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OLLSCOIL NA GAILLIMHE
UNIVERSITY OF GALWAY

Function of the Degenerate Disc: The Significance of Intra Discal Vacuum Phenomenon (IDVP) in the Lumbar Spine.

A thesis submitted to the University of Galway as partial fulfilment of the requirements
for degree of Doctor of Philosophy (PhD) in Surgery

By

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Submitted: 30th April 2024

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Certificate of Authorship Final Thesis Submission

Doctor of Philosophy (PhD) in Surgery

Discipline of Surgery, School of Medicine, University of Galway

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Title of Submission: Function of the Degenerate Disc: The Significance of Intra Discal Vacuum Phenomenon (IDVP) in the Lumbar Spine.

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List of Publications & Presentations

Cawley DT, Simpkin A, Abraham E et al. Intradiscal vacuum phenomenon matches lumbar spine degeneration patterns in an ageing population. *European Spine Journal*. 2024 Feb 28;1-8.

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Cawley DT, McDonnell A, Simpkin A, et al. Intra-discal vacuum phenomenon with advanced lumbar spine disc degeneration: complementary findings from both MRI and CT. *BMC Medical Imaging*. 2025 Mar 20;25(1):94.

Cawley DT. Motion attenuation surgery in the degenerative lumbar spine: Is cement discolplasty a safe and effective option?. *Brain & spine*. 2025 Mar 4;5:104220.

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Affiliated publication since the start of this PhD:

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Research presentations have been made at by different members of the research team:

- Irish Spine Society 12th November 2022: 2 oral presentations, 1 poster
- Atlantic Orthopaedic Club Meeting 19th November 2022: 2 oral presentations
- Royal Academy of Medicine Intern Day : 1 presentation
- European Spine Society, Frankfurt October 2023: 1 poster.
- BIR annual congress, November 2023: 1 oral presentation
- European Orthopaedic Research Society 2023: 1 presentation
- British Association of Spine Surgeons, March 20-22 2024: 2 presentations, 2 posters.
- European Spine Society, Vienna October 2024, 2 posters.

Abbreviations

CD: cement discoplasty

CT: computed topography

IDVP: Intra Discal Vacuum Phenomenon

LBP: Low back pain

LL: lumbar lordosis

MMUH/MPH: Mater Misericordiae University Hospital and Mater Private Hospital

MRI: magnetic resonance imaging

OR: Odds Ratio

PI: pelvic incidence

PLIF: Posterior lumbar interbody fusion

PMMA: polymethylmethacrylate cement

SPECT: Single-photon emission computed tomography

TLIF: Trans-foraminal (posterolateral) lumbar interbody fusion

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1. Introduction

The degenerative process within the lumbar spine has become a large part of spine surgery in westernised society. It encompasses muscular, intra-discal, ligamentous contributions and with advanced aging, bone health and more global sagittal balance disequilibrium. Studies of the spinal column have over the last 30 years included significant analyses of its architecture and morphology. Where deficits present from degeneration of the lumbar spine, most of this is from collapse of the intervertebral disc, which wears out, becoming empty and degenerate and leads to a loss of posture in the aging lumbar spine. The empty disc often remains mobile and manifests as an intradiscal vacuum phenomenon (IDVP), the significance of which we investigate as a central theme in this thesis.

This PhD investigates IDVP beyond the limited published scientific evidence. Through analyses of CT scans of the abdomen, we have shown that IDVP is more prevalent than previously thought. Having identified these we explore the morphological patterns that pertain to IDVP which further our understanding of the function of the degenerative spine. We have focussed on normal subjects over 60 years of age and have deliberately avoided symptomatology to uncover normative population data.

Our hypothesis is that IDVP forms a part of the functioning degenerative spine, reflective of a dynamic process that allows for erect standing, an intra-spinal compensatory mechanism, to counter the kyphogenic attributes of growing older, in other words, one's tendency to stoop. These contributing elements include disc degeneration, osteoporotic fracture, spondylolisthesis, adjacent ankylosis and degenerative scoliosis, and are closely correlated to the spino-pelvic relationship. In other words, we use IDVP to help straighten up in the presence of degenerative factors such as those listed above.

It is not possible nor feasible to investigate motion activity within the intervertebral disc with an imaging system. All we can do is, from supine CT (computed topography) scans, analyse what occurs within the human intervertebral disc. Previous studies have shown early understanding of IDVP in this regard, in that CT highlights IDVP, which is an empiric marker for intra-discal movement, as discussed later. Thus our work thus infers what occurs in vivo while moving the degenerative spine. The spine is always included on CT of the abdomen and therefore, readily available for analysis. A dataset of 2200 subjects is set, with an expected positive diagnostic rate of 40%, involving the aid of a team of junior researchers, who receive training specific to identifying and characterising IDVP.

We identify subjects who also had a second CT scan over seven years previously, so as to characterise the natural history of IDVP- a phenomenon yet undescribed. Further metrics are performed to pursue the aims

as outlined above, which largely include grading the IDVP, measuring angle of pelvic incidence (which eclipses the spinopelvic relationship) and identifying further diagnoses. Subsets of diagnoses are analysed separately as listed above. The most salient of these is degenerative scoliosis, with asymmetric IDVP, requiring a separate analysis and research paper.

A separate cohort of subjects who had both CT and MRI are analysed to identify the complementary role of CT in analysis of advanced disc degeneration and in particular, how that pertains to IDVP. This cohort includes subjects with appropriate spinal symptoms, excluding other factors that require CT & MRI scanning, such as neoplasm, infection and trauma. Thus 200 scans are required to yield 60 appropriate subjects (in keeping with similar papers on this subject).

We explore the literature on a new treatment option for symptomatic IDVP, cement discoplasty and outline some cases as examples.

Finally we discuss unifying aspects of the five research themes described above.

2. Literature Review

2.1 Evolution and “Devolution” of the Vertebrate

We cannot know where we are going until we know where we have come from.

As vertebrates, we have a skeletal architecture that protects the neuroaxis, the spinal cord, a projection of the brain (Figure 2.1). Between each vertebral bone lie the intervertebral discs (Figure 2.2).

Humans are understood to be biped, to have the ability to walk on two feet for up to the last seven million years (Figure 2.3). This contrasts with our ability to form a blood clot which is at least 50 million years old¹. The ability to stand up straight is not that old and thus a **genetically fragile function**. This challenge is relevant in an era of sedentary lifestyles, including sitting desk jobs, working at computers or digital tablets, enjoying television or computer games, where our expression of an erect spine is further modified into a persistent flexion position (Figure 2.4). This overloads the discs and under-utilises the gluteal and core abdominal muscles².

Where deficits present from degeneration of the lumbar spine, wear and then collapse of the intervertebral disc lead to a loss of posture in the aging lumbar spine. Degenerative conditions of the spine will therefore affect its most vulnerable spot- the lumbosacral junction, where it carries everything above it, and where a mobile vertebral unit (L5) articulates with a steady base below (sacrum and pelvis). It is well recognized that approximately one fifth of all GP consultations are for low back pain, as manifestation of this vulnerability³.



Figure 2.1: Human vertebral column. The shape of the spine includes extension (lordosis) of the flexible cervical and lumbar sections of the spine, and flexion (kyphosis) of the rigid thoracic and sacral sections of the spine. Most low back pain originates from the degeneration of discs in the lumbar spine (Lateral view of the vertebral column, Plate 111, Gray's Anatomy).

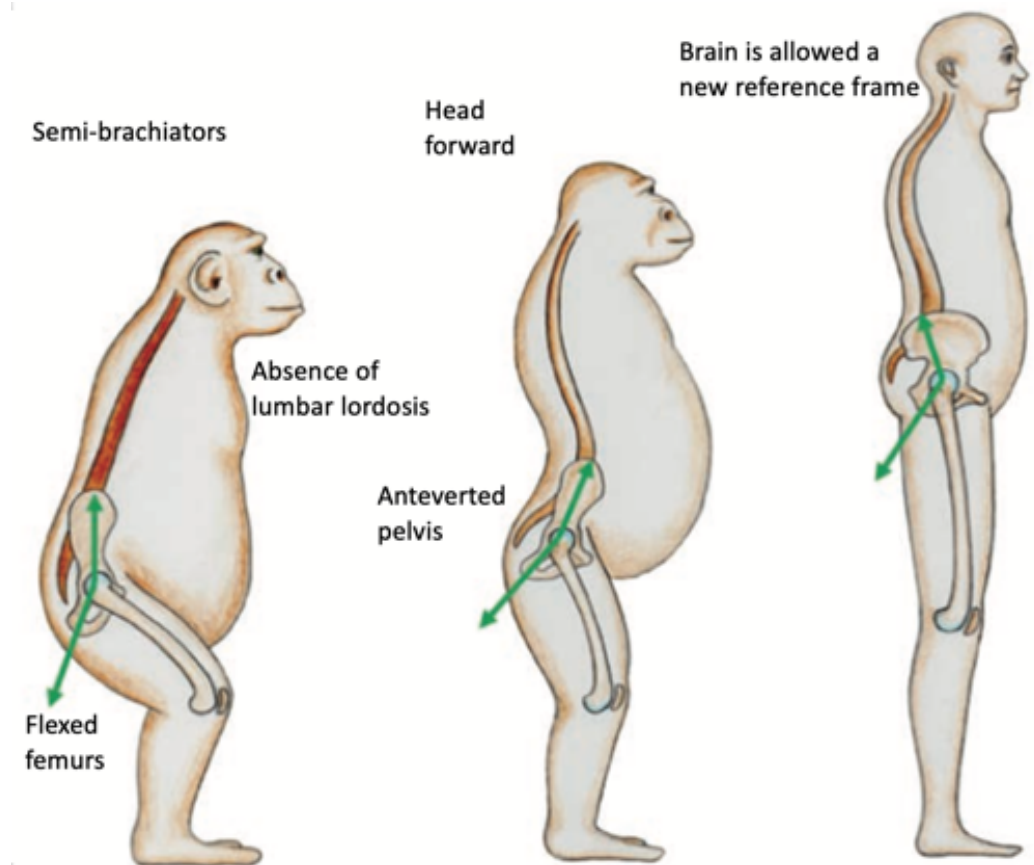


Figure 2.3: Evolution of the Spine. Gorilla (semi-brachiator), Lucy (hominin species *Australopithecus afarensis*, 3.2million years), modern human. Evolution of upright posture involves widening of the pelvis, hip extension, lumbar lordosis and retraction of the head. Spinal Anatomy: Modern Concepts. Vital JM, Cawley DT.

