.92	3.32	1.17518			
Supine L3/4	DLBP	31	18.01	3.70	.66483	-2.462	0.019*	-3.44746
	Asymptomatic	8	21.46	2.68	.94718			
Supine L4/5	DLBP	31	19.47	4.93	.88602	-0.681	0.500	-1.40181
	Asymptomatic	8	20.87	6.16	2.17943			
Supine L5/S1	DLBP	31	18.17	5.28	.94826	-2.651	0.012*	-5.61927
	Asymptomatic	8	23.79	5.61	1.98471			
Prone Extension L1/2	DLBP	30	17.68	3.53	.64412	-3.040	0.004*	-4.84629
	Asymptomatic	7	22.52	4.90	1.85126			
Prone Extension L3/4	DLBP	30	17.73	3.39	.61906	-3.706	0.001*	-5.14133
	Asymptomatic	8	22.88	3.86	1.36348			
Prone Extension L4/5	DLBP	30	18.05	4.04	.73694	-1.090	0.283	-1.90000
	Asymptomatic	6	19.95	2.96	1.20867			
Prone Extension L5/S1	DLBP	30	18.03	5.00	.91210	-1.307	0.200	-2.77700
	Asymptomatic	7	20.81	5.37	2.03055			

Key: * = significant difference between asymptomatic and DLBP subjects ($p < .05$), SD = standard deviation, SEM = standard error of the mean, sig value = significance value, flex sit = Flexed sitting, ext sit = Extended sitting, EIL – Prone extension

The remaining non-parametric data were analysed using the Mann-Whitney U test and the results are displayed in table 6.12.13.

Table 6.12.13: Results of Mann-Whitney U test for axial pMRI scan data for asymptomatic and DLBP subjects

	group	N	Mean Rank	Sum of Ranks	Asymp sig (2 tailed)
Neutral Sit L1/2	DLBP	33	18.24	602.00	0.073
	Asymptomatic	5	27.80	139.00	
Extended Sit L1/2	DLBP	28	15.29	428.00	0.016*
	Asymptomatic	5	26.60	133.00	
Prone Extension L2/3	DLBP	30	16.60	498.00	0.002*
	Asymptomatic	8	30.38	243.00	

Key: * significant difference $p < 0.05$, asymp sig = asymptotic significance

The Mann-Whitney U test was non-significant for axial NP posterior migration in neutral sitting at L1/2. This indicates that there were comparable levels of posterior migration for asymptomatic subjects and those with DLBP in this position at this level.

However, there was a significant difference in posterior NP migration at L1/2 in extended sitting ($p < 0.016$) and L2/3 in prone extension ($p < 0.002$). The value of mean rankings indicates that the asymptomatic subjects had significantly greater posterior NP migration than the DLBP subjects.

From Table 6.12.12 and 6.12.13 it can be seen that there was a greater mean or mean ranking for posterior migration of the NP in all the asymptomatic subjects at all levels and position.

6.13: Discussion

The final phase of this study was conducted to investigate the effect of different positions on the behaviour of the lumbar IVDs in subjects with DLBP. The aim of this phase was to establish a database of the extent of sagittal plane NP migration in DLBP subjects in different functional positions (Objective 6, section 1.8) and then finally to compare the extent of sagittal plane NP migration between asymptomatic and DLBP subjects (Objective 7, section 1.8).

The sample was equally balanced in terms of gender with a mean age (39 years) reflective of the younger age for DLBP. From the consultant radiologist reports of the pMRI scans, the majority of the group (91%) demonstrated changes in the IVD with L5/S1 having the greatest number of bulges, prolapses and herniations. Eleven subjects (32%) demonstrated impingement of at least one nerve root or the conus medullaris. Based on the pMRI scans, nine subjects (27%) were recommended for surgical opinion.

6.13.1: Behaviour of the intervertebral disc from sagittal pMRI scans

From the results it was evident that there was a significant effect of position on the sagittal NP migration in subjects with DLBP ($p=0.001$). Post-hoc testing identified significant differences in the sagittal NP position for the Neutral and Flexed sitting positions compared to the other four positions (Extended sitting, Standing, Supine and Prone extension) ($p<0.001$). In total there were eight out of a possible 15 significant differences found and these are presented in table 6.13.1.

Table 6.13.1: Statistically significant differences ($p < 0.003$) in Nucleus Pulposus migration from sagittal positional Magnetic Resonance Imaging scans in DLBP subjects

Position	Greater posterior NP migration than
Flexed sitting	Standing Extended sitting Supine Prone extension
Neutral sitting	Standing Extended sitting Supine Prone extension

In Neutral sitting, there was statistically significant greater posterior migration of the NP compared to Extended sitting, Standing, Supine and Prone extension. The mean difference ranged from 2.38mm to 3.12mm. The greatest mean difference in NP migration occurred between Neutral sitting and the unloaded positions (Supine and Prone extension, 2.75mm and 3.12mm respectively). In Flexed sitting there was also a statistically significant greater amount of posterior NP migration compared to Extended sitting, Standing, Supine and Prone extension. The mean difference ranged from 3.22mm to 4.14mm. The greatest mean difference in NP migration again occurred between Flexed sitting and the unloaded positions (Supine and Prone extension, 3.71mm and 4.14mm respectively). Of all comparisons, Flexed sitting and Prone extension (greatest amount of flexion and greatest amount of extension) produced the greatest mean difference in NP migration (4.14mm).

In the sagittal plane, these results support the theory of sagittal plane IVD behaviour (posterior NP migration in flexion and anterior NP migration in extension) in DLBP subjects. In addition the results from the DLBP subjects demonstrate for the first time the significant effect of position upon sagittal plane IVD behaviour in DLBP subjects. This theory has been proposed (McKenzie and May 2003) but has not been demonstrated in DLBP subjects using pMRI in the literature to date.

Previous authors have reported the sagittal plane behaviour of the NP in different positions. An early study by Zamani et al (1998) reported results for 25 LBP subjects and 5 asymptomatic subjects that had Neutral sitting, Flexed sitting, and Extended sitting and Supine sagittal scans performed in a 0.5T Open MRI system. They reported that there was no definite change noted between Supine and Neutral sitting positions for posterior IVD bulge. This is in contrast to the findings reported in the current study for the DLBP subjects but the methodological flaws in the study by Zamani et al (1998) reduce the confidence in their results for comparison with the present study. The main weakness in Zamani et al's (1998) results is the lack of objective measurements in the assessment of posterior IVD bulge. The authors simply carried out a visual assessment of the posterior IVD boundary. Therefore the key finding that Extended sitting increased the posterior IVD bulge in 27% (24/90 IVDs) cannot be viewed with confidence nor can it be classed as comparable with the NP migrations measurements performed in this thesis.

A more recent study by Ferreiro-Perez et al (2007) assessed 45 LBP patients in Supine and Neutral sitting using pMRI sagittal and axial scans. The authors reported a descriptive analysis where 8% (2/24) of posterior IVD herniations were seen only on Neutral sitting images and 58% (14/24) of the posterior IVD herniations increased in size in Neutral sitting compared to Supine. Although this is a descriptive result and the authors did not carry out any statistical tests to determine significance, the findings support those reported in the current study for the DLBP subjects.

Morishita et al (2008) performed sagittal T1W and T2W FSE kMRI scans in Neutral sitting, Flexed sitting and Extended sitting in 587 LBP patients. Despite the authors carrying out multiple measurements and analysis, they reported minimal information in the article. Morishita et al (2008) did report a significant increase in IVD herniations in Flexed and Extended sitting compared to Neutral sitting images but there was no data or analysis provided to support this finding. On face value alone, this finding supports the current results for the DLBP subjects in that there was greater posterior migration in Extended sitting compared to Neutral sitting. However, Morishita et al's (2008) finding that there was greater herniation in Flexed sitting compared to Neutral sitting is in opposition to the DLBP subjects' results. An explanation for this can be proposed in that Morishita et al (2008) were evaluating posterior IVD herniation

whereas the current study was evaluating subjects with a DLBP presentation, not specifically herniation. From table 6.12.2 it can be seen that IVD herniation was reported in only one subject at L5/S1 by the Consultant Radiologist.

Therefore the two studies are not directly comparable.

In a large study by Zou et al (2009) involving pMRI scans performed in Neutral, Flexed and Extended sitting in 513 LBP patients, they reported similar results for all the healthy IVDs as was found in the present study. The IVDs migrated anteriorly in extension and posteriorly in flexion, although these trends were not found to be statistically significant in the study by Zou et al (2009). They also noted that in degenerated IVDs, the migration trends were less predictable. A limitation of Zou et al's study was that the principal aim was to investigate the dynamic bulging of the IVD in IVD degeneration and there was no method included to describe the migration effect measurement or analysis.

Despite some positive trends reported in the literature that support the results of the current study, there is more research required to be carried out to establish the exact behaviour of the IVD in different positions in the sagittal plane from pMRI sagittal scans. It is important that future research reporting methods fully describe the measurement methods, their reliability and analysis performed as was employed in the current study. By ensuring rigorous reporting methods, the results from future research projects will have greater credibility.

6.13.2: Behaviour of the intervertebral disc from axial pMRI scans

From the results it was evident that there was a significant effect of position on the sagittal NP migration in subjects with DLBP on axial pMRI scans ($p=0.001$). The matched-pairs t-test identified significant differences in the sagittal plane NP migration for Standing, Neutral, Flexed and Extended sitting and this is demonstrated in table 6.13.2.

Table 6.13.2: Statistically significant differences ($p < 0.003$) in Nucleus Pulposus migration from axial positional Magnetic Resonance Imaging scans in DLBP subjects

Position	Greater posterior NP migration than
Standing	Prone extension
Flexed sitting	Standing Extended sitting Supine Prone extension
Neutral sitting	Extended sitting Standing Supine Prone extension
Extended sitting	Prone extension

Standing demonstrated significantly less posterior migration of the NP compared to Neutral and Flexed sitting but significantly greater posterior NP migration compared to Prone extension. Mean differences in NP position ranged from 1.44mm to 1.78mm.

Neutral sitting demonstrated statistically significant greater posterior NP migration in comparison to Extended sitting, Supine and Prone extension. Mean NP differences ranged from 1.8mm to 3.04mm. The largest mean differences occurred between Neutral sitting and the unloaded positions (Supine and Prone extension, 2.17mm and 3.04mm respectively).

Flexed sitting demonstrated statistically significant greater posterior NP migration in comparison to Extended sitting, Supine and Prone extension. Mean NP differences ranged from 1.46mm to 3.15mm. The largest mean NP differences again occurred between Flexed sitting and the unloaded positions (Supine and Prone extension, 1.95mm and 3.15mm respectively).

The position of Extended sitting demonstrated statistically greater posterior NP migration compared to Prone extension with a mean NP difference of 1.63mm. The sagittal plane NP migration in the axial pMRI scans produced the same results as the sagittal pMRI scans for Flexed and Neutral sitting. However, the axial pMRI scans produced further significant differences for the two other loaded positions (Standing and Extended sitting) in comparison to Prone extension. As there has been no literature published regarding axial pMRI scans

and NP behaviour in the sagittal plane, it is unclear whether these additional significant results are of importance.

Imaging studies normally report sagittal or axial measurements separately. There is no literature available that compares results between imaging planes. For this study, the significant results reported as mean differences (mm) for the sagittal and axial scans are demonstrated in table 6.13.3 below.

Table 6.13.3: Mean differences (mm) for significant results between sagittal and axial positional Magnetic Resonance Imaging scans

	Sagittal NP mean difference	Axial NP mean difference	Difference between imaging planes
Neutral sit – extended sit	2.54	1.8	0.74
Neutral sit – standing	2.38	1.44	0.94
Neutral sit – supine	2.75	2.17	0.58
Neutral sit – prone extension	3.12	3.04	0.08
Flexed sit – extended sit	3.22	1.46	1.76
Flexed sit – standing	3.36	1.71	1.65
Flexed sit – supine	3.71	1.95	1.76
Flexed sit – prone extension	4.14	3.15	1.25

In each significant result, the sagittal scans measured a greater posterior NP migration compared to the axial scans for all comparisons. What this means in terms of which image plane should be used for measurement of sagittal plane NP migration is unclear. Fazey et al (2006, 2011) have reported that a single line measurement in sagittal scans may not reflect the full NP profile. However, from the current results the sagittal measurements, although consistently greater than the axial scans, are not erratic and follow the same trend between positions as the axial measurements.

Further research is required in this area in order to identify whether measurements should be performed from the sagittal or axial pMRI scans, or

indeed if both are required to create a balanced picture of the IVD. Ideally 3-dimensional imaging of the NP peak profile would be preferred (such as that used by Perie et al 2001, 2003; Violas et al 2007 and Perie & Curnier 2010) but this area is still in its development phase and requires further work before becoming clinically useful.

6.13.3: Between group differences in intervertebral disc behaviour for asymptomatic and Discogenic low back pain subjects

6.13.3.1: Sagittal pMRI scans

From the results it was evident that there was greater posterior migration of the NP in the asymptomatic subjects for all positions and levels (except Standing at L4/5, Supine at L5/S1 and Prone extension at L5/S1), than the DLBP subjects. This is an interesting finding as none of the asymptomatic subjects reported any discomfort moving immediately from Flexed sitting to Extended sitting, yet this was painful for some of the DLBP subjects. As the asymptomatic subjects had greater posterior migration, it would have been logical to assume that they would have had a greater potential to have a problem in moving into extension. Reasons for this difference can be theorised to be caused by differences in IVD creep rate and compressive loading effects between the two groups (Adams et al 2006, Barbir et al 2011, O'Connell et al 2011). It is acknowledged that creep rate is affected by different factors such as age, loading history, degenerative changes, hydration levels, IVD area, posture and compressive loading (Twomey and Taylor 1982, Adams et al 2006, O'Connell et al 2011). However, additional factors such as visco-elastic changes due to injury or damage in the IVD along with AF deformation (Solomonow et al 2003, Adams et al 2006) may slow the creep rate in DLBP subjects so that there is a smaller amount of NP migration compared to asymptomatic subjects.

As the asymptomatic group demonstrated greater posterior migration of the NP, it could be theorised that the DLBP group's experience of discomfort could be due to chemically mediated pain rather than a mechanical mechanism. As the results from this study are the first to report this difference in behaviour between asymptomatic and DLBP subjects, it would warrant further research with larger samples to investigate the differences fully for statistical and clinical significance.

Of the 30 comparisons between the asymptomatic and DLBP subjects, only ten were statistically significantly different and occurred mainly in the upper IVD levels (L1/2 and L2/3). This is presented in table 6.13.4.

Table 6.13.4: Intervertebral disc level demonstrating statistically significant differences between positions for asymptomatic and DLBP subjects

Position	Intervertebral disc level
Neutral sitting	L2/3, L4/5, L5/S1
Flexed sitting	L2/3
Extended sitting	L1/2, L2/3
Standing	L1/2, L2/3
Supine	L1/2, L2/3

Of the positions investigated, Neutral sitting demonstrated significant differences between the two groups at three levels (L2/3, L4/5 and L5/S1). Extending sitting, Standing and Supine demonstrated significant differences at L1/2 and L2/3. Flexed sitting only demonstrated significant differences at L2/3. As noted in the results, Prone extension did not demonstrate significant differences between the two groups at any lumbar IVD segmental level. These results support the need for DLBP subjects to be investigated in loaded positions (especially Neutral sitting for the lower lumbar spine). The Prone extension position did not identify any significant differences between the two groups and Supine only demonstrated differences at the upper two IVD levels. As it has been demonstrated that the lower IVD levels have the highest incidence of DLBP problems (Knopp-Jergas et al 1996), the only position that identified significant differences between the two groups at these levels was Neutral sitting. Indeed, the unloaded positions support prior clinical experience by the author where rMRI reports have failed to identify any IVD pathology in patients presenting with significant symptoms.

Previous MRI studies investigating the response of the lumbar NP to flexion and extension found that anterior migration was most apparent in the upper 4 lumbar IVDs, but this was in unloaded and nonfunctional, recumbent positions (Fennel, Jones & Hukins 1996; Edmondston et al 2000). The results from the

current study differ in that sagittal plane NP migration behaved differently in loaded, functional positions in asymptomatic and DLBP subjects. The upper IVD levels (L1/2 and L2/3) demonstrated significant posterior NP migration and this may be due to the loaded effects on the IVD.

A possible theory to explain the differences between the two groups in the current results would perhaps be due to the DLBP group experiencing pain with their condition. Pain can limit movement and lead to altered movement strategies (O'Sullivan 2005), therefore the DLBP may have adopted the positions required for each pMRI scan but may not have moved as far or as freely as the asymptomatic subjects. The present study did not assess the range of movement in each subject for each position and this is a limitation of the study. However, future research of IVD behavior should include measurements of segmental and global lumbar range of movement to investigate this theory.

6.13.3.2: Axial pMRI scans

From table 6.12.6 (mean values for asymptomatic and DLBP subjects), at L1/2 the greatest posterior migration occurred in Flexed sitting (28.73mm) for the asymptomatic subjects and in Neutral sitting for the DLBP subjects (20.26mm). The least amount of posterior migration for both groups occurred in Prone extension (22.52mm and 17.68mm respectively). At this level, the asymptomatic subjects had a mean 6.21mm change in NP position while the DLBP subjects had a mean 2.58mm change in NP position.

At L2/3 the greatest posterior migration occurred in Flexed sitting for both groups (27.52mm and 21.3mm respectively). The least amount of posterior migration of the NP occurred in Extended sitting for both groups also (22.59mm and 17.75mm respectively). At this level, the asymptomatic subjects had a mean NP change in position of 5.13mm and the DLBP subjects had a mean change of 3.55mm.

At L3/4 the greatest NP posterior migration occurred in Neutral sitting for the asymptomatic subjects (25.63mm) and Flexed sitting for the DLBP subjects (21.34mm). The least amount of posterior NP migration occurred in Extended sitting for the asymptomatic subjects and Prone extension for the DLBP subjects (20.93mm and 17.73mm respectively). At this level the asymptomatic subjects

had a mean NP change in position of 4.7mm and the DLBP subjects had a mean change of 3.61mm.

At L4/5 the greatest posterior migration occurred in Flexed sitting for the asymptomatic subjects and Neutral sitting for the DLBP subjects (27.48mm and 21.66mm respectively) although this was only 0.03mm greater than Flexed sitting for this group. The least amount of posterior NP migration occurred in Prone extension for both groups (19.95mm and 18.05mm respectively). At this level, the asymptomatic subjects had a mean change in NP position of 7.53mm and the DLBP subjects had a mean change of 3.61mm.

At L5/S1, the greatest posterior migration occurred in Flexed sitting for the asymptomatic subjects and Extended sitting for the DLBP subjects (27.19mm and 21.37mm respectively). The least amount of posterior migration occurred in Prone extension again for both groups (20.81mm and 18.03mm respectively). At this level, the asymptomatic subjects had a mean change in NP position of 6.38mm and the DLBP subjects had a mean change of 3.34mm. Table 6.13.5 presents the asymptomatic and DLBP subjects data.

Table 6.13.5: Greatest, least and mean change in Nucleus pulposus migration (mm) at each intervertebral disc level for asymptomatic and DLBP subjects

level	Asymptomatic subjects			DLBP subjects		
	Greatest	Least	Mean change	Greatest	Least	Mean change
L1/2	F.Sit 28.73	EIL 22.52	6.21	N.Sit 20.26	EIL 17.68	2.58
L2/3	F.Sit 27.52	E.Sit 22.59	5.13	F.Sit 21.3	E.Sit 17.75	3.55
L3/4	N.Sit 25.63	E.Sit 20.93	4.7	F.Sit 21.34	EIL 17.73	3.61
L4/5	F.Sit 27.48	EIL 19.95	7.53	N.Sit 21.66	EIL 18.05	3.61
L5/S1	F.Sit 27.19	EIL 20.81	6.38	E.Sit 21.37	EIL 18.03	3.34

Key: F.Sit = flexed sitting, N.Sit = Neutral sitting, E.Sit = Extended sitting, EIL = Prone extension

These results again demonstrate the greater NP migration occurring in the asymptomatic subjects compared to the DLBP subjects. In terms of percentage

shift across the sagittal plane diameter of the IVD the asymptomatic subjects' NP migrated between 17 – 26% of the diameter as opposed to a 10 – 13% migration in the DLBP subjects. These results reflect those found for the sagittal pMRI scans compared between the asymptomatic and DLBP subjects. Whether these results demonstrate a clinical significance remains to be established. The same theories for the results obtained from the sagittal pMRI scans can be applied for the axial pMRI scan asymptomatic and DLBP subject's results comparison. As was reflected in the sagittal pMRI comparison between the asymptomatic and DLBP subjects, there is further research required with larger numbers to identify clinically significant results of NP behaviour in subjects with DLBP that can inform conservative clinical management of this condition.

Chapter 7: Discussion

This chapter consists of a general discussion to bring together the three phases of this study that have been previously discussed in detail (see sections 4.5, 5.5 and 6.13). Although the results from this study mainly provide evidence regarding lumbar IVD behaviour, the implications from this for physiotherapy practice and the conservative management of DLBP are discussed. The final section of this chapter will then consider the strengths and limitations of this thesis and suggest areas for improvement for future research.

7.1: Asymptomatic subjects

The first phase of this study aimed to establish the reliability of the Osiris software system and to establish a database of lumbar NP migration from a group of asymptomatic subjects (Objective 1 and 3, Section 1.8). As discussed in Section 4.5, these objectives were addressed and demonstrated reliable measurements of NP migration obtained using the Osiris software system. The asymptomatic subjects demonstrated a significant effect of position on the sagittal plane NP migration in the lumbar spine in both sagittal and axial pMRI scans ($p < 0.001$). The results from this phase support previous studies using rMRI and upright/open MRI scanners in asymptomatic subjects where flexed positions cause a posterior migration of the NP and extended positions cause anterior migration (Beattie et al 1994, Fennel, Jones and Hukins 1996, Brault et al 1997, Edmondston et al 2000, Fredericson et al 2001, Nazari et al 2012). These results lend support to the first two hypotheses (Section 1.6), in that this study has demonstrated the lumbar NP will migrate posteriorly in flexed positions and anteriorly in extended positions in asymptomatic subjects. Therefore we can reject the null hypothesis and accept the first two experimental hypotheses for asymptomatic subjects.

7.2: 3SPACE Fastrak™

The second phase of this study aimed to establish the reliability of the FT system in measuring three-dimensional lumbar movement and also to establish a database of three-dimensional lumbar movement. From this it was then aimed

to investigate if a relationship existed between three-dimensional lumbar spine movement and the pattern of NP migration (Objectives 2, 4 and 5, Section 1.8). As was discussed fully in Section 5.5, despite strategies to enhance reliability, the results demonstrated that only five out of the 12 movements performed achieved ICC values of *substantial* or better reliability (0.61 and above). The sagittal plane movements in particular only demonstrated *slight to fair* reliability (Flexion = 0.17 and extension = 0.4). In addition, the flexion and extension ROM reported in this phase was consistently less than that reported in previous studies of lumbar ROM (Mannion and Troke 1999, Yang et al 2008, Lee et al 2011, Ha et al 2012).

As the current FT system used within the School of Health Sciences demonstrated low reliability and under reported spinal ROM, the system was deemed to require further development (including investigation of the FT system, the user interface and data collection protocols) to establish reliable and accurate spinal ROM measurements prior to future use.

In the initial stages of this study, it was hoped to establish if there was a relationship between the pattern of NP migration between different positions and three-dimensional spinal movement (Objective 5, Section 1.8). As the clinical examination of LBP routinely incorporates the assessment (subjective or objective) of spinal ROM, it was hoped that by establishing any relationship between NP behaviour and three-dimensional spinal ROM this could ultimately enhance or inform future clinical practice. As discussed in Section 5.5.3, it became immediately apparent that both systems (FT and pMRI) were incompatible at this time.

It was decided that although the FT system has previously been shown to be reliable in the measurement of three-dimensional spinal ROM, the current system used within the School of Health Sciences required further development to establish reliability and accuracy. In addition, as the FT system and pMRI scans were incompatible at this time, it was decided that the remainder of this thesis would focus on the use of the pMRI only to investigate NP behaviour. Therefore, this study was unable to establish support for or against the proposed experimental and Null hypotheses investigating the relationship between NP migration and three-dimensional spinal ROM.

7.3: Discogenic low back pain subjects

The third phase of this study aimed to investigate the effect of different positions on the sagittal NP migration in DLBP subjects as well as compare the sagittal NP migration between asymptomatic and DLBP subjects (Objective 6 and 7, Section 1.8).

The results again demonstrated a significant effect of position on the sagittal NP migration in both sagittal and axial pMRI scans ($p=0.001$). This is the first time that the effect of position on the sagittal plane migration of the NP in DLBP subjects has been clearly demonstrated using pMRI.

These results again lend support for the first two hypotheses, in that this study has demonstrated the lumbar NP will migrate posteriorly in flexed positions and anteriorly in extended positions in DLBP subjects. Therefore we can reject the Null hypothesis and accept the first two experimental hypotheses for asymptomatic and DLBP subjects.

7.4: Between group comparisons

The third phase of this study also aimed to compare the extent of NP sagittal migration between asymptomatic and DLBP subjects in sagittal and axial pMRI scans. The results demonstrated that there was greater posterior sagittal plane NP migration in the asymptomatic subjects for all positions and IVD levels in the sagittal (except standing at L4/5, Supine at L5/S1 and Prone extension at L5/S1) and axial pMRI scans compared to the DLBP subjects. This is the first time that the sagittal plane NP behaviour has been compared using pMRI. The results challenge some clinically based theories of mechanical compression of the nerve root by the IVD causing pain (McKenzie and May 2003). These results suggest that the NP of DLBP subjects do not migrate posteriorly as far as asymptomatic subjects. Therefore, further research is required to extend this study with larger numbers to investigate this phenomenon in greater detail alongside its clinical implications.

As nine DLBP subjects (27%) were recommended for surgical opinion by the consultant radiologist based on their pMRI scans, it is interesting to consider this in light of the group comparison results. The group comparisons suggest that the NP of DLBP subjects does not migrate posteriorly as much as those of asymptomatic subjects. The radiologist recommendation for these nine subjects reflects the fact that in clinical practice they do not rely on one plane of images

in their clinical examination but view sagittal, axial and coronal images of the IVD. The fact that this study did not incorporate coronal views may account for some of the differences suggested between the radiologist opinion and the results in this study. Coronal views enable visualisation of the exiting nerve roots and although not a factor required for this study, it is important in the clinical examination. Additionally, a radiologist will view the entire IVD not just the NP, therefore although the NP may not migrate as far in DLBP subjects, the AF may have a role to play. Further research, especially the use of three-dimensional imaging, would enable further clarification of the effect of position on the NP and AF.

7.5: Implications for clinical practice

The results from this study provide a number of implications for clinical practice and all health professionals (such as GPs, Physiotherapists, osteopaths, chiropractors, and occupational health physicians) involved in DLBP management. Figure 7.5.1 presents a DLBP pathway of the clinical implications discussed below.

Assessment	Management	Investigation
<ul style="list-style-type: none"> • symptoms affected by loading, position and sustained position 	<ul style="list-style-type: none"> • advice to remain active avoiding sustained positions • advice on changing positions (loaded and unloaded) • postural education inc. lumbar support in sitting • pain physiology education • acupuncture 	<ul style="list-style-type: none"> • pMRI in sitting (Neutral, Flexed and Extended)

Figure 7.5.1: Clinical implications for DLBP

7.5.1: Subclassification

As was demonstrated in the earlier review of literature (Section 2.3.2), it is important for clinicians to sub-classify patients presenting with back pain (Fersum et al 2010). By sub-classifying LBP, appropriate management strategies can be implemented and matched to the sub-group identified. Current sub-classification theories that would suggest a discogenic problem are the MDT, TBC and the patho-anatomic systems (Delitto, Erhard and Bowling 1995, McKenzie and May 2003, Petersen et al 2003) due to the presence of centralisation from loading strategies and movements utilised in their assessments. However, there is a lack of literature to support any of these systems individually in terms of accuracy and validity for DLBP. The current results relate to the presence of centralisation as a sub-class being linked to the IVD as the behaviour of the NP in the sagittal plane reflected previously published research where the NP migrates posteriorly in flexion and anteriorly in extension. Further research is warranted to investigate the IVD behaviour in DLBP patients demonstrating centralisation.

In the case of the DLBP sub-group, the subjective history recorded during the clinical assessment could be enhanced by including questions regarding loading effects and positional change effects on patient's symptoms. Patients reporting loading and positional effects on their symptoms would then enable clinicians to consider a DLBP classification, which they could examine further during the objective examination.

7.5.2: Clinical management of Discogenic low back pain

Lumbar sagittal plane NP migration in response to position has been suggested to be an important element in NSLBP treatment (Zou et al 2009). However, this suggestion has not been supported by the literature to date as most studies investigating IVD behaviour have reported IVD bulging and limited descriptive analyses (Ferreiro-Perez et al 2007, Morishita et al 2008, Zou et al 2009). Although there have been animal and asymptomatic human studies performed that support the theory of IVD response (Schnebel et al 1988, Scannell and McGill 2009), the current study is the first to report the sagittal plane behaviour of the NP and IVD to different positions in subjects with DLBP. These findings

support the theory of posterior NP migration in flexed postures and anterior NP migration in extended postures.

From the results of the present study, clinicians should consider advising patients appropriately regarding positional loading/postures and activity in the clinical management plan. The current LBP guidelines (NICE 2009) recommend physical activity and the provision of advice to keep moving, but this should be tailored with a patient-centred focus so that patients feel confident to maintain activity within the confines of their symptoms.

The subjective history information gathered on loading and positional effects on patient symptoms can enable clinicians to confidently advise patients on optimum strategies to manage their condition. For example, the results from this study would suggest that clinicians can recommend unloaded positions as well as supported (extended) sitting positions to DLBP patients as these positions will lead to less posterior migration of the NP within the IVD. In addition, the effect of sustained upright loaded positions can be identified in a subjective assessment and clinicians can then advise patients regarding frequent position change which could include unloaded and loaded positions to minimise the effect of spinal creep. Currently Prone extension is a commonly used treatment position and the results of this study support the fact that this position creates greater anterior NP migration than Neutral sitting or Flexed sitting. However, as there was no difference in NP migration between the Supine and Prone extension positions in this study, it can be concluded that either lying position should be equally effective. Current UK clinical guidelines (NICE 2009) emphasise the need for LBP patients to remain active. Historically, patients in the past were managed with bed rest but this has been shown to be an ineffective management plan for LBP patients. However, the results from this study demonstrate that unloaded lying positions (supine or prone extension) may be a therapeutic option for the management of DLBP. This supports the advice currently provided by NHS inform (2013). This approach should not be applied across the board for all LBP, but rather used as part of a clinically reasoned management plan for the short term in DLBP patients until they can return to full function and gain control of their symptoms. Further research is required to investigate the effectiveness of this approach for DLBP.

Clinical management of DLBP can utilise different movements, exercises and postures as part of the treatment. The MDT method commonly uses sagittal plane movements such as extension in standing and lying as a therapeutic technique (McKenzie and May 2003). In subjects classified as having posterior derangement, MDT advocates extension exercises as one method to reduce the stress on the pain-sensitive posterior AF by causing anterior migration of the NP (McKenzie and May 2003). The MDT centralisation phenomenon has been reported as being linked to DLBP and is associated with positive outcomes (Berthelot et al 2007, Murphy, Hurwitz and McGovern 2009, Broetz, Burkard and Weller 2010, Albert and Manniche 2012). However, some authors have reported that although centralisation can improve symptoms it does not cause any changes on MRI features (Broetz et al 2008). The MRI scans carried out in Broetz et al's (2008) study were performed in a recumbent position and, from the results of the current study; those authors may have arrived at a different conclusion if they had used pMRI. Donelson et al (1997) have also reported that the MDT defined concept of centralisation is strongly associated with a competent AF compared to peripheralisation. While the present study supports the theory of sagittal plane NP posterior migration in flexion and anterior migration in extension (Kolber and Hanney 2009) for DLBP and asymptomatic subjects, the results of comparisons between the two groups do not fully support the concept of the IVD being associated with centralisation. This could also be due to the fact that as Donelson et al (1997) suggests, centralisation is related to AF competency whereas this study has focused upon the NP behaviour. Further research is required to investigate the effect of position on the IVD (AF and NP) using pMRI in patients demonstrating the centralisation phenomenon.

The results of the two group's comparison revealed that there was significantly greater sagittal plane NP posterior migration in the asymptomatic subjects compared to the DLBP subjects. This result challenges the assumption of posterior NP migration causing the symptoms of DLBP as accepted within the MDT method. The results from this comparison do not support the concept of using extension exercises to induce anterior NP migration to reduce stress upon the sensitive posterior AF or adjacent nerve roots. This result may be explained in part by the IDD model where inflammatory substances secreted by the NP cause symptoms as they track into radial fissures located within the posterior AF

and stimulate nerve endings that have ingrown deeper into the AF due to injury or degeneration (Stefanakis, Key and Adams 2012). Therefore the NP of DLBP subjects would not need to migrate a greater posterior distance than the asymptomatic subjects NP before this effect was stimulated. In addition, DLBP symptoms can also be partly explained by poor or statically maintained positions (such as sitting or bending) causing mechanical stress on posterior spinal structures which in turn activates chemically sensitised nociceptors located around the IVD (Stefanakis, Key and Adams 2012). This effect can be modified by changing position so that the mechanical stress is altered and is another reason why clinicians would recommend DLBP patients to change position frequently and also to support the lumbar lordosis in sitting.

This chemical sensitisation concept also supports the clinician advising patients to change position frequently and to avoid statically held positions such as sitting at a desk at work for too long. By advising patients to sit with their lumbar spine supported into extension via a lumbar roll, clinicians can enable patients to adopt "better" positions that consequently create less stress and stimulation of the chemically sensitised nociceptors and therefore less pain. Although this study has demonstrated Extended sitting to be a "better" sitting position in terms of the lumbar IVD, there remains a need for further investigation of the optimal sitting position for the overall spine as there is still discrepancies between physiotherapists regarding the best sitting position for the spine (O'Sullivan et al 2012).

The findings reported here support clinician reassurance to patients regarding their subjective experience of pain. In the absence of red flag signs and symptoms, reassurance and increasing the patient's confidence around managing their symptoms, is an important part of DLBP management. A clear explanation of chemically and inflammatory mediated pain controlled by higher centres rather than the IVD compressing the nerve root as the source of the pain is an important concept to convey to patients (Roussel et al 2013). It has been shown in two randomised controlled trials (Moseley 2002, Moseley, Nicholas and Hodges 2004) that pain physiology education significantly improves treatment effectiveness as well as reducing pain, pain catastrophising and pain beliefs with effects maintained at one year follow-up in CLBP patients. These

results support researchers such as Dr Mick Thacker who called for clinicians to shift away from “mechanical based therapies” and become more aware of neuro-immunology factors in pain in his keynote speech delivered at Physiotherapy 2012 (The Chartered Society of Physiotherapy 2012). Further research is required to investigate the effect of pain physiology education and subsequent patient confidence in the management (and self-management) of DLBP as there is minimal literature available on this area at present.

Overall, the clinical applications of this study discussed above, can be incorporated into patient advice via portals such as NHS Choices (2013) that patients can access individually or be guided to by physiotherapists. This website does provide information on exercise, advice to remain active and advice on posture. However, further expansion of the information to include advice regarding changing position (including loaded and unloaded positions) and advice to remain active while avoiding sustained positions should be included. In addition, consideration should be given to include pain physiology information/education at the same time so that patients have all available evidence around DLBP provided for them to access. This development requires further research to identify the optimum level of information that is required for patients as well as the optimum mode of delivery (for example online, telephone, face to face). Patients with DLBP should also be consulted to establish their views and needs for service development in this area. This is a timely recommendation as the Physiotherapy Pain Association (PPA), in conjunction with the Chartered Society of Physiotherapy, is currently working to develop a competency framework for physiotherapists in pain management (PPA 2013). As the results of this study demonstrated less posterior migration in flexion of the NP in patients with DLBP, and therefore suggests greater influence of chemically and centrally mediated pain, it is important that physiotherapists can provide effective pain management and education for patients with DLBP.

7.5.3: pMRI investigation of Discogenic low back pain

If DLBP patients are not improving after a course of conservative management and are subsequently being referred for further investigation via imaging, they should be considered for pMRI rather than recumbent MRI. The author

recognises however, that current access to pMRI centres in the UK is limited (both geographically and financially).

As was demonstrated in the sagittal pMRI between group comparisons (asymptomatic and DLBP subjects), the sitting positions (Neutral, Flexed and Extended sitting) were significantly different at the lower IVD levels (L4/5 and L5/S1). These IVDs have been recognised as the levels most frequently affected by DLBP (Hammer 2002, Hadjipavlou et al 2008).

In terms of identifying appropriate positions to include in a full pMRI investigation of DLBP, these results would support sagittal pMRI scans being performed in the sitting positions (Neutral, Flexed and Extended) as between the three positions significant differences were demonstrated in four out of the five IVD levels (L1/2, L2/3, L4/5 and L5/S1). No significant differences were demonstrated in any position for L3/4.

The results also support previously published literature (Ferreiro-Perez et al 2007, Keorochana et al 2011) and clinical opinion in that Supine imaging does not reflect the true status of the IVD and so inconclusive or incorrect results may be reported. Indeed, the sagittal pMRI scans in the Supine position only identified significant differences at the upper IVD levels (L1/1 and L2/3) in the current study. The lower IVD levels (L4/5 and L5/S1) have greater forces acting on them in the lordotic up-right spine compared to the upper IVD levels and the removal of these forces in lying may result in less significant behaviour in the lower IVD levels.

The results would also support the use of axial scans performed in the sitting positions (Neutral and Flexed sitting) as between these two positions significant differences were demonstrated in four out of the five IVD levels (L1/2, L2/3, L4/5 and L5/S1). Supine axial scans only identified significant differences in three out of the five IVD levels (L1/2, L3/4 and L4/5).

Regardless of the fact that the asymptomatic group had greater posterior migration, these results have demonstrated for the first time that there are different IVD behaviours between asymptomatic subjects and those with DLBP. Further research in this area is required with larger sample sizes defined by specific DLBP inclusion criteria (which requires to be defined by international

consensus within the research community) in order to examine this phenomenon further. This will then lead to greater understanding and further development of theories underlying IVD behaviour.

There is support from the results for the avoidance of using the Standing position in pMRI scans as significant differences were only identified at upper IVD levels (L1/2 and L2/3) in both the sagittal and axial scans. As the sitting positions also identified significant differences, the results would support only scanning in the sitting positions and so avoiding the risk of fainting that has been demonstrated in the clinical use of standing for these scans.

A further recommendation would be that subjects with DLBP undergoing a pMRI scan should be advised to get up and change position/ walk about when going from Flexed sitting to Extended sitting to avoid the discomfort and risk of fainting as reported in the DLBP subjects. Personal communication with the pMRI staff identified that prior to the current study no subjects undergoing a pMRI scan had fainted or reported discomfort with the Extended sitting position. A possible explanation for it occurring in this study could be due to the multiple positions imaged (six versus three in normal clinical practice) therefore increasing the time spent in static positions and the creep response in the spinal tissues as well as increasing stimulation of sensitised nociceptors in the spine. An alternative measure would be to alter the scan position order so that Extended sitting does not follow Flexed sitting. A limitation of this study was that all subjects had the pMRI scans performed in the same order, whereas the results may have differed if the scanning positions were randomised between each subject (thus altering the creep effect on the IVDs over the scanning time). To investigate this further and establish the optimum pMRI scanning position order additional research is required to be carried out with a DLBP population.

7.6: Strengths and limitations of the study

While it is difficult to ensure a sample was included that only had DLBP due to a lack of accurate clinical tests for this condition; the present sample did meet specific inclusion criteria identified from current literature to reflect DLBP subjects seen in clinical practice. The results demonstrate significant differences

between the asymptomatic and DLBP groups that cannot be judged to occur by chance.

7.6.1: Sample size

The sample size in phase 1 and 2 were smaller than originally planned due to a slow recruitment process for subjects. Although the asymptomatic subjects sample detected statistically significant differences in sagittal plane NP migration between different positions, this effect was not observed at every lumbar IVD level or in every position scanned. Additionally, the results from the FT subjects presented a wide variation in reliability with the majority of measurements demonstrating lower reliability compared to previously reported ICCs.

Although the intended sample size was recruited for the DLBP group (N = 34), not every position scanned had a full dataset of subjects. Table 6.12.1 displays that only 25 out of the 34 subjects had complete data collected (i.e. sagittal and axial scans were performed in all six positions). Of the six positions scanned, only Neutral sitting provided a complete sample of data in all 34 subjects. Additional recruitment to ensure 34 complete sets of positions were scanned would have been of benefit as this may have enabled greater confidence in determining disc behaviour in the various positions. Future investigations of the IVD behaviour in DLBP subjects should consider larger sample sizes with complete datasets for each position scanned. This would be achieved by over-recruitment of subjects to ensure full data sets for each position and to allow for any unusable data. Sample size calculations should consider smaller differences in NP migration as for this study the calculations included a 5mm difference. In addition, sample size calculations should be based upon the data from the DLBP subjects as this group had smaller changes in NP migration between the positions studied here.

A convenience sampling strategy was employed in all three phases of this study (see section 3.1) with the author involved in recruitment for each phase as well as physiotherapists for the DLBP subjects.

Recruitment and data collection of DLBP subjects took place over a four month period, resulting in a possible 38 subjects. This was far less than anticipated as

the NPLBPA (NHS QIS 2008) reported that NHS Grampian had over 5,000 LBP patients referred in 2007. This equates to around 430 patients per month. However, there are several reasons for this small number achieved over the four month period. The potential NSLBP subjects may not all have been issued with the recruitment packs by the physiotherapists due to time pressures and other work priorities. It is also possible interested subjects were willing to participate but forgot to fill in the reply slip and post it back. There was also no direct benefit to subjects for taking part in any of the three phases, which may have influenced the motivation of potential subjects. Those who did take part in phase 1 and 3 expressed a desire to have a MRI scan performed and also to help other LBP sufferers (*ad hoc* comments noted by the author during data collection). Future research investigating DLBP with pMRI should therefore aim to carry out sample size calculations to ensure adequately powered studies are conducted that recruit large samples of subjects that reflect the DLBP population (Polgar and Thomas 2011).

7.6.2: Gender of subjects

The asymptomatic subject sample contained fewer females than the DLBP subject sample (36% versus 50% respectively). Despite this, the results can still be viewed with confidence as there has been no gender bias identified in NSLBP (Maniadakis and Gray 2000, Mortimer et al 2006), therefore this may not present a major limitation for this part of the analysis. In addition, the DLBP sample had an even split for gender which is what would be required based on reports of incidence of DLBP.

7.6.3: Age of subjects

The DLBP sample was on average three years older than the asymptomatic sample (39 years versus 36 years respectively). However, this difference was not significant. As stated previously (Section 2.3.5), DLBP has been observed in younger patients peaking between 20-40 years of age (Awad and Moskovich 2006, Casey 2011). Therefore the mean age of both samples in these studies

reflects the age group of interest although both are at the higher end of the range.

7.6.4: Height and weight of subjects

There were minimal, non-significant differences between the asymptomatic and DLBP samples for height and weight; the lack of significant differences means that any bias due to these two parameters is eliminated (Polgar and Thomas 2011).

7.6.5: Measurement tool

Osiris software was employed for measurement of the pMRI scans and its reliability has been established and discussed fully (see Section 5.1.1). Despite this however, there still remains potential sources of error in any tool; such as human error in carrying out the measurements. Every effort was made to limit potential sources of error in this study but they cannot be ruled out completely. Measurements were also dependent on the resolution of the pMRI images to visually identify anatomical structures. This was especially evident in the axial measurements as anatomical structures with similar hydration levels anterior to the IVD anterior boundary (such as anterior longitudinal ligament and connective tissue) made it difficult to identify the anterior boundary with confidence in some cases. This limited the data available for analysis in the axial scans. This limitation has been taken forward in initial discussion with Dr Russell Horney from Monash University, Australia. His PhD study involved identification of anatomical structural edges in CT scans and discussion has now begun on the possibility of this process being remodelled for use in pMRI scans to identify the IVD outer edge as well as the AF/NP boundary (in healthy, non-degenerate IVDs) within the IVD. A recent publication demonstrating the ovine "structural gradation" between the iAF and NP (Wade et al 2012) will challenge the identification of the *in vivo* iAF/NP boundary. Nevertheless, further research to identify this will be of benefit to improving understanding of IVD behaviour as well as increasing measurement accuracy.

One consultant radiologist reviewed all pMRI scans throughout this study. It would have strengthened this project to include at least one additional musculoskeletal radiologist to arrive at a consensus report for each subject as well as both radiologists classifying degenerative changes in each lumbar IVD for each subject using a scale such as the Pfirrmann scale (Pfirrmann et al 2001). This study did not classify nor analyse positional effect on the IVD dependent on degenerative grade as this was outwith the objectives of this thesis. This may limit the confidence in the results obtained as it has been acknowledged that the sagittal plane behaviour of the NP demonstrated here is less predictable in degenerate IVDs (Schnebel et al 1988, Zou et al 2009). Future research in this area should endeavour to include multiple radiologists for reporting and classifying pMRI scans with sub-analyses based on IVD degenerative grade.

7.6.6: Data collection protocol

The demographic data set for all subjects only included their age, height and weight. It is a limitation that was recognised at a later stage that a more detailed data set would have enhanced this study. Inclusion of clinical information such as pain time frames, numerical rating scales for pain, previous history of back pain, self report of pain location and distribution as well as the use of outcome measures such as the Roland Morris Functional Disability Scale (Roland and Morris 1983) would have improved the rigour of this study. Additionally, the use of a reliable and accurate tool such as the FT system to measure lumbar range of movement would have added to the data set as well. Recording detailed clinical history of the DLBP subjects could have identified variables that may have impacted upon the results and may have provided opportunity for sub-group analysis in that group. However, this study overall was primarily concerned with investigating the behaviour of the IVD in asymptomatic and DLBP subjects and the age, height and weight data enabled both groups to be compared. As this study has identified areas for further research, future projects can aim to include detailed clinical information from symptomatic subjects to address the limitations identified here.

The data collection protocol resulted in all subjects' data being included in the Neutral sitting position, therefore it can be concluded that the protocol was

suitable for this section of the data analysis. However, several subjects were excluded from the other positions for data analysis due to discomfort causing motion/blurring of the images and in one case the breakdown of the pMRI gantry. Despite initial piloting of the position order for scanning and refinement of the protocol, subjects still found some positions too uncomfortable to remain still for the duration of the image acquisition. In clinical practice, the pMRI staff reported they do not normally have any problems with patients in the Flexed and Extended sitting positions and it was only the Standing positions that they reported as a risk factor for fainting. The time spent in each position (10 minutes) would have induced a creep effect upon the tissues of the IVD so it is logical to assume that Flexed sitting in DLBP subjects would cause posterior migration of the NP and hence posterior bulging of the AF. By moving straight into Extended sitting, this may not have provided sufficient time for the NP to migrate posteriorly & hysteresis to occur in the AF. This theory was supported in practice by asking each subject to get up from the pMRI chair and walk around for approximately one minute while the pMRI protocol was set up for the next image (between Flexed sitting and Extended sitting). By adding in this short time of movement/position change and thus time for the NP and AF to recover from Flexed sitting, all subjects were able to tolerate this order of scans with no further problems reported or fainting. From this effect it could also be concluded that this group of subjects had IVDs that did not respond as quickly to changes in position leading to mechanical effects which would further support the inclusion of them in this project. Further research to examine this behaviour is recommended.

A further limitation of the scanning protocol was that all subjects were asked to adopt the position for each scan that they felt they could maintain without moving for the duration of the scan. Therefore, no end range positions were adopted, and this may have reduced the strength of the results. However, until pMRI technology advances to enable faster image acquisition time this is something that cannot be addressed or investigated at this time. This limitation, does not detract from the significant findings of this study.

The combination of scanning time (1.5 – 2 hours per subject) and pMRI scanning performed in clinically provocative positions may mean that in future

perhaps fewer positions should be scanned for research and clinical purposes as was suggested above. Further research and pMRI development is recommended to ensure images with excellent resolution at all levels are produced while limiting time spent in the scanner for subjects.

7.6.7: Inclusion/exclusion criteria

The inclusion criteria for this project were based upon the current literature surrounding DLBP. As was demonstrated in the review of literature on the clinical examination of LBP and sub-classification of DLBP (see section 2.3.9), there are no reliable and accurate assessments to identify DLBP. Inclusion criteria were created to reflect the literature but on reflection may have been interpreted too leniently by clinicians, leading to subjects other than DLBP patients being included which will have affected the results of this study. However, the significantly different differences between the asymptomatic and DLBP subjects' means some confidence can be attributed to the inclusion criterion employed although this only supports differences between those with back pain and those with no symptoms. There remains lack of clarity regarding the homogeneity of the DLBP group. Further research is recommended to investigate positional effects on the IVD in NSLBP and specific sub-groups such as DLBP with clearly identified inclusion and exclusion criteria.

Although this study provides support towards a chemically mediated/neuro-immunology response in DLBP, patho-anatomic causes cannot be completely ruled out. As discussed above, the inclusion/exclusion criteria had limitations and an additional one would be that all DLBP presentations were included i.e. acute and chronic DLBP subjects. It has been demonstrated that the IVD can be vulnerable to injury and has some limited capability to heal (Stefanakis et al 2012). An acute first episode of DLBP may be due to a pathoanatomical event where there is impingement upon the adjacent tissues such as the NR or herniation of NP material through the AF which can be visualised on MRI. However, due to the acute injury, a healing response is triggered which has, as part of the process, an inflammatory stage with the associated release of chemical mediators (Watson 2013). The inflammatory stage is a normal event in the healing process with a rapid onset which peaks and then settles down

over the next few weeks in a standard tissue. Due to the lack of vascular supply to the IVD, it could be theorised that this process could take place over a longer period. This initial event could then be attributed as the factor leading to sensitisation of nerve endings around the IVD and an eventual neuro-immunologic pathway generating repeated episodes of DLBP or chronic long-lasting DLBP. Further research is required to investigate this theory as not every person with an initial episode of DLBP goes on to develop chronic or episodic DLBP. Future research should aim to identify reliable and accurate assessments for DLBP that are accepted internationally. From this, further research can then consider the behaviour of the IVD in acute and chronic DLBP subjects.

7.6.8: 3SPACE Fastrak™

The initial aim for phase two of this study was to use 3-dimensional motion analysis (3SPACE Fastrak™) to investigate lumbar spine motion in DLBP and then investigate any correlations to pMRI scanning of the lumbar spine. The initial objective was to investigate the reliability of the FT system. However, after analysis of the data it was decided to focus the remainder of this study on the pMRI work as the FT system was unreliable for lumbar spine motion analysis (see section 5.5.1). In addition, the pMRI and FT systems were incompatible at this time in that the pMRI involved 2-dimensional images gained from statically held positions whereas the FT system involved 3-dimensional motion analysis from dynamic movement.

Further work to resolve the FT system reliability issues will enable future research into 3-dimensional motion analysis of the lumbar spine in DLBP subjects.

Chapter 8: Conclusion

8.1: Key findings

This project has identified for the first time the effect of position on the lumbar IVD in the sagittal plane in asymptomatic subjects and those with DLBP. The results support previously reported IVD behaviour in that the NP migrates posteriorly in flexed positions and anteriorly in extended positions. However, for the first time, this project has identified that asymptomatic subjects demonstrate greater posterior migration and a greater range of migration than DLBP subjects.

8.2: Implications for clinical practice and further research

In terms of clinical practice, there is a need to recognise that current LBP assessment, guidelines and management strategies may not be appropriate for patients presenting with DLBP, that have a positional effect on their symptoms. In addition, for DLBP patients that are not responding to conservative management after 6 weeks, they may benefit from further investigation via pMRI.

8.2.1: Implications for physiotherapy practice:

- The subjective physiotherapy assessment should consider the effect of loading and position on DLBP patient's symptoms
- Appropriate advice should be given to DLBP patients regarding positional loading, postures and physical activity
- Use of appropriate exercises and positioning that improve symptoms for DLBP patients
- Reassurance and explanation to patients regarding neurophysiology of pain, rather than the IVD as a pain source

8.2.2: Implications for imaging of discogenic low back pain

- If DLBP patients are not improving and further imaging is being considered, pMRI should be used rather than rMRI

- Sagittal pMRI scans should include sitting positions (Neutral, Flexed and Extended)
- Axial pMRI scans should include sitting (Neutral and Flexed) and Supine positions
- Standing scans should be avoided
- DLBP patients should be encouraged to move between Flexed and Extended sitting scans

8.3: Suggestions for further research

The results of this study suggest that further research is indicated in the following areas:

- International consensus should be reached on the definition of DLBP
- Repeating this study (asymptomatic and DLBP subjects) with larger samples (using improved DLBP definition for inclusion) using recommended sagittal and axial scanning positions and including a LBP group for comparison
- Include additional musculoskeletal radiologist for reporting and include degenerative grading of IVDs for separate analysis of degeneration grade and IVD positional effects
- Include Nazari et al (2012) IVD measurements for comparison to this study's measurements in asymptomatic and DLBP subjects
- Continue to increase the numbers of subjects in the asymptomatic and DLBP databases

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Appendices

1. Ethical approval
2. Participant information sheet – Asymptomatic subjects
3. Consent form – Asymptomatic subjects
4. pMRI screening form
5. Intervertebral disc article (Alexander et al 2007)
6. Participant information sheet – 3SPACE Fastrak™
7. Consent form - 3SPACE Fastrak™
8. Source and sensor placement and Sequence of movements
9. Letter of invitation - DLBP subjects (Private practice)
10. Letter of invitation – DLBP subjects (NHS)
11. Participant information sheet – DLBP subjects (Private practice)
12. Participant information sheet – DLBP subjects (NHS)
13. Consent form – DLBP subjects
14. Data collection form – DLBP subjects
15. Asymptomatic subjects' sagittal pMRI additional results
16. Asymptomatic subjects' axial pMRI additional results
17. DLBP subjects' sagittal pMRI additional results
18. DLBP subjects' axial pMRI additional results
19. Re-print permission

Appendix 1: Ethical Approval



Grampian Local Research Ethics Committee (2)

Summerfield House
2 Eday Road
Aberdeen
AB15 6RE

Telephone: 01224 558503
Facsimile: 01224 558609

21 July 2006

Mrs I A Alexander
Physiotherapist/Research Practitioner
NHS Grampian
Physiotherapy Department
Chalmers Hospital
Clunie Street,
BANFF
AB45 1JA

Dear Mrs Alexander

Full title of study: An analysis of lumbar spine motion and response of the intervertebral disc to functional positions using positional MRI and 3SPACE Fastrak
REC reference number: 06/S0802/40

Thank you for your letter of 6 July 2006, responding to the Committee's request for further information on the above research and submitting revised documentation.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised.

Ethical review of research sites

The favourable opinion applies to the research sites listed on the attached form.

Conditions of approval

The favourable opinion is given provided that you comply with the conditions set out. You are advised to study the conditions carefully, in particular:

Condition 1: Annual Progress Report

Under the Central Office of Research Ethics Committees (COREC) regulations NHS Research Ethics Committees are required to monitor research with a favourable opinion. This is to take the form of an annual progress report which should be submitted to the Grampian Research Ethics Committee 12 months after the date on which the favourable opinion was given. Annual reports should be submitted thereafter until the end of the study.

Points to note:

- The first annual progress report should give the commencement date for the study. This is normally assumed to be the date on which any of the procedures in the protocol are initiated. Should the study not commence within 12 months of approval a written explanation must be provided in the 1st annual progress report.
- Progress reports should be in the format prescribed on the COREC website (www.corec.org.uk/applicants/apply/progress.htm).
- Progress reports must be signed by the Principal Investigator/Chief Investigator.
- Failure to submit a progress report could lead to a suspension of the favourable ethical opinion for the study.
- Please note the Annual Progress Report is a short 3 page form which is extremely easy to complete.

Condition 2: Notification of Study Completion/Termination

Under the Central Office of Research Ethics Committees (COREC) regulations researchers are required to notify the Ethics Committee from which they obtained approval of the conclusion or early termination of a project and to submit a Completion/Termination of Study Report. Researchers should follow the instructions on the COREC website (www.corec.org.uk/applicants/apply/endofproject.htm).

Points to note:

- For most studies the end of a project will be the date of the last visit of the last participant or the completion of any follow-up monitoring and data collection described in the protocol.
- Final analysis of the data and report writing is normally considered to occur after formal declaration of the end of the project.
- A Final Report should be sent to the GREC within 12 months of the end of the project.
- The summary of the final report may be enclosed with the end of study declaration, or sent to the REC subsequently.
- There is no standard format for final reports. As a minimum we should receive details of the end date and information on whether the project achieved its objectives, the main findings and arrangements for publication or dissemination of research, including any feedback to participants.
- Please note the Completion/Termination of Study Report need only be a summary document and should, therefore, be easy to prepare.

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

SF1 list of approved sites

<i>Document</i>	<i>Version</i>	<i>Date</i>
Application	1	28 March 2006
Investigator CV		28 March 2006
Protocol	1	28 March 2006
Covering Letter		28 March 2006
Covering Letter		6 July 2006
Advertisement	1	28 March 2006
Letter of invitation to participant	2	6 July 2006
GP/Consultant Information Sheets	1	28 March 2006
Participant Information Sheet	2	6 July 2006
Participant Consent Form	1	28 March 2006
Response to Request for Further Information		6 July 2006
Summary CV for Supervisor (Student research)		28 March 2006

Research governance approval

The study should not commence at any NHS site until the local Principal Investigator has obtained final research governance approval from the R&D Department for the relevant NHS care organisation.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

06/S0802/40	Please quote this number on all correspondence
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With the Committee's best wishes for the success of this project

Yours sincerely

Carol Bai

ff
Dr Sheila Simpson
Chair

Enclosures: Standard approval conditions
 Site approval form

SF1 list of approved sites

North of Scotland Research Ethics Committee (2)

Summerfield House
2 Eday Road
Aberdeen
AB15 6RE

Tel: 01224 558474
Fax: 01224 558609

08 February 2010

Mrs Lyndsay Alexander
School of Health Sciences
Faculty of Health and Social Care
Robert Gordon University
Garthdee Road
ABERDEEN
AB10 7QG

Dear Mrs Alexander

Study title: An analysis of lumbar spine motion and response of the intervertebral disc to functional positions using positional MRI and 3SPACE Fastrak
REC reference: 06/S0802/40
Amendment number: AM01
Amendment date: 26 January 2010

The above amendment was reviewed at the meeting of the Sub-Committee held on 04 February 2010 by the Sub-Committee in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
Participant Information Sheet	3	26 January 2010
Participant Information Sheet	2	22 June 2006
Notice of Substantial Amendment (non-CTIMPs)	AM01	26 January 2010
Covering Letter		26 January 2010

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

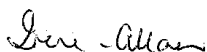
Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

06/S0802/40:

Please quote this number on all correspondence

Yours sincerely



**Mrs Irene Allan
Committee Co-ordinator**

Enclosures: List of names and professions of members who took part in the review

Copy to: NHSG R&D Department

Research and Development

Foresterhill House Annexe
Foresterhill
Aberdeen
AB25 2ZB



Date 11/01/07
Ethics 06/S0802/40
R&D Ref: 2007RG001

Mrs Lyndsay Alexander
Physiotherapy Department
Chalmers Hospital
Clunie Street
Banff
AB45 1JA

Enquiries to Katy Booth
Extension 54656
Direct Line 01224 554656
Email k.booth2@nhs.net

Dear Mrs Alexander,

Project title: An analysis of lumbar spine motion and response of the intervertebral disc to functional positions using positional MRI and 3SPACE Fastrak

Thank you very much for sending all relevant documentation. I am pleased to confirm that the project is now registered with the NHS Grampian Research & Development Office. The project has R & D Management Approval to proceed locally.

Please note that if there are any other researchers taking part in the project that are not named on the original Ethics application, please advise the Ethics Committee in writing and copy the letter to us so that we may amend our records and assess any additional costs.

Wishing you every success with your research

Yours sincerely

Katy Booth
Data Co-ordinator

Proposal Number: SHS10/04
Name Lyndsay Alexander
Short Title: An analysis of lumbar spine motion and response of the intervertebral disc to functional positions using Positional MRI and 3SPACE FASTRAK®.

Research Outcome

This proposal was considered by SRRG on 23 February 2010. _____

Decision

Full approval of proposal

The group approved the amendments

Lyndsay already had approval for this project, but at the time approval was to use NHS patients for data collection. Lyndsay has reviewed this and will now be using private sector patients. There was no change to the patient consent information.

The proposal had already been passed via NOSRES.

Signature: Date:

Dr Sue Barnard, Convenor of SRRG, or designated alternate



Appendix 2 Participant Information Sheet (Asymptomatic subjects)

STUDY: The effect of position and movement on the intervertebral disc

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish.

- Part 1 tells you the purpose of this study and what will happen to you if you take part.
- Part 2 gives you more detailed information about the conduct of the study.

Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Part 1

What is the purpose of the study?

People suffering from back pain are a common occurrence in society. Despite this, doctors, physiotherapists and other clinicians are still trying to understand how the spine works and moves in the upright position. We would like to invite you to help us improve our understanding of the spine in people without back pain. This will then allow us to compare how a pain free spine works compared to someone with back pain. In order to help you make up your mind, I have outlined what taking part would or would not involve. This project is a PhD research project.

Why have I been chosen?

The study will involve 11 volunteers that have no back pain. These volunteers will be recruited from the Robert Gordon University Campus.

Do I have to take part?

No. It is up to you to decide whether or not to take part. If you do, you will be given this information sheet to keep and be asked to sign a consent form. You are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time,

or a decision not to take part, will not affect the standard of care you receive in the future.

What will happen to me if I take part?

You will be invited to attend the Positional MRI Centre at Woodend Hospital, Aberdeen by the researcher. During this visit you will have 2 assessments, a MRI scan of your back (in standing sitting and lying down), and a motion analysis of your spine while you perform different movements (such as bending, arching, side bending and twisting). Both assessments are painless and will take a maximum of 2 hours to complete.

What do I have to do?

You will have to stand, sit and lie down in the MRI scanner for about 10 minutes in each position. The assessments will be easier if you can bring comfortable clothing such as a t-shirt, track suit bottoms or shorts to wear. There are changing facilities within the Positional MRI Centre that you can use.

What are the possible risks of taking part?

A MRI scan or motion analysis does not include any potential risks for the participant.

What are the possible benefits of taking part?

We cannot promise the study will help you but the information we get might help improve the treatment of people with back pain.

What happens when the research study stops?

A summary of the results from this research project will be sent to all participants.

What if there is a problem?

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2. A contact number for any complaints is Mrs E Hancock (Head of School, Health Sciences, Robert Gordon University, Aberdeen): 01224 263251

Will my taking part be kept confidential?

Yes. All the information about your participation in this study will be kept confidential. The details are included in Part 2.

Contact details

Further information can be obtained from: **Lyndsay Alexander, School of Health Sciences, Faculty of Health and Social Care, Robert Gordon University, Garthdee, Aberdeen**

Tel: 01224 263264

This completes Part 1 of the Information Sheet.

If the information in Part 1 has interested you and you are considering participation, please continue to read the additional information in Part 2 before making any decision.

Part 2

What will happen if I don't want to continue with the study?

If you withdraw from the study, we will destroy all your identifiable samples, but we will need to use the data collected up to your withdrawal.

What if there is a problem?

Complaints: If you have a concern about any aspect of this study, you should ask to speak with the researchers who will do their best to answer your questions (Contact number: 01224 263264). If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be obtained from the Positional MRI Centre.

Harm: In the event that something does go wrong and you are harmed during the research study there are no special compensation arrangements. If you are harmed and this is due to someone's negligence then you may have grounds for a legal action for compensation against (Robert Gordon University, or NHS Grampian) but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you.

Will my taking part in this study be kept confidential?

All information which is collected about you during the course of the research will be kept strictly confidential.

Involvement of your General Practitioner

With your consent, your GP will be informed of your participation in this study and the results of the MRI scans will be sent to them.

What will happen to any samples I give?

All data collected by the researcher will be securely stored on CD/DVDs as images of the spine and numerical data of the motion analysis. All data will be analysed by the researcher and information will be coded and any identifying information will be

removed. All data from this study will be securely stored within the Robert Gordon University.

What will happen to the results of the study?

The study results will be published in medical journals and a summary will be sent to all participants. The overall project will also be written up as part of a PhD study by the researcher.

Who is organising and funding the research?

The research has been funded by a SHERT/TYSON Fellowship award to the principal researcher which has paid for all the MRI scans and allowed the researcher to be released from her clinical work to carry out the project.

Who has reviewed this study?

This study was given a favourable ethical opinion for conduct in the NHS by the Grampian REC.

All participants will be given a copy of the information sheet and a signed consent form to keep.

Thank you for taking time to read this information sheet and considering taking part in this study.

Consent by patient to participate in:

A study to evaluate back pain using positional MRI and Fastrak motion tracking system.

Name of patient:

Name of study: **An investigation into low back pain using positional MRI and Fastrak**

Principal investigator: Dr Ioannis Agouris, Research Fellow, faculty of Health and Social Care, Robert Gordon University.

I have read the patient information sheet on the above study and have had the opportunity to discuss details with the researcher and ask questions. The researcher has explained to me the nature and purpose of the study to be undertaken and i understand fully what is proposed to be done.

I have agreed to take part in this study as it has been outlined to me, but i understand that I am completely free to withdraw from the study or any part of the study at any time I wish and that this will not affect any continuing medical treatment in any way.

I understand that this study is part of a research project designed to promote medical knowledge, and may be of no benefit to me personally. The Grampian Research Ethics Committee of NHS Grampian has approved this study.

I hereby fully and freely consent to participate in this study which has been fully explained to me.

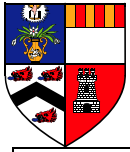
Signature of patient:

Date:

I confirm I have explained to the patient named above, the nature and purpose of the test to be undertaken.

Signature of investigator:

Date:

**CONFIDENTIAL**

To be completed by patient		
full name:	date of birth:	weight:

To be completed by MRI staff	
MRI scan number:	referring clinician / dept:
CHI number:	Unit number:

The MRI scanner uses a very strong magnet and radio-waves to make images. This may be dangerous for some people. This questionnaire is designed to find out if it is safe for you to have an MRI scan.

Patients **must** complete this form before the examination.
This information will be retained within your confidential medical record.

Please circle **Yes** or **No**

1) Do you have a heart pacemaker or implanted cardiac defibrillator?	1	Yes	No
2) Have you had any brain or heart surgery?	2	Yes	No
Do you have:			
3) an aneurysm clip?	3	Yes	No
4) an implanted nerve stimulator?	4	Yes	No
5) any artificial limbs or joints?	5	No	Yes
6) any metal plates or screws in your body?	6	Yes	No
7) a middle ear implant?	7	Yes	No
8) a hydrocephalus shunt (if yes, please give details over the page)?	8	Yes	No
9) any other implant, heart valve, coil, stent, catheter or artificial object in your body?	9	No	Yes
10) any metal fragments in your body (such as shrapnel or bullets)?	10	Yes	No
11) a false eye?	11	Yes	No
12) dentures, dental plates or braces?	12	Yes	No
13) a wig or hairpiece?	13	Yes	No
14) a hearing aid?	14	No	Yes
15) a medication patch (nicotine / contraceptive)?	15	Yes	No
16) tattoos or tattooed eyeliner?	16	Yes	No
17) any body piercing jewellery?	17	Yes	No
18) any allergies?	18	No	Yes
19) Have you had other operations (if yes, give details over the page)?	19	No	Yes
20) Have you ever had metal fragments in your eye?	20	Yes	No

Females Only

21) Are you or could you be pregnant?	21	Yes	No
22) Are you breast feeding?	22	Yes	No
23) Do you have a contraceptive coil?	23	No	Yes

If you have answered yes to any of the questions, please give additional information here

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IMPORTANT NOTES

- The University of Aberdeen cannot be held liable for any injury / death to the patient which arises as a direct result of any failure by the patient to disclose accurate and complete information on this form.
- **PLEASE DO NOT TAKE ANY METAL OBJECTS, COINS, BANK OR CREDIT CARDS, WATCHES ETC. INTO THE SCANNING ROOM. LEAVE THEM IN THE LOCKER PROVIDED IN THE CHANGING CUBICLE**

I confirm that I have read and understood the section entitled "Important Notes" above. I further confirm that the information I have given on this form is correct and complete to the best of my knowledge.

signed (patient):	date:
-------------------	-------

or

signed (on behalf of patient):	date:
print name:	relationship to patient:

signed (MRI Authorised Person):	date:
---------------------------------	-------

The Response of the Nucleus Pulposus of the Lumbar Intervertebral Discs to Functionally Loaded Positions

Lyndsay A. Alexander, BSc,* Elizabeth Hancock, MSc,* Ioannis Agouris, PhD,*
Francis W. Smith, MD,† and Alasdair MacSween, PhD*

Study Design. Asymptomatic volunteers underwent magnetic resonance imaging to investigate how different positions affect lumbar intervertebral discs.

Objective. To quantify sagittal migration of the lumbar nucleus pulposus in 6 functional positions.

Summary of Background Data. Previous studies of the intervertebral disc response in the sagittal plane were limited to imaging of recumbent positions. Developments of upright magnetic resonance imaging permit investigation of functional weight-bearing positions.

Methods. T2-weighted sagittal scans of the L1–L2 to L5–S1 discs were taken of 11 volunteers in standing, sitting (upright, flexed, and in extension), supine, and prone extension. Sagittal migration of the nucleus pulposus was measured (mm) as distance from anterior disc boundary to peak pixel intensity. Lumbar lordosis (Cobb angle) was measured in each position.

Results. Fifteen comparisons between positions showed significant positional effects (14 at L4–L5, L5–S1, the most mobile segments). Prone extension and supine lying induced significantly less posterior migration than sitting. Flexed and upright sitting, significantly more than standing at L4–L5, as did flexed sitting compared with extended.

Conclusion. These results support for the first time the validity of clinical assumptions about disc behavior in functional positions: sitting postures may increase risk of posterior derangement, and prone and supine may be therapeutic for symptoms caused by posterior disc displacement.

Key words: upright MRI, nucleus pulposus, intervertebral disc, functional positions. **Spine 2007;32:1508–1512**

Intervertebral disc (IVD) problems, principally excessive migration of the nucleus pulposus (NP) and disruption of the annulus fibrosus (AF), are generally accepted to be one of the main causes of nonspecific back pain.^{1–4} Around 40% of people with low back pain are thought to have pain of discogenic origin.^{5,6} The apocryphal “slipped disc,” disc bulging or ultimately prolapse leading to impingement, is a major cause of work absence in industrialized societies.⁷ The assumption that (primarily) exten-

sion and flexion cause, predictable and repeatable, anterior and posterior (respectively), migrations of the NP underlies popular conservative therapeutic interventions, such as the McKenzie regimen,⁸ where exercises and postural corrections, designed to reduce such migrations and resultant impingement, are prescribed. While some *in vivo* work is available, the evidence base for such treatments is extremely limited as *in vitro* study of the response of IVD to everyday postures, such as sitting, standing, and bending, has not previously been reported. Magnetic resonance imaging (MRI), which allows visualization of IVDs, has hitherto been restricted due to imaging of cadavers,^{9,10} or nonfunctional recumbent positions, which remove the effects of both gravity and forces generated by functional muscle work due to scanner design.^{11–14} Moreover, the limited space permitted in the completely enclosed scanners used, due to magnet bore, has been noted to limit subject’s movements.¹²

Beattie *et al*¹³ examined supported supine flexion and extension (lying on a lumbar roll) in 20 normal female subjects. They reported the distance from the posterior boundary of the NP, to the posterior boundary of the AF, decreased significantly in extension (*vs.* flexion) at L3–L4, L4–L5, and L5–S1 levels. While there was also a reduction trend in the anterior distances, this was not significant, suggesting perhaps an anterior compression of the NP, in extension, but no significant migration. Fennell *et al*¹² examined neutral, extended, and flexed side lying, in 3 normal subjects and found a similar pattern. Brault *et al* investigated the issue through measurement of “peak pixel intensity,” which occurs at the center of the NP representing the peak area of hydration within the disc.¹⁴ They reported significantly greater anterior migration in extended compared with flexed, supported supine lying, at L1–L2, L2–L3, and L3–L4 levels. Edmondston *et al*¹¹ used the same technique and positions, with 10 asymptomatic volunteers, reporting a significant anterior migration at L1–L2, L2–L3, and L5–S1 in supported supine extension.