2.2 Anatomy of the Disc

The **anatomy** of the intervertebral disc includes a central nucleus pulposus and annular fibrosis. The main mechanical functions of the disc are to absorb the axial stresses and to resist the load applied to the spinal column by the force of gravity. The function of the disc is to act as a shock absorber and as an energy converter (a lesser known but at least equally important role). The closed space of the nucleus allows a suspension mechanism, with compression of type 2 collagen. The surrounding annulus fibrosis contains type 1 collagen fibres arranged in 10–20 layers. The collagen fibres in AF are at 30 degrees to each other so the normal disc deforms approximately 10% in compression and rotates. When acting in sequence, this

allows an active rotation with passive counter-rotation of the shoulders versus the pelvis while walking or running.

Due to its viscoelastic properties, the intervertebral disc allows flexibility when subjected to limited loads, becoming increasingly rigid as the load increases. Of the total axial load borne by the intact disc, 75% is on the *nucleus pulposus* and 25% on the *annulus*⁴.

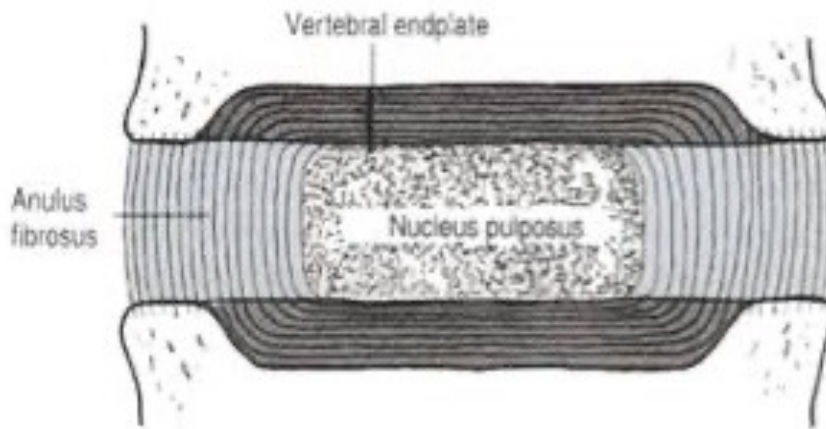


Figure 2.2: Intervertebral disc. The disc is a composite structure with two main components: the fibrous border (*Annulus fibrosus*) which encircles the disc, mostly composed of Type 1 collagen (which resist tensile forces) and the gelatinous centre (*Nucleus pulposus*), mostly composed of Type 2 collagen (which resist compressive forces). This gelatinous centre, with advanced disc degeneration, is no longer present in IDVP.

The young intervertebral disc displays clear physical and molecular differences between the outer *Annulus fibrosus* and inner *Nucleus pulposus* (Figure 2.2), which become less distinct in the adult⁵.

2.2 Normal aging

With increasing age comes variation in both the synthesis and degradation of the macromolecules, particularly aggrecan, and their structures⁶. **Are these changes by design, to adapt to the altered environment of the aging spine?**

It is recognised that lumbar lordosis decreases with the normal aging process, mostly due to disc degeneration⁷. Those who can adapt appropriately will, often unknowingly, cope with instituting a series of intra- and extra-spinal compensatory measures and manage well.

It is commonly thought that the degradative changes are detrimental to disc function, particularly given its inability to remove and replace accumulated degradation products. The rate at which these detrimental changes occur may vary between individuals because of genetic, biomechanical, and nutritional differences⁸. Diverse etiological factors are thought to serve as primary initiating events, including genetic predisposition, smoking, infection, abnormal biomechanical loading, decreased nutrient transport across the endplate and ageing⁹. As degeneration proceeds, there are elevated levels of inflammatory cytokines, enhanced aggrecan and collagen degradation, changes in disc cell phenotype¹⁰.

Yet imaging findings of spine degeneration are present in high proportions of asymptomatic individuals, increasing with age¹¹. It is therefore likely that an event secondary to a structural deficit, such as injury or leakage of NP material through annular fissures results in recruitment of immune cells to the disc which then triggers pain generation.

2.3 Low back pain in an aging population

The developed world has seen a steady increase in the **prevalence** of low back pain (LBP) over the last 20 years¹². This is considered due to the diverse reasons as cited above, including an aging population, a more sedentary younger population (Figure 2.4) and co-morbidities such as obesity. The **natural history** of low back pain is that it resolves or at least, improves to a manageable level in at least 75% of cases¹³.

By far, the greatest clinical findings in the LBP patient is the combination of weak buttock and abdominal muscles, and tight hip flexors and spinal extensors. This is called **lower crossed syndrome**². It was originally described in 1979 as Unterkreuz syndrome, by Janda (a Czech physician with a specialist interest in physiotherapy, who himself was a polio sufferer) through neurophysiological testing in sedentary older patients who spent the day sitting, then not seen in younger persons who were working in manual occupations including industry or farming, or previously hunting and gathering food etc. Interestingly, upper crossed syndrome exists for neck pain with similar characteristics. It most likely underpins most causes of current back pain.

Efforts to reduce back pain are wholesale in the workplace, including manual handling techniques and ergonomic changes such as desk/chair/computer screen height adjustments. Adjusting seat and desk heights are unproven with regard to preventing back pain. The key deficit with these is the failure to tackle the **pre-disposing risk factors** that lead to that point: that despite all, the person is **still sitting**. This gives rise to such muscle imbalances as outlined above, particularly the overworked secondary paraspinal extensors, which can tear on (even minimal) exertion and are, hate to say it, are the straw that...

By contrast, **regular exercise** continues to outperform all other measures as a preventative strategy.

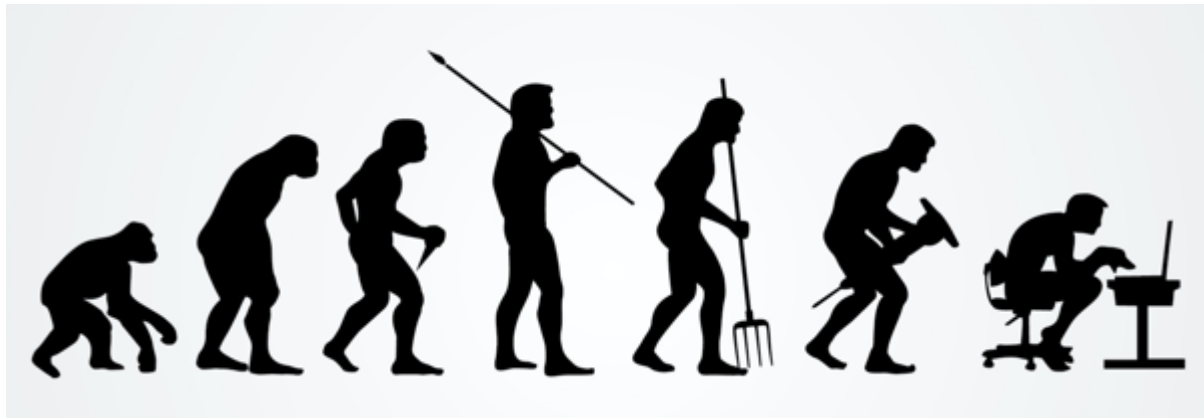


Figure 2.4: Devolution of the Human Spine.

2.4 Morphology of the Lumbo-Pelvic Spine

Over the past 30 years there has been a renewed interest in research in this area. This is because of the increasing prevalence of degenerative spinal conditions, the ability to visualise and measure dynamic and upright parameters of the spine and the growing market for innovative therapies- both surgical and non-surgical. A landmark discovery was the recognition of the pelvis as an indicator of what the individual shape of the lumbar spine should resemble. This was eclipsed as the angle of **pelvic incidence (PI)**, attributed to Duval-Beaupère (Paris) ¹⁴.

PI is an angular method to assess the antero-posterior size of the pelvis (Figure 4). A large pelvis requires a large lumbar lordosis (LL) angle, and a small pelvis, a small LL. This is a constant value for each individual, assuming that there is negligible movement across the sacroiliac joints. This angle should equal the angle of lordosis of the lumbar spine. Thus, if a sufferer of back pain presents with evidence of disc

degeneration in the lumbar spine, they will have an accompanying stoop, largely from the loss of angular lumbar lordosis. A reference parameter for what their normal lumbar lordosis angle should equate to, is the PI, within about 10 degrees.