With the development of upright positional MRI (pMRI) scanners, it is possible to image the spine in both upright/functional and recumbent positions, the great diagnostic advantage being imaging of the spine in the load-bearing postures which trigger symptoms.^{15–17} Initial work by Jinkins and Dworkin¹⁶ has documented pMRI scanning of subjects with degenerative spinal conditions sitting in normal, flexed, and extended positions and supine. They reported pronounced differences between loaded and unloaded positions and that pathology

From the *Robert Gordon University, Aberdeen, U.K.; and †Positional MRI Centre, Woodend Hospital, Aberdeen, U.K.

Acknowledgment date: June 29, 2006. First revision date: November 3, 2006. Acceptance date: December 8, 2006.

The manuscript submitted does not contain information about medical device(s)/drug(s).

No funds were received in support of this work. No benefits in any form have been or will be received from a commercial party related directly or indirectly to the subject of this manuscript.

Address correspondence and reprint requests to Lyndsay A. Alexander, BSc, School of Health Sciences, Faculty of Health and Social Care, Robert Gordon University, Garthdee Road, Aberdeen, AB10 7QG, U.K.; E-mail: l.a.alexander@rgu.ac.uk



Figure 1. Examples of scanning position used: extended sitting, standing, flexed sitting and prone extension.

such as dysfunctional intersegmental motion was revealed only under axial loading.¹⁶ The present study investigated the response of the NPs, of the lumbar IVDs of normal subjects in 6 different functional positions: standing (referred to as P1), sitting (upright, P2; flexed, P3; and in extension, P4), supine (P5), and prone extension (P6).

■ Materials and Methods

A convenience sample of 11 healthy volunteers was recruited by response to a general notice and word of mouth. Approval was obtained from both Grampian NHS and Robert Gordon University ethics committees, and all subjects gave informed written consent before their participation in this project. Subjects were included if they had no present back pain and no history of requiring treatment for back pain, no cognitive, mental, or communication impairment preventing informed consent, and age between 18 and 60 years. Subjects were excluded from the study if they had any contraindications to an MRI

procedure or shoulder/hip width greater than 45 cm (width of pMRI).

A 0.6 Tesla, positional “Upright” MRI (Fonar Corp., Melville, NY) was used to carry out the scans. This scanner can image in supine, erect (weight-bearing), and seated positions in both neutral and other (*e.g.*, flexed/extended) postures.^{15,18} Sagittal (TR-3848, TE-120) weighted images through the 5 lumbar IVDs were taken: field of view = 30 cm, slice thickness = 4.5 mm, slice interval = 5 mm, acquisition matrix = $180 \times 256/3\text{NEX}$, imaging time = 4 to 5 minutes per sequence. The same radiographer carried out each scan at the same time each day (to minimize diurnal effects¹⁹), in the same order: standing, sitting (upright, flexed, and in extension), supine, and prone extension (Figure 1). Initial pilot work revealed that this sequence minimized subject discomfort. Sitting in extension and prone extension were maintained passively using foam rolls and wedges. Subjects were required to maintain each position for approximately 10 minutes per scan.

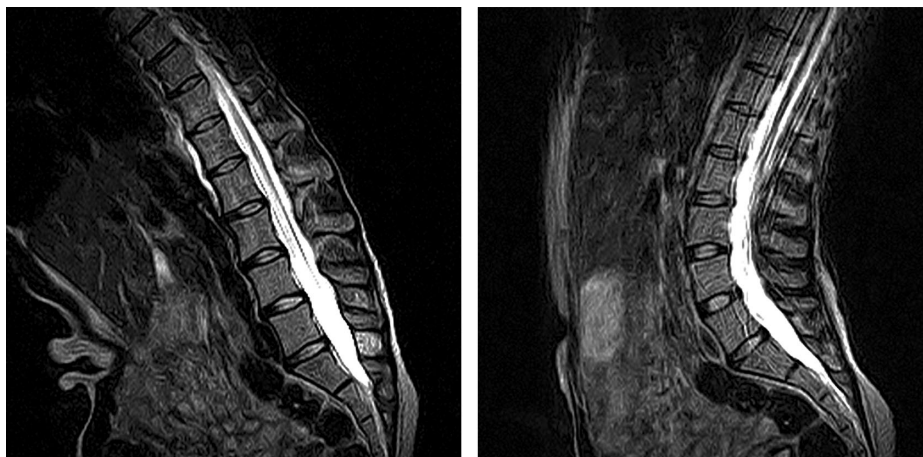


Figure 2. Example mid-sagittal slice scans of a subject in extended and flexed sitting.

All images were transferred to CD ROM, and subsequent measurements were taken with the Osiris 4.19 software program (University of Geneva, Geneva, Switzerland) by the same researcher. In addition, all images were examined and reported by a consultant radiologist (Figure 2, examples of scan images).

The midsagittal slice image was identified for each subject, in each position. To examine if the different positions affected the extent of lumbar lordosis, the Cobb angle (the angle between the superior vertebral endplates of L1 and S1) for each posture was measured.²⁰ The same researcher then located the center of the NP in each image using the peak pixel intensity method of Brault *et al.*¹⁴ This is where the mid-disc line and the point of peak pixel intensity on that line are identified. The distance from the anterior disc boundary to this point was then recorded in millimeters and defined as the extent of sagittal migration of the NP; therefore, greater values represented greater posterior migration. Before analyzing the effect of position on NP migration, the intraoperator reliability of locating the NP center was assessed by measuring each midsagittal scan, for each subject, at each level and each position, 3 times on a blind basis.

Separate intraclass correlation coefficients (ICCs), for each level, in each position, were calculated to quantify the intraoperator reliability of location of the NP center. Before inferential testing, normality of distribution was examined with the Shapiro-Wilk test. Where distribution was not within acceptable limits of normality ($P < 0.05$), nonparametric models were applied. To determine the effect of the 6 positions measured on lumbar lordosis, differences between the Cobb angles in each position were tested with repeated measures ANOVA. Where significant effects were found, *post hoc* testing (paired *t* tests) of all possible comparisons was applied. With Bonferroni correction (15 tests), statistical significance was determined at $P < 0.003$.

The effect of the positions on the sagittal migration of each of the NPs was investigated using separate Friedman's tests for the NPs at L1–L2 and L2–L3 (NP1 and NP2, respectively) and separate repeated-measures analysis of variance (ANOVA) for the NPs at L3–L4, L4–L5, and L5–S1 (NP3, NP4, and NP5, respectively). Statistical significance was determined at $P < 0.05$. Where significant effects were found, *post hoc* testing (Wilcoxon for Friedman's tests and paired *t* tests for ANOVAs) of all possible comparisons between positions, at each NP, were applied. With Bonferroni correction (15 tests), statistical significance was determined at $P < 0.003$.

■ Results

Seven females and 4 males completed the study: all except one were employed; age (mean \pm SD), 36 ± 9 years; height 1.72 ± 0.08 m; and weight, 72.09 ± 14.25 kg.

A high level of intratester reliability was found for the NP translation measurements (performed with the OSIRIS 4.19 software program) with ICC for each position ranging from 0.71 to 0.97 (mean \pm SD, 0.89 ± 0.06). While the consultant radiologist did identify degenerative changes in 6 subjects, these were indicative of normal, age-appropriate “wear and tear” in a healthy spine. The mean Cobb angles for sitting positions were as follows: P3, flexed $1.6^\circ (\pm 7.2^\circ)$, P2, upright $21.5^\circ (\pm 10.1^\circ)$, and P4, extended $50.2^\circ (\pm 8.1^\circ)$ with, P5, supine lying $51.4^\circ (\pm 6.4^\circ)$, P1, standing $52.8^\circ (\pm 12.9^\circ)$, and P6, prone extension $61.4^\circ (\pm 7.1^\circ)$. Significant differences were found (ANOVA), and *post hoc* testing indicated that upright and flexed sitting were significantly lower (less lordosis) than every other position ($P < 0.001$) and prone extension significantly greater (increased lordosis) than every other position except standing ($P < 0.001$). While not significantly different between every successive step, this rank order supports the anticipated effect of these functional positions on lumbar lordosis.

The ANOVA and Friedman's analysis revealed that at all levels position exerted a statistically significant influence on the sagittal migration of the NP. To determine between which positions the significant differences lay, *post hoc* analysis was performed, and the results are presented in Table 1.

The NPs of the lowest IVD levels, NP4 and NP5 (IVDs L4–L5 and L5–S1, respectively), were the most affected by position, in that every position was significantly different from at least one other. Fifteen significant differences were found: 11 from comparison of loaded and unloaded and 4 from unloaded positions. The magnitude and direction of the significant differences between loaded positions are presented in Table 2.

Table 1. Results of Pairwise Post Hoc Comparisons of the Effect of Six Different Positions on the Posterior Migration (mm) of Individual Nucleus Pulposus of the Lumbar Vertebrae

	P2	P3	P4	P5	P6
P1	NP4, NP5	NP4			
P2				NP4, NP5	NP3, NP4, NP5
P3			NP4	NP4, NP5	NP4, NP5
P4				NP5	NP5

P1 indicates standing; P2, upright sitting; P3, flexed sitting; P4, sitting in extension; P5, supine; P6, prone extension; NP3, significant difference between positions ($P < 0.003$) for nucleus pulposus 3; NP4, significant difference between positions ($P < 0.003$) for nucleus pulposus 4; NP5, significant difference between positions ($P < 0.003$) for nucleus pulposus 5.

Both upright and flexed sitting induced significantly more posterior migration of NP4 than did standing, with the same effect observed for upright sitting at NP5. The magnitude and direction of the significant differences in NP sagittal migration, from the comparisons between loaded and unloaded positions, are presented in Table 3.

Discussion

The aim of this study was to investigate the NP response to different functional positions in normal subjects. While it is difficult to guarantee a sample with completely normal spines, the present sample did meet specific inclusion criteria and all scans were classified as within normal limits by a consultant radiologist.

Previous authors^{12,13} visually identified both anterior IVD margin and NP boundary but did not report ICCs. Peak pixel intensity was used in this study to identify the NP center. This yielded a mean ICC of 0.89; Edmondston *et al* reported 0.71 with the same technique.¹¹ This more objective technique may yet yield greater benefits when scanning degenerative discs where visual identification of boundaries may be even more difficult.

Initial analysis showed that the NPs of the lowest IVD levels, NP4 and NP5 (IVDs L4–L5 and L5–S1, respectively), displayed the greatest differences in sagittal migration between position: 14 of the 15 significant differ-

Table 2. Mean Difference (mm, 95% CI, and % of Anteroposterior Disc Width) and Direction of the Statistically Significant Differences in the Posterior Migration of Individual Nucleus Pulposus of the Lumbar Vertebrae From the Comparisons Between Loaded Positions

	P2 > P1	P3 > P1	P3 > P4
NP4	5.7 2.6–8.9 17.8%	6.1 2.6–9.7 19.1%	5.1 2.5–7.7 15.9%
NP5	6.9 3.2–10.6 22.1%	NS	NS

> indicates significantly greater posterior migration than; NP4, nucleus pulposus 4; NP5, nucleus pulposus 5; P1, standing; P2, upright sitting; P3, flexed sitting; P4, sitting in extension; NS, not significant.

Table 3. Mean Difference (mm, 95% CI, and % of Anteroposterior Disc Width) and Direction of the Statistically Significant Differences in the Posterior Migration of Individual Nucleus Pulposus of the Lumbar Vertebrae From the Comparisons Between Loaded (Standing, Upright, Flexed, and Extended Sitting) and Unloaded (Supine and Prone Extension) Positions

	P2 > P6	P3 > P6	P4 > P6	P2 > P5	P3 > P5	P4 > P5
NP3	4.7 2.9–6.4 14.9%					
NP4	6.3 4.6–8.1 19.7%	6.7 3.4–10.1 20.9%		5.2 3.2–7.3 16.3%	5.6 2.5–8.8 17.5%	
NP5	8.7 5.8–11.5 27.9%	6.3 2.9–9.7 20.2%	6.4 3.0–9.8 20.5%	9.5 6.3–12.6 30.5%	7.1 3.3–10.9 22.8%	7.2 3.6–10.9 23.1%

> indicates significantly greater posterior migration than; NP3, nucleus pulposus 3; NP4, nucleus pulposus 4; NP5, nucleus pulposus 5; P1, standing; P2, upright sitting; P3, flexed sitting; P4, sitting in extension; P5, supine; P6, prone extension.

ences found occurred at NP4 and NP5. This finding accords with the theoretical model of posterior migration, leading to disc bulging and ultimately pathology, in that previous studies report that most disc derangements occur at the most mobile motion segment, L4–L5.^{21,22} Previous MRI studies investigating the response of the NP to flexion and extension found that anterior migration was most apparent in the upper 4 lumbar discs, but this was in unloaded and nonfunctional, recumbent positions.^{11,12} The present results differ in that NP migration was different in these loaded, functional, positions. This accords with the generally accepted clinical finding of disc derangement at lower levels in that no significant differences in posterior migration were found at higher (L1–L2, L2–L3) levels; and at NP3 (L3–L4), only the difference between prone extension and upright sitting was significant.

In the comparisons of loaded positions both P2, upright and P3, flexed sitting induced significantly more posterior migration of NP4 than did P1, standing; with the same effect observed for upright sitting at NP5. Flexed sitting also induced significantly more posterior migration than sitting in extension at NP4. This suggests that standing may well be preferable, in terms of reduced risk of posterior derangement than the classically “poor” sitting postures: upright and flexed. Interestingly, sitting in extension, which is generally accepted as a “better” sitting posture, did not differ significantly from standing, which would suggest that, for normal subjects, both standing and sitting in extension are preferable. Flexed sitting induced significantly greater posterior migration of NP4 than sitting in extension. This latter finding, in conjunction with the Cobb angle analysis, which verified that the positions tested had the expected effects on lumbar lordosis, supports the hypothesis that maintenance of the lumbar lordosis, when sitting, should reduce the risk of posterior disc derangement, at the most commonly affected level, L4–L5.²¹

The results from the comparisons of the loaded and unloaded positions also revealed the pattern of significant positional effect at NP4 and NP5 (with only 1 exception, upright sitting being greater than prone extension at NP3) discussed earlier. Prone extension, a posture commonly used as a treatment technique in physical therapies,⁸ induced significantly less posterior migration than any of the 3 sitting positions. Interestingly, supine lying also showed significantly less posterior migration than any of the 3 sitting positions at the same levels. Moreover, there was no appreciable pattern of difference in the levels of mean difference or the 95% confidence intervals in the significant comparisons of sitting to prone extension and supine. This finding may suggest support for the hypothesis that this popular therapeutic technique may in fact be no better than simply lying down in terms of posterior disc derangement. This apparent lack of support for this popular treatment may have reflected the fact that, due to the scanning technique, prone extension (and all other positions measured) was maintained for approximately 5 minutes, as opposed to active, full range repeated but not sustained prone extension, which is used as a therapeutic exercise. In contrast, the Cobb angle analysis revealed that prone extension induced greater mean lordosis (61.4°) than did supine (51.4°). While this difference was nonsignificant, it does at least support the assertion that greater lordosis did occur but perhaps not end of range. Until such time as real-time active scanning is possible, this limitation is unavoidable.

■ Key Points

- To our knowledge, this is the first study of sagittal migration of nucleus pulposus in functional positions.
- We used upright MRI to see the effect of different functional positions on the nucleus pulposus.
- Our results support previously reported theories and models of disc behavior.

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Appendix 6: Information sheet (3SPACE Fastrak™)



A pilot study to establish the reliability and validity of the 3SPACE Fastrak in the analysis of lumbar spine kinematics

Study Information Sheet

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Please talk to others about the study if you wish.

Part 1 below tells you about the purpose of the study and what you would be required to do if you take part

Part 2 gives you more detailed information about the conduct of the study

Ask us if there is anything that is not clear or if you would like more information, contact details are given below. Take time to decide whether or not you wish to take part.

Part 1

The purpose of the study

Our project aims to find out how accurate and reliable a painless measurement device is in measuring back movements. Identifying this would allow physiotherapists to use more accurate tools to measure spine movements in patients with back pain.

Why have I been chosen?

In order to carry out the study we require 20 people (male or female) with no back problems at the present time, over 18 years of age to volunteer. We have

placed adverts in the RGU staff and students email, the RGU newsletter and have provided information to student groups in the faculty.

Do I have to take part?

NO. It is up to you to decide whether to take part or not. If you do you will be given this information sheet to keep and asked to sign a consent form. You are still free to withdraw at any time and without giving a reason. If you decide not to take part or start but decide to withdraw you can do this at any time. If you withdraw from the study we will not contact you again in relation to this.

What will happen to me if I take part?

Once you sign the consent form you will be asked to attend the Human Performance Laboratory on level 1 in the Faculty of Health and Social Care building on two occasions spaced two weeks apart. The first visit will last around 3 hours and the second one will last around 2 hours. During these visits painless sensors will be attached to your back and you will be asked to perform everyday movements such as bending forward, backward, side to side, and twisting in both standing and sitting positions as well as standing up from sitting down. These movements will be assessed using 2 pieces of equipment which are pain free and record movements of your spine via the sensors on your back.

What do I have to do?

There are no restrictions while taking part in this study and you can carry out your normal routine in between the two visits for testing.

What are the side effects of the treatment?

There are no side effects for people having assessments performed using the 3SPACE Fastrak and Vicon.

What are the other disadvantages and risks of taking part?

There are no disadvantages or risks in taking part in this study. Both the 3SPACE Fastrak and the Vicon are painless examinations of movement.

What are the potential benefits of taking part?

There are no intended direct benefits to volunteers taking part in this study. The information we get from this study will help us establish if the 3SPACE Fastrak is a reliable piece of equipment to assess back movements which may help in the assessment and treatment of back problems in the future.

What if there is a problem?

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. Detailed information on this aspect is given in Part 2 of this information sheet.

Will my taking part in the study be kept confidential?

Yes. All the information about your participation in this study will be kept confidential. Details are included in Part 2.

Contact details

Lyndsay Alexander, School of Health Sciences, Faculty of Health and Social Care, RGU, Garthdee Road, Aberdeen. Tel: 01224 263264

Kay Cooper, School of Health Sciences, Faculty of Health and Social Care, RGU, Garthdee Road, Aberdeen. Tel: 01224 263283

This completes Part 1 of the information sheet. If the information in Part 1 has interested you and you are considering taking part, please continue to read the additional information in Part 2 before making any decision.

Part 2

What if relevant new information becomes available?

Sometimes, during the course of a research project, new information becomes available about the treatment being studied. If this happens the research physiotherapist will tell you about it and discuss whether you want to, or should, continue in the study. If you decide not to carry on you will stop participation in the study immediately. If you decide to continue in the study you will be asked to sign an updated consent form.

If the study is stopped for any reason you will be told why.

What if there is a problem?

If you have a complaint about how you have been treated by a member of the study team, in the first instance you should contact: Mrs Elizabeth Hancock, Head of School, The Robert Gordon University, Faculty of Health and Social Care,

School of Health Sciences, Garthdee Road, Garthdee, Aberdeen AB10 7QG, Tel: 01224 263257.

In the event that something does go wrong and you are harmed during the research study there are no special compensation arrangements. If you are harmed and this is due to someone's negligence then you may have grounds for a legal action for compensation against The Robert Gordon University but you may have to pay your legal costs.

Will my taking part in the study be kept confidential?

Yes. Information collected during the study will be saved on a laptop computer and then transferred to a desktop computer that is in a secure office at the Robert Gordon University. It will be retained for a period of 5 years. Only the researchers and authorised personnel from RGU will have access to study information. All will have a duty of confidentiality to you as a research participant and nothing that could reveal your identity will be disclosed outside the research site.

Processes for handling, processing, storage and destruction of your information will comply with the Data Protection Act 1998.

What will happen to the results of the study?

If you wish to know the outcome of the study you will be sent a summary of the findings once all information has been analysed. Please give the researcher your contact details if you would like a summary of the findings.

Reports will be written for publication in relevant medical journals and presented at conferences from the final results obtained in this study. In such reports and presentations no personal data will be included and participants will be anonymous.

Who is organising and funding the research?

This study is being organised by staff at the Robert Gordon University and its personnel will not receive any funding for your inclusion in the study.

Who has reviewed the study?

This study was given a favourable ethical opinion for conduct by the School of Health Sciences Ethics Committee. This means it has undergone an approval process for research being undertaken within RGU.

Thank you for taking the time to read this information sheet. If you are interested in taking part in this study or have further questions you would like answered before making a decision please contact Lyndsay Alexander tel: 01224 263264, email l.a.alexander@rgu.ac.uk or Kay Cooper tel: 01224 262677, email: k.cooper@rgu.ac.uk who will be happy to answer any further questions that you may have.

Appendix 7: Consent form (3SPACE Fastrak™)



Volunteer Identification Number for this trial:

CONSENT FORM

A pilot study to establish the reliability and validity of the 3SPACE Fastrak in the analysis of lumbar spine kinematics

Name of Researcher:

- 1 I confirm that I have read and understand the information sheet dated 17/07/07 (version 1) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

- 2 I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my legal rights being affected.

- 4 I understand that data collected during the study, may be looked at by responsible individuals from The Robert Gordon University, where it is relevant to my taking part in this research. This data will be stored under a code and will not identify me.

- 7 I agree to take part in the above study.

Please initial box

_____	_____	_____
Name of Volunteer	Date	Signature
_____	_____	_____
Name of Person taking consent (if different from researcher)	Date	Signature
_____	_____	_____
Researcher	Date	Signature

When completed, 1 for Volunteer; 1 for researcher site file (original).

Appendix 8: Source and sensor placement and sequence of movements

Sensors are attached vertically to the skin over the spinous process of the first lumbar vertebrae (L1) and the sacrum (S2) via double sided sticky tape (3M) in a semi-flexed position to minimise the effect of full flexion displacement due to skin traction (Maffey-Ward et al 1996, Swinkels & Dolan 1998, Swinkels & Dolan 2000). The skin over L1 & S2 will be cleaned with alcohol wipes to remove sweat and any surface oil that may affect the adherence of the tape to the skin (Burnett et al 1998).

The spinous process of L1 and S2 are located via palpation of the spine in a relaxed semi-flexed standing position and marked with a cosmetic pencil (Dolan & Swinkels 1998, Mannion & Troke 1999, Swinkels & Dolan 2000). L1 is identified as the third spinous process above the L4 spinous process where L4 or L4/5 interspace is identified as the spinous process level with the superior iliac crests (Burnett et al 1998). S2 is identified as the midpoint between the dimples of Venus on the sacrum (Swinkels & Dolan 1998).

The 3SPACE Fastrak source is securely fixed onto a wooden pedestal placed directly behind the subject within the recommended operational range of the device as carried out by previous authors (Mannion & Troke 1999, Lee & Wong 2002, Burnett et al 2004). The Fastrak® manufacturer specifies that the distance between the transmitter and sensors is 30 inches/76cm. The wooden pedestal is also height adjustable to allow the transmitter to remain level with the sensors in both standing and sitting.

Neutral Standing position

Feet placed comfortably apart (measured to ensure same distance used for re-test), arms by side, head in neutral position with gaze facing directly in front (Swinkels & Dolan 1998, Mannion & Troke 1999, Lee & Wong 2002).

Neutral Sitting position

Seated on stool in upright position and instructed to "sit tall" and look straight ahead with hands resting by sides. Subject's hips, knees and ankles are in a position of 90° flexion with the stool height adjusted for each subject to ensure this alignment and feet placed hip distance apart (Amiri et al 2003, O'Sullivan et al 2003).

Standing

- **Flexion**

Starting in a neutral standing position, the subject is asked to bend forward/down as far as they are able to go to touch their toes, keeping their

knees straight then return to their starting position (Barrett et al 1999, Mannion & Troke 1999, Swinkels & Dolan 2003).

- **Extension**
Starting in a neutral standing position, subjects are asked to lean backwards, reaching down the back of their thighs with their hands, keeping their knees straight then return to the starting position (Barrett et al 1999).
- **Side Flexion**
Starting in a neutral standing position with arms by their side, subject is asked to side bend sliding one hand down the side of their leg as far as possible keeping both feet flat on the ground then return to the starting position. The subject then repeats the manoeuvre to the opposite side (Mannion & Troke 1999).
- **Rotation**
Starting in a neutral standing position, arms crossed over chest, subjects are asked to turn head to one side and follow with their trunk and pelvis as far as possible and then return to the starting position. The subject then repeats the manoeuvre to the opposite side (Mannion & Troke 1999).

Sitting

- **Flexion**
Starting in neutral sitting position, subject is asked to bend forward/down as far as they are able to go sliding their hands down the side of their calves, keeping their bottom on the stool then return to the starting position.
- **Extension**
Starting in a neutral sitting position with arms hanging by their side, subject is asked to arch backwards as far as possible maintaining gaze straight ahead at all times, then return to starting position.
- **Side Flexion**
Starting in the same neutral sitting position as for extension in sitting, subject is asked to bend to the side as far as possible without bending forward or backward during the movement. They then return to the starting position. The movement is then repeated to the other side.
- **Rotation**
Starting in a neutral sitting position with arms crossed over their chest, subjects are asked to turn head to one side and follow with their trunk and pelvis as far as possible and then return to the starting position. The subject then repeats the movement to the opposite side

Appendix 9: Letter of invitation (Private practice)



**ROBERT GORDON
UNIVERSITY•ABERDEEN**

Letter of Invitation.

Study: The effect of position and movement on the intervertebral disc.

We would like to invite you to participate in the above study. This study is currently being carried out in Aberdeen at the Positional MRI Centre based in Woodend Hospital as part of a PhD project.

Your physiotherapist has given you this letter of invitation and an information sheet to read. We would like you to take time to read the information sheet and decide if you would like to take part in this project.

If you would like to take part, you can respond directly by completing the tear off slip on the bottom of this letter and sending it back to the researcher in the self addressed envelope.

Should you have any questions in the meantime please contact me on 01224 263264.

Thank you for your time.

Lyndsay Alexander

(Lecturer)

Name: _____

Address: _____

Telephone Number: _____

Please complete and return in the self addressed envelope.

Appendix 10: Letter of invitation (NHS)



**ROBERT GORDON
UNIVERSITY • ABERDEEN**

Letter of Invitation.

Study: The effect of position and movement on the intervertebral disc.

We would like to invite you to participate in the above study. This study is currently being carried out in Aberdeen at the Positional MRI Centre based in Woodend Hospital as part of a PhD project.

Your physiotherapist has given you this letter of invitation and an information sheet to read. We would like you to take time to read the information sheet and decide if you would like to take part in this project.

If you would like to take part, you can respond directly by completing the tear off slip on the bottom of this letter and sending it back to the researcher in the self addressed envelope.

Should you have any questions in the meantime please contact me on 01224 263264.

Thank you for your time.

Lyndsay Alexander

Name: _____

Address: _____

Telephone Number: _____

Please complete and return in the self addressed envelope.

Appendix 11: Information sheet (Private practice)



**ROBERT GORDON
UNIVERSITY • ABERDEEN**

Patient Information Sheet

STUDY: The effect of position and movement on the intervertebral disc

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish.

- Part 1 tells you the purpose of this study and what will happen to you if you take part.
- Part 2 gives you more detailed information about the conduct of the study.

Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Part 1

What is the purpose of the study?

People suffering from back pain are a common occurrence in society. Despite this, doctors, physiotherapists and other clinicians are still trying to understand how the spine works and moves in the upright position. We would like to invite you to help us improve our understanding of the spine in people with back pain. This will then allow us to compare how a spine works in someone with back pain compared to someone without back problems. In order to help you make up your mind, I have outlined what taking part would or would not involve. This project is a PhD research project.

Why have I been chosen?

We are inviting patients with back and/or leg pain that are attending private physiotherapy to take part.

Do I have to take part?

No. It is up to you to decide whether or not to take part. If you do, you will be given this information sheet to keep and be asked to sign a consent form. You are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive in the future.

What will happen to me if I take part?

The researcher will telephone you at home in about a week to ask if you are interested in taking part in this study. She can answer any further questions you may have about taking part in this project. You will be invited to attend the Positional MRI Centre at Woodend Hospital, Aberdeen by the researcher at this time also. During the visit to the

Positional MRI Centre, you will have a MRI scan of your back performed (in different standing, sitting and lying down positions) this assessment is painless and will take a maximum of 1.5 hours to complete.

What do I have to do?

You will have to stand, sit and lie down in the MRI scanner for about 10 minutes in each position. The assessments will be easier if you can bring comfortable clothing such as a t-shirt, track suit bottoms or shorts to wear. There are changing facilities within the Positional MRI Centre that you can use.

What are the possible risks of taking part?

A MRI scan does not include any potential risks for the participant. Some of the positions may be uncomfortable for people with back pain (such as sitting or bending forward), should you feel uncomfortable with any position at any time you can halt the assessments. As the MRI scan uses a magnetic effect to take the images no metallic objects or clothing should be worn whilst having a MRI scan performed. The radiographer performing your MRI scan will check for anything metal before you have your scan.

What are the possible benefits of taking part?

We cannot promise the study will help you but the information we get might help improve the treatment of people with back pain.

What happens when the research study stops?

After you have the MRI scans at the Positional MRI Centre, you will continue with your standard physiotherapy treatment.

What if there is a problem?

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2. A contact number for any complaints is Mrs E Hancock (Head of School, Health Sciences, Robert Gordon University, Aberdeen): 01224 263251

Will my taking part be kept confidential?

Yes. All the information about your participation in this study will be kept confidential. The details are included in Part 2.

Contact details

Further information can be obtained from: **Lyndsay Alexander, School of Health Sciences, Faculty of Health and Social Care, Robert Gordon University, Garthdee, Aberdeen**

Tel: 01224 263264

This completes Part 1 of the Information Sheet.

If the information in Part 1 has interested you and you are considering participation, please continue to read the additional information in Part 2 before making any decision.

Part 2

What will happen if I don't want to continue with the study?

If you withdraw from the study, we will destroy all the data already collected up to that point unless you give consent for us to include that data. We would like to use the collected data, with your consent, in order to investigate if there is any pattern or common findings, in the scans taken from subjects who choose to withdraw from the study.

What if there is a problem?

Complaints: If you have a concern about any aspect of this study, you should ask to speak with the researchers who will do their best to answer your questions (Contact number: 01224 263264).

Harm: In the event that something does go wrong and you are harmed during the research study there are no special compensation arrangements. If you are harmed and this is due to someone's negligence then you may have grounds for a legal action for compensation against (Robert Gordon University, or NHS Grampian) but you may have to pay your legal costs.

Will my taking part in this study be kept confidential?

All information which is collected about you during the course of the research will be kept strictly confidential.

Involvement of your General Practitioner

With your consent, your GP will be informed of your participation in this study and the results of the MRI scans will be sent to them.

What will happen to any samples I give?

All data collected by the researcher will be securely stored on CD/DVDs as images of the spine. All data will be analysed by the researcher and information will be coded and any identifying information will be removed. All data from this study will be securely stored within the Robert Gordon University.

What will happen to the results of the study?

The study results will be published in medical journals and a summary will be sent to all participants. The overall project will also be written up as part of a PhD study by the researcher. At all times no participant will be identified in any way in the reports or publications.

Who is organising the research?

The research is organised by Mrs Lyndsay Alexander (lecturer at Robert Gordon University) as part of her PhD studies.

Who has reviewed this study?

This study was given a favourable ethical opinion for conduct in the NHS by the North of Scotland Research Ethics Service and by the School of Health Sciences, Research Management Group, Robert Gordon University.

All participants will be given a copy of the information sheet and a signed consent form to keep.

Thank you for taking time to read this information sheet and considering taking part in this study.

Appendix 12: Information sheet (NHS)



**ROBERT GORDON
UNIVERSITY • ABERDEEN**



Patient Information Sheet

STUDY: The effect of position and movement on the intervertebral disc

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Talk to others about the study if you wish.

- Part 1 tells you the purpose of this study and what will happen to you if you take part.
- Part 2 gives you more detailed information about the conduct of the study.

Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

Part 1

What is the purpose of the study?

People suffering from back pain are a common occurrence in society. Despite this, doctors, physiotherapists and other clinicians are still trying to understand how the spine works and moves in the upright position. We would like to invite you to help us improve our understanding of the spine in people with back pain. This will then allow us to compare how a spine works in someone with back pain compared to someone without back problems. In order to help you make up your mind, I have outlined what taking part would or would not involve. This project is a PhD research project.

Why have I been chosen?

We are inviting patients referred to physiotherapy to take part.

Do I have to take part?

No. It is up to you to decide whether or not to take part. If you do, you will be given this information sheet to keep and be asked to sign a consent form. You are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive in the future.

What will happen to me if I take part?

The researcher will telephone you at home in about a week to ask if you are interested in taking part in this study. She can answer any further questions you may have about taking part in this project. You will be invited to attend the Positional MRI Centre at Woodend Hospital, Aberdeen by the researcher at this time also. During the visit to the Positional MRI Centre, you will have a MRI scan of your back performed (in different standing, sitting and lying down positions) this assessment is painless and will take a maximum of 1.5 hours to complete.

What do I have to do?

You will have to stand, sit and lie down in the MRI scanner for about 10 minutes in each position. The assessments will be easier if you can bring comfortable clothing such as a t-shirt, track suit bottoms or shorts to wear. There are changing facilities within the Positional MRI Centre that you can use.

What are the possible risks of taking part?

A MRI scan does not include any potential risks for the participant. Some of the positions may be uncomfortable for people with back pain (such as sitting or bending forward), should you feel uncomfortable with any position at any time you can halt the assessments. As the MRI scan uses a magnetic effect to take the images no metallic objects or clothing should be worn whilst having a MRI scan performed. The radiographer performing your MRI scan will check for anything metal before you have your scan.

What are the possible benefits of taking part?

We cannot promise the study will help you but the information we get might help improve the treatment of people with back pain.

What happens when the research study stops?

After you have the MRI scans at the Positional MRI Centre, you will continue with your standard physiotherapy treatment.

What if there is a problem?

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2. A contact number for any complaints is Mrs E Hancock (Head of School, Health Sciences, Robert Gordon University, Aberdeen): 01224 263251

Will my taking part be kept confidential?

Yes. All the information about your participation in this study will be kept confidential. The details are included in Part 2.

Contact details

Further information can be obtained from: **Lyndsay Alexander, School of Health Sciences, Faculty of Health and Social Care, Robert Gordon University, Garthdee, Aberdeen**

Tel: 01224 263264

This completes Part 1 of the Information Sheet.

If the information in Part 1 has interested you and you are considering participation, please continue to read the additional information in Part 2 before making any decision.

Part 2

What will happen if I don't want to continue with the study?

If you withdraw from the study, we will destroy all the data already collected up to that point unless you give consent for us to include that data. We would like to use the collected data, with your consent, in order to investigate if there is any pattern or common findings, in the scans taken from subjects who choose to withdraw from the study.

What if there is a problem?

Complaints: If you have a concern about any aspect of this study, you should ask to speak with the researchers who will do their best to answer your questions (Contact number: 01224 263264). If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be obtained from the Positional MRI Centre.

Harm: In the event that something does go wrong and you are harmed during the research study there are no special compensation arrangements. If you are harmed and this is due to someone's negligence then you may have grounds for a legal action for compensation against (Robert Gordon University, or NHS Grampian) but you may have to pay your legal costs. The normal National Health Service complaints mechanisms will still be available to you.

Will my taking part in this study be kept confidential?

All information which is collected about you during the course of the research will be kept strictly confidential.