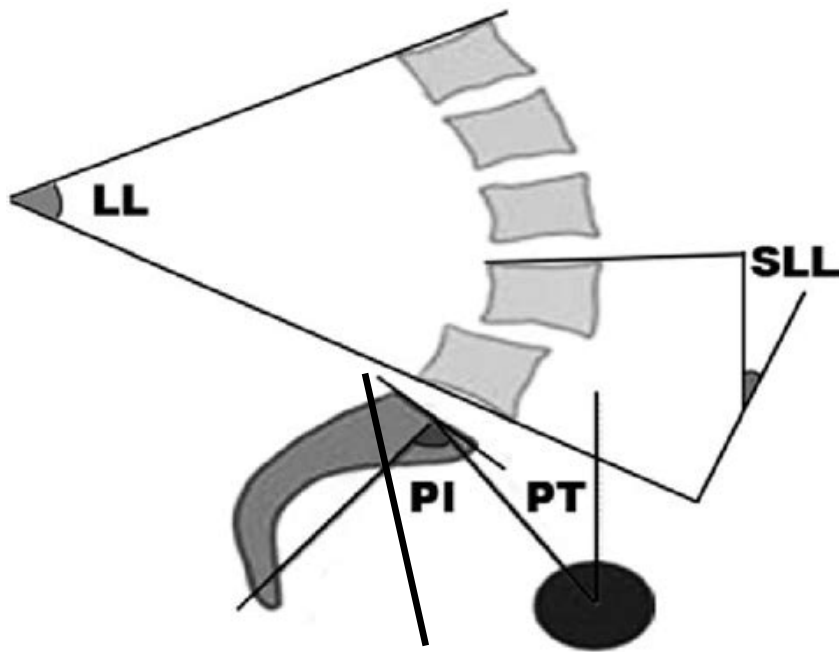


Figure 2.5: Pelvic Incidence (PI), a metric of sagittal alignment constitution and key predictor of lumbar lordosis. The **distribution of LL** also follows a pattern, in that most LL is within the lower lumbar areas, L4/S1. With a greater PI, the LL is distributed more across the L1-L5 region whereas with a low PI, LL mostly originates at the L5/S1 region. SLL is segmental LL. PT is Pelvic Tilt.

2.5 The Degenerative Process

Disc Degeneration

Given that the disc is a structure of low blood supply, its regenerative ability is non-existent. The start of the degenerative process for a disc is an annular tear, which disrupts the integrity of the ligament and may allow the inner *Nucleus* to degenerate or herniate to beyond its normal position, also known as a slipped disc. Reasons for a tear in the disc are to do with a deficiency in the annular fibrosis type 1 collagen, a

molecule that is designed to provide **tensile strength**. A disc herniation through the annular tear posteriorly into the spinal canal can cause nerve or spinal cord compression.

The gross morphology of disc degeneration was graded by Thompson et al in 1990¹⁵ (Table 1). It is worth noting the increasing prevalence of “clefts” in advanced disc degeneration. This is the histological manifestation of a void within the disc, a phenomenon that is reflected as IDVP on sagittal imaging, such as CT.

Grade	Nucleus	Anulus	Endplate	Vertebral Body
I	Bulging gel	Discrete fibrous lamellas	Hyaline, uniformly thick	Margins rounded
II	White fibrous tissue peripherally	Mucinous material between lamellas	Thickness irregular	Margins pointed
III	Consolidated fibrous tissue	Extensive mucinous infiltration; loss of anular demarcation	Focal defects in cartilage	Early chondrophytes or osteophytes at margins
IV	Horizontal clefts parallel to endplate	Focal disruptions	Fibro-cartilage extending from subchondral bone, irregularity and focal sclerosis in subchondral bone	Osteophytes less than 2 mm
V	Clefts extend through nucleus and annulus	-	Diffuse sclerosis	Osteophytes greater than 2 mm

Table 1: Thompson’s morphologic classification of disc degeneration.

Disc degeneration can be graded on MRI as proposed by Pfirrmann in 2001⁵. They proposed a five- stage **MRI classification** according to the following criteria: structure and colour (white/black), nucleus/annulus distinction, signal intensity, intervertebral disc height. The classification was descriptive and progressive. Greatest inter-observer disagreements from the Pfirrmann classification are regarding disc height, signal of the nucleus and for lumbosacral transitional vertebrae. These disagreements reflect the interpretation of signals from within the moderately degenerative disc, particular between grades 3 and 4⁵. Further Pfirrmann modifications include grade progressions of disc height collapse, signifying directionality of height collapse as the pathogenesis¹⁶Error! Bookmark not defined.

Advanced degeneration in both classifications included a hypointense nucleus signal, whereas with IDVP, disagreement can arise from an intense intradiscal signal consistent with fluid imbibement. In contrast, CT based imaging becomes more accurate in these cases, demonstrating accompanying end-plate sclerosis and differentiates between water and vacuum.

Because the traditional teachings of anatomy were from prosection of supine specimens¹⁷, dynamic anatomical components have only recently been captured in the scientific literature, through conventional imaging and software capabilities. It is worth noting that MRI (magnetic resonance imaging) was invented after CAT (computer-aided tomography) but CT (computed tomography) with its associated digital reconstructions post-dated MRI. Sagittal imaging of the spinal column through CT was borne from this technological advancement. While MRI best depicts soft-tissue, CT best depicts the most and least dense structures, namely bone and air, neither of whom are well visualized on MRI. Sagittal CT allows an appreciation of the profile of the intervertebral disc to highlight where there is no *Nucleus pulposus*, an intradiscal vacuum phenomenon (IDVP).

Endplate inflammatory effects can be observed as described by Modic et al over 30 years ago¹⁸ and remain the subject of much research and debate. MRI serves to highlight varying degrees of water, thus where oedema is depicted along the end plate, it indicates recent inflammation. With chronicity of inflammation, this changes to include greater fat infiltration, to then hardening and displaying sclerosis. There is a varying correlation of Modic changes with low back pain. Some who have Modic 1 changes (Bruised/Active) do not progress to Modic 2 (Fat deposition/settling). Both phenomena can exist at the same time and at the same level. There is a Modic 3 burnt-out phase with endplate sclerosis and biological dormancy. What is not apparent from either classification is the extent to which IDVP is present in degenerative discs.

There are two theories on the origins of disc degeneration-the former relates to constant extension and distraction of the spine which creates micromotion between adjacent vertebrae, low-solubility nitrogen within the negative pressure area and cavity expansion. The latter theory relates to endplate sclerosis which blocks the transfer of nutrients and metabolites to the inner disc, leading to disc degeneration and entrapment of gases¹⁹.

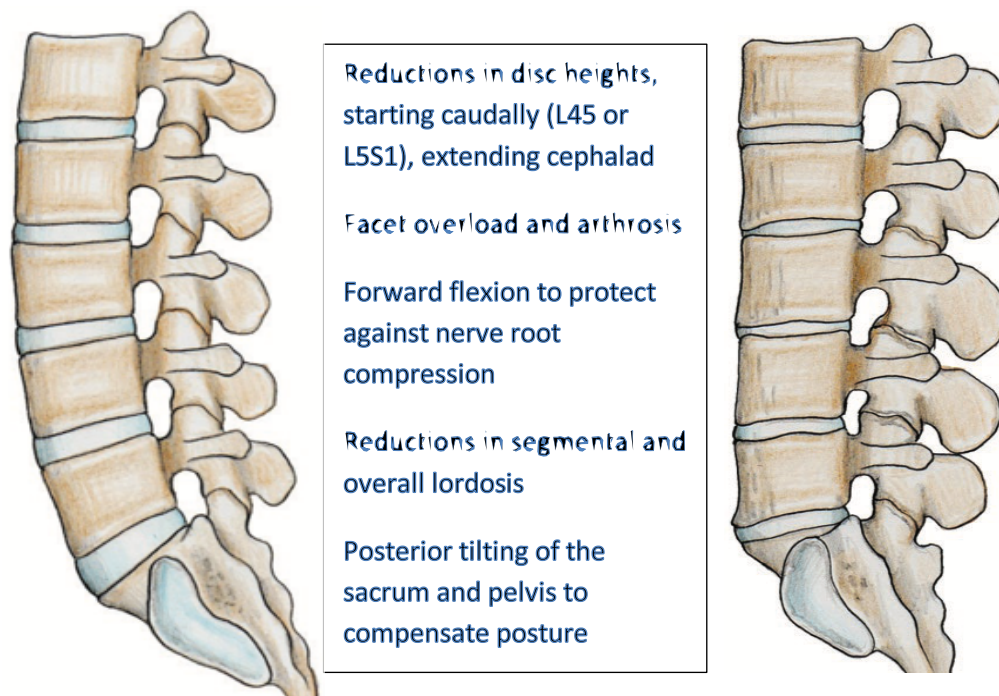


Figure 2.6: Spinal Degeneration. Evolution toward kyphosis with respect to the initial state by disc height narrowing, articular hypertrophy, hypertrophy of the spinous processes with interspinous contact.

2.6 Adult Spinal Deformity

The loss of disc height causes a loss of lordosis in the lumbar spine⁷. The prevalence of lower lumbar disc degeneration is higher than upper lumbar disc degeneration. It is recognised that low back pain sufferers often lose their lower LL with respect to upper LL. It is therefore relevant to identify if IDVP distribution is also reflective of pelvic incidence, a marker for lordosis distribution and if IDVP occurs along patterns of predictable disc degeneration.

The ability to remain upright, or bipedal relies on multiple compensatory mechanisms which keep us standing or walking within a range of angles relative to the vertical, also known as the “cone of economy”¹. With a loss of LL, one develops a stoop, or “sagittal disequilibrium”. To mitigate against this, there are intra- and extra-compensatory measures to help optimize posture²⁰. Extra-spinal compensatory measures include backward tilt (retroversion) of the pelvis, hip extension and knee flexion. Intra-spinal compensatory

measures include neck and thoracic extension. As mentioned, some extend the upper lumbar spine which frequently causes fatigue type pain.

Adult spinal deformity patients have shown a discrepancy in trunk flexion between standing and walking of 7.6°, which is particularly correlated with lumbo-pelvic (PI-LL) mismatch²¹. Muscular fatigue and/or claudication are accepted drivers of progressive kyphosis (stoop), but the evidence is limited. MRI studies showing the spinal muscle cross-sectional area in patients with flatback have been shown to be a marker for worsening kyphosis while walking²². However, paraspinal mapping with electromyographic studies did not differentiate between those with spinal stenosis and asymptomatic volunteers, with a reported sensitivity of 30%²³. In fact, kyphosis patients have shown greater muscle activity in the lower back in the resting standing position with greater muscle fatigue at the upper lumbar spine than patients with lumbar spinal canal stenosis²⁴.

With lumbar disc herniation, there develops a coronal translation, causing a scoliosis which with resolution of symptoms, either with time or surgery often reverses²⁵. While a stoop manifests affecting sagittal alignment^{26, 27}, in some older subjects, the associated **kyphoscoliosis** becomes a fixed or at least an uncorrected deformity. Sequential disc degenerations, invariably starting at either L4/5 or L5/S1 disc levels, progressing in a cephalad direction leading to a flattening of the lumbar spine, or loss of LL, to a variable degree of tolerance, as described above¹ (Figure 2.6).

2.7 Intra Discal Vacuum Phenomenon (IDVP)

A vacuum disc represents a 90% nitrogen gas accumulation where a cavity opens in a supine position, lowering the pressure and generating an intradiscal bubble²⁸. Magnusson reported that the vacuum, subsequently filled by gas, requires a reduction of barometric pressure within the disc of up to 0.05 atmosphere ($0.0505 \times 105 \text{ Pa}$). The significance of IDVP, because of the absence of structurally intact tissue, is that of potential “vertical instability”, a term used by Robert Mulholland in 2008 to refer to post-fusion yet symptomatic patients²⁹. In 2010, Goel et al proposed that acute or chronic weakness of paraspinal muscles secondary to disuse, abuse, or injury lead to telescoping of the spinal segments related to subtle or manifest listhesis at the facet articulation³⁰. The latter definition of the term fits better with IDVP as outlined above.

Lewandrowski et al surveyed 273 spine surgeons who mostly recognized IDVP as a sign of advanced disc degeneration and as a collapsing lumbar motion segment (182/273; 66.7%), that it preceded anterolateral lumbar instability (187/273; 68.5%), may cause vertical instability with symptomatic dynamic foraminal & lateral recess stenosis (222/273; 81%), mechanical back pain (201/273; 73.1%), and may cause sciatica-type low back and leg pain (179/273; 66.3%). The majority of surgeons indicated that vacuum phenomenon on radiographic studies is associated with vertical instability and collapse resulting in dynamic foraminal and lateral recess stenosis and should be treated surgically (199/266; 73.7%)³¹.

A supine lateral radiograph may demonstrate a IDVP if the trajectory of the radiograph is parallel to the disc space, observed in up to 20% in elderly patients³² and reported in almost 50% of chronic LBP patients¹⁹. Given the effects of gravity, these are not easily seen on erect radiographs. MRI scans identify fat (T1 imaging) and water (T2), thus serve as a useful imaging modality for soft tissue but intra-discal gas will not demonstrate high resonance or contrast to the surrounding bone³³. Secondly, given that MRI is a lengthy scan, the supine position will allow fluid to flow into a cavity and may yield a false negative disc signal³⁴. While a vacuum may collapse on erect radiograph imaging, it may conversely be highlighted with a supine radiograph in extension over a cushion support (Figure 2.7).

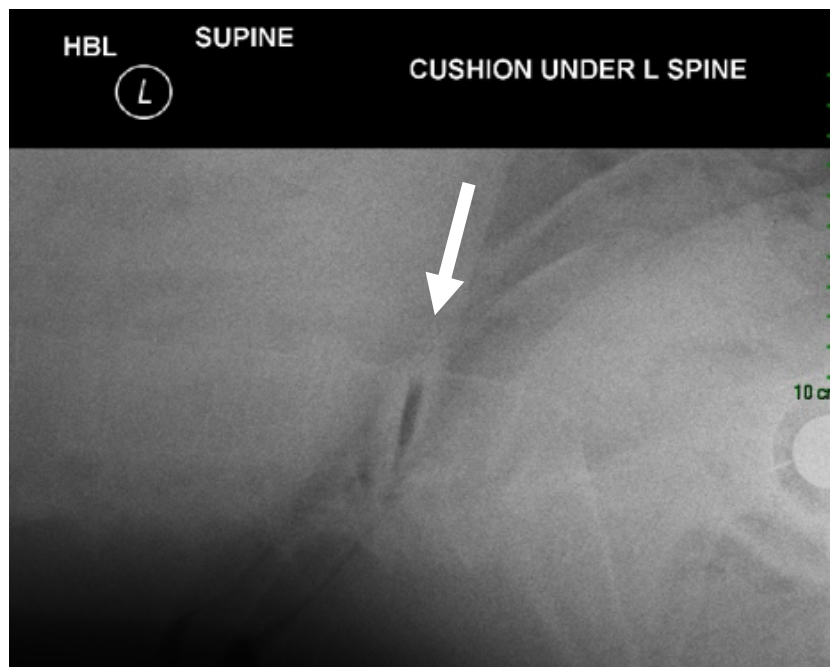


Figure 2.7: Radiograph displaying IDVP. The lumbar spine is extended over a cushion which opens the (black) vacuum at L4/5 (white arrow). The patient subsequently received an oblique anterior fusion, which both stabilised L4/5 and restored lordosis. Plain radiographs were not used in the research given the unpredictable rate of diagnosis.

CT on the other hand is a quicker supine scan and an intradiscal bubble is more likely to form. Accumulation of gas is a very rapid process, whereas the accumulation of fluid is a relatively slower

dynamic process³⁵. With disc degeneration and progression of vacuum as a proportion of the disc space, there is an accompanying progression of end-plate sclerosis³⁶. This corresponds to Modic Grade 3 changes, as referred to above. It is a radiological observation of hardening of the vertebral endplate, in association with advanced disc degeneration. This finding also serves as a guide to appropriate cement discoplasty, discussed later.

Radiological evidence of IDVP has been associated with LBP-in the morning, when standing up or rolling over³⁷. In a Turkish study, 12,450 consecutive patients with chronic LBP were investigated with CT and MRI. 219 (1.8%) were found to have IDVP, who had associated findings of disc degeneration, Modic change and spinal stenosis³⁸. Patients with severe IVDD were eight times more likely to have IDVP, increasing to 24 times at L5S1. Higher IVP severity scores at each lumbar level significantly predicted presence of severe disc degeneration and/or Modic changes at the corresponding lumbar level.

While this thesis outlines the aforementioned vertical instability that is evident with IDVP (telescoping spine³⁰), a correlate of this in the fracture environment is the intravertebral cleft vacuums that occur with non-union of fractures, often accompanied by signs of clinical instability, including back pain, spasm, stiffness and augmented by a support such as a brace or crutches^{34,39}.

The *Annulus fibrosus* that contains IDVP is relatively intact, as evidenced by the isolated case reports of vacuum cysts within the spinal canal^{40,41,42}.

However, there is no evidence that IDVP, separate from disc degeneration is causative of back pain symptoms. Similarly, while disc degeneration is associated with low back pain, there is an incidence of advanced disc degeneration, increasing with increasing age, as seen on MRI without significant symptoms¹¹. Brinjikji et al evaluated 33 articles reporting imaging findings for 3110 asymptomatic individuals. The prevalence of disc degeneration in asymptomatic individuals increased from 37% of 20-year-old individuals to 96% of 80-year-old individuals, similarly for disc bulges, disc protrusions and annular fissures. IDVP may be correlative with disc degeneration but not causative of it. For this reason, it may also be a necessary compensatory opening of the disc to allow for postural correction, in the presence of advanced disc degeneration.

Distribution of IDVP is most commonly within the anterior aspect of the intervertebral disc, with twice the prevalence of other patterns, including centrally, central-posterior or anterior-posterior⁴³ (Figure 2.6). In terms of intra-discal pressure, this can be interpreted as the area of greatest negative pressure.

While IDVP is a radiological finding, cadaveric analysis has shown that at a histological level, there is evidence of intra-discal cleft progression with advanced degeneration. Posterior concentric tears are first to

appear, with radial and perinuclear tears coalescing to become transdiscal tears⁴⁴. Similar to previous works, there is ingrowth of vascularized reparative tissue and while minor cracks may be filled by scar formation, complete healing of large tears is not possible owing to constant motion between the tear margins^{45,46}.

As a surrogate marker, IDVP signifies persistent movement in the presence of advanced degeneration^{19,47,48}. Studies of range of motion on cadaveric degenerate discs would indicate an increase in segmental motion (widening of the neutral zone) in moderate disc degeneration but with a restabilisation with severe disc degeneration^{48,49}. This is reflected as increases up to grade IV but decreases when disc degeneration advances to grade V⁴⁹.

2.8 Conclusion

As IDVP has not been studied in relation to its biomechanical significance or function, this thesis investigates, from a cohort of CT scans, these characteristics.

Our objectives show the associations of IDVP with disc degeneration:

- through the morphology of the lumbopelvic spine and sagittal based degenerative changes
- through its association with degenerative scoliosis, reflecting coronal based degenerative changes
- through its natural history, over an average of ten years
- compared with the most popular investigation for disc degeneration, MRI
- and in the context of an emerging treatment, cement discoplasty.