Involvement of your General Practitioner

With your consent, your GP will be informed of your participation in this study and the results of the MRI scans will be sent to them.

What will happen to any samples I give?

All data collected by the researcher will be securely stored on CD/DVDs as images of the spine. All data will be analysed by the researcher and information will be coded and any identifying information will be removed. All data from this study will be securely stored within the Robert Gordon University.

What will happen to the results of the study?

The study results will be published in medical journals and a summary will be sent to all participants. The overall project will also be written up as part of a PhD study by the researcher. At all times no participant will be identified in any way in the reports or publications.

Who is organising the research?

The research is organised by Mrs Lyndsay Alexander (lecturer at Robert Gordon University) as part of her PhD studies.

Who has reviewed this study?

This study was given a favourable ethical opinion for conduct in the NHS by the North of Scotland Research Ethics Service.

All participants will be given a copy of the information sheet and a signed consent form to keep.

Thank you for taking time to read this information sheet and considering taking part in this study.

Appendix 13: Consent form – DLBP subjects



**ROBERT GORDON
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Patient Identification Number for this trial:

CONSENT FORM

Title of Project: The effect of position and movement on the intervertebral disc

Name of Researcher: Mrs Lyndsay Alexander

Please initial box

1. I confirm that I have read and understand the information sheet dated 28/1/10

(version 3) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily.

2. I understand that my participation is voluntary and that I am free to withdraw at any time,

without giving any reason, without my medical care or legal rights being affected.

3. I understand that relevant sections of any of my medical notes and data collected during

the study, may be looked at by responsible individuals from Robert Gordon University, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.

4. I agree to my GP being informed of my participation in the study.

5. I agree to take part in the above study.

Name of Patient

Date

Signature

Name of Person taking consent
(if different from researcher)

Date

Signature

Researcher

Date

Signature

Appendix 14: Data collection form – DLBP subjects



Study

Number:

Study title: The response of the intervertebral disc to functional positions

Name:

Address:
.....
.....

Tel Number:.....

Date of Birth:

Physiotherapists name:.....

Physiotherapy dept:

GP Name:

GP Practice:.....
.....

.....

Height:

Weight:

Job title:

Are you signed off work due to back pain at the moment?

Yes

(Please tick)

No

If Yes, how long have you been signed off?

Appendix 15: Asymptomatic subjects' sagittal pMRI additional results

Further investigation of the positional effect in the sagittal plane was investigated using the paired t-test with graphical output to demonstrate the paired differences. This is presented in Table 15.1 and Figure 15.1 to 15.15.

Figure 15.1 to 15.15 all use a reference line (thick black line) positioned vertically on the x-axis at zero. Any significant differences between positions are displayed visually via a bias of the data to one side or the other of the histogram.

Table 15.1: Results of the paired t-test for sagittal plane Nucleus Pulposus migration from sagittal positional Magnetic Resonance Imaging scans.

	Mean	N	Mean difference	T value	Significance (2-tailed)
Standing	17.61	55	-3.72	-5.537	0.001*
Neutral sitting	21.32	55			
Standing	17.61	55	-3.56	-5.824	0.001*
Flexed sitting	21.17	55			
Standing	17.61	55	-0.73	-1.035	0.305
Extended sitting	18.33	55			
Standing	17.61	55	0.24	0.381	0.705
Supine	17.37	55			
Standing	17.61	55	1.53	2.602	0.012
Prone extension	16.08	55			
Neutral sitting	21.32	55	0.15	0.279	0.781
Flexed sitting	21.17	55			
Neutral sitting	21.32	55	2.99	5.641	0.001*
Extended sitting	18.33	55			
Neutral sitting	21.32	55	3.95	6.089	0.001*
Supine	17.37	55			

Neutral sitting	21.32	55	5.24	10.184	0.001*
Prone extension	16.08	55			
Flexed sitting	21.17	55	2.84	5.067	0.001*
Extended sitting	18.33	55			
Flexed sitting	21.17	55	3.80	6.079	0.001*
Supine	17.37	55			
Flexed sitting	21.17	55	5.09	9.126	0.001*
Prone extension	16.08	55			
Extended sitting	18.33	55	0.96	1.388	0.171
Supine	17.37	55			
Extended sitting	18.33	55	2.26	3.777	0.001*
Prone extension	16.08	55			
Supine	17.37	55	1.29	2.80	0.007
Prone extension	16.08	55			

Key: * = significant at p<0.003 level

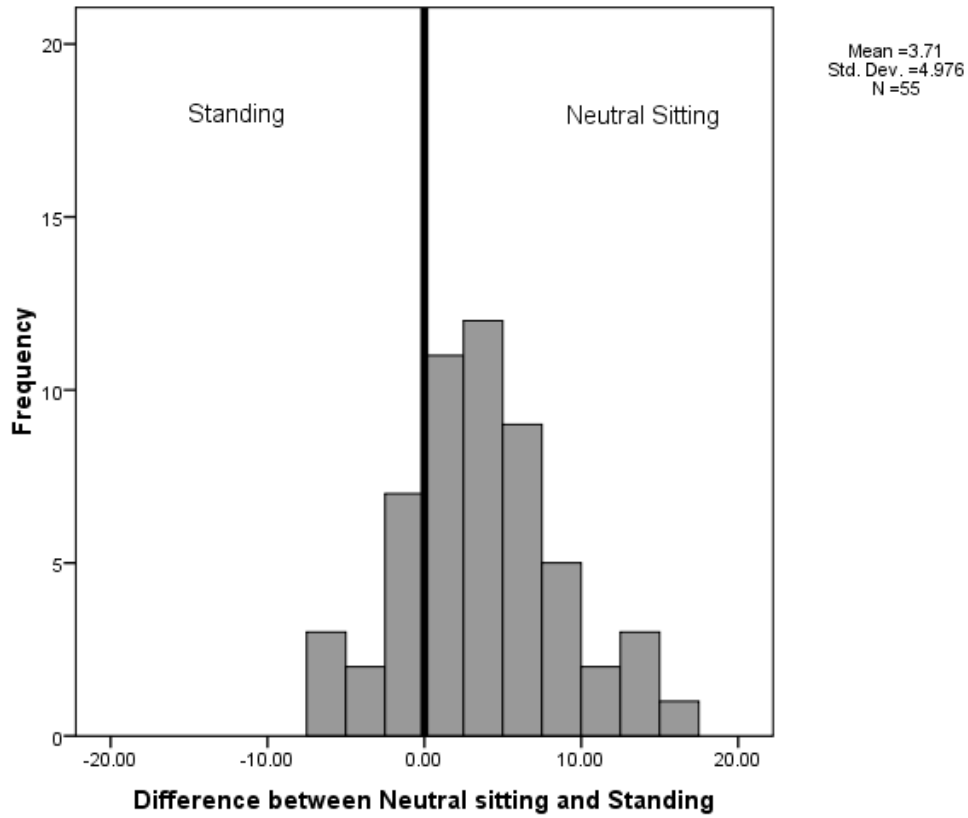


Figure 15.1: Asymptomatic subjects' sagittal positional Magnetic Resonance Imaging scan paired differences between Neutral Sitting and Standing (significant difference demonstrated, $p < 0.001$).

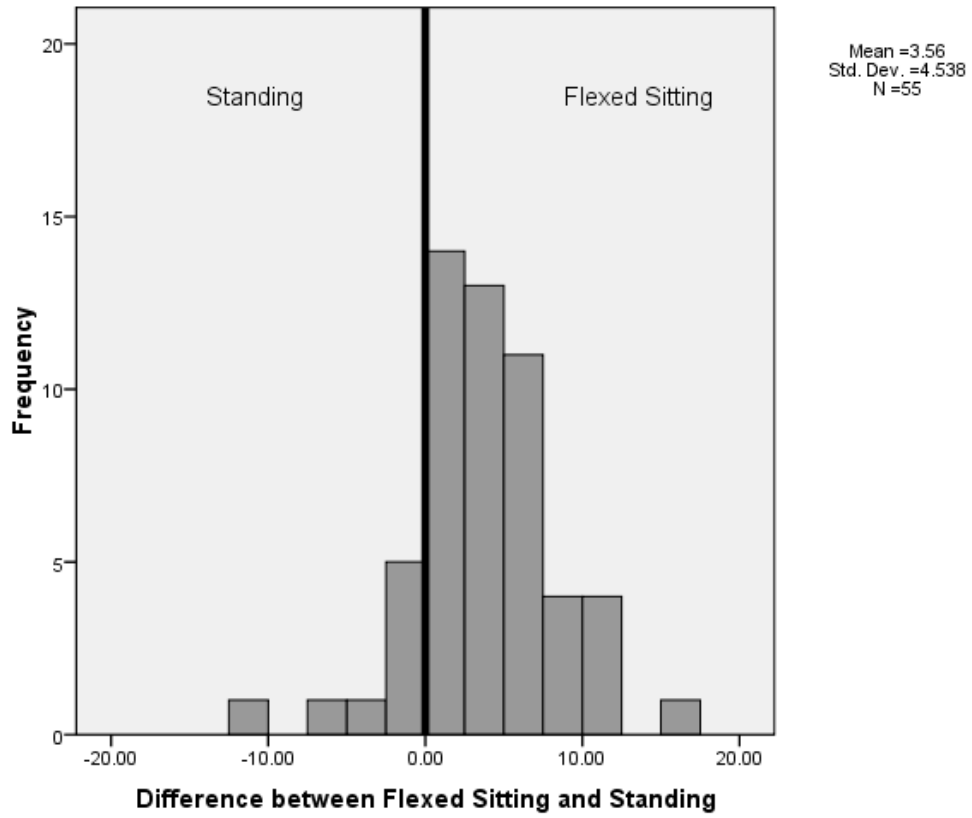


Figure 15.2: Asymptomatic subjects' sagittal positional Magnetic Resonance Imaging scan paired differences between Flexed Sitting and Standing (significant difference demonstrated, $p < 0.001$).

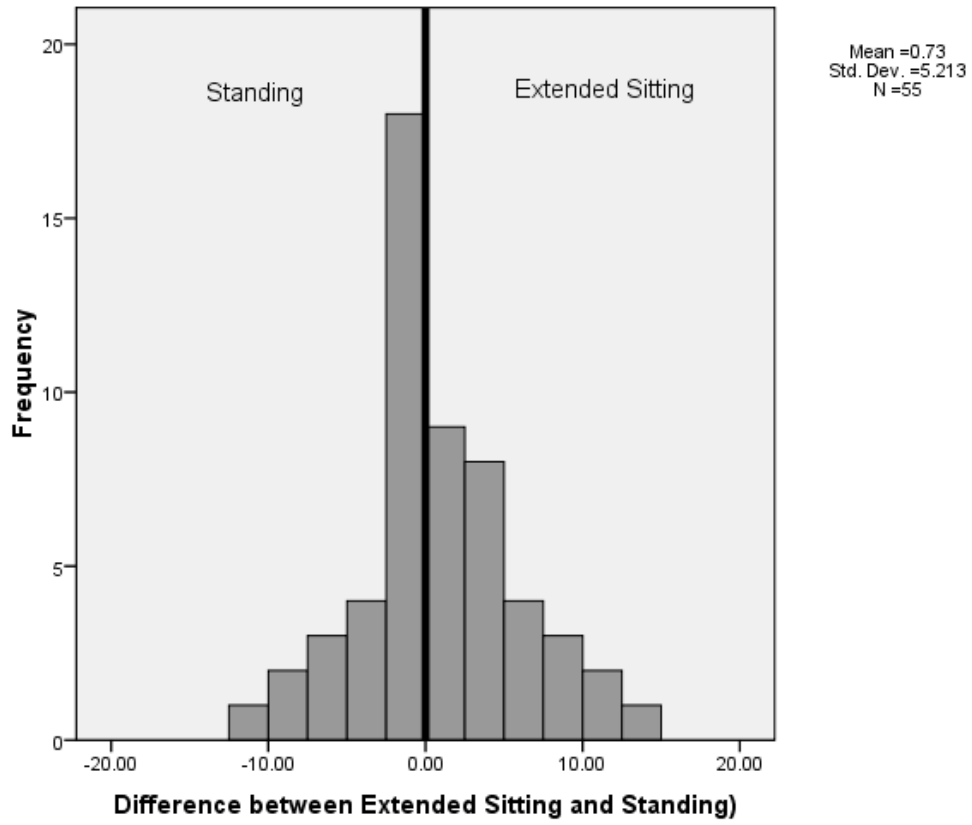


Figure 3.2.8: Asymptomatic subjects' sagittal positional Magnetic Resonance Imaging scan paired differences between Extended Sitting and Standing (non-significant difference demonstrated, $p=0.305$).

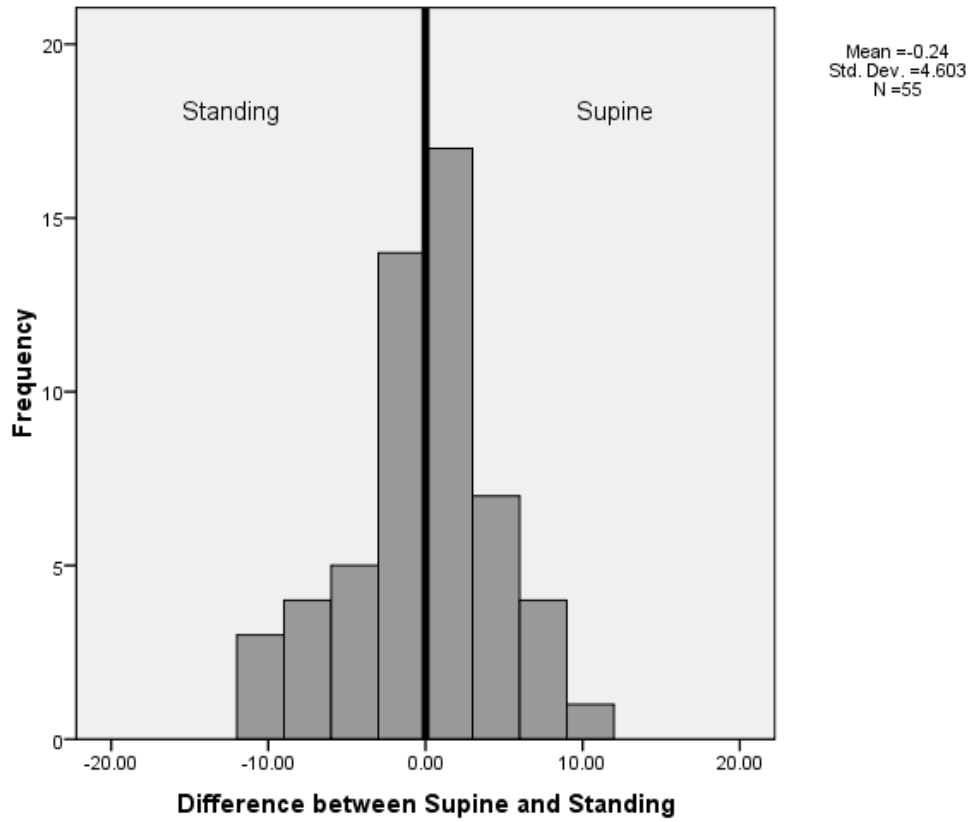


Figure 3.2.9: Asymptomatic subjects' sagittal positional Magnetic Resonance Imaging scan paired differences between Supine and Standing (non-significant difference demonstrated, $p=0.705$).

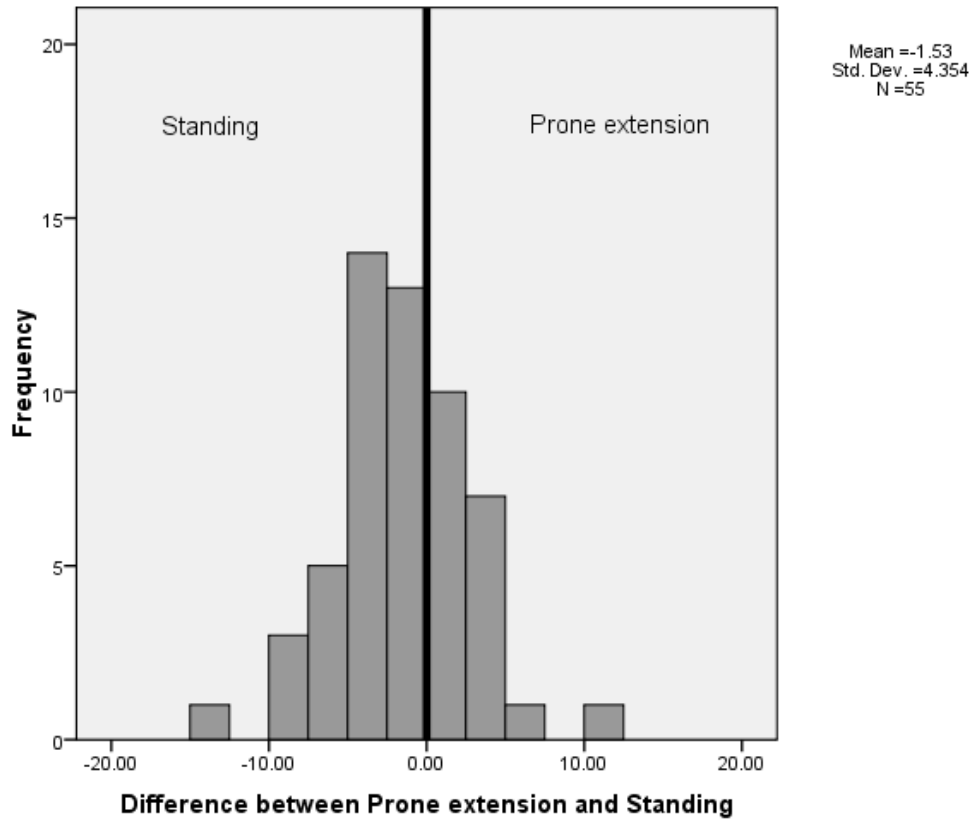


Figure 3.2.10: Asymptomatic subjects' sagittal positional Magnetic Resonance Imaging scan paired differences between Prone extension and Standing (non-significant difference demonstrated, $p=0.012$).

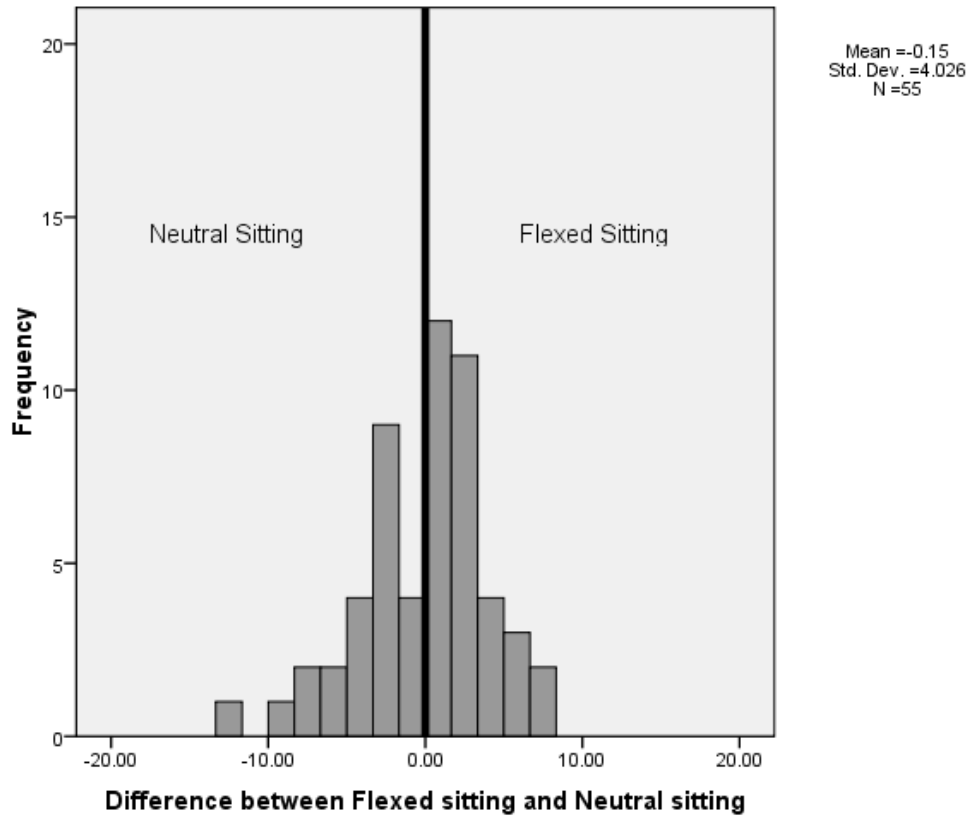


Figure 3.2.11: Asymptomatic subjects' sagittal positional Magnetic Resonance Imaging scan paired differences between Flexed sitting and Neutral sitting (non-significant difference demonstrated, $p=0.781$).

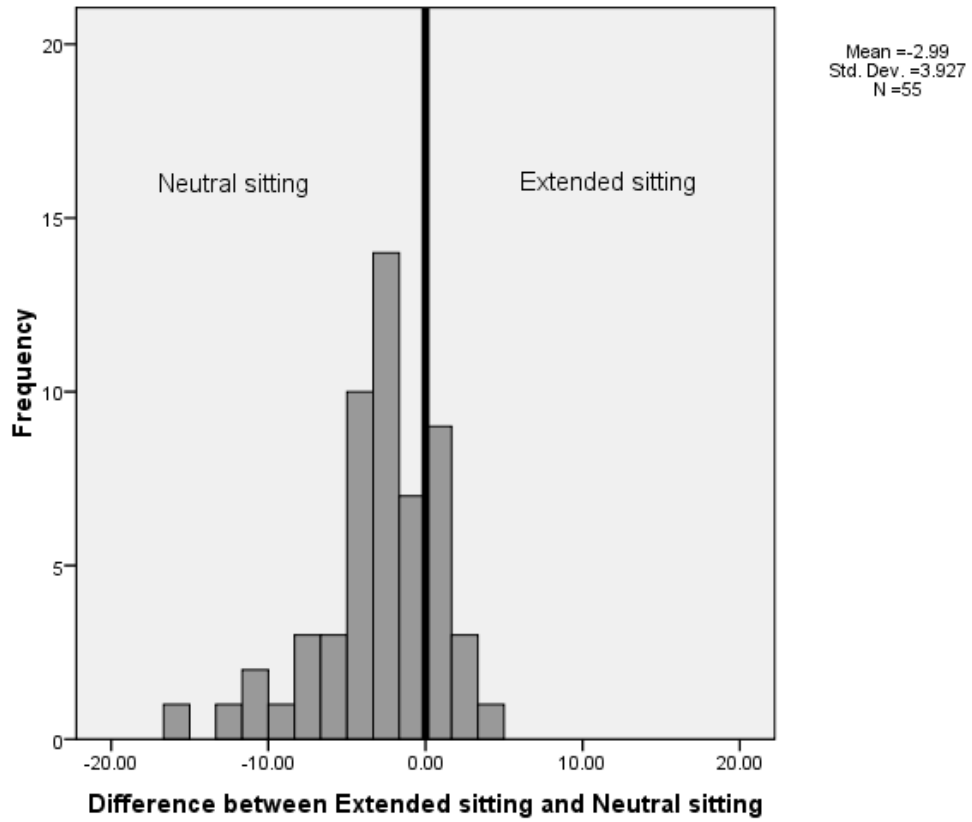


Figure 3.2.12: Asymptomatic subjects' sagittal positional Magnetic Resonance Imaging scan paired differences between Extended sitting and Neutral sitting (significant difference demonstrated, $p < 0.001$).

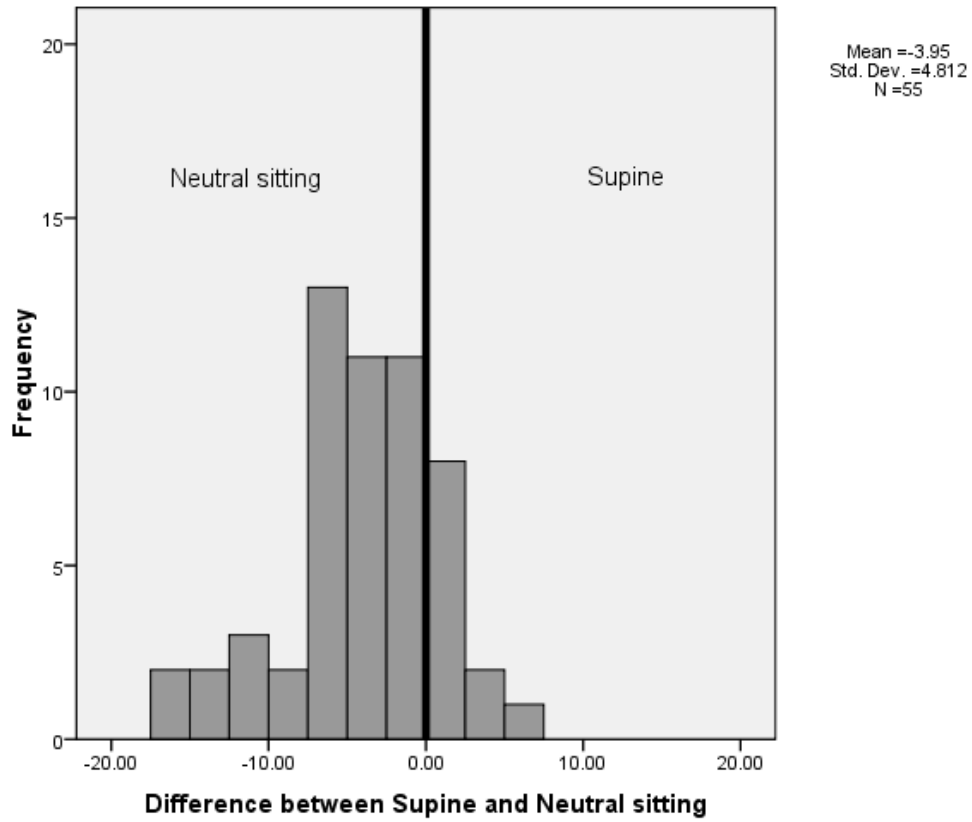


Figure 3.2.13: Asymptomatic subjects' sagittal positional Magnetic Resonance Imaging scan paired differences between Supine and Neutral sitting (significant difference demonstrated, $p < 0.001$).

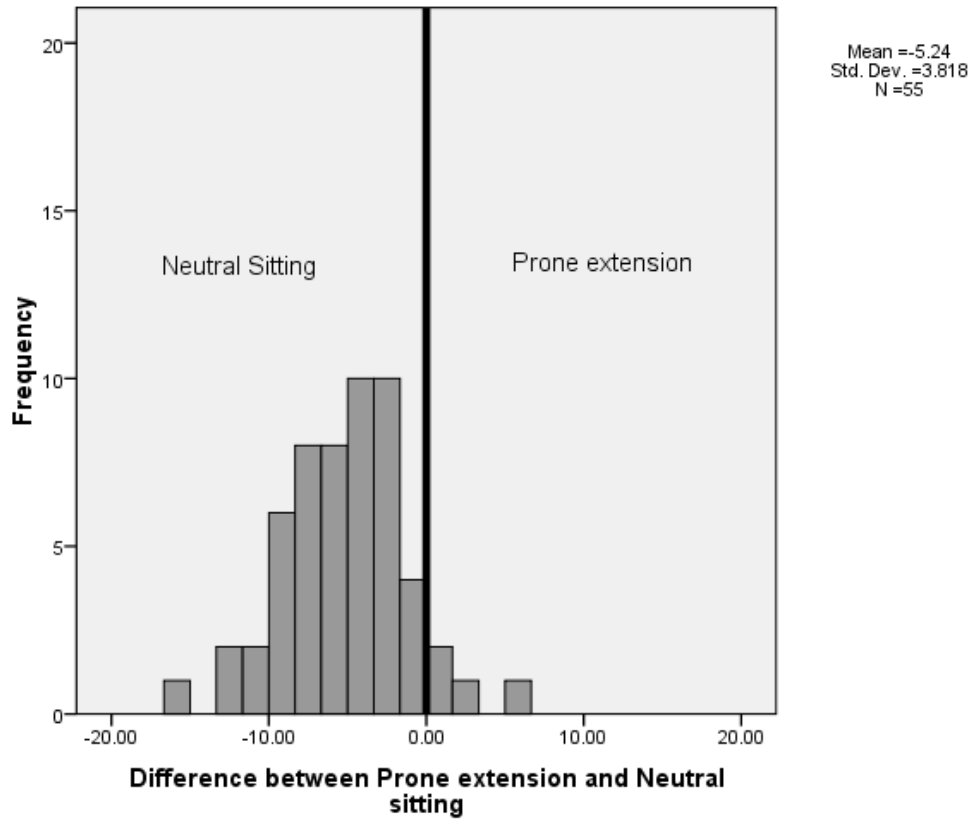


Figure 3.2.14: Asymptomatic subjects' sagittal positional Magnetic Resonance Imaging scan paired differences between Prone extension and Neutral sitting (significant difference demonstrated, $p < 0.001$).

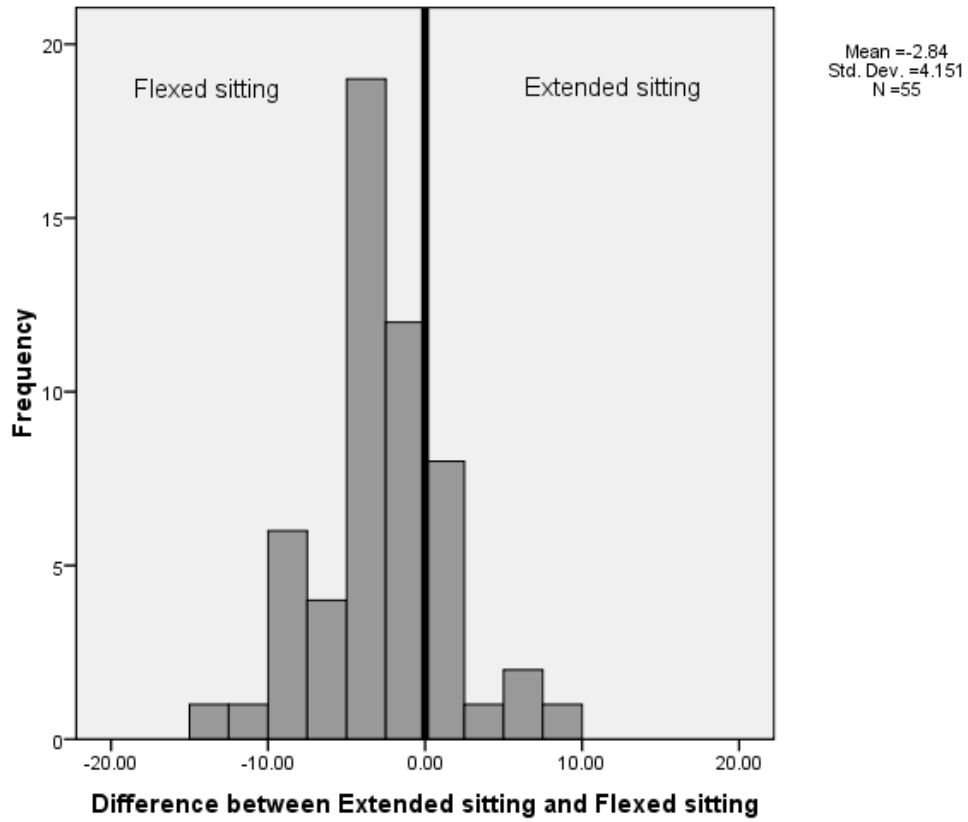


Figure 3.2.15: Asymptomatic subjects' sagittal positional Magnetic Resonance Imaging scan paired differences between Extended sitting and Flexed sitting (significant difference demonstrated, $p < 0.001$).

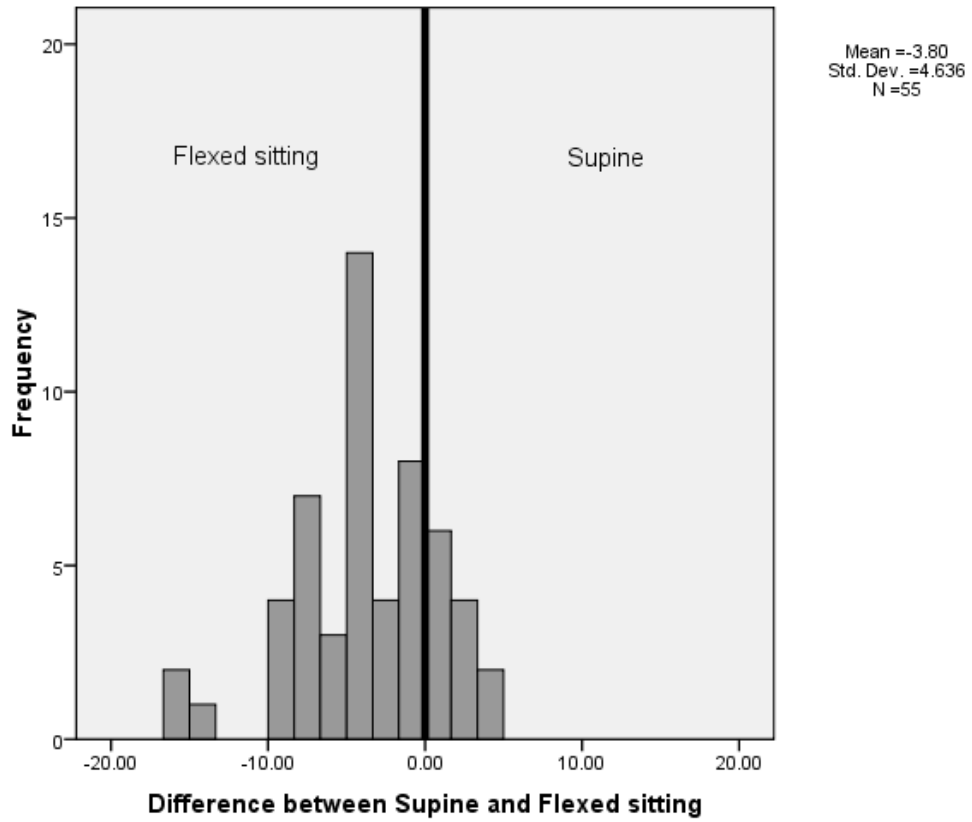


Figure 3.2.16: Asymptomatic subjects' sagittal positional Magnetic Resonance Imaging scan paired differences between Supine and Flexed sitting (significant difference demonstrated, $p < 0.001$).

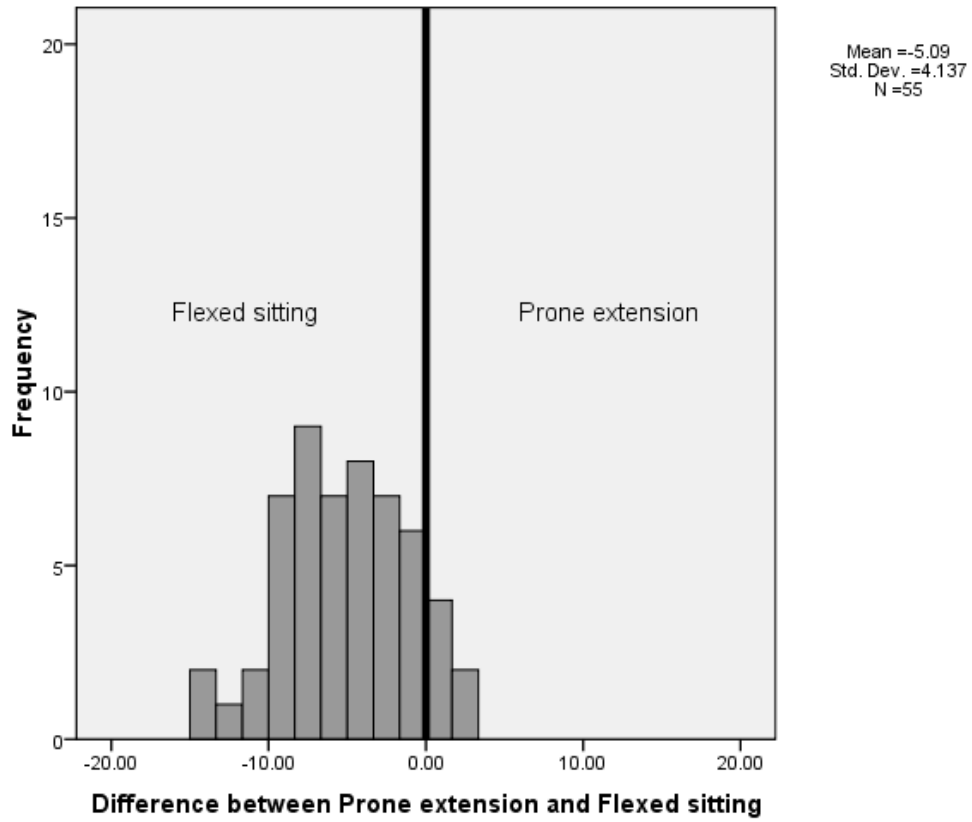


Figure 3.2.17: Asymptomatic subjects' sagittal positional Magnetic Resonance Imaging scan paired differences between Prone extension and Flexed sitting (significant difference demonstrated, $p < 0.001$).

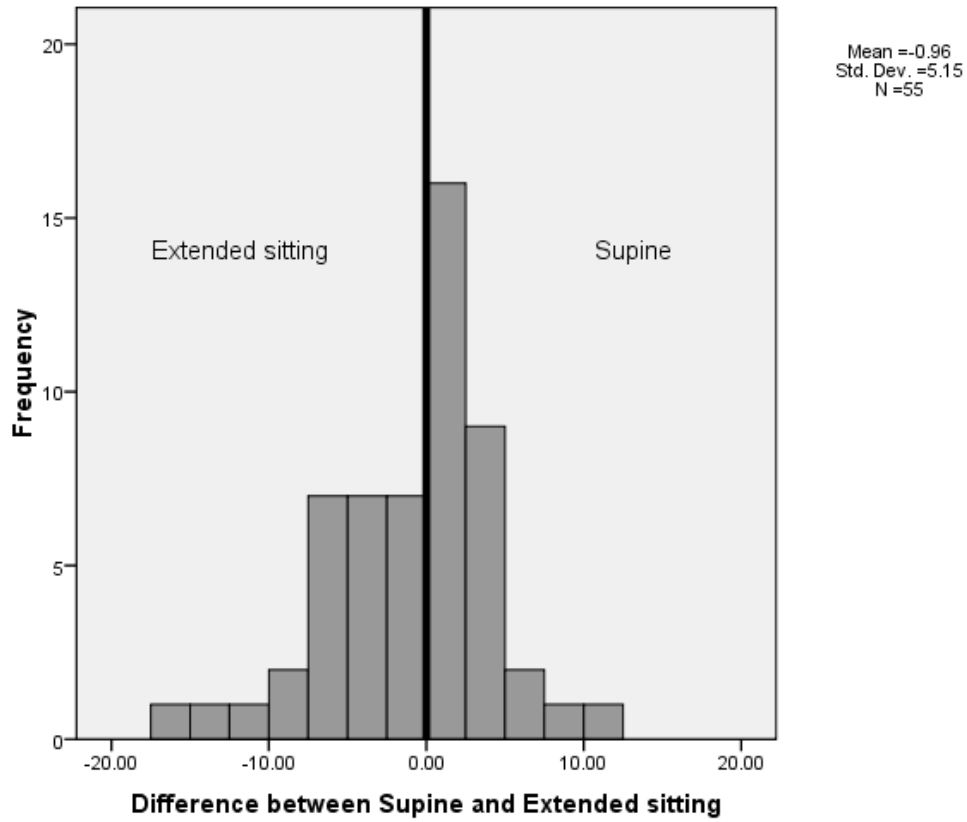


Figure 3.2.18: Asymptomatic subjects' sagittal positional Magnetic Resonance Imaging scan paired differences between Supine and Extended sitting (non-significant difference demonstrated, $p=0.171$).

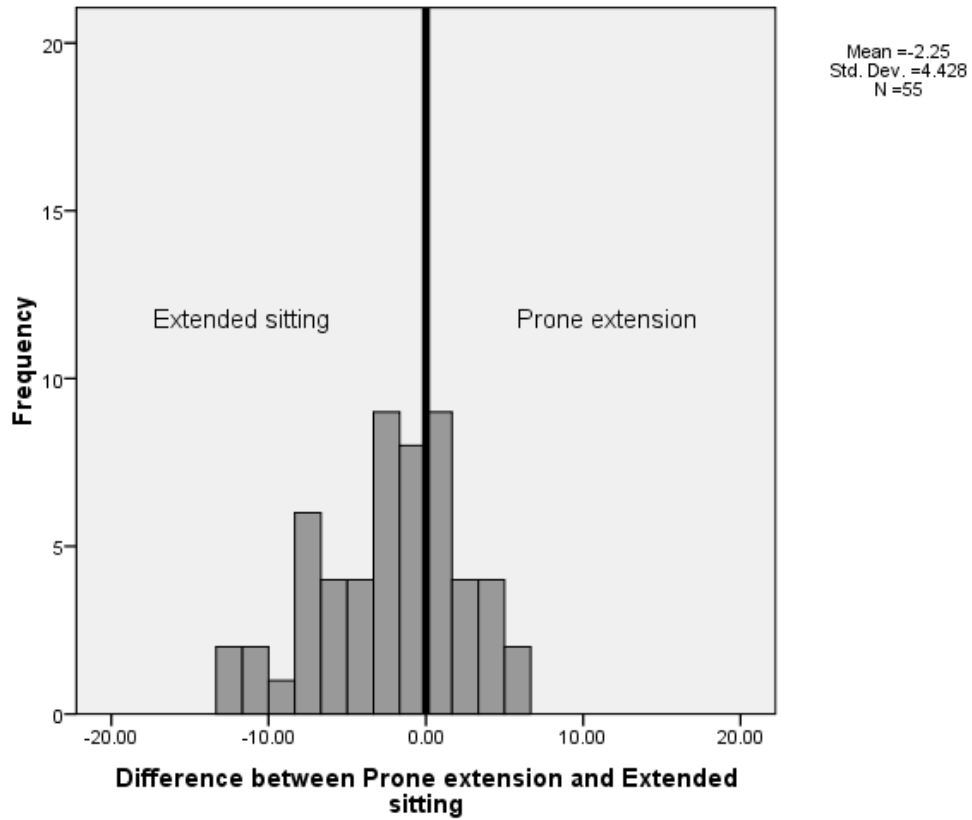


Figure 3.2.19: Asymptomatic subjects' sagittal positional Magnetic Resonance Imaging scan paired differences between Prone extension and Extended sitting (significant difference demonstrated, $p < 0.001$).

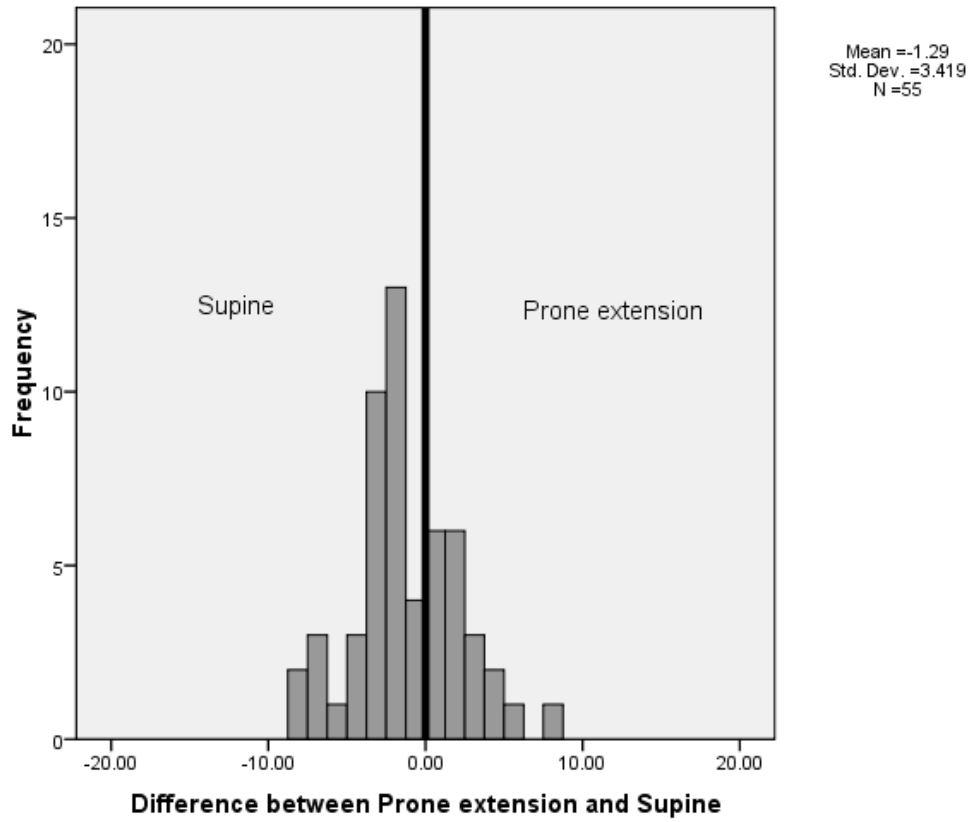


Figure 3.2.20: Asymptomatic subjects' sagittal positional Magnetic Resonance Imaging scan paired differences between Prone extension and Supine (non-significant difference demonstrated, $p=0.007$).

Appendix 16: Asymptomatic subjects' axial pMRI additional results

Further investigation of the positional effect from the axial pMRI scans was investigated using the paired t-test with graphical output to demonstrate the paired differences. This is presented in Table 16.1 and Figure 16.1 to 16.15.

Following the same principle as Appendix 15, Figure 16.1 to 16.15 all use a reference line (thick black line) positioned vertically on the x-axis at zero. Any significant differences between positions are displayed visually via a bias of the data to one side or the other of the histogram.

Table 16.1: Results of paired t-test for sagittal plane Nucleus Pulposus migration from axial positional Magnetic Resonance Imaging scans.

	Mean	N	Mean Difference	T value	Significance (2-tailed)
Standing	22.50	35	-2.81	-4.011	.001*
Neutral sitting	25.31	35			
Standing	22.64	30	-3.75	-3.695	.001*
Flexed sitting	26.39	30			
Standing	22.77	37	-.96	-1.217	.231
extended sitting	23.73	37			
Standing	22.50	35	-.76	-.903	.373
Supine	23.26	35			
Standing	22.54	33	.80	.887	.382
Prone extension	21.74	33			
Neutral sitting	25.64	26	-.77	-.874	.391
Flexed sitting	26.41	26			
Neutral sitting	25.40	34	1.80	2.083	.045
Extended sitting	23.61	34			
Neutral sitting	25.42	37	2.24	2.513	.017
Supine	23.18	37			
Neutral sitting	25.30	34	3.43	4.071	.001*
Prone extension	21.86	34			
Flexed sitting	26.70	31	2.64	3.809	.001*

Extended sitting	24.06	31			
Flexed sitting	26.84	27	3.36	3.359	.002*
Supine	23.48	27			
Flexed sitting	26.78	26	4.49	3.561	.002*
Prone extension	22.30	26			
Extended sitting	24.17	35	1.19	1.255	.218
Supine	22.98	35			
Extended sitting	23.84	32	1.41	1.386	.176
Prone extension	22.44	32			
Supine	23.80	35	1.74	1.854	.072
Prone extension	22.06	35			

Key: * = significant at p<0.003 level

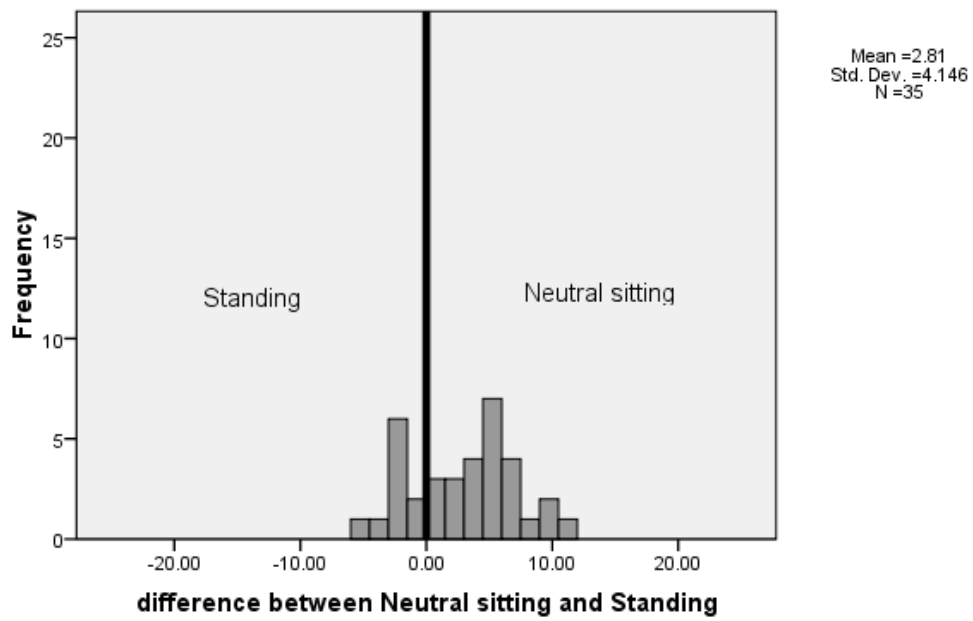


Figure 16.1: Asymptomatic subjects' axial positional Magnetic Resonance Imaging scan paired differences between Neutral Sitting and Standing (significant difference demonstrated, $p < 0.001$).

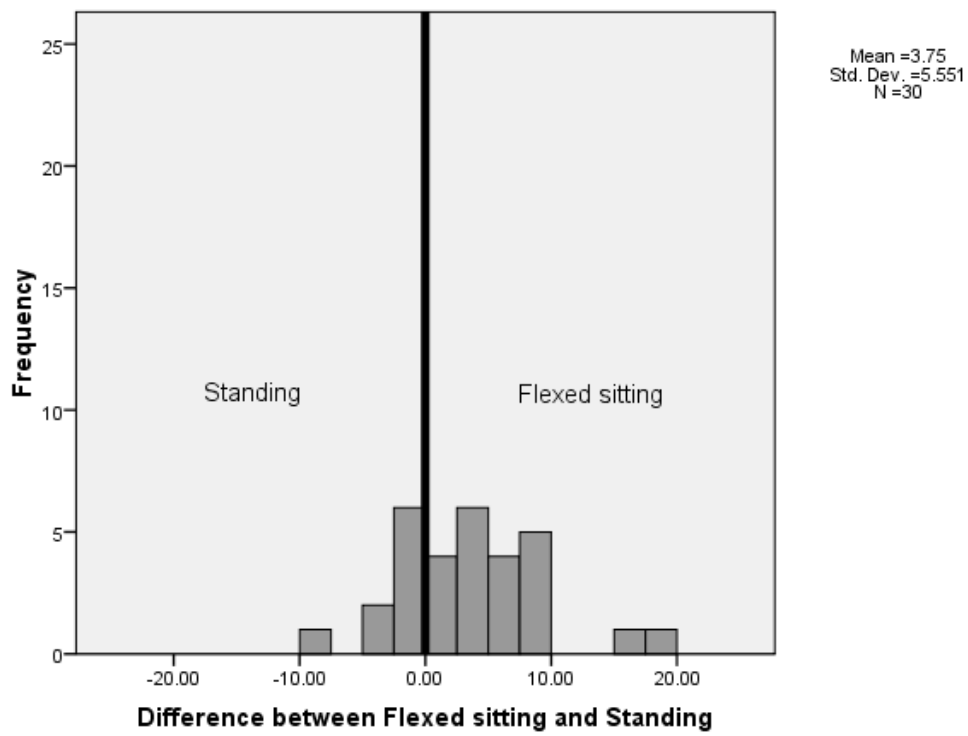


Figure 16.2: Asymptomatic subjects' axial positional Magnetic Resonance Imaging scan paired differences between Flexed Sitting and Standing (significant difference demonstrated, $p < 0.001$).

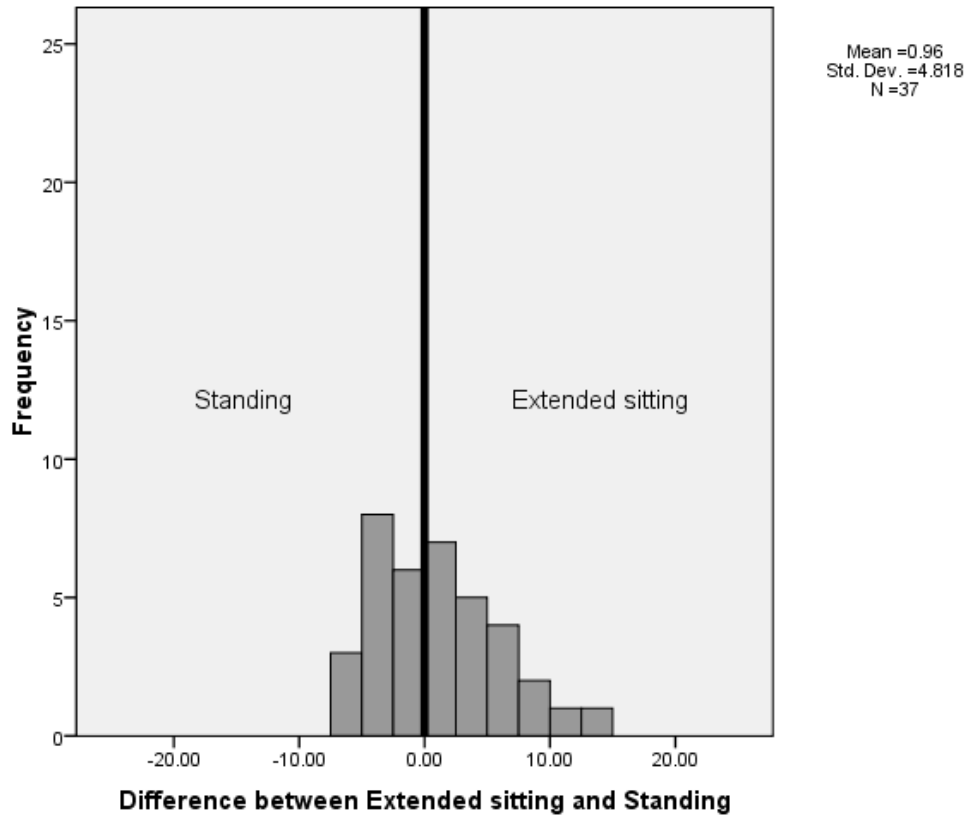


Figure 3.2.23: Asymptomatic subjects' axial positional Magnetic Resonance Imaging scan paired differences between Extended Sitting and Standing (non-significant difference demonstrated, $p=0.231$).

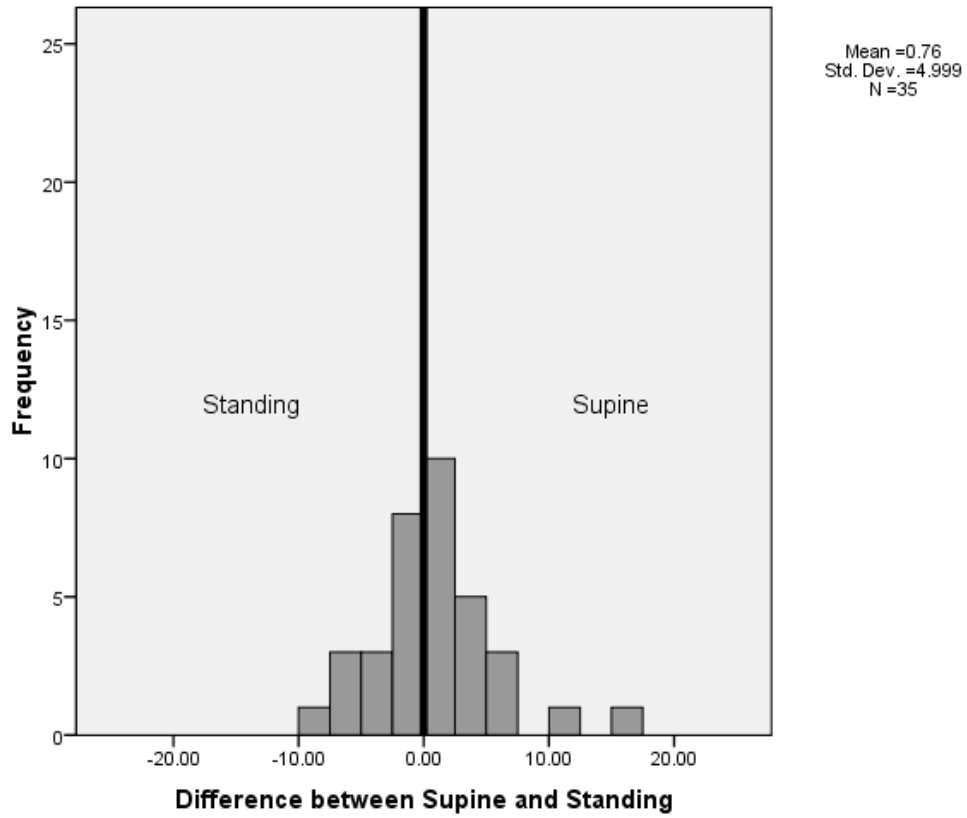


Figure 3.2.24: Asymptomatic subjects' axial positional Magnetic Resonance Imaging scan paired differences between Supine and Standing (non-significant difference demonstrated, $p=0.373$).

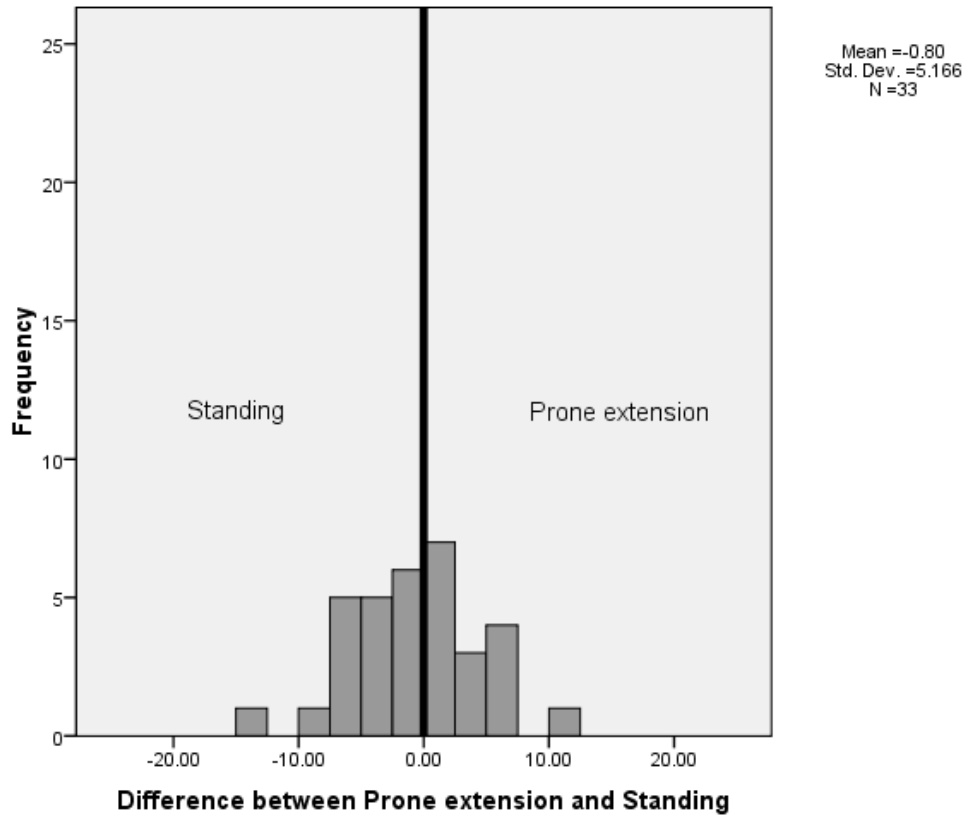


Figure 3.2.25: Asymptomatic subjects' axial positional Magnetic Resonance Imaging scan paired differences between Prone extension and Standing (non-significant difference demonstrated, $p=0.382$).

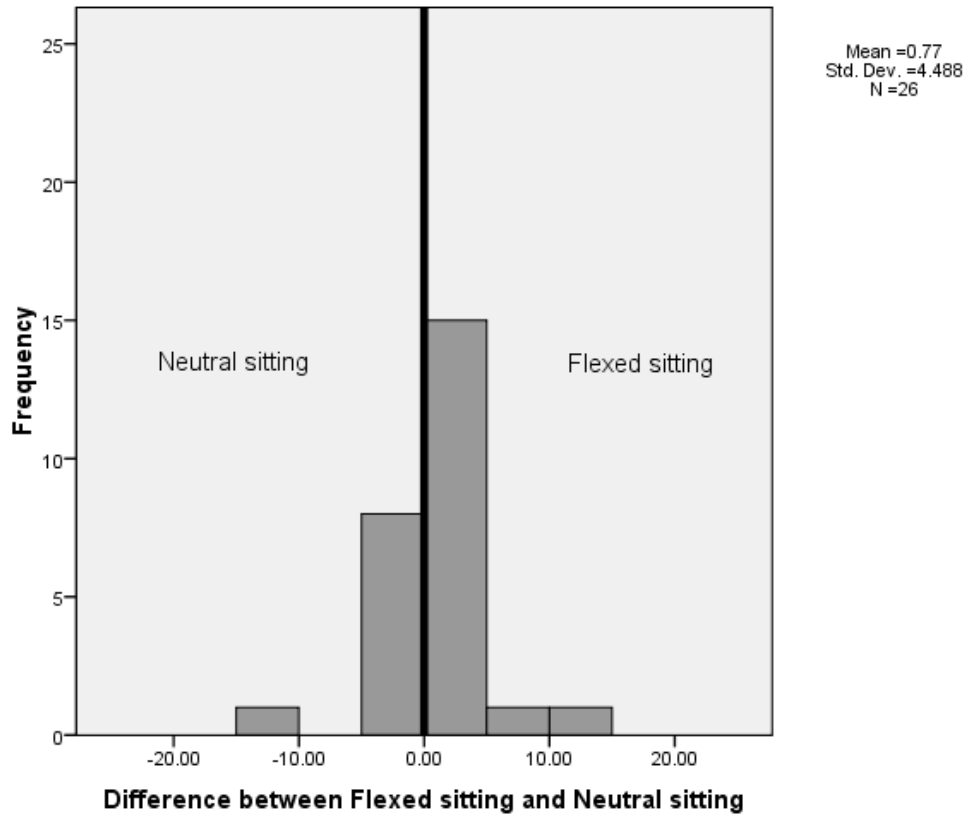


Figure 3.2.26: Asymptomatic subjects' axial positional Magnetic Resonance Imaging scan paired differences between Flexed sitting and Neutral sitting (non-significant difference demonstrated, $p=0.391$).

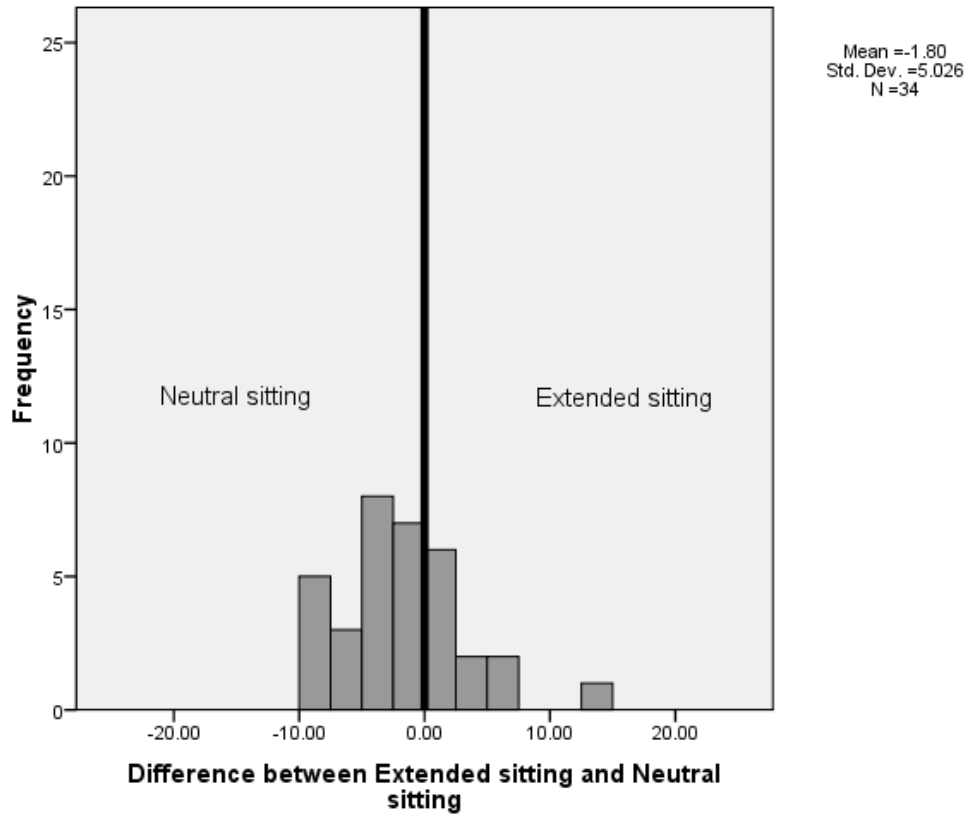


Figure 3.2.27: Asymptomatic subjects' axial positional Magnetic Resonance Imaging scan paired differences between Extended sitting and Neutral sitting (non-significant difference demonstrated, $p=0.045$).

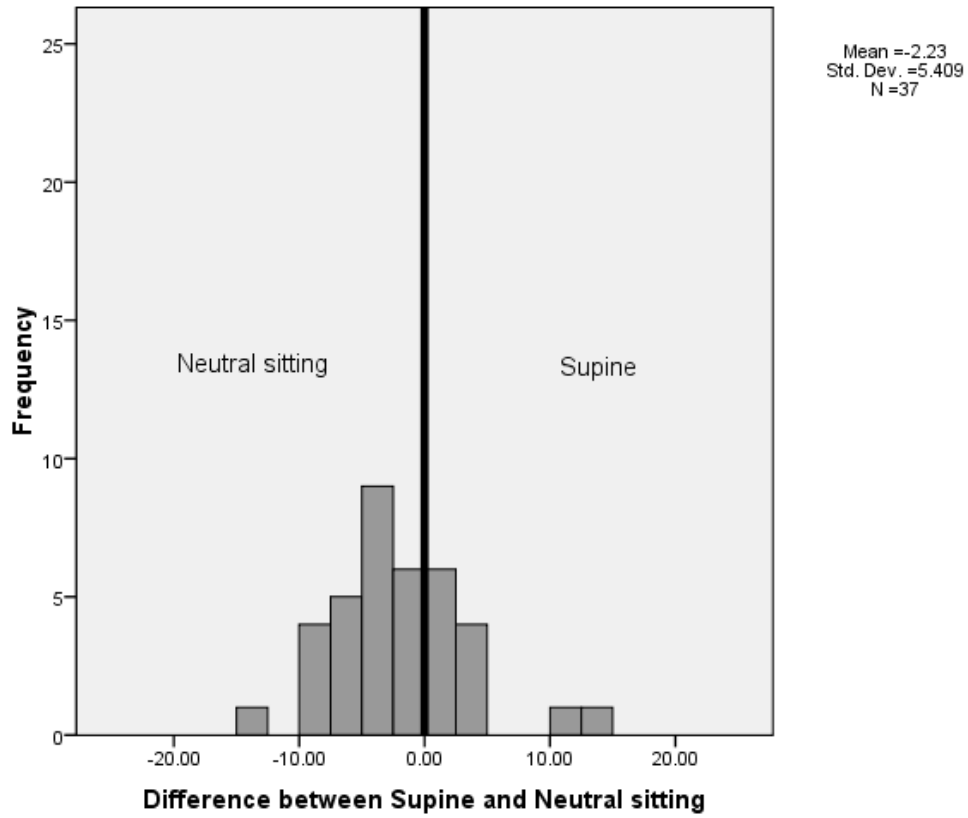


Figure 3.2.28: Asymptomatic subjects' axial positional Magnetic Resonance Imaging scan paired differences between Supine and Neutral sitting (non-significant difference demonstrated, $p=0.017$).

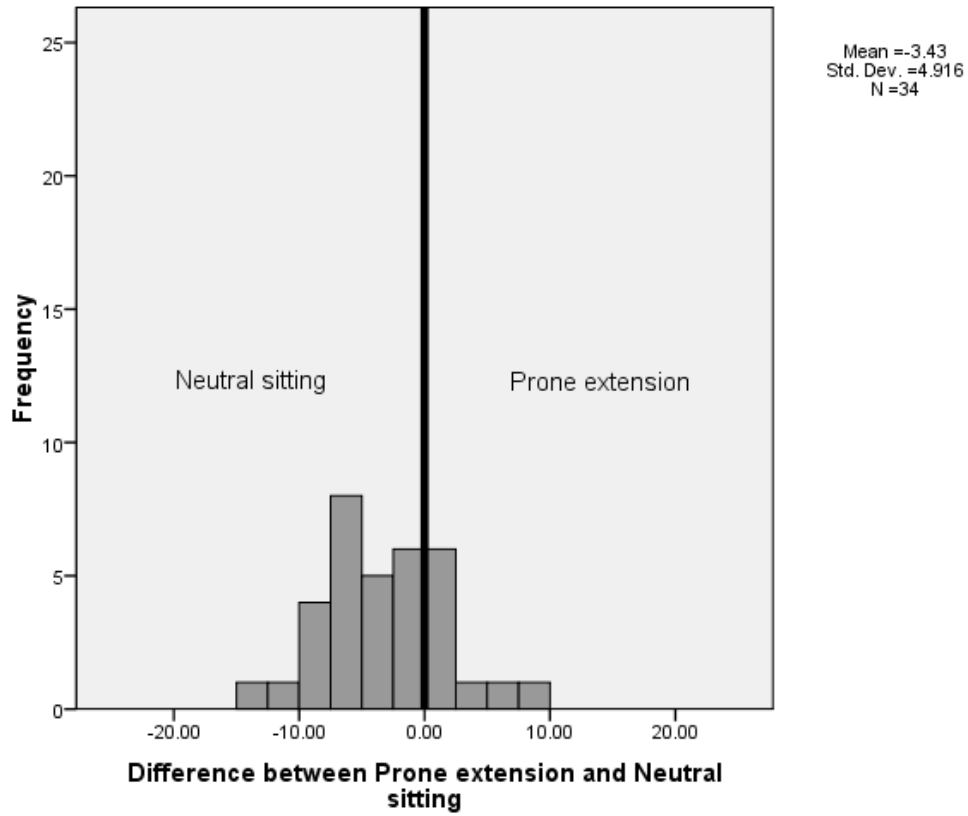


Figure 3.2.29: Asymptomatic subjects' axial positional Magnetic Resonance Imaging scan paired differences between Prone extension and Neutral sitting (significant difference demonstrated, $p < 0.001$).