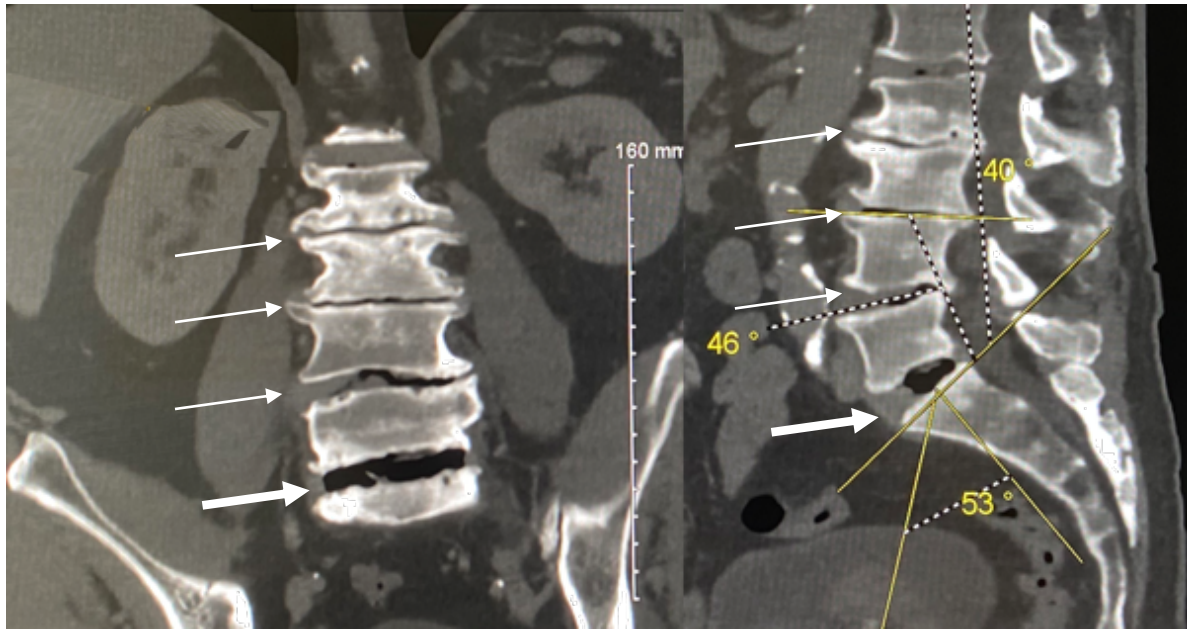


Figure 2.8: CT scan with coronal and sagittal reconstructions. Large IDVP noted at L5S1 (big arrow) with lesser IDVP noted at additional levels (small arrows). Additional evidence of disc degeneration was evident including disc osteophytes, end plate sclerosis and collapse.

3. Intra-Discal Vacuum Phenomenon matches Lumbar Spine Degeneration Patterns in an Aging Population.

3.1 Introduction

As mentioned, IDVP has not been evaluated in the context of lumbopelvic morphology or the associated degenerative pathologies that affect sagittal balance or spinal compensatory mechanisms. The objective of this study was to identify IDVP prevalence in an aging population, with respect to lumbar spine morphology and associated degenerative pathologies.

3.2 Methods

After approval from the institutional review board, subjects only included historic scans of those over 60 years of age without implication for treatment, without acute or relevant spinal pathology, who underwent CT scans of the abdomen for symptoms unrelated to the spine, with 1- 3 mm image cuts, over a defined time period (01/01/2012 onwards). All patient data were anonymized at the source and image interpretation data were collected in a secure database. The exclusion criteria were as follows: duplicate scans, insufficient quality or detail, pelvic or hip abnormality, acute spinal findings, destructive spinal pathology (tumor or infection), previous neuromodulation, or previous spine instrumentation.

All abdominal CT scans were performed using 64-MDCT scanners, with the subject in a supine position, with digital sagittal and coronal reconstructions (McKesson Radiology™). The selected scans had full visualization of the lumbar spine and pelvis (including the femoral heads), without spinal indications for CT scanning. CT scans were assessed by two experienced musculoskeletal clinicians who underwent IDVP-specific training in a consensus reading for the presence, location, and severity of intervertebral IDVP.

Degenerative pathologies were identified and also analysed separately, including isthmic spondylolisthesis, degenerative listhesis, prior lumbar fracture, lumbosacral transitional vertebrae (LSTV) and autofused segment(s). Categorization of IDVP was performed according to the classification of Wilhuber et al.³⁶, including mild (air/disc ratio 1:2, less air than disc tissue), partial (1:1, equal distribution), and total (2:1, with more air than disc tissue). Spinal analysis included sagittal lumbopelvic reconstructions to assess for IDVP and pelvic incidence (PI).

3.2.1 Statistical Analysis

All patient data were analyzed using the statistical software R v4.1 [R Core Team 2021]. Vienna, Austria]. Demographic and clinical details were compiled and summarized with respect to IDVP. Intra- and inter-observer agreements for the presence of IDVP on CT were assessed. Those with and without degenerative pathologies were selected and analyzed using ANOVA.

The variables for inclusion in univariate and multivariate were age, PI, Position (upper-middle-lower) and Involvement (single or multiple levels). These were used to answer the research questions posed above. These were used for a regressive stepwise progression so as to avoid including unnecessary variables.

Continuous variables were compared using the Mann-Whitney test, while categorical variables were compared using either the χ^2 or Fisher's exact test, where appropriate. The presence of IDVP was modelled using binary logistic regression to investigate associations with age (years), PI (degrees), and position (upper lumbar, equally upper and lower, and lower lumbar). Univariate models for each of the three predictors and mutually adjusted multivariable regression are presented.

Among those with IDVP, the prevalence and severity (Mild/Partial/Total) within levels (L1-S1) was recorded. The prevalence across positions was assessed using the χ^2 test for association. Severity was modelled using ordinal logistic regression to investigate associations with age and PI (degrees) at each level (L12, L23, L34, L45, L5S1) separately. Associated degenerative pathologies (as listed above) were selected and analyzed using ANOVA.

3.3 Results

The prevalence of lumbar spine IDVP was 50.3% (955/1898) and increased with age (125 exclusions). The distribution is outlined in Table 3.1. This increased in severity towards the lumbosacral junction (L1L2 8.3%, L2L3 10.9%, L3L4 11.5%, L4L5 23.9%, and L5S1 46.3%, Figure 3.1). A lower PI yielded a higher incidence of IDVP, particularly at L5S1 ($p<0.01$, Figure 3.2). A total of 292 patients had IDVP with additional degenerative pathologies (Figure 3.3, Table 3.2), which were more likely to occur at the level of isthmic spondylolisthesis, adjacent to a previous fracture or suprajacent to a lumbosacral transitional vertebra ($p<0.05$). Examples are shown in Figure 3.4

Characteristic	N	not seen, N = 940 ¹	vacuum seen, N = 663 ¹	p-value ²
PI	832	54 (11)	51 (11)	<0.001
Age	1,592	72 (8)	76 (9)	<0.001
Position (where positive)	649			0.010
Lower lumbar			412 (63%)	
Equal (upper & lower)			131 (20%)	
Upper lumbar			106 (16%)	
Involvement	1,498			<0.001
None		847 (95%)		
Unilevel			305 (46%)	
Multilevel			346 (52%)	

Table 3.1: Demographic Details and IDVP Regions. *p<0.05. ¹n (%); Mean (SD). ²Fisher's exact test; Pearson's Chi-squared test; Wilcoxon rank sum test. Data was missing for some subjects, including age and PI.

<u>292 IDVP with Lumbar Degenerative Pathologies</u>	<u>PI</u>	<u>Associated IDVP Level</u>
31 Isthmic spondylolisthesis (IDVP within level)*	62.6	L5S1
19 Degenerative listhesis (IDVP within level)	55.9	L45
89 Prior fracture (IDVP at adjacent level)*	51.5	Level of fracture
94 Lumbosacral transitional vertebrae (adjacent) *	61.4	L4L5
52 Adjacent auto-fused segment (adjacent)	50.3	-
7 Multiple diagnoses	61.5	-

Table 3.2: Cohort of IDVP with associated degenerative pathologies, which had a higher incidence of IDVP than those without associated degenerative pathologies. PI did not influence this. *p<0.05

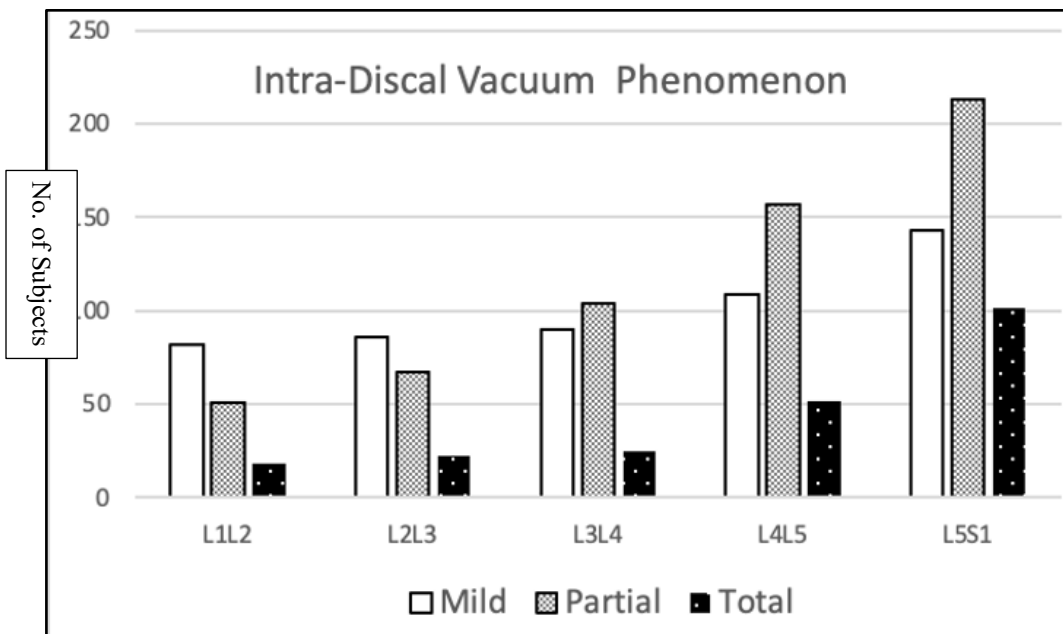
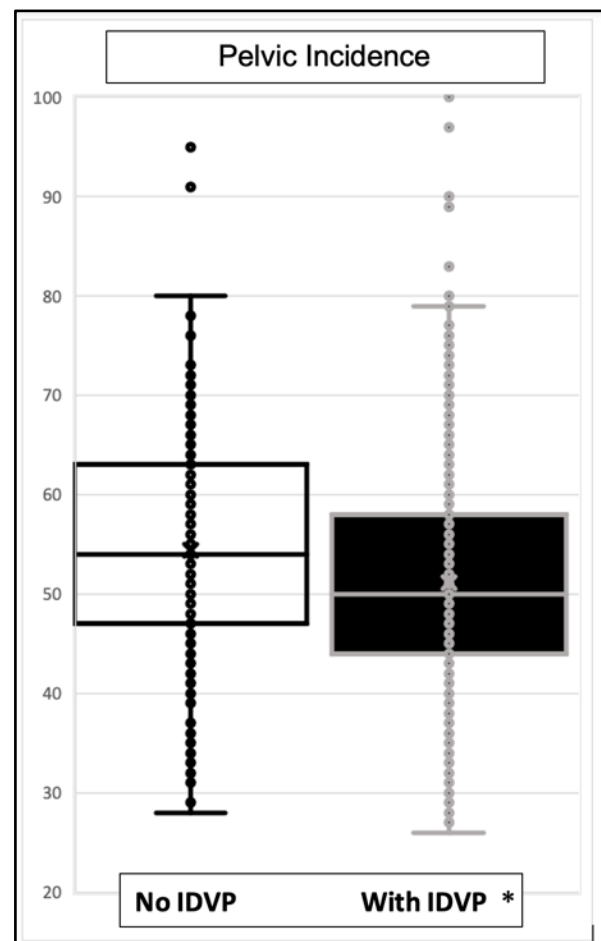