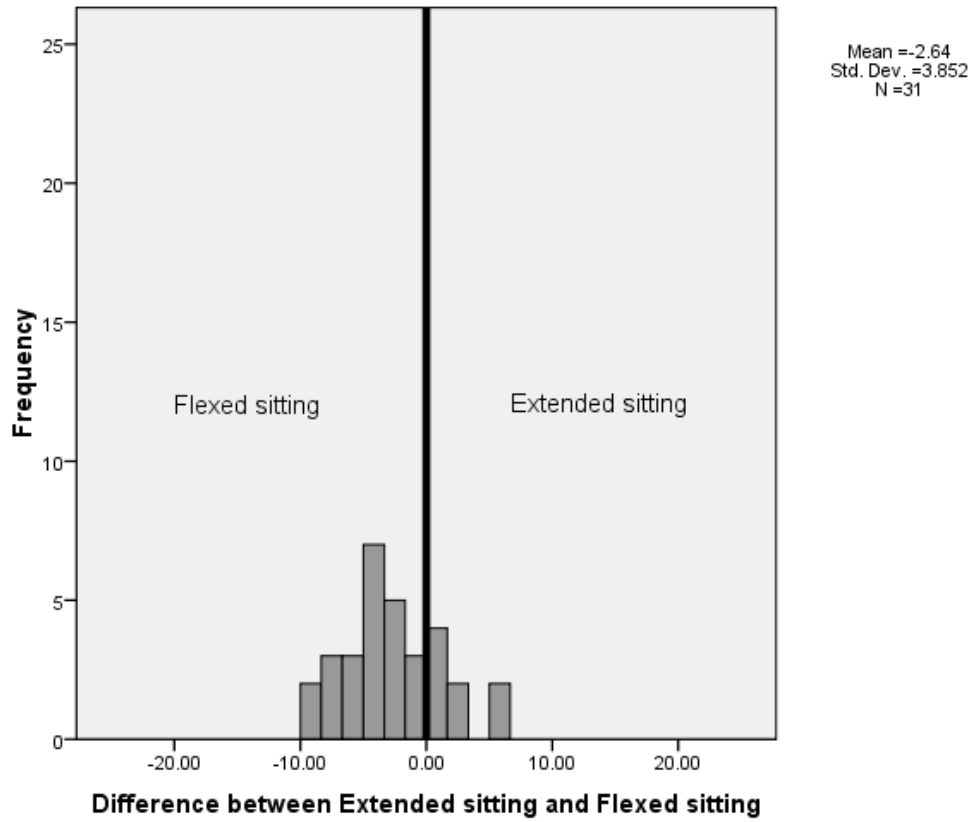


Figure 3.2.30: Asymptomatic subjects' axial positional Magnetic Resonance Imaging scan paired differences between Extended sitting and Flexed sitting (significant difference demonstrated, $p < 0.001$).

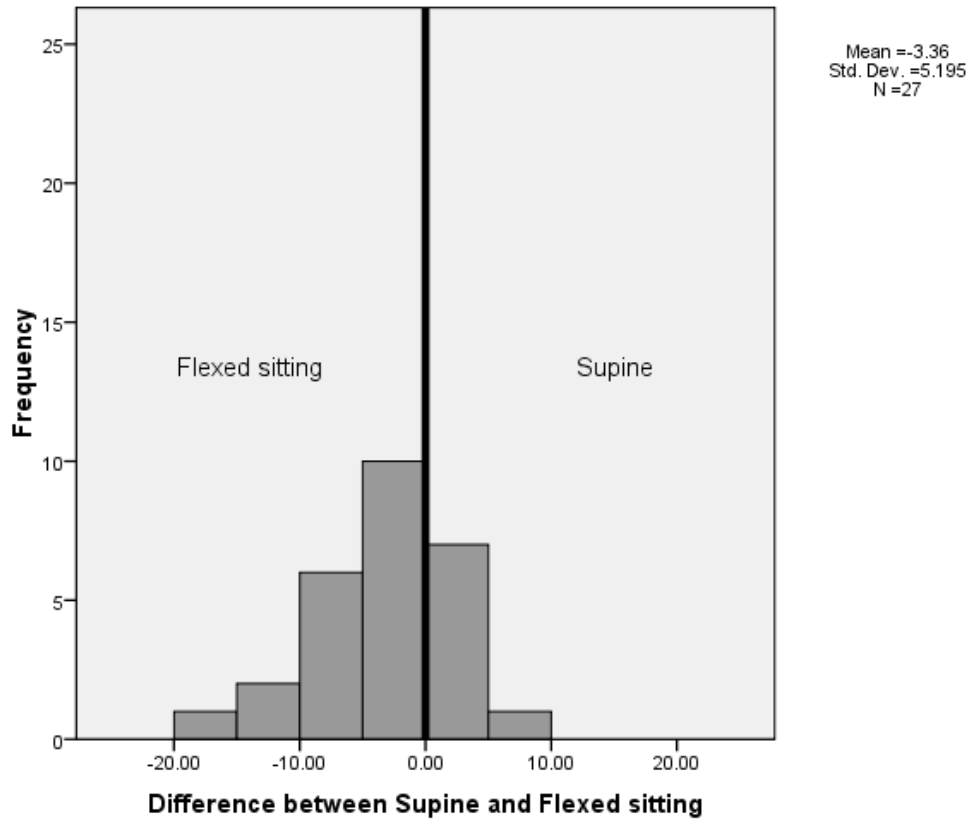


Figure 3.2.31: Asymptomatic subjects' axial positional Magnetic Resonance Imaging scan paired differences between Supine and Flexed sitting (significant difference demonstrated, $p < 0.002$).

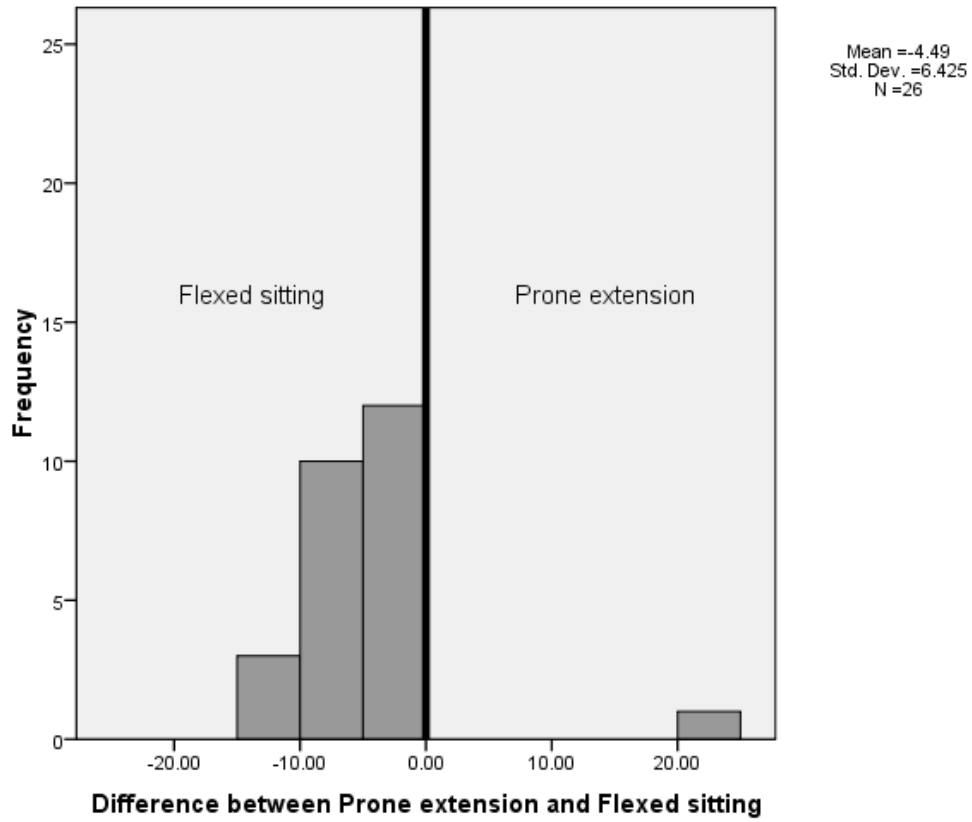


Figure 3.2.32: Asymptomatic subjects' axial positional Magnetic Resonance Imaging scan paired differences between Prone extension and Flexed sitting (significant difference demonstrated, $p < 0.002$).

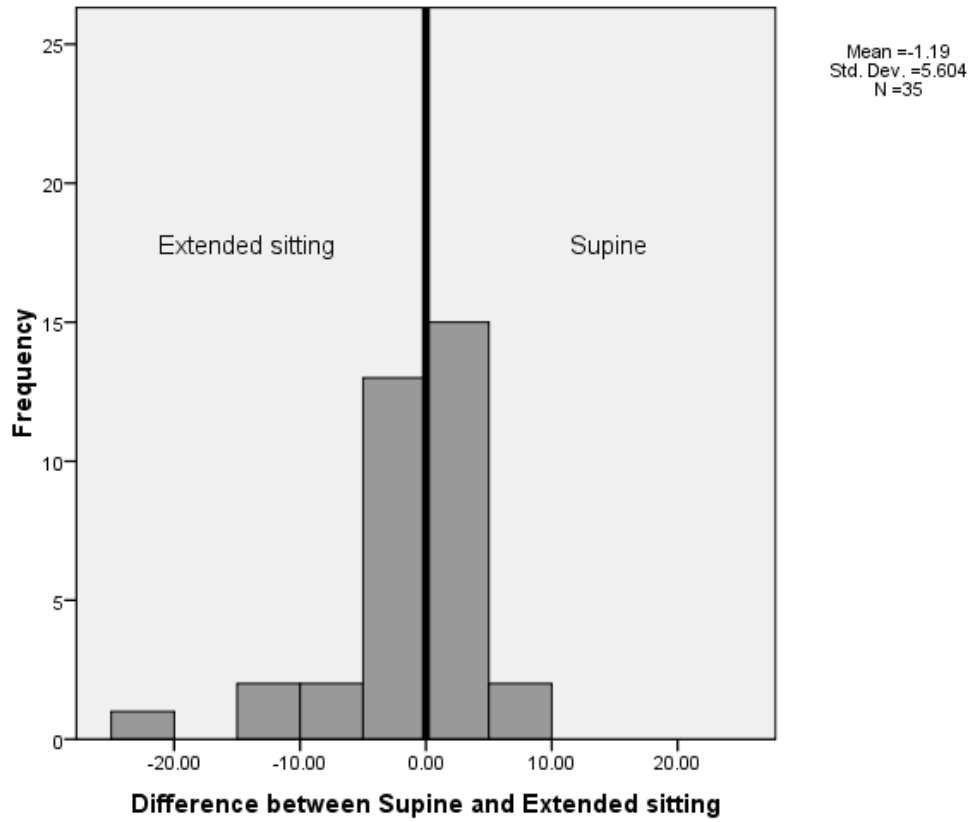


Figure 3.2.33: Asymptomatic subjects' axial positional Magnetic Resonance Imaging scan paired differences between Supine and Extended sitting (non-significant difference demonstrated, $p=0.218$).

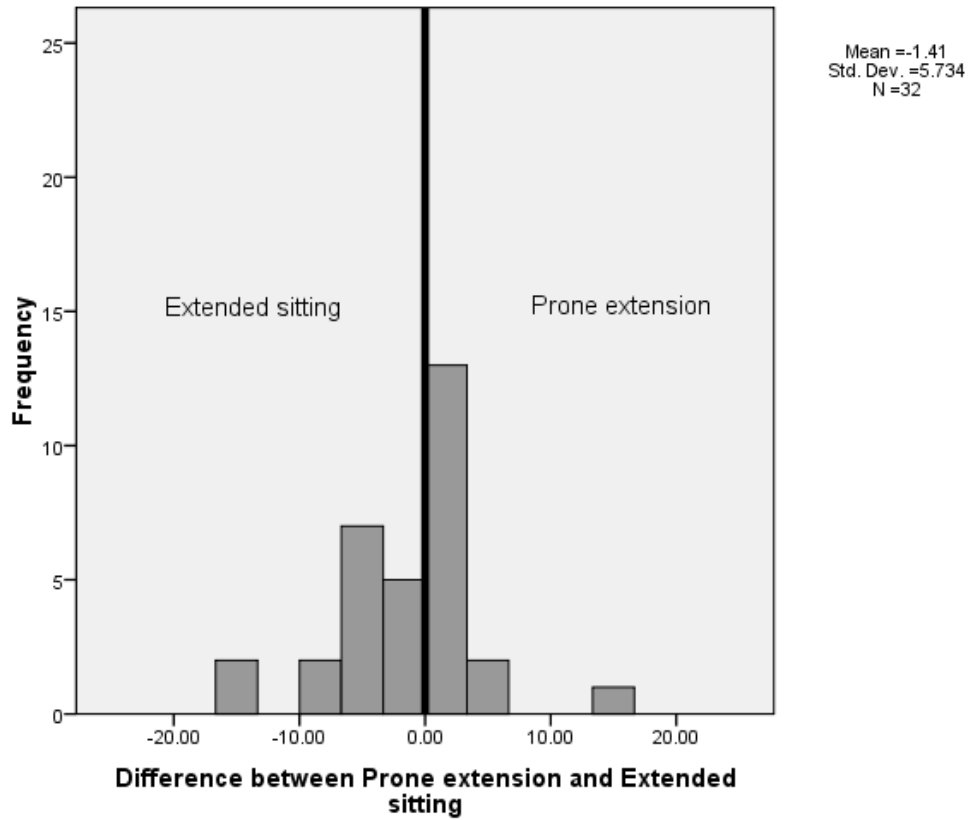


Figure 3.2.34: Asymptomatic subjects' axial positional Magnetic Resonance Imaging scan paired differences between Prone extension and Extended sitting (non-significant difference demonstrated, $p=0.176$).

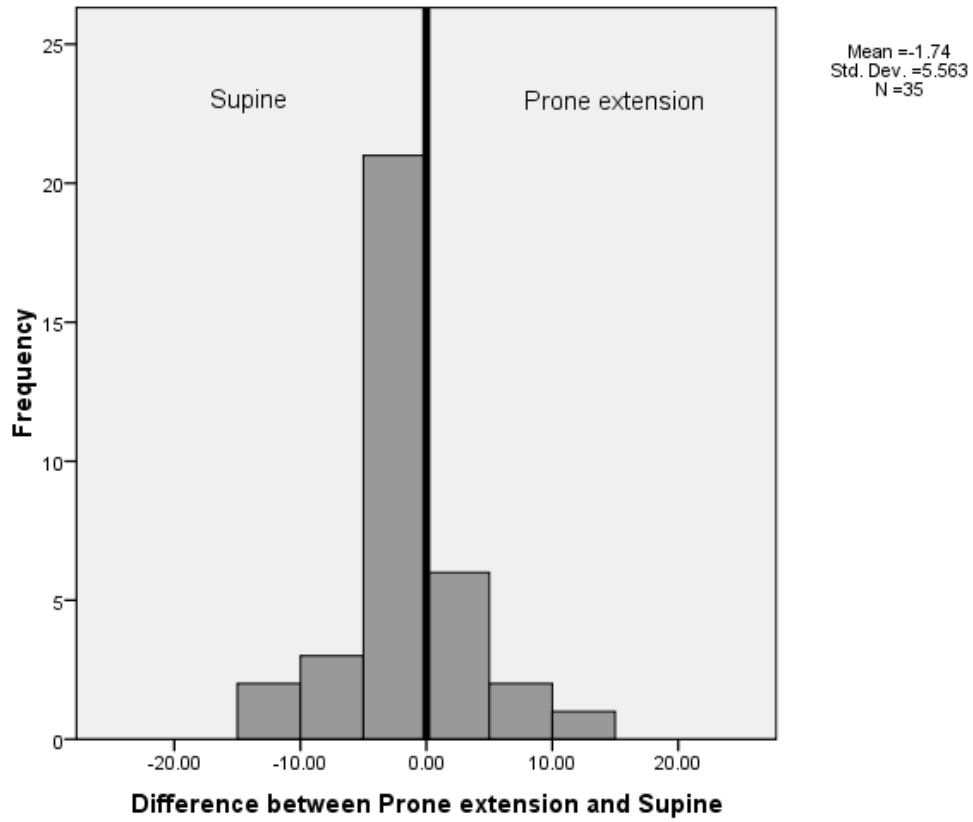


Figure 3.2.35: Asymptomatic subjects' axial positional Magnetic Resonance Imaging scan paired differences between Prone extension and Supine (non-significant difference demonstrated, $p=0.072$).

Appendix 17: DLBP subjects' sagittal pMRI additional results

Further investigation of the positional effect in the sagittal plane was investigated using the paired t-test with graphical output to demonstrate the paired differences. This is presented in Table 17.1 and Figure 17.1 to 17.15.

Figure 17.1 to 17.15 all use a reference line (thick black line) positioned vertically on the x-axis at zero. Any significant differences between positions are displayed visually via a bias of the data to one side or the other of the histogram.

Table 17.1: Paired t-test results for different effects between positions

Comparison	N	Group means	Mean difference	t-value	Significance level (2 tailed)
N.Sit & F.Sit	165	N.Sit = 17.8421 F.Sit = 18.7072	-0.86515	-2.014	0.046
N.Sit & E.Sit	150	N.Sit = 17.9995 E.Sit = 15.4601	2.53940	4.791	0.001*
N.Sit & St	150	N.Sit = 17.8172 St = 15.4401	2.37713	4.920	0.001*
N.Sit & Supine	160	N.Sit = 17.7911 Supine = 15.0458	2.74537	5.596	0.001*
N.Sit & EIL	154	N.Sit = 17.6834 EIL = 14.5626	3.12078	6.597	0.001*
F.Sit & E.Sit	145	F.Sit = 18.9197 E.Sit = 15.7037	3.21607	6.343	0.001*
F.Sit & St	145	F.Sit = 18.8554 St = 15.4989	3.35648	6.677	0.001*
F.Sit & Supine	155	F.Sit = 18.9206 Supine = 15.2065	3.71419	7.441	0.001*

F.Sit & EIL	149	F.Sit = 18.8683 EIL = 14.7291	4.13913	8.130	0.001*
E.Sit & St	145	E.Sit = 15.3748 St = 15.5541	-0.17931	-0.345	0.730
E.Sit & Supine	145	E.Sit = 15.2370 Supine = 14.9057	0.33131	0.601	0.548
E.Sit & EIL	139	E.Sit = 15.1296 EIL = 14.5970	0.53259	1.090	0.278
St & Supine	145	St = 15.3196 Supine = 14.6827	0.63690	1.288	0.200
St & EIL	144	St = 15.2894 EIL = 14.5485	0.74090	1.520	0.131
Supine & EIL	154	Supine = 14.8809 EIL = 14.5626	0.31831	0.653	0.515

Key: N.Sit – Neutral sitting; F.Sit = flexed sitting; E.Sit = extended sitting; St = standing; EIL = prone extension; * significant at the $p < 0.003$ level (with Bonferroni correction).

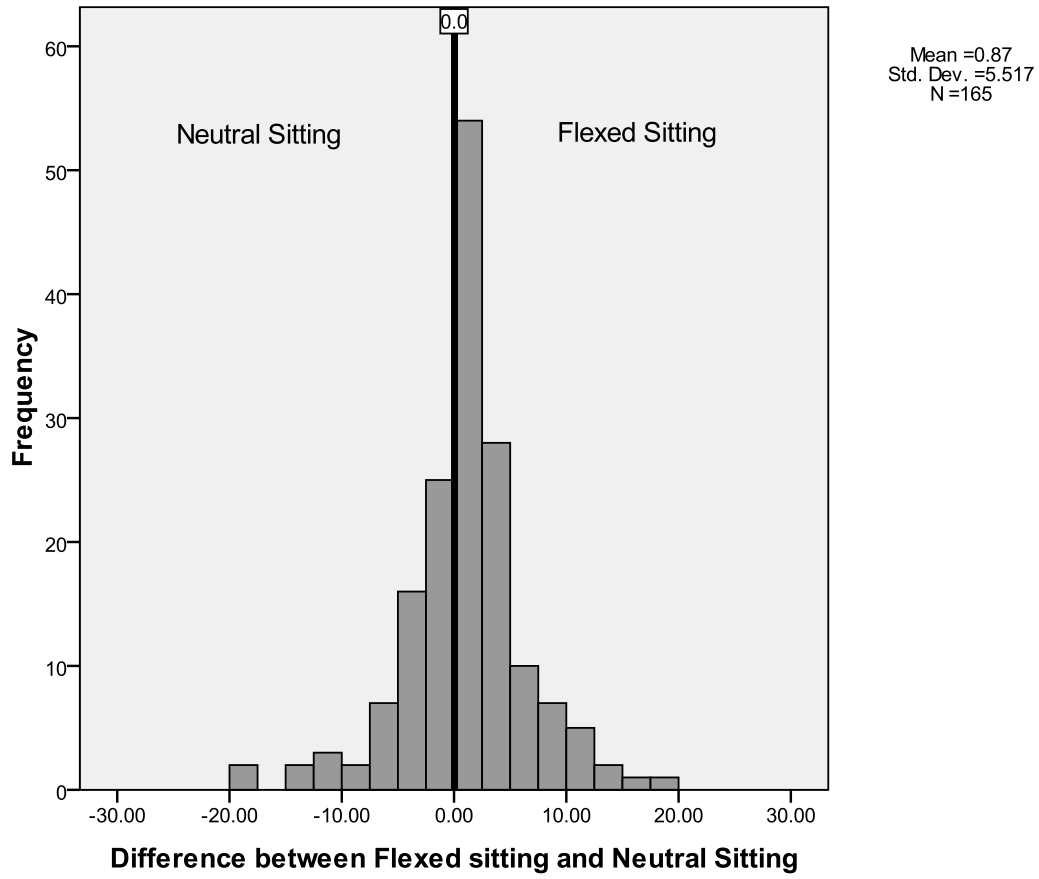


Figure 17.1: Sagittal paired differences between Flexed sitting and Neutral sitting (Non-significant difference, $p=0.046$)

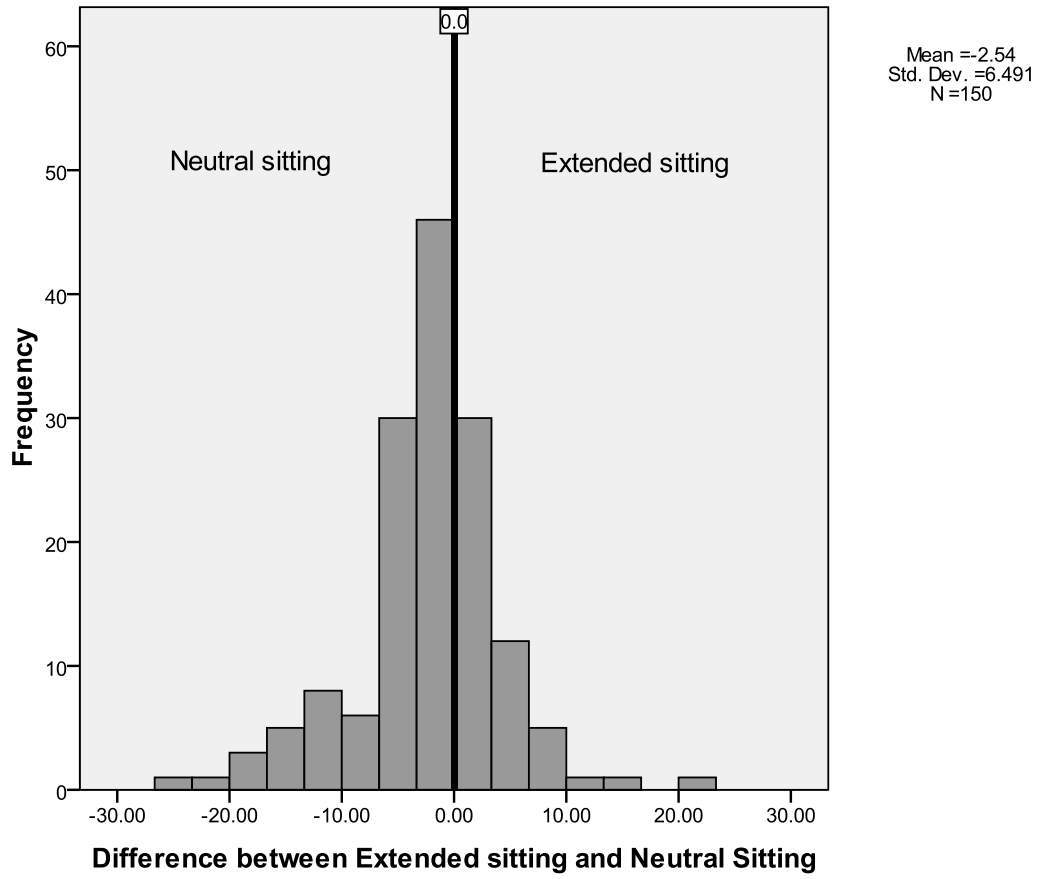


Figure 17.2: Sagittal paired differences between Extended sitting and Neutral sitting (significant difference demonstrated, $p < 0.001$)

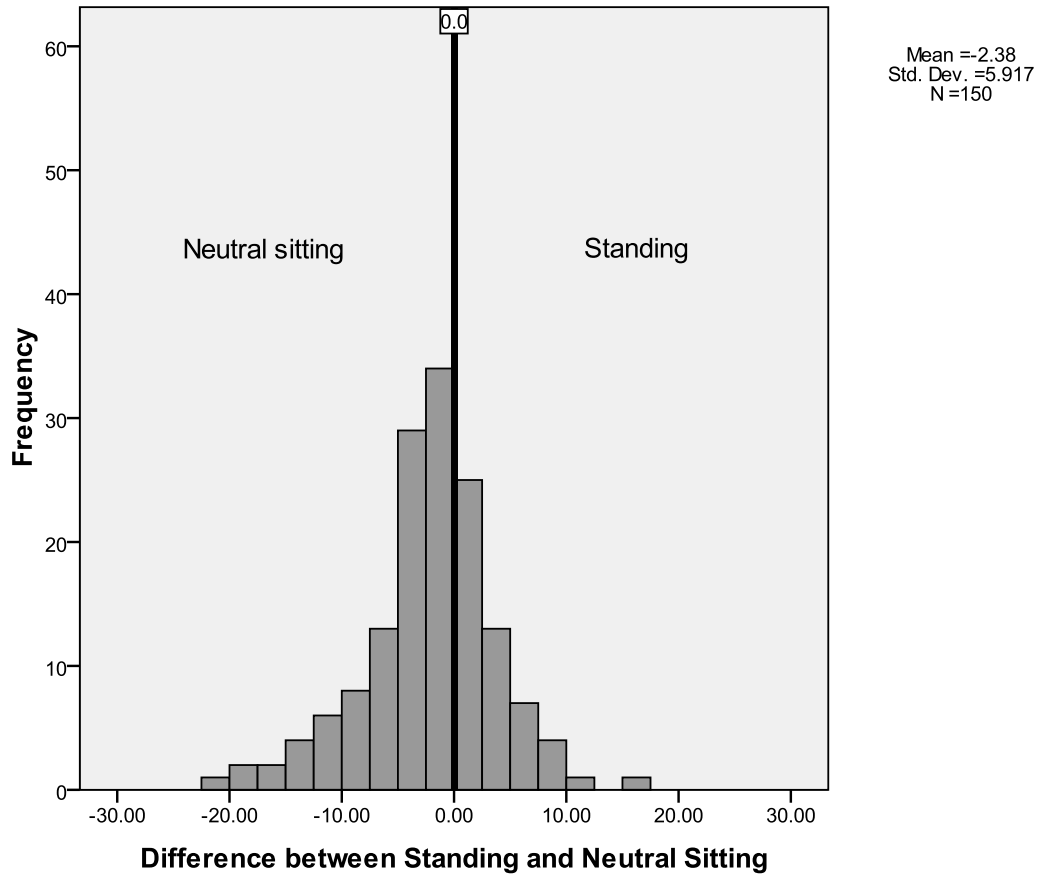


Figure 17.3: Sagittal paired differences between Standing and Neutral sitting (significant difference demonstrated, $p < 0.001$)

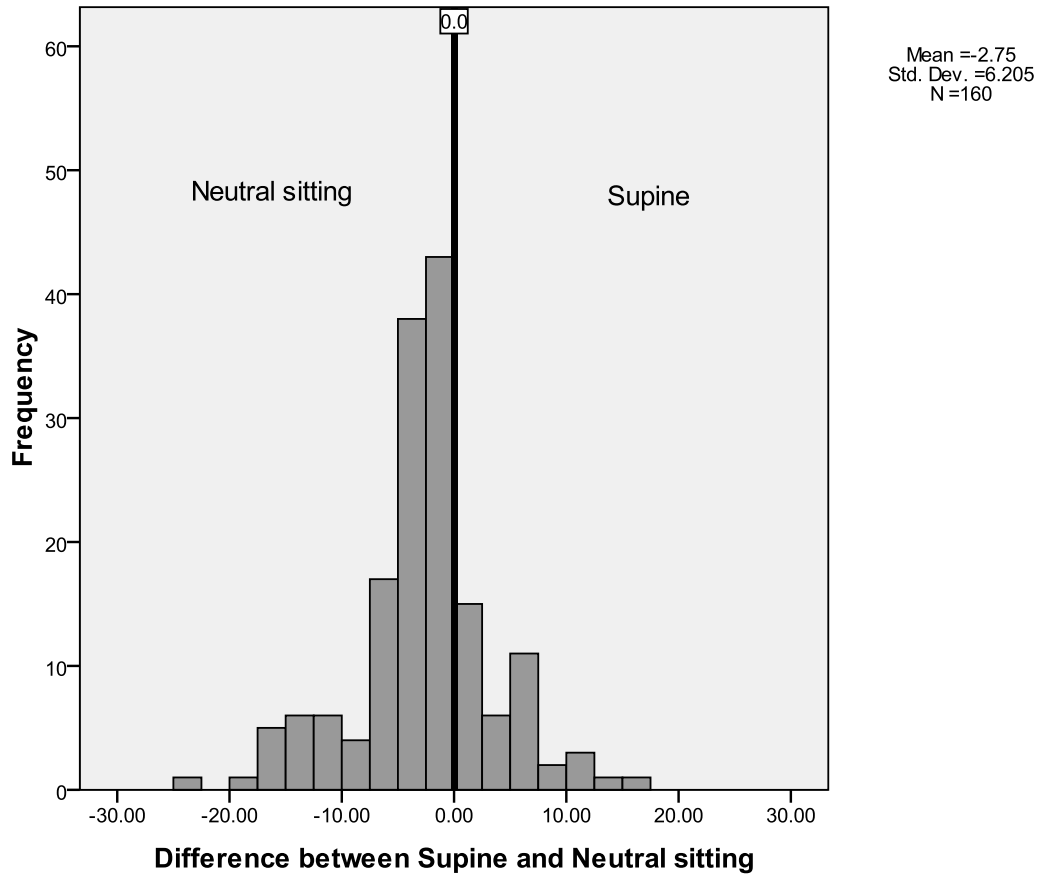


Figure 17.4: Sagittal paired differences between Supine and Neutral sitting (significant difference demonstrated, $p < 0.001$)

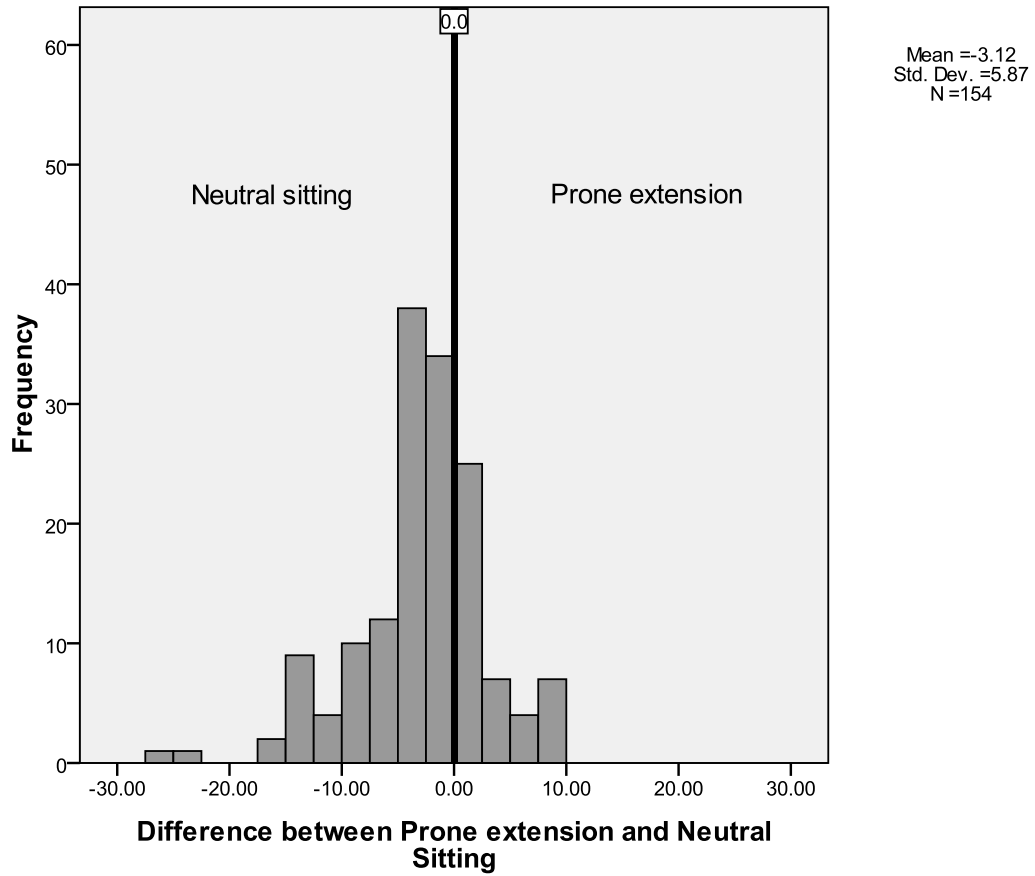


Figure 17.5: Sagittal paired differences between Prone extension and Neutral sitting (significant difference demonstrated, $p < 0.001$)

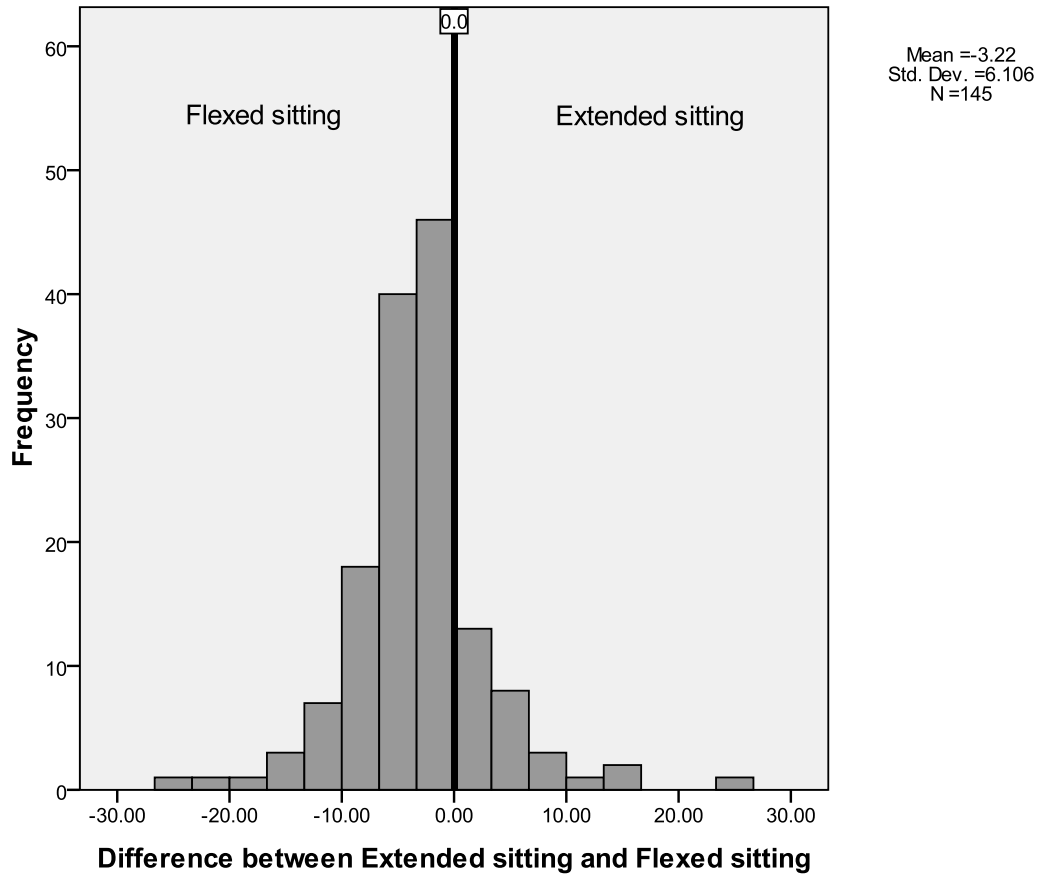


Figure 17.6: Sagittal paired differences between Extended sitting and Flexed sitting (significant difference demonstrated, $p < 0.001$)