Figure 3.1: IDVP for each lumbar segment, with increases in prevalence and severity from L1L2 to L5S1 ($p < 0.001$).

Figure 3.2: Box plot/histogram of Pelvic Incidence for categories of No IDVP v With IDVP. * $p < 0.05$.



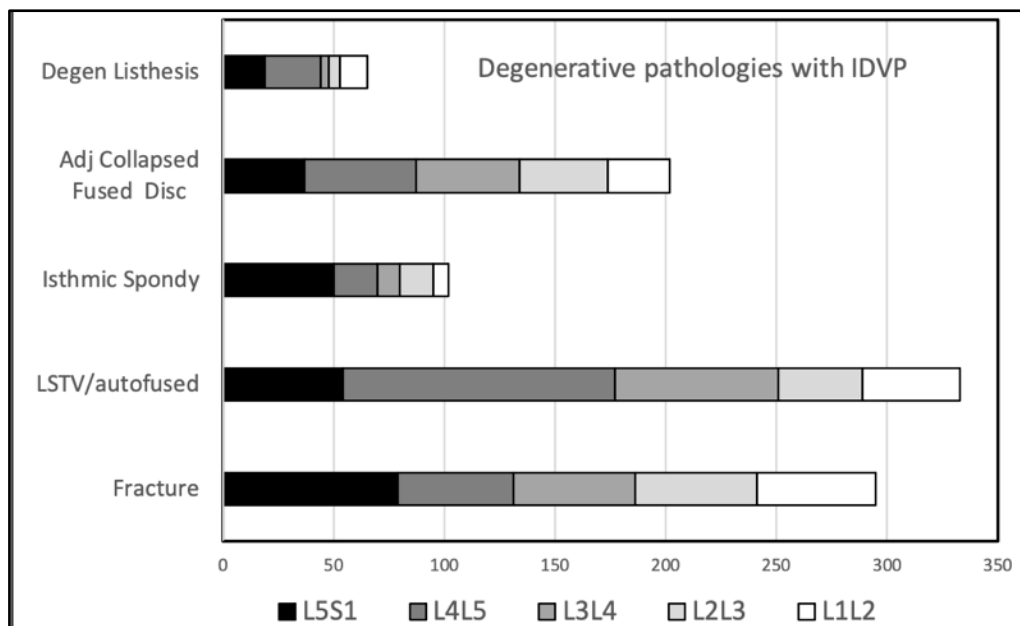


Figure 3.3: 292 subjects IDVP with degenerative pathologies, outlined at each different level and with weighted severity scoring. Isthmic spondylolisthesis, while invariably occurring at L5S1, displayed associated IDVP mostly at L5S1 but also at additional or other levels, similarly for lumbosacral transitional vertebrae at L45 and similarly for IDVP adjacent to fracture at the affected level.

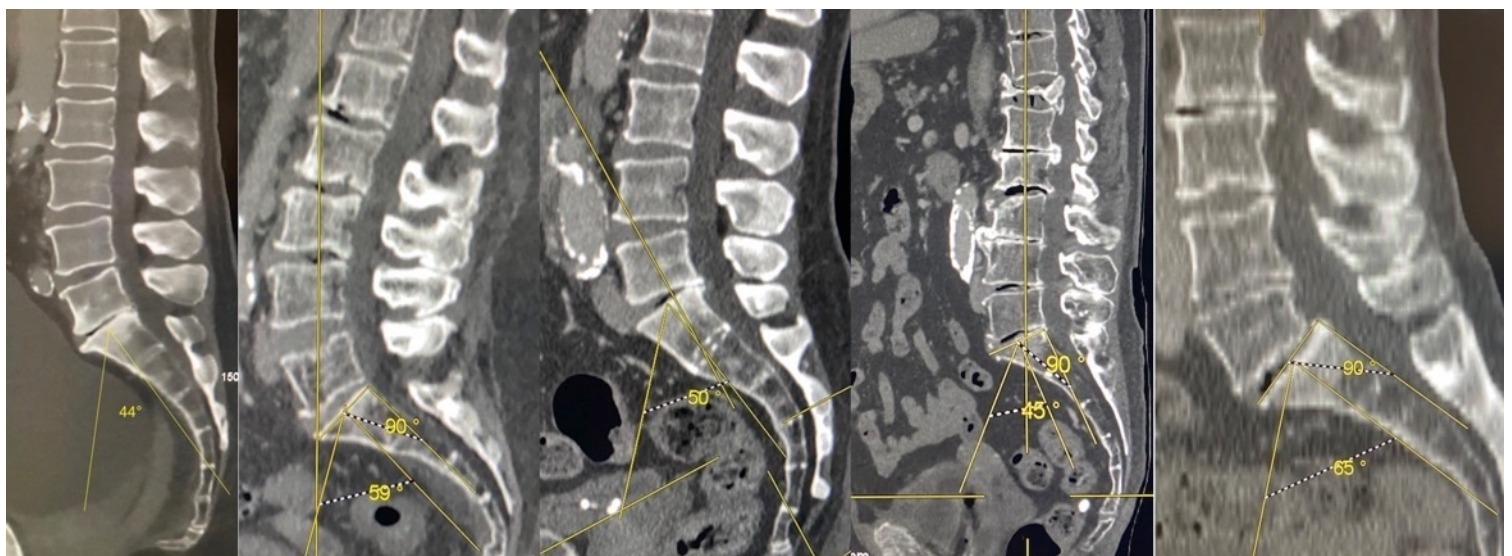


Figure 3.4: IDVP Examples. Findings indicative of lumbar spinal morphology and associated degenerative pathologies. A: Low PI° (Narrow pelvis, 44°) with IDVP L5S1. B: High PI (Wide pelvis, 59°) with IDVP L1L2L3L4. C: Lumbosacral transitional vertebra with IDVP L4L5. D: Fracture L3, T12 and Autofusion L3L4, each with adjacent IDVP. E: Isthmic Spondylolisthesis with IDVP L5S1.

3.4 Conclusion

Analysis of almost 2000 subjects revealed novel insights regarding IDVP. This study evidences the prevalence of IDVP in aging spines, associated with disc degeneration. IDVP occurs in 50% of adults over 60 years of age, significantly higher than previously cited, radiograph-based studies^{28,31,32,34}. This may reflect the increasing prevalence of degenerative disc disease, or the superior diagnostic ability of CT to radiograph, whose recent digital sagittal reconstructions post-date the invention of MRI. Where an IDVP occurs, it is more likely to occur at more than one level. It is expected that disc degeneration is increased in the lower lumbar spine, and this pattern has also been demonstrated with IDVP. Furthermore, this is particularly evident at L5S1 with a lower mean Pelvic Incidence (PI) and in association with degenerative pathologies, such as at L45 with sacralized L5S1 (LSTV), at L5S1 with isthmic spondylolisthesis, or adjacent to the level of a previous fracture.

While the associated diagnoses above cause disc degeneration from different biomechanical forces, the resulting IDVP, an empiric marker for movement, and in particular opening of the disc space, correlates with an extension moment on the spine in all cases. The acute lordotic angle at L5S1 in the setting of low PI is recognized as a significant risk factor in disc degeneration⁵⁰, and also outlined above. Similarly, Kanna et al noted in their series, where L5S1 had the highest prevalence of IDVP, that angular instability was the most important predictive factor in the pathogenesis of IDVP, more than translation¹⁹. The anterior shear forces associated with isthmic spondylolisthesis reflect correlative findings of disc degeneration and degree of slip. LSTV has degenerative effects at the suprajacent level for the disc and facet, and spinal stenosis. A vertebral fracture causes disc degeneration, regardless of the level. As outlined in the introduction, this would preferentially support the negative pressure theory over the endplate degeneration theory of IDVP¹⁹. The former relates to constant extension and distraction of the spine which creates micromotion between adjacent vertebrae, low-solubility nitrogen within the negative pressure area and cavity expansion. The latter theory relates to endplate sclerosis which blocks the transfer of nutrients and metabolites to the inner disc, leading to disc degeneration and entrapment of gases.

Recent studies of CT scans have shown considerable insight on IDVP, including that of Murata et al⁴³, who outlined increased severity of IDVP with worsening grade of disc degeneration, particularly with central (“island”) IDVP that also involved the anterior annulus. We effectively consider their three-level grading of IDVP severity (spot- linear-island) to be similar to that of Kanna’s (dot-linear-dense) or Wilhuber’s CT classification of endplates³⁶.

This study was designed not to identify clinical correlations or associated symptoms as those studies exist, but to establish morphological-based patterns in an aging population. Established disc degeneration affects sagittal alignment, even at a young age. It is especially correlated with low PI, lower arc lordosis, and axial-type compressive forces⁵⁰. Conversely, high PI values tended to indicate degeneration at the L3L4 and L4L5 discs. Both PI patterns were reflected in this population, occurring at the level of challenges to sagittal alignment. The associated degenerative pathologies also accelerated disc degeneration at the affected level(s).

However, this study had some limitations. This series would provide a more comprehensive analysis as a prospective series with a detailed analysis of symptomatology. Retrospective symptomatology in a population over 60 years of age may yield little, given the potential for exclusion and inclusion (α and β) errors—memory decay regarding historical back-related symptoms and a high incidence of an episode of back pain, respectively. It is also possible that despite efforts to normalize the cohort, these subjects may not be as healthy as those who would not avail of health services. The use of contrast was not controlled for and may have affected results. A comparison with erect imaging would provide further insight into the IDVP. No erect CT exists, but this would best analyze this.

Finally, it is worth noting a well-recognized high prevalence of disc degeneration in asymptomatic patients aged over 60 years. To further differentiate those with pathological versus age-related changes, correlative studies of both MRI and CT would provide valuable insights, as outlined in Chapter 6. The reasons why a significant minority do not develop IDVP go beyond the remit of this research, which is based on yet-unknown genetic elements and associated phenotypes. Nonetheless this study highlights those who with IDVP potentially display an adaptive mechanism as a result of suboptimal spinal biomechanics.

4. Patterns of Intra-Discal Vacuum Phenomenon in Adult Degenerative Scoliosis

4.1 Introduction

Degenerative scoliosis occurs with asymmetric disc and facet degeneration and vertebral wedging. Intra-Discal Vacuum Phenomenon (IDVP) is associated with advanced disc and facet degeneration, but typically poorly visualised on x-ray or MRI, and has not been reported in the context of degenerative scoliosis. Controversies exist over the progression of degenerative scoliosis, particularly with regard to the mechanical stability of the deformity and the implications for reconstructive surgery, which carries a risk of over 35% for mechanical complications and a significant economic burden⁵¹. Yet, in cases where surgery is indicated, it improves overall health-related quality of life, with differential benefits from sagittal and coronal corrections⁵². Conservative options have a limited role^{53,54} as have surgical decompression, limited spinal fusion and cement discolasty^{55,56}. A subset of the cohort outlined in Chapter 3 was isolated to further investigate degenerative scoliosis through evaluation and characterisation of IDVP.

4.2 Methods

Methods were similar for the cohort outlined in Chapter 3. The lumbar spine was analysed for severity, distribution, symmetry, scoliosis, pelvic incidence and listhesis. The definition for de novo degenerative scoliosis was taken as a Cobb angle of 10° on coronal reconstruction, as outlined in previous studies^{57,58}. An S-shape curve was considered if the secondary curve was also greater than 10°, otherwise it was considered a C-shape curve. The prevalence of scoliosis was calculated along with demographic details including age, gender and ethnicity. Exclusions were imaging for recent trauma or disease monitoring such as infection or tumor.

Statistical analysis

All subject data were analyzed with the statistical software R v4.1 (R Core Team (2021). <https://www.R-project.org>). Demographic and clinical details were compiled and summarized with respect to scoliosis. Continuous variables were compared using Mann-Whitney tests, while categorical variables were compared using either a χ^2 or Fisher's exact test where appropriate. The presence of scoliosis was modelled using binary logistic regression to investigate associations with pelvic incidence (PI, degrees), and position within the lumbar spine (lower (L4L5S1), equally both, upper (L1L2L3)) and back pain (yes/no).

Univariate models for each of the predictors, and a mutually adjusted multivariable regression are presented, to adjust for confounding. Clinically significant back pain details were recorded and analysed.

4.3 Results

148 subjects with scoliosis were identified (Table 4.1). 140 (95%) scoliotic subjects displayed IDVP. Subjects with S-shape curves accounted for 76% (112) and C-shape curve in 24% (36). 108 (97.3%) with an S-curve had multilevel contralateral IDVP compared to 8 (23%) of C-curves (Figure 4.1). IDVP position was distributed more towards the upper lumbar spine and with increased asymmetry (concavity-based). Examples are shown in Figures 4.2 and 4.3.

Characteristic	scoliosis, N = 148
Age	80 (9)
Gender	39M:109F
Back Pain	63 (43%)
PI	54 (11)
Position of IDVP	
Upper Lower	37 (28%)
Equal Lower/Upper	41 (31%)
Lower Lumbar	56 (42%)
Asymmetric IDVP levels	132 (95%)
IDVP Level Involvement	
None	9 (6.2%)
Unilevel	24 (16%)
Multilevel	113 (78%)

Table 4.1: Subject characteristics by scoliosis

Figure 4.1: Distribution of IDVP in scoliotic cases: C curve with 27/35 displaying unilateral IDVP patterns. S curve (most common) with 108/111 displaying contralateral IDVP patterns. Values and corresponding percentages are weighted to represent increasing severity of IDVP.

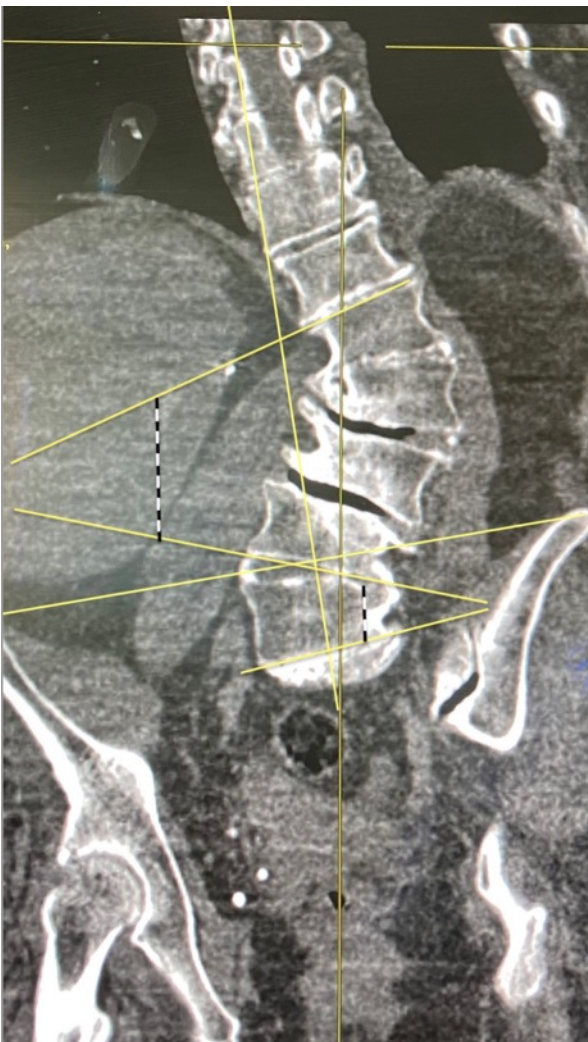
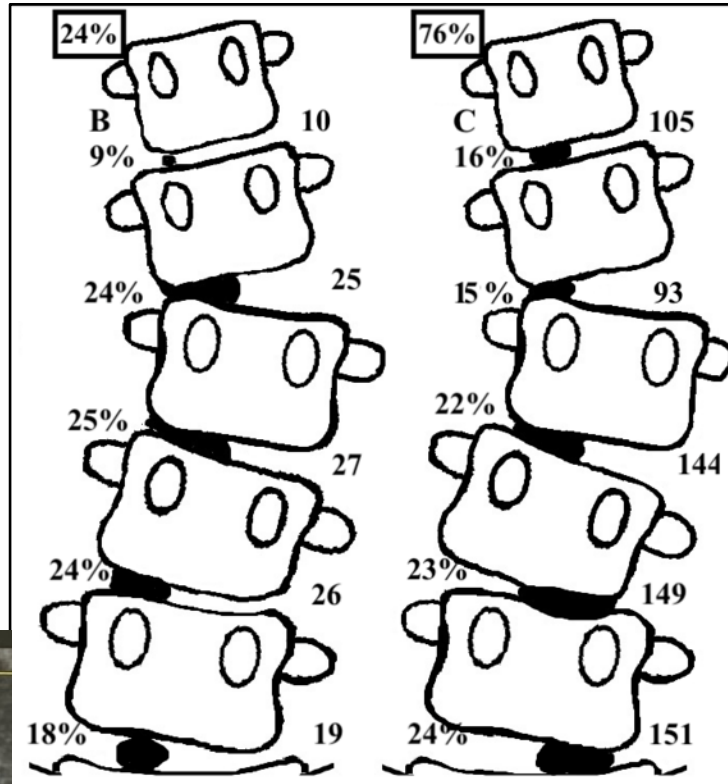
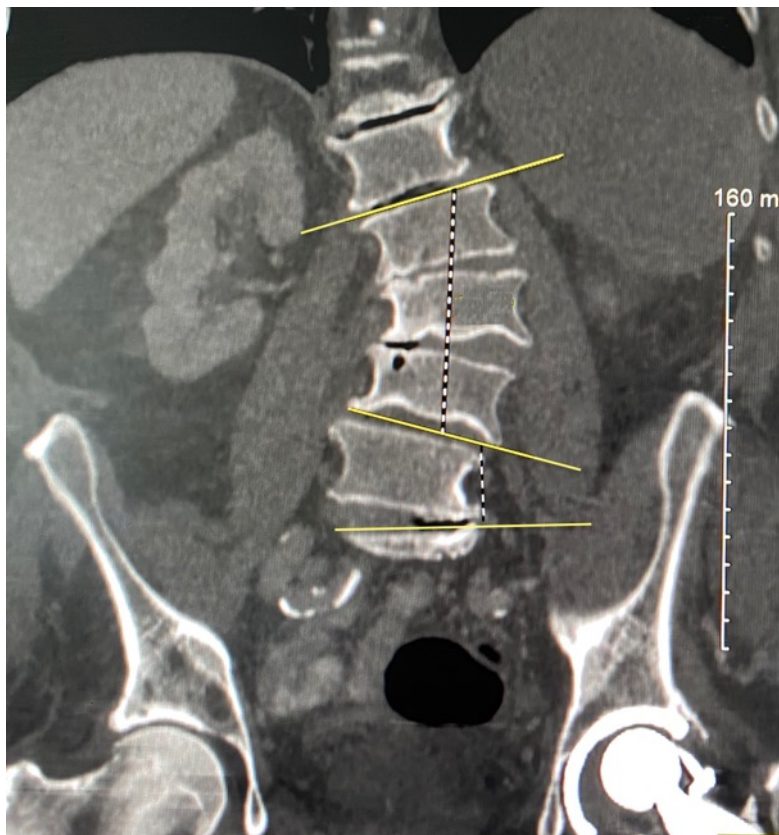