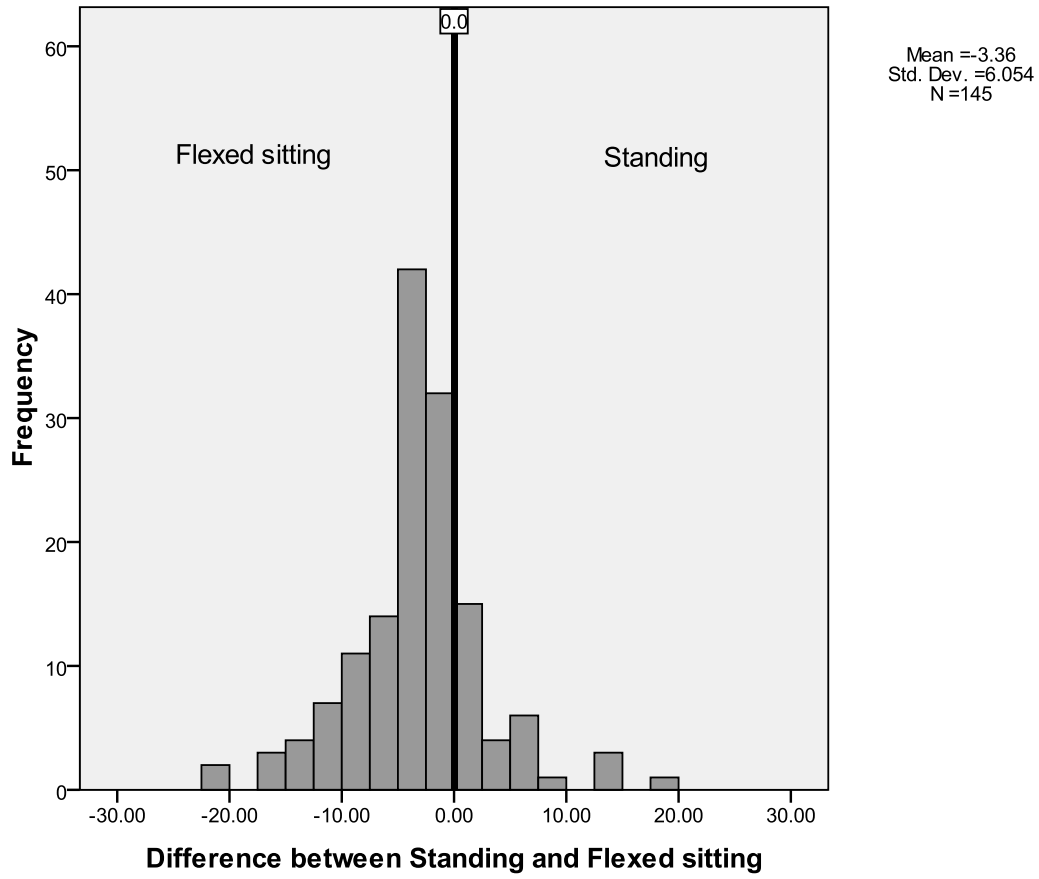


Figure 17.7: Sagittal paired differences between Standing and Flexed sitting (significant difference demonstrated, $p < 0.001$)

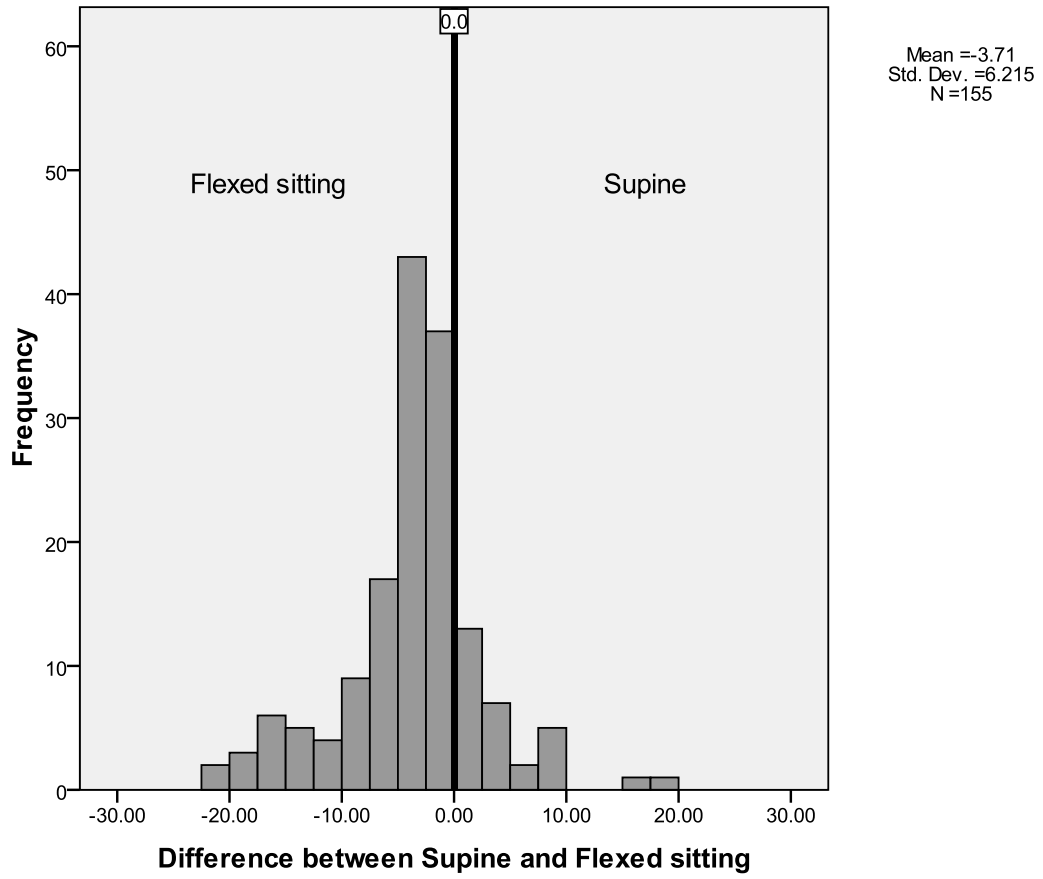


Figure 17.8: Sagittal paired differences between Supine and Flexed sitting (significant difference demonstrated, $p < 0.001$)

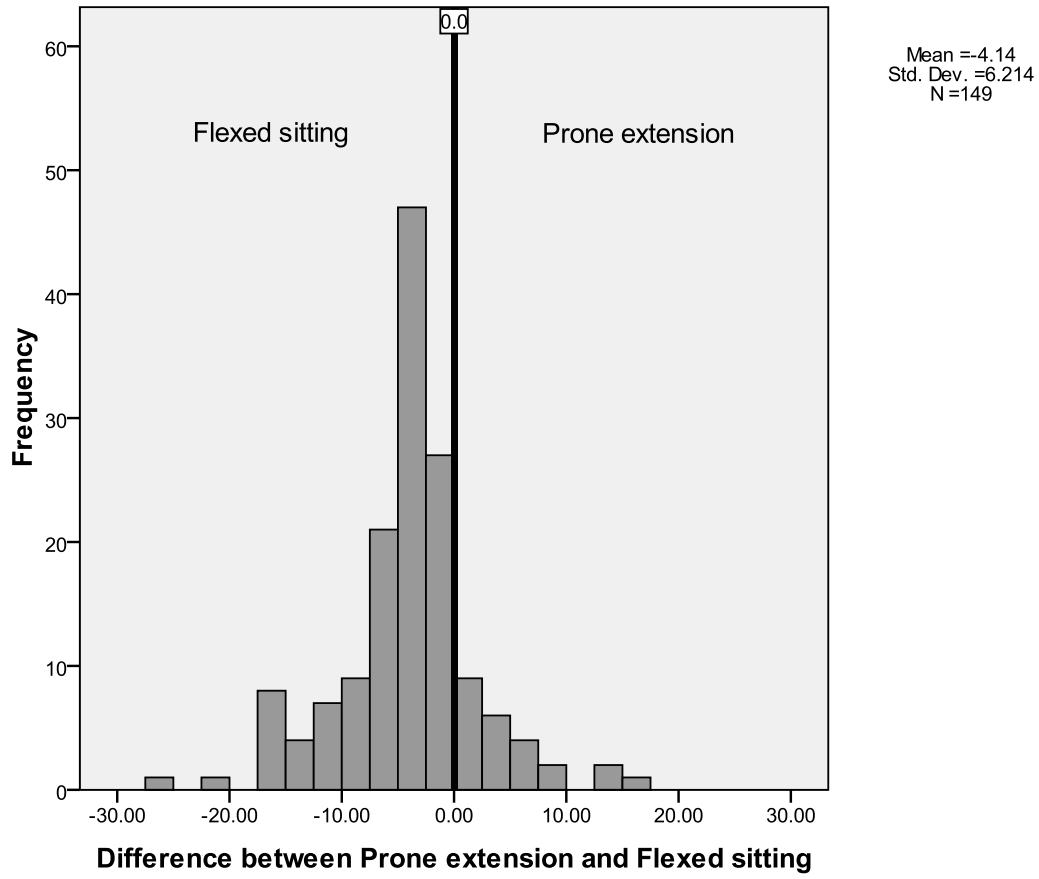


Figure 17.9: Sagittal paired differences between Prone extension and Flexed sitting (significant difference demonstrated, $p < 0.001$)

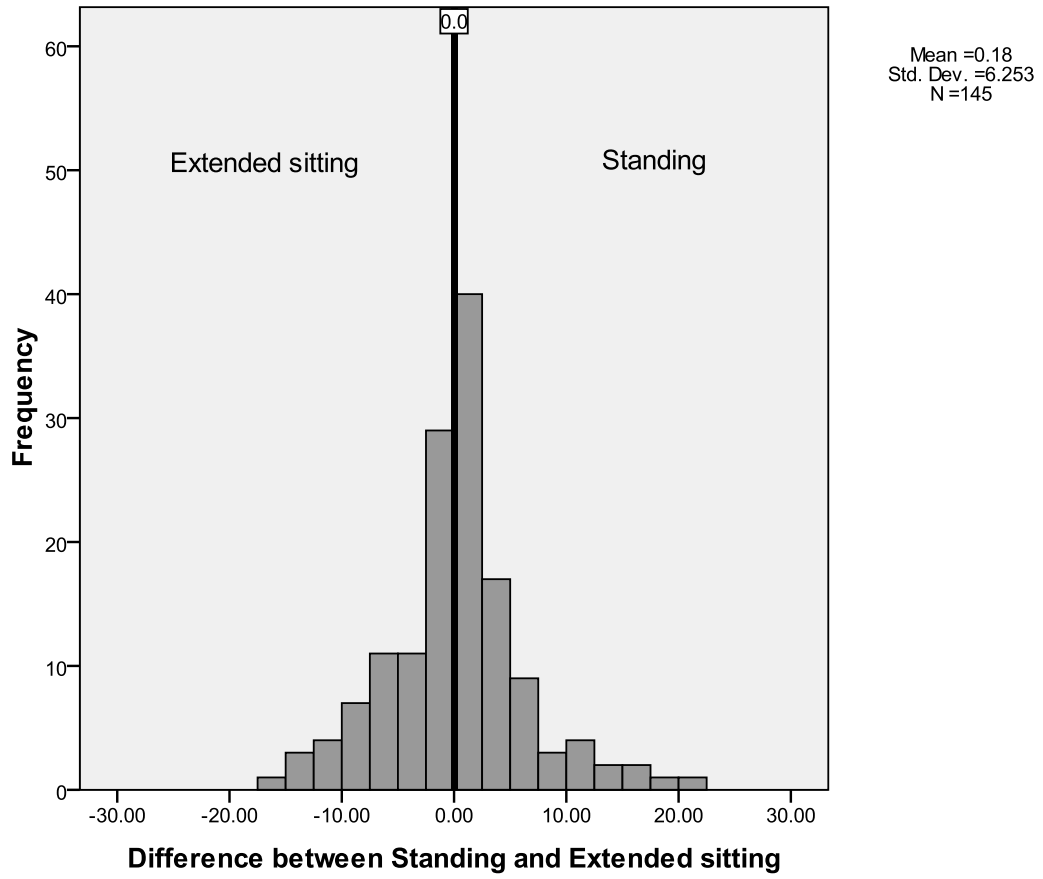


Figure 17.10: Sagittal paired differences between Standing and Extended sitting (Non-significant difference demonstrated, $p=0.730$)

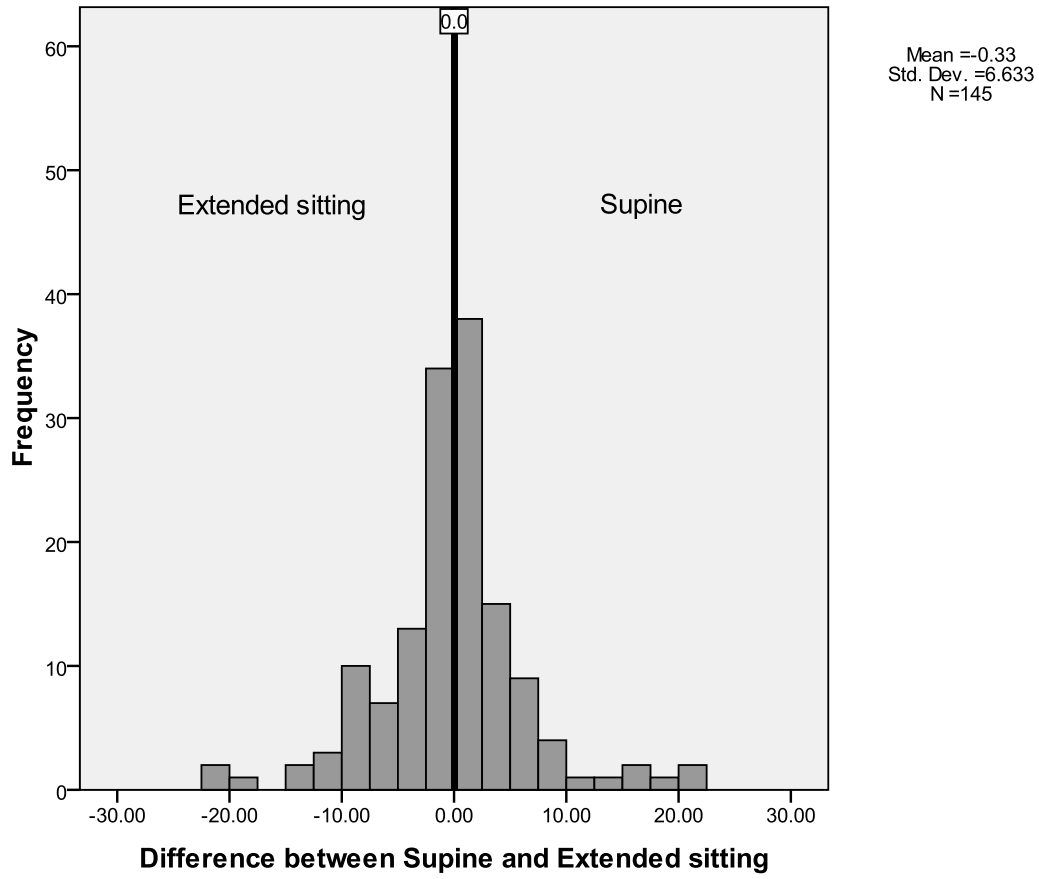


Figure 17.11: Sagittal paired differences between Supine and Extended sitting (Non-significant difference demonstrated, $p=0.548$)

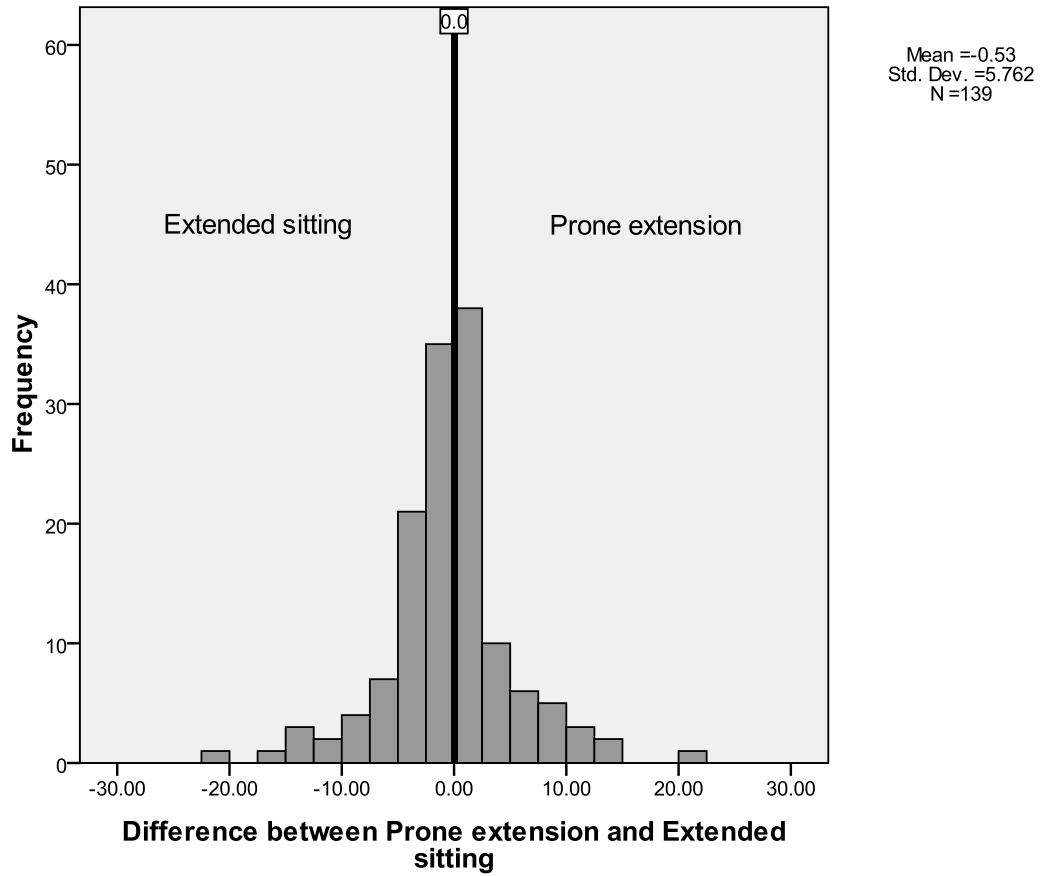


Figure 17.12: Sagittal paired differences between Prone extension and Extended sitting (Non-significant difference demonstrated, $p=0.278$)

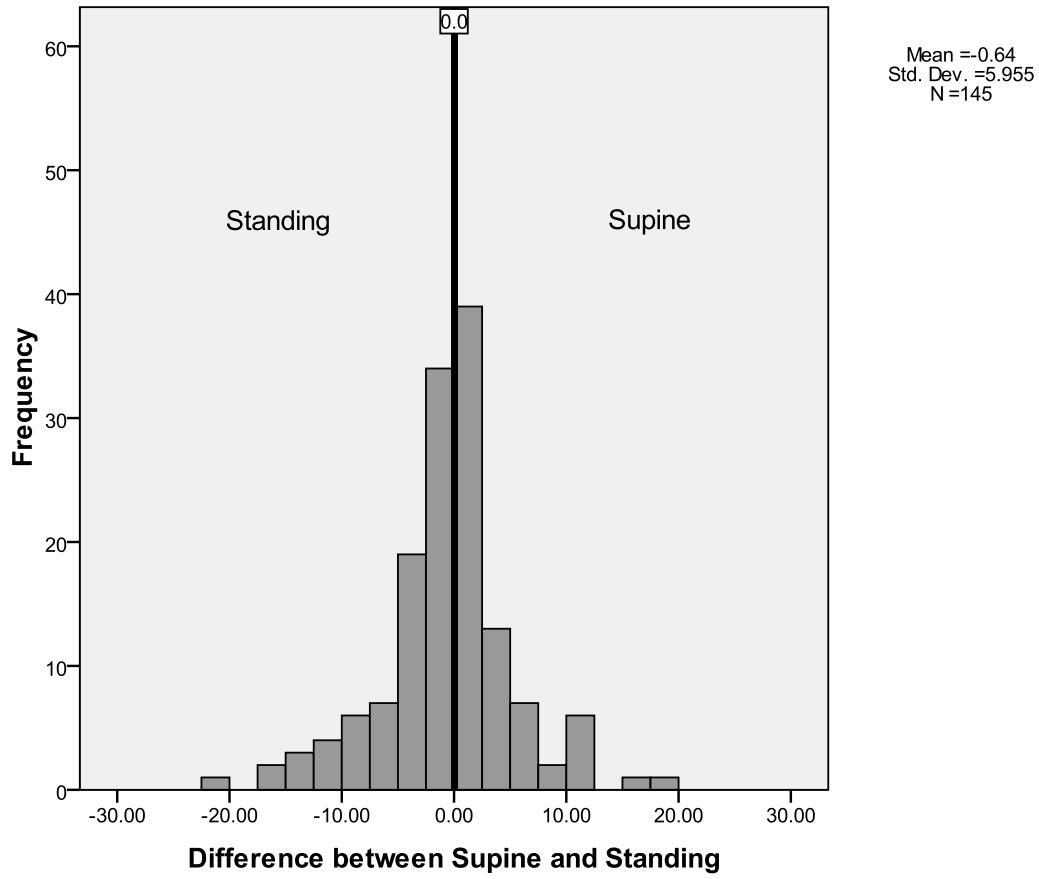


Figure 17.13: Sagittal paired differences between Supine and Standing (Non-significant difference demonstrated, $p=0.2$)

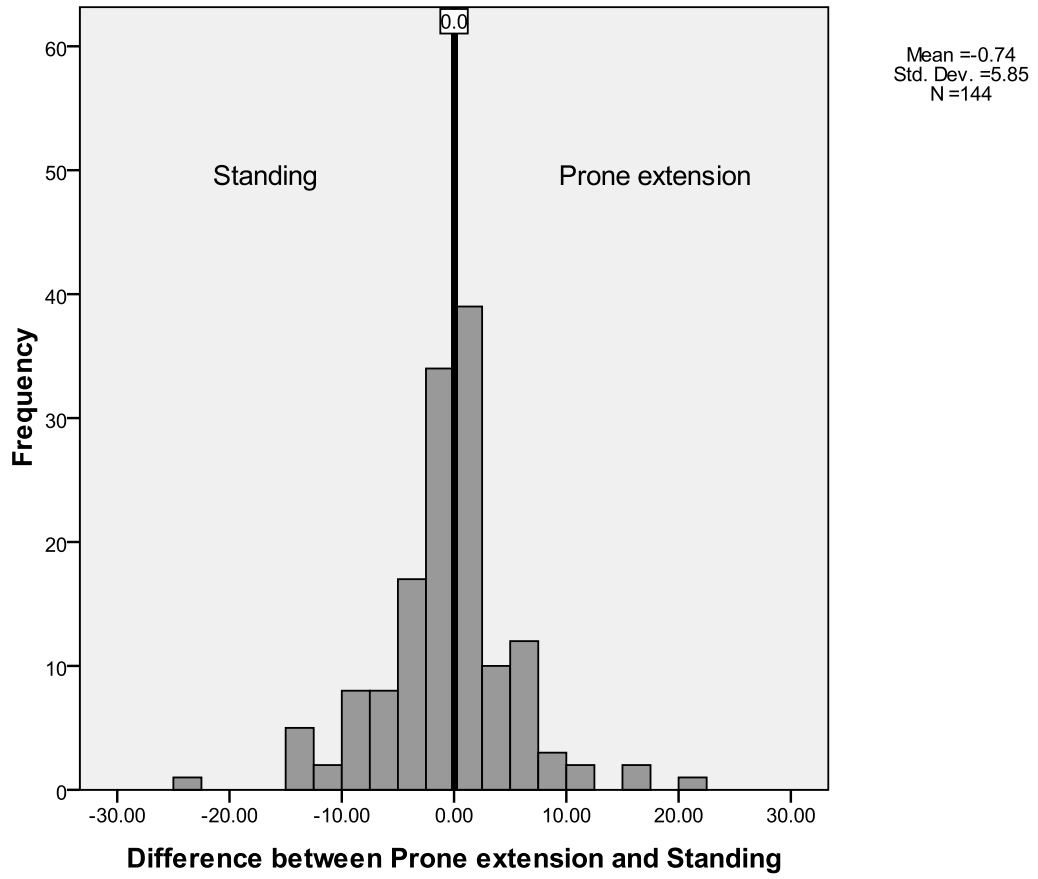


Figure 17.14: Sagittal paired differences between Prone extension and Standing (Non-significant difference demonstrated, $p=0.131$)

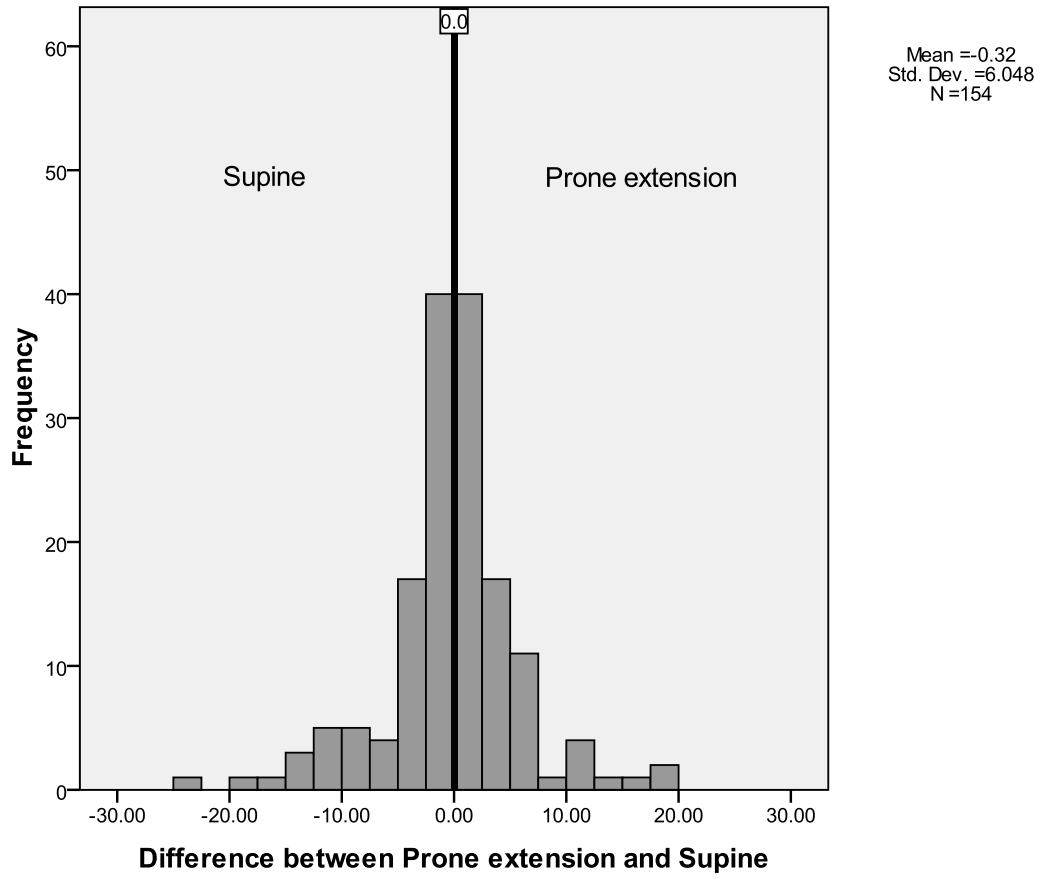


Figure 17.15: Sagittal paired differences between Prone extension and Supine (Non-significant difference demonstrated, $p=0.515$)

Appendix 18: DLBP subjects' axial pMRI additional results

Further investigation of the positional effect in the sagittal plane was investigated using the paired t-test with graphical output to demonstrate the paired differences. This is presented in Table 18.1 and Figure 18.1 to 18.15.

Figure 18.1 to 18.15 all use a reference line (thick black line) positioned vertically on the x-axis at zero. Any significant differences between positions are displayed visually via a bias of the data to one side or the other of the histogram.

Table 18.1: Matched pairs t-test results for axial pMRI scan data

	Mean	N	Mean	T value	Sig. (2 tailed)
Standing	19.64	132	-1.44040	-3.057	0.003*
Neutral sitting	21.08	132			
Standing	19.65	127	-1.71370	-3.852	0.001*
Flexed sitting	21.36	127			
Standing	19.81	122	0.28664	0.616	0.539
Extended sitting	19.52	122			
Standing	19.35	127	0.80031	1.892	0.061
Supine	18.55	127			
Standing	19.45	122	1.77852	4.775	0.001*
Prone extension	17.68	122			
Neutral sitting	21.01	151	-0.20417	-0.618	0.537
Flexed sitting	21.21	151			
Neutral sitting	21.26	126	1.79740	3.647	0.001*
Extended sitting	19.46	126			
Neutral sitting	20.82	141	2.17321	4.558	0.001*
Supine	18.65	141			
Neutral sitting	20.82	137	3.03469	6.098	0.001*
Prone extension	17.78	137			
Flexed sitting	21.19	126	1.46008	3.136	0.002*
Extended sitting	19.73	126			
Flexed sitting	20.79	141	1.95213	3.983	0.001*
Supine	18.84	141			
Flexed sitting	20.98	137	3.15036	6.579	0.001*

Prone extension	17.83	137			
Extended sitting	19.48	126	0.67960	1.246	0.215
Supine	18.80	126			
Extended sitting	19.56	117	1.62658	3.170	0.002*
Prone extension	17.93	117			
Supine	18.76	137	0.89788	2.572	0.011
Prone extension	17.86	137			

Key: * significant at $p < 0.003$ level

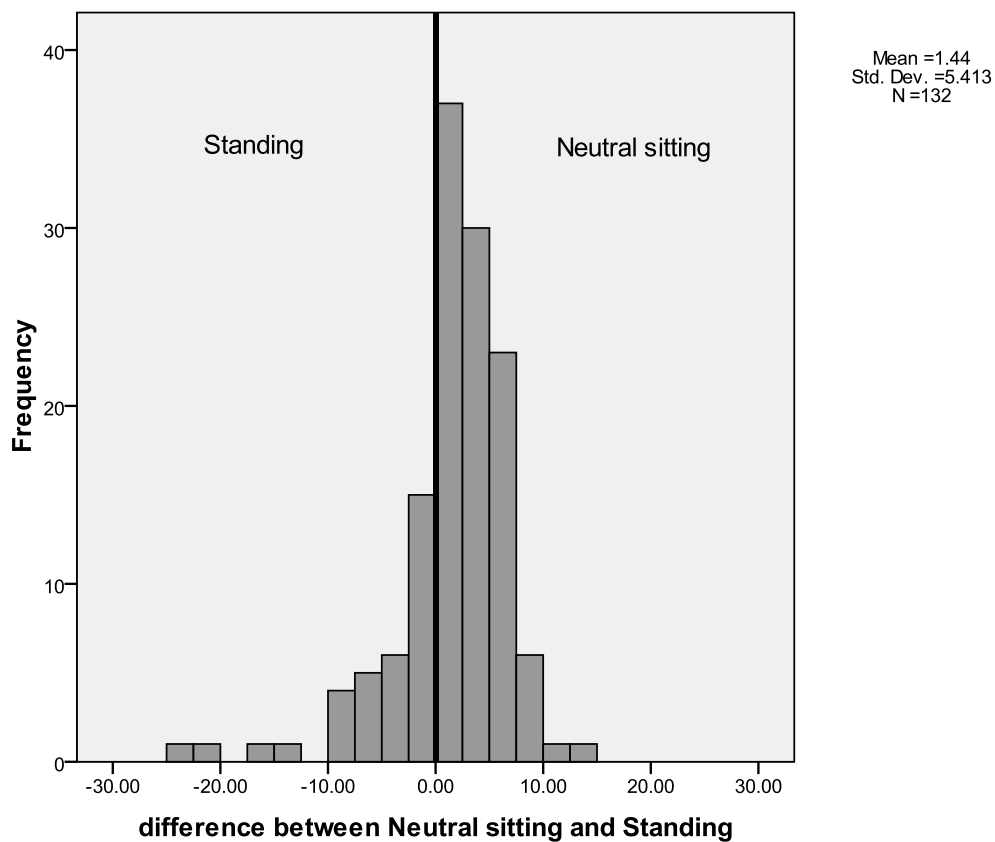


Figure 18.1: Axial paired differences between Neutral sitting and Standing (significant difference demonstrated, $p = 0.003$)

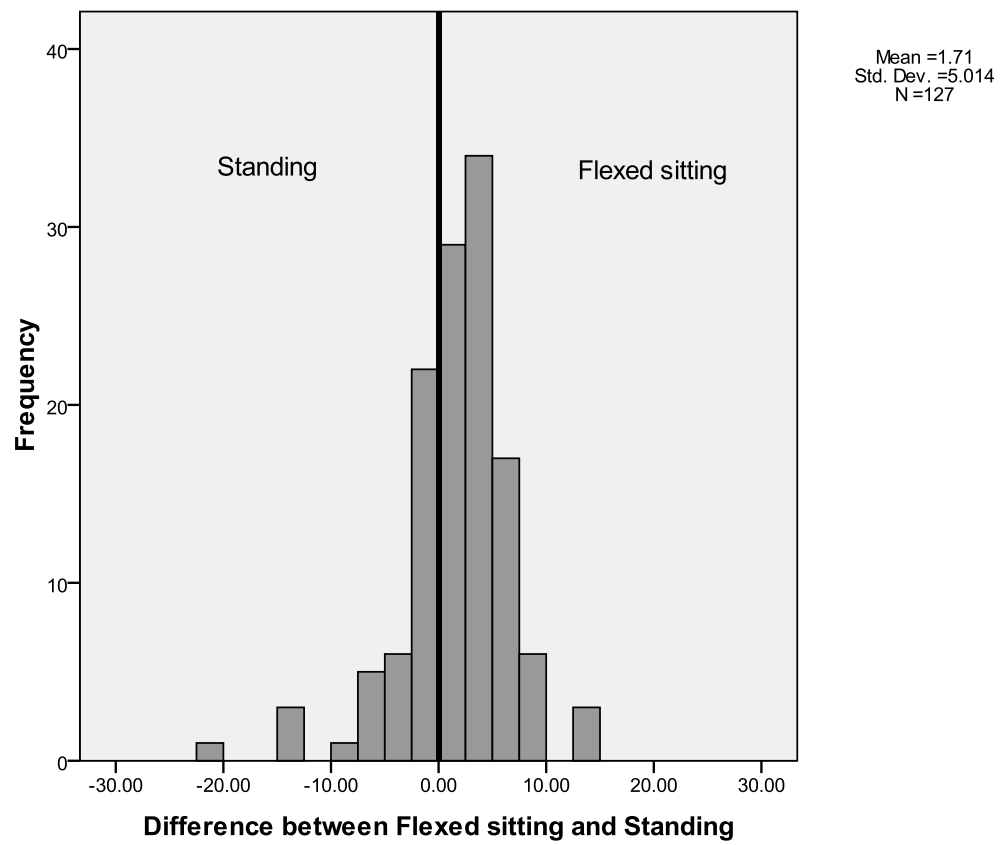


Figure 18.2: Axial paired differences between Flexed sitting and Standing (significant difference demonstrated, $p=0.001$)

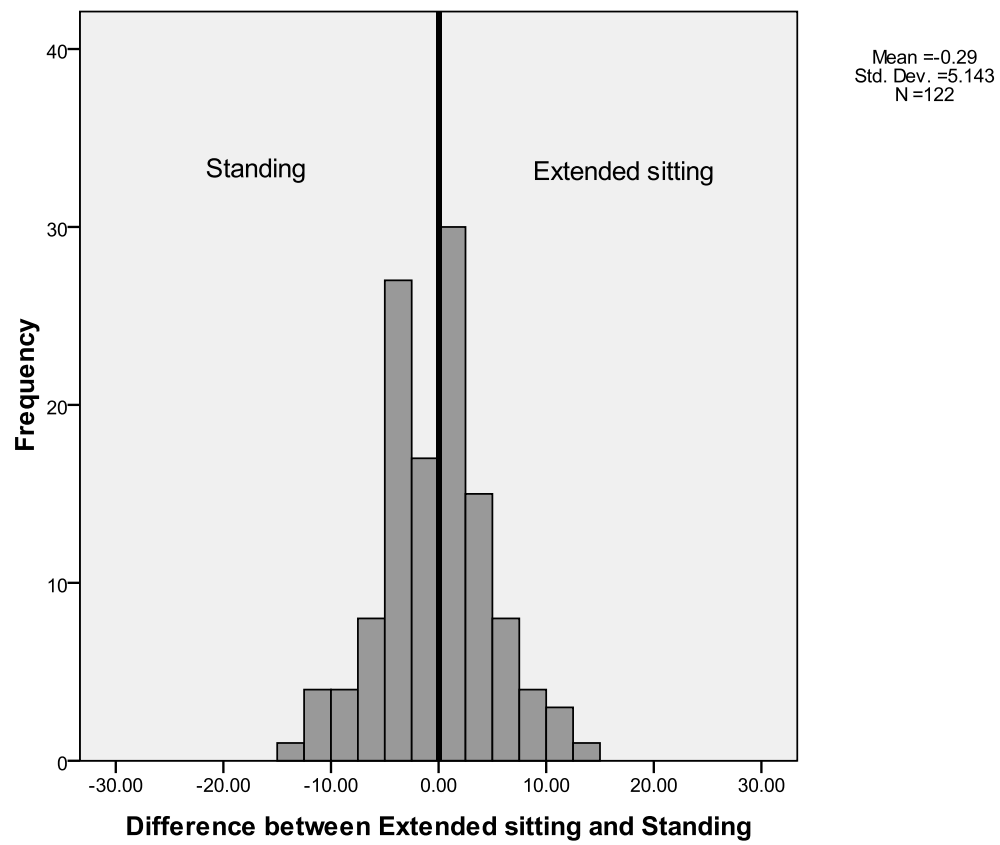


Figure 18.3: Axial paired differences between Extended sitting and Standing (Non-significant difference demonstrated, $p=0.539$)

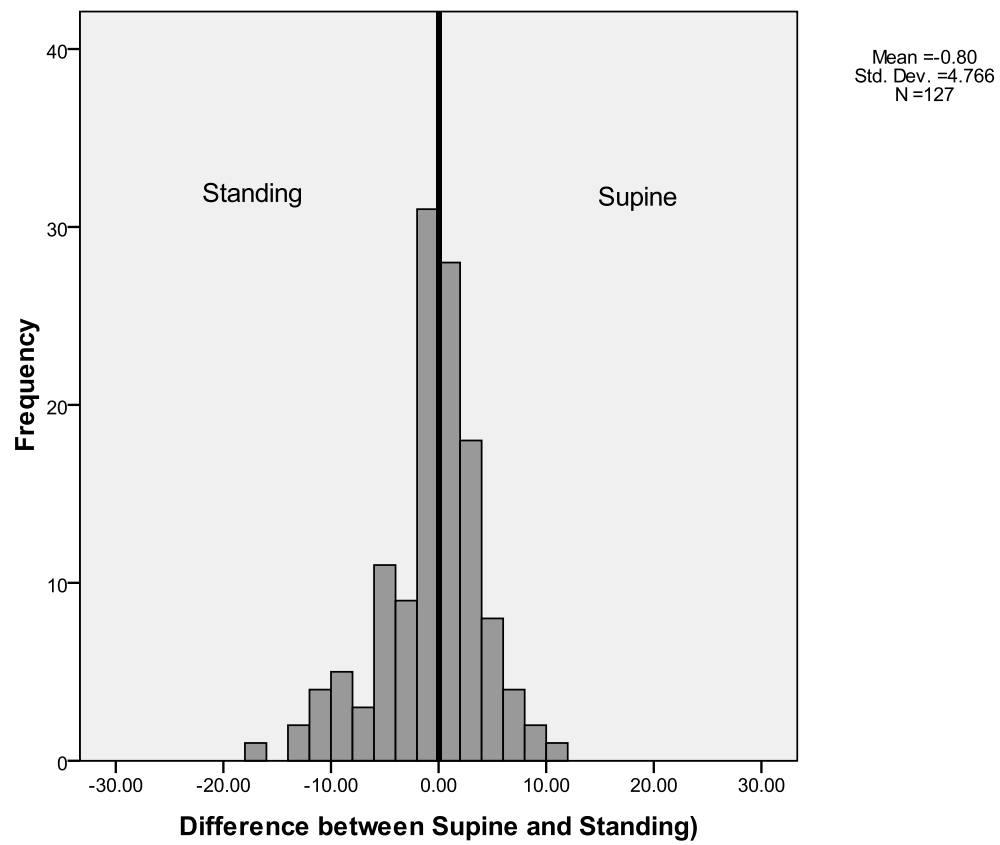


Figure 18.4: Axial paired differences between Supine and Standing (Non-significant difference demonstrated, $p=0.061$)

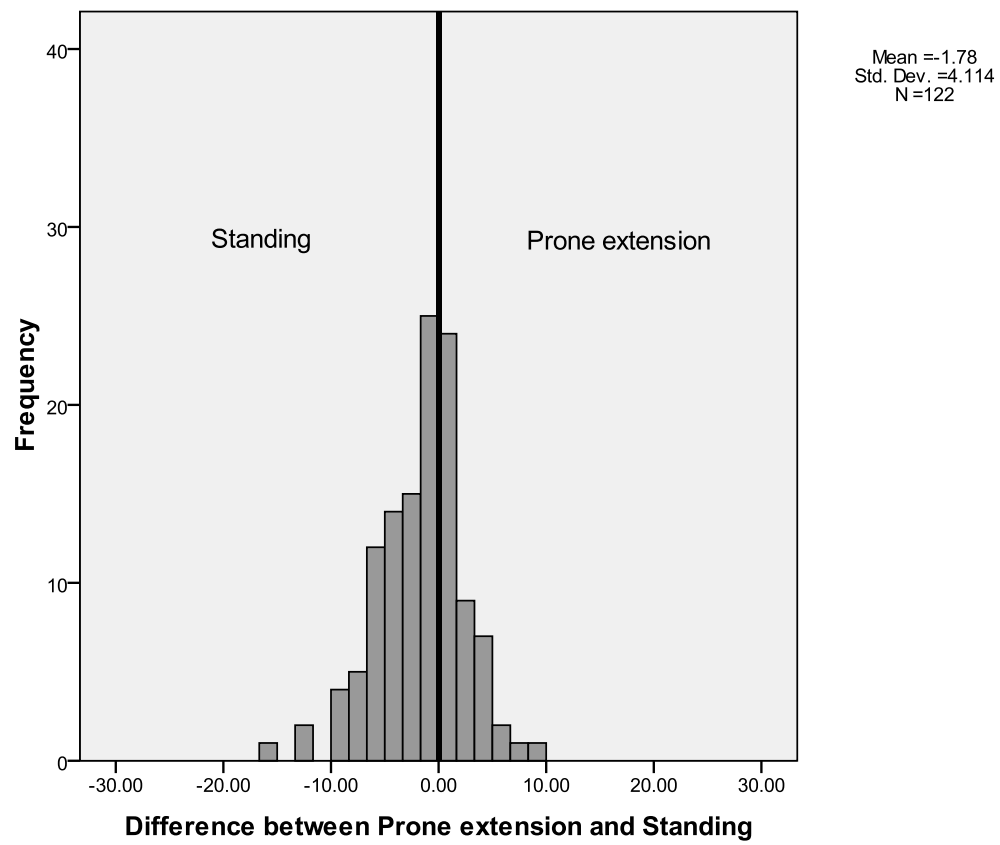


Figure 18.5: Axial paired differences between Prone extension and Standing (significant difference demonstrated, $p=0.001$)

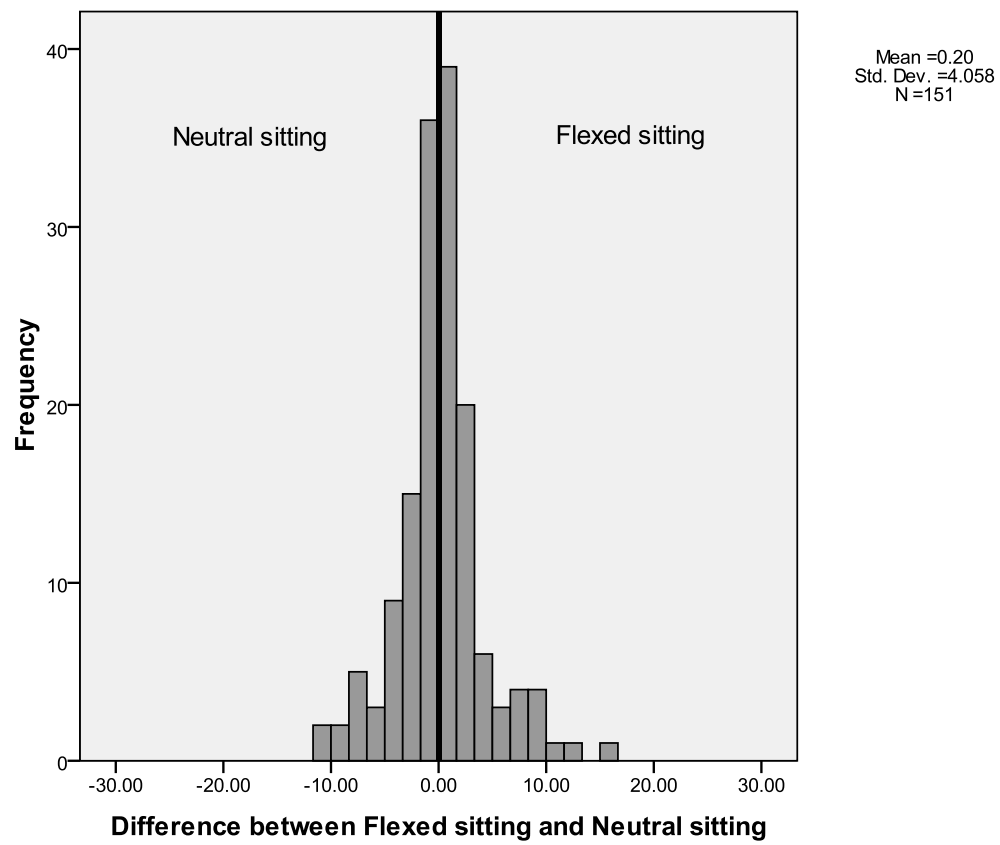


Figure 18.6: Axial paired differences between Flexed sitting and Neutral sitting (Non-significant difference demonstrated, $p=0.537$)

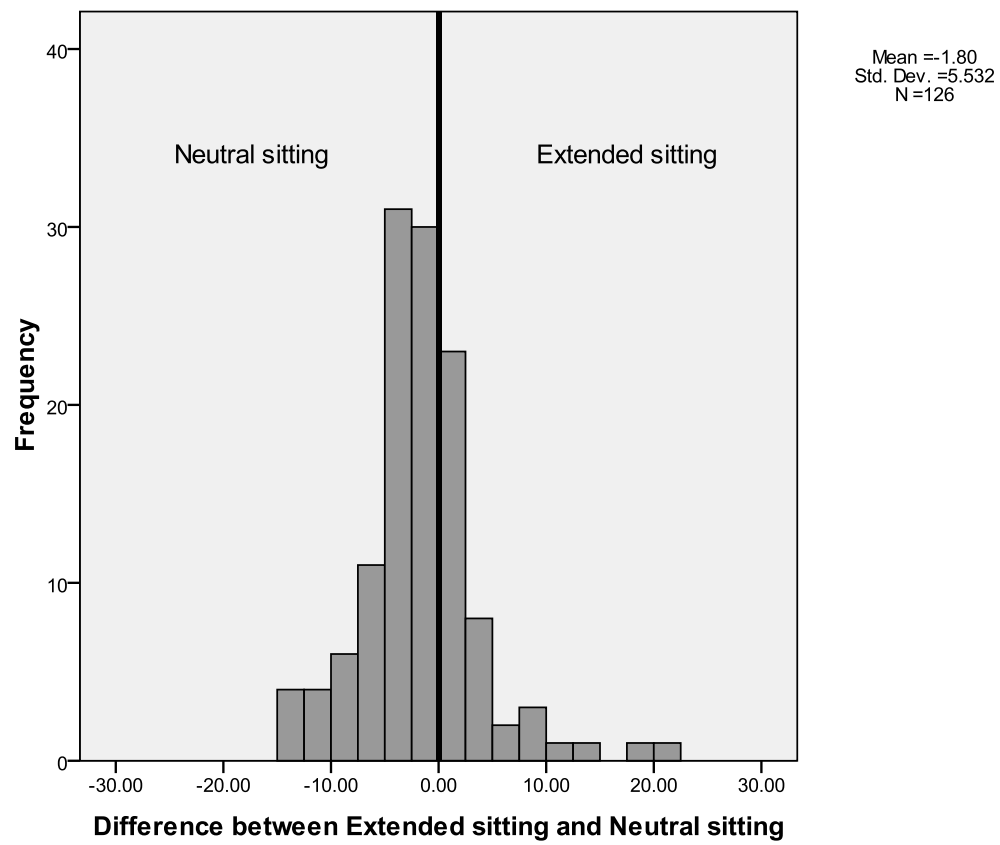


Figure 18.7: Axial paired differences between Extended sitting and Neutral sitting (significant difference demonstrated, $p=0.001$)

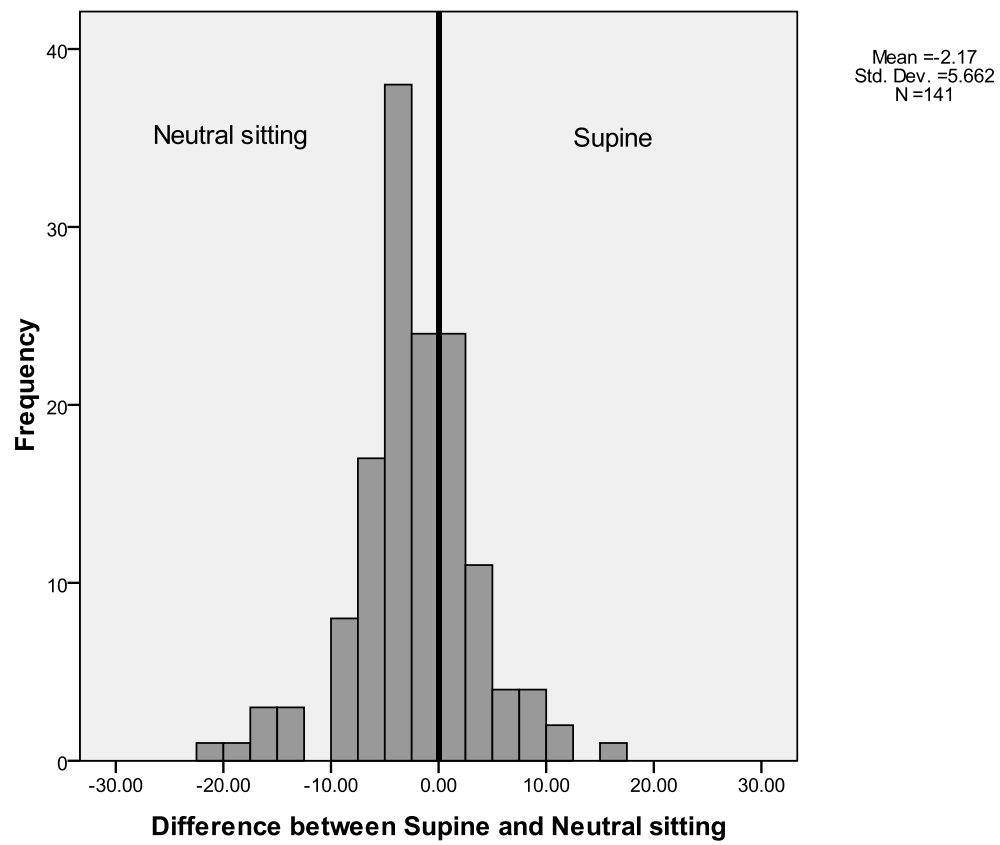


Figure 18.8: Axial paired differences between Supine and Neutral sitting (significant difference demonstrated, $p=0.001$)

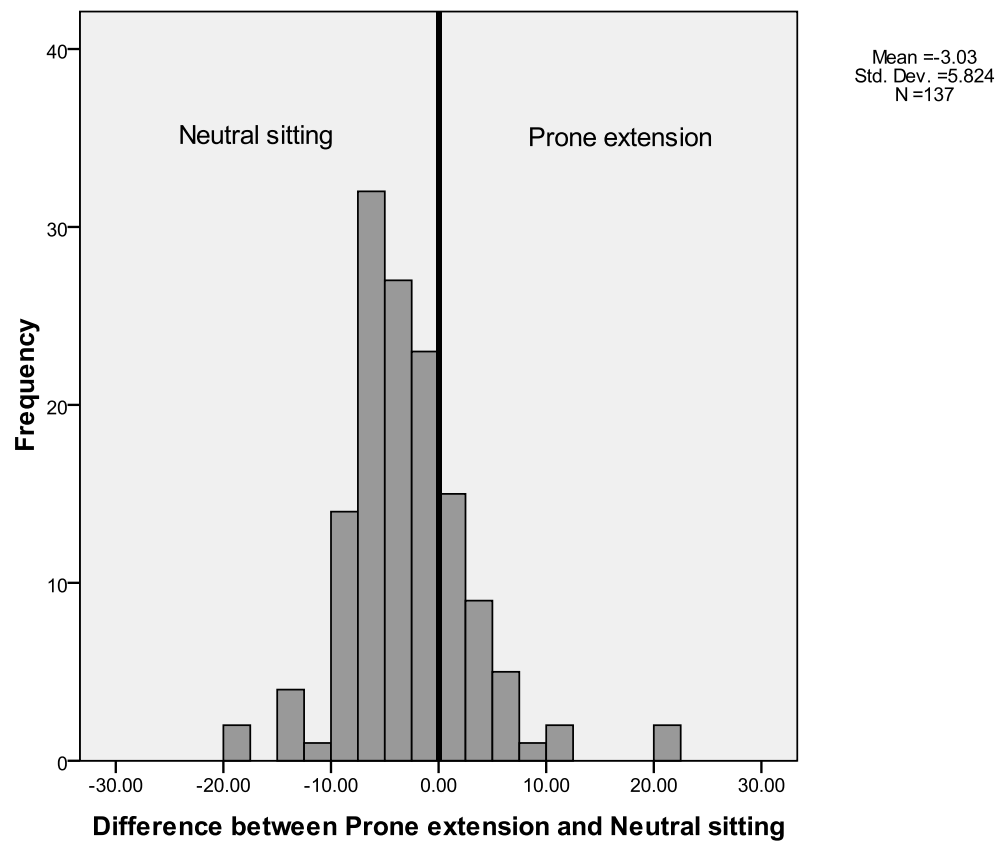


Figure 18.9: Axial paired differences between Supine and Neutral sitting (significant difference demonstrated, $p=0.001$)

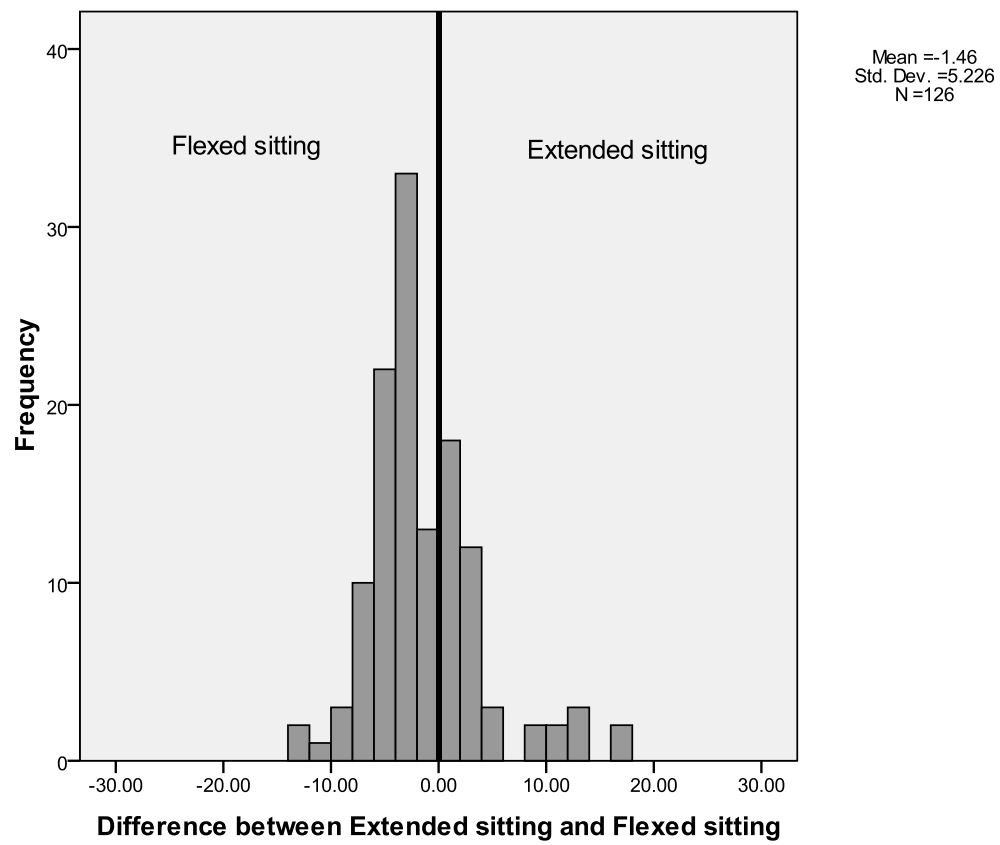


Figure 18.10: Axial paired differences between Extended sitting and Flexed sitting (significant difference demonstrated, $p=0.002$)

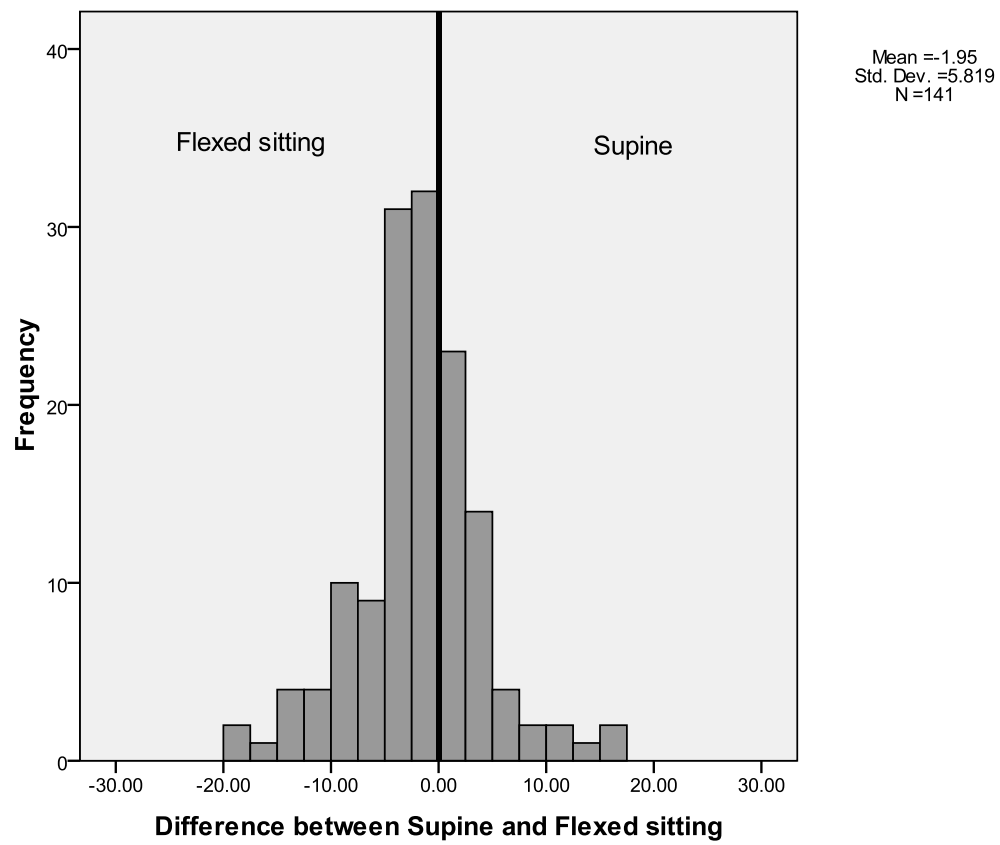


Figure 18.11: Axial paired differences between Extended sitting and Flexed sitting (significant difference demonstrated, $p=0.001$)

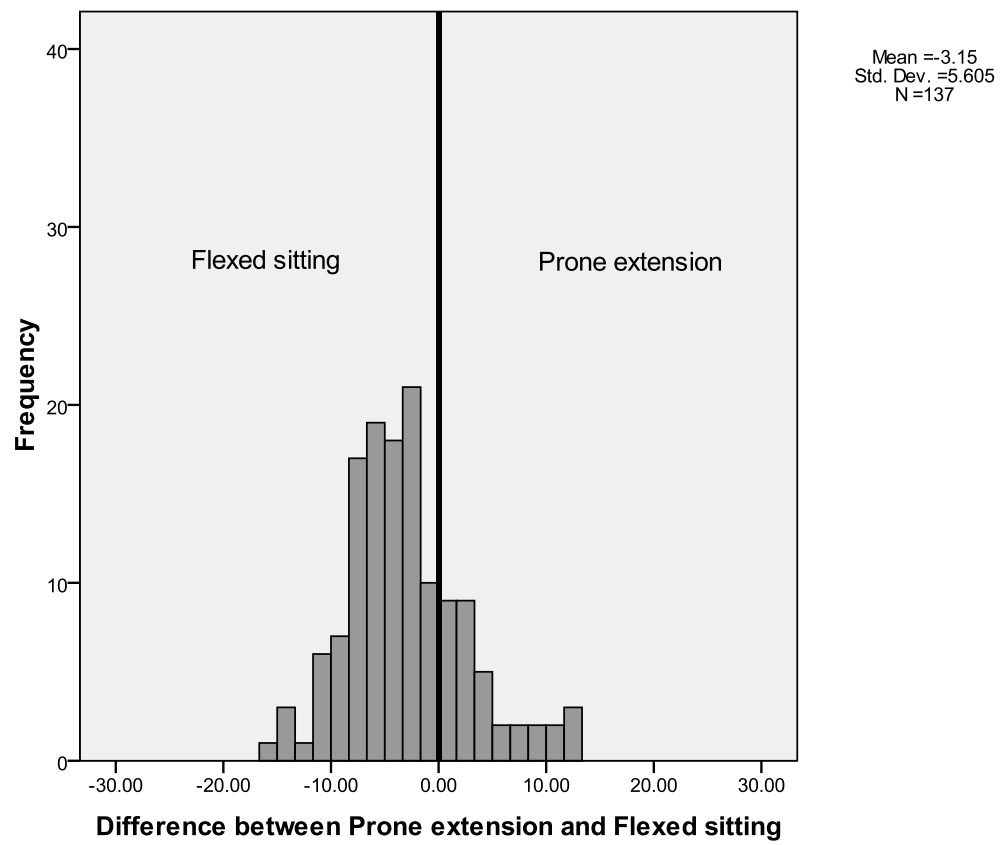


Figure 18.12: Axial paired differences between Prone extension and Flexed sitting (significant difference demonstrated, $p=0.001$)

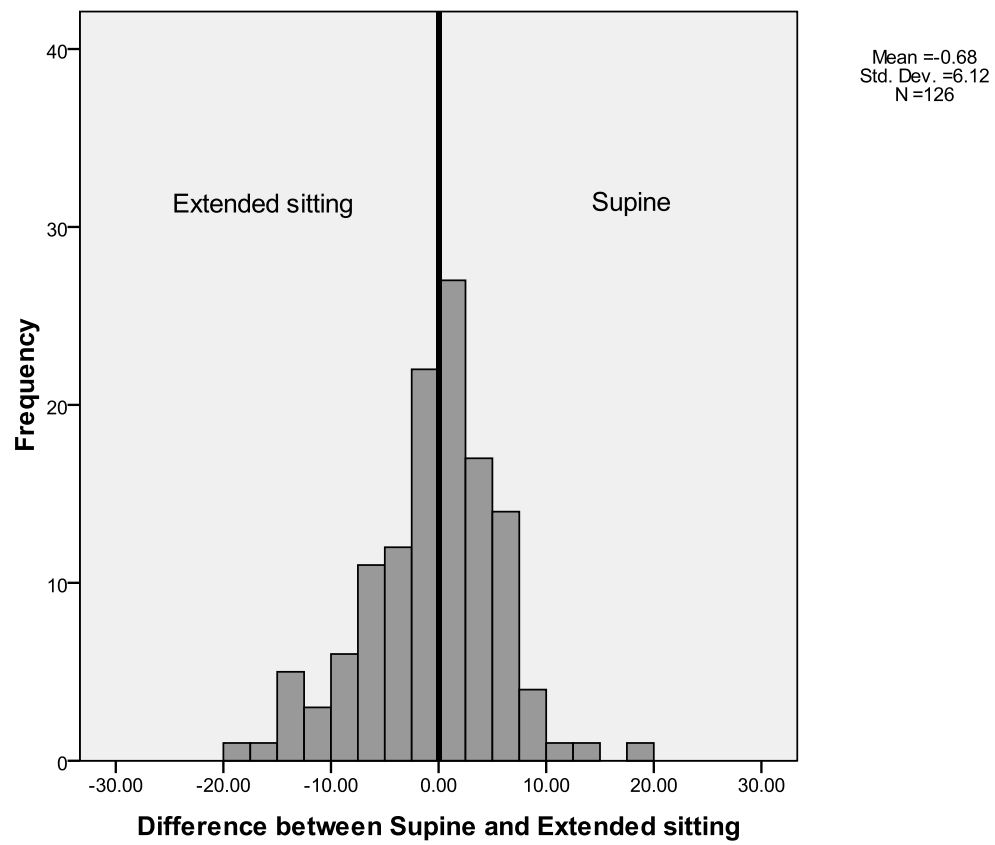


Figure 18.13: Axial paired differences between Supine and Extended sitting (Non-significant difference demonstrated, $p=0.215$)

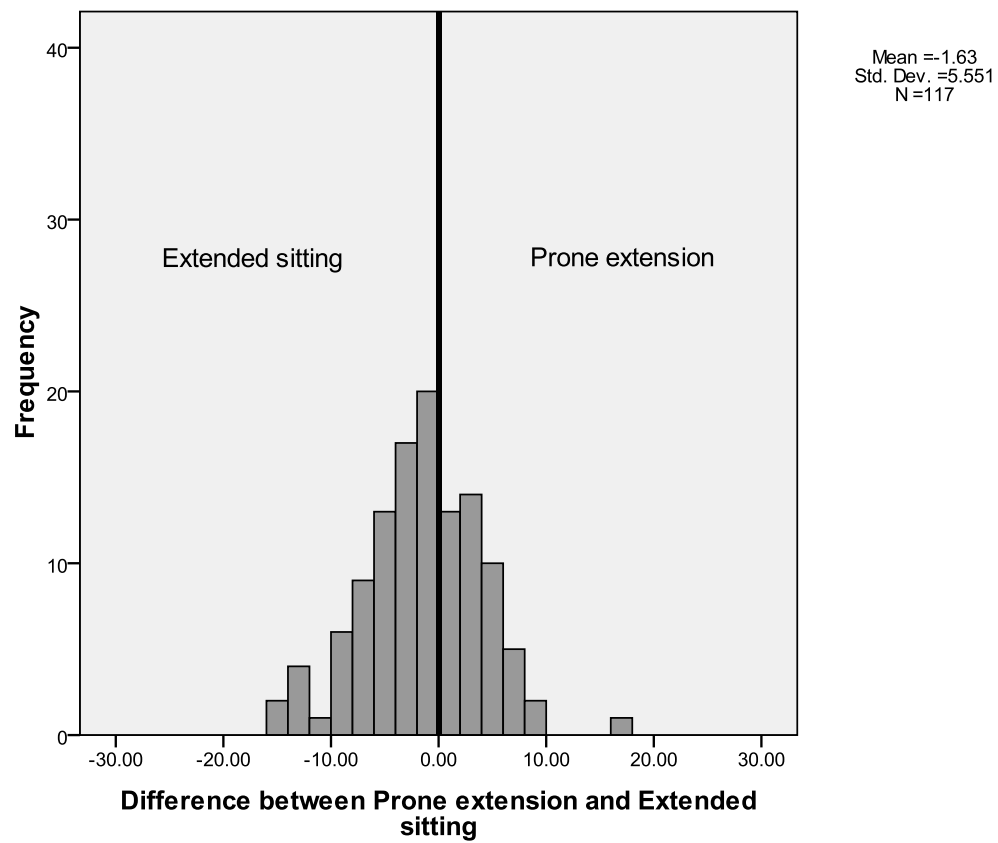


Figure 18.14: Axial paired differences between Prone extension and Extended sitting (significant difference demonstrated, $p=0.002$)

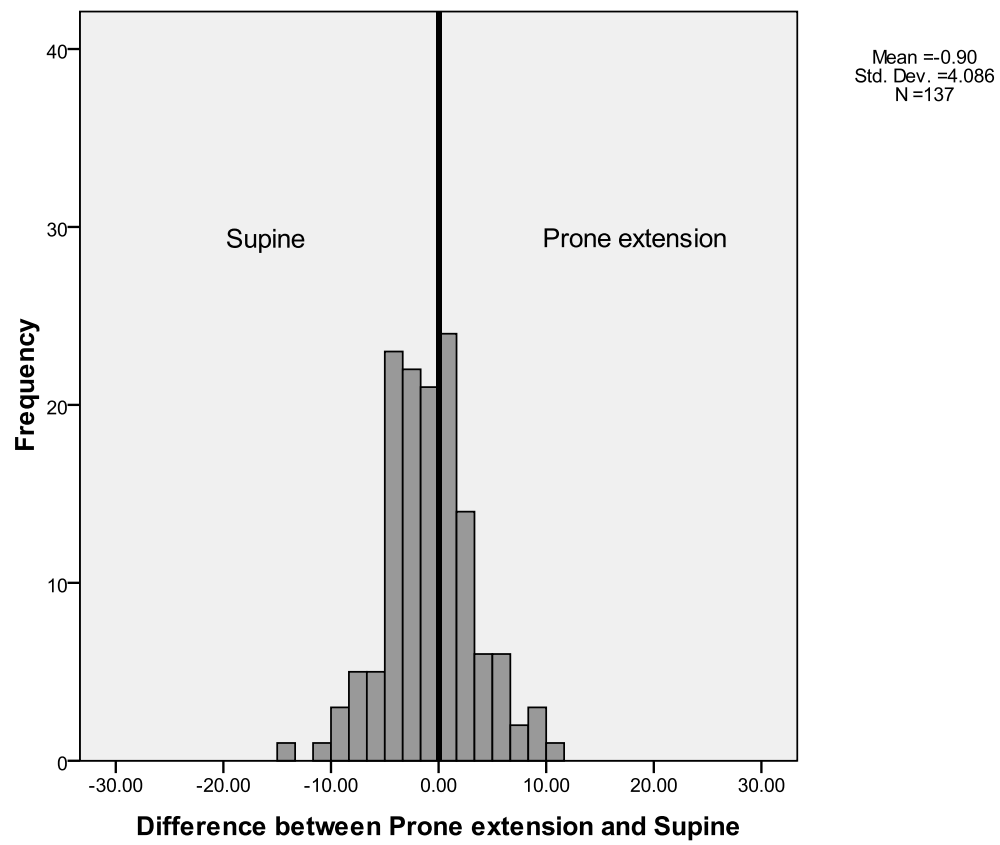


Figure 18.15: Axial paired differences between Prone extension and Supine (Non-significant difference demonstrated, $p=0.011$)

Appendix 19: FIGURE 2.4.1 Permission

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Senior Editor, HowStuffWorks.com
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