Figure 4.2: Degenerative S-curve scoliosis with IDVP at L2L3 and L3L4, associated L2 wedging, endplate sclerosis and disc osteophytes. Deformity and prior autofusion noted at L4L5 and L5S1. Incidental vacuum noted at contra-lateral (to concavity of curve) left sacroiliac joint.

Figure 4.3: Degenerative S-curve scoliosis with multilevel contra-lateral IDVP, total IDVP at T12L1, right side partial IDVP at L1L2 and L3L4, left side partial at L5S1. Incidental (worn out) hip replacement on the left side, which may have previously influenced coronal alignment (Trendelenberg gait).



4.4 Conclusion

This is the first study to report on the characteristics of IDVP in degenerative scoliosis, from an aging population. IDVP accompanied adult lumbar scoliosis in 95% of over 60 year-old subjects. Importantly, there were clear patterns of IDVP, reflected most in multilevel contralateral IDVP in those with S-shape curves (76%), with accompanying lateral listhesis and increased Cobb angle. The distribution of IDVP was different to that seen in an overall over-60s cohort, as reported in Chapter 3, with a high prevalence of upper lumbar IDVP. It is recognized that patients with degenerative scoliosis have higher pathologic spinopelvic parameters (such as sagittal and coronal imbalance), single leg support time when walking, center of mass, and increased head sway and lower extremity neuromuscular activity^{59,60}. It is likely that the varied distribution in IDVP that is different to non-scoliotic cases is relevant to differences in gait and postural patterns.

IDVP as a surrogate marker for intersegmental movement^{19,47,48} provides insight on how degenerative scoliosis behaves and implications for both minimalist and corrective surgeries. These include cement discoplasty which can stabilize a scoliotic curve, offload the associated foraminal stenosis and allow partial sagittal and coronal correction without the heavy morbidity of corrective surgery, particularly in frail or elderly patients.

Concavity based IDVP, outlines the secondary disc degeneration that occurs in response to a contralateral disc degeneration, which invariably progresses in a caudal to cephalad distribution with a primary asymmetry in the caudal lumbosacral area. This facilitates increased coronal deformity where multiple levels are involved, with the most common apex at L3. These degenerative coronal changes are invariably coupled to sagittal based changes.

One may consider the observed multilevel contralateral IDVP and S-curve scoliosis as an ongoing and functional spinal shape. It may act as an intraspinal coronal compensatory mechanism in the degenerative spine to remain within the “cone of economy”, as described previously¹. The coexistence of vacuum, end plate sclerosis and disc osteophyte provide insight onto the loading and unloading on the concave aspect of a C-shape or on opposing aspects of the S-shape curves (Figures 4.2 and 4.3).

5. Natural History of IntraDiscal Vacuum Phenomenon and its role in Advanced Disc Degeneration.

5.1 Introduction

Having shown the presence of IDVP in sagittal (Chapter 3) and coronal (Chapter 4) based pathologies, this study was designed to identify the behavior of IDVP over time. The natural history of disc herniation is well described. However, our knowledge of the endpoints of natural history of disc degeneration remains unknown. MRI loses accuracy with advanced degeneration, becoming hyporesonant and indistinct. Cadaveric specimens display adaptive changes in the disc with loss of the hydrostatic capacity of the nucleus, increased intra-discal clefts and end-plate impermeability^{44,45}. IDVP is associated with advanced disc degeneration and CT is the optimal modality to visualise this^{35,43}.

5.2 Methods

Similar inclusion and exclusion criteria were applied in this study to those used in Chapters 3 and 4. Subjects only included historic CT abdomen scans of those over 60 years of age without acute or relevant spinal pathology, with a diagnosis of at least one level with IDVP on the original CT scan and all of whom had a similar scan >7 years later. A history of clinically significant back pain was also recorded.

Recorded demographic details included age, ethnicity and gender. Symptoms of back pain were recorded from clinical charts where there was evidence of clinically significant back pain, as defined by pain over 3 months, with radiographic imaging or MRI scan of the lumbar or thoracic spine or any spinal intervention or injection, during the study period. There was no comparative data used for subjects without IDVP.

Statistics

As per relevant studies on the topic, a cohort of 60 subjects were chosen to power the study^{5,16}. All patient data were analysed with the statistical software Rv4.1 [Core Team (2021)]. Demographic and clinical details were compiled and summarised with respect to the natural history of IDVP and for disc height over time (autofused/same/worsened). Continuous variables were compared using Mann-Whitney tests, while categorical variables were compared using either a χ^2 or Fisher's exact test where appropriate. Intra- and inter-observer agreements for the presence of IDVP on CT were assessed.

The natural history (autofused/same/worsened) was modelled using ordinal logistic regression (both baseline and follow-up data together using a random effect) to investigate associations with age (years), follow-up time (years), back pain (yes/no), involvement of other levels (yes/no), worst level (L1L2, L2L3, L3L4, L4L5, L5S1), and type (Uni- or Multilevel). Univariate models for each of the predictors, and a

mutually adjusted multivariable regression are presented. Disc height categories were analysed for IDVP negative and each level of IDVP positive severity and compared using ANOVA (analysis of variance) and Tukey's HSD (honestly significant difference). Statistical significance was set as less than 0.05.

5.3 Results

CT scans included 360 levels in 29 males and 31 females (mean 68.9 years), displaying 82 levels of IDVP, with a second scan included after a mean of 10.3 years, (Table 5.1). Most levels displayed the same level of severity (persisted, 45) compared to where some progressed (26), regressed (8) and fused (3) ($p < 0.01$, Table 5.2). There was also an increased incidence, 37/60 (62%) of developing IDVP at another level. Disc heights were reduced with increased severity of IDVP. A record of back pain was evident in 31/60 subjects, which was not significantly worse in those with worsening severity or additional level involvement over the study period.

Age at entry	68.9 years (SD 7.75 years)					
Gender	29 male, 31 female					
Time period since index scan	10.3 years (SD 2.4 years, Range 7-15 years)					
Levels analysed	360 levels with 82 IDVP					
Incidence of	T12L1	L1L2	L2L3	L3L4	L4L5	L5S1
IDVP at index scan	3M	3M	3M,4P	5M,4P,1T	9M,11P,5T	9M,13P,12T
	6.7%	5%	11.7%	16.7%	41.7%	60%

Table 5.1: Demographic and Index Scan Details. SD: Standard Deviation. M:Mild, P:Partial, T:Total.

194 (54%) IDVP remained negative	<u>45 (13%) Persisted same severity</u> 10 Mild 18 Partial 17 Total	<u>26 (7%) Progressed in severity</u> 16 Partial 10 Total	(1 Improved, progressed at another level)
65 (18%) Additional IDVP levels developed	<u>14 (4%) Autofused</u> 8 Previously autofused 6 Additionally autofused (3 were originally Partial IDVP levels, 3 were originally IDVP negative)		7 (2%) Exclusions (fractures, Schmorl nodes) 8 (2%) Regressed in severity

Table 5.2: Outcome of 360 levels from the second scan.

	Unadjusted				Unadjusted		
	Odds Ratio	95% CI	p		Odds Ratio	95% CI	p
Age	1.00	0.95, 1.06	0.46		1.01	0.95, 1.07	0.38
Follow up	1.05	0.85, 1.29	0.32		0.94	0.73, 1.21	0.32
Back pain	0.73	0.26, 1.97	0.27		1.13	0.36, 3.62	0.42
Other levels	3.45	1.17, 11.31	0.02*		3.26	1.02, 11.89	0.03*
Involvement	0.77	0.27, 2.19	0.31		0.87	0.24, 3.15	0.41
Worst level L23	3.50	0.15, 137.93	0.23		1.68	0.06, 75.14	0.38
Worst level L34	11.24	0.65, 359.61	0.06		4.41	0.19, 176.06	0.19
Worst level L45	47.66	3.55, 1284.54	0.00*		30.86	2, 926.53	0.01*
Worst level L5S1	26.83	2.2, 677.6	0.01*		16.13	1.08, 469.48	0.03*

Table 3. Univariate (left) and multivariate (right) logistic regression models of IDVP. Worst levels were identified as compared to L12. *p<.05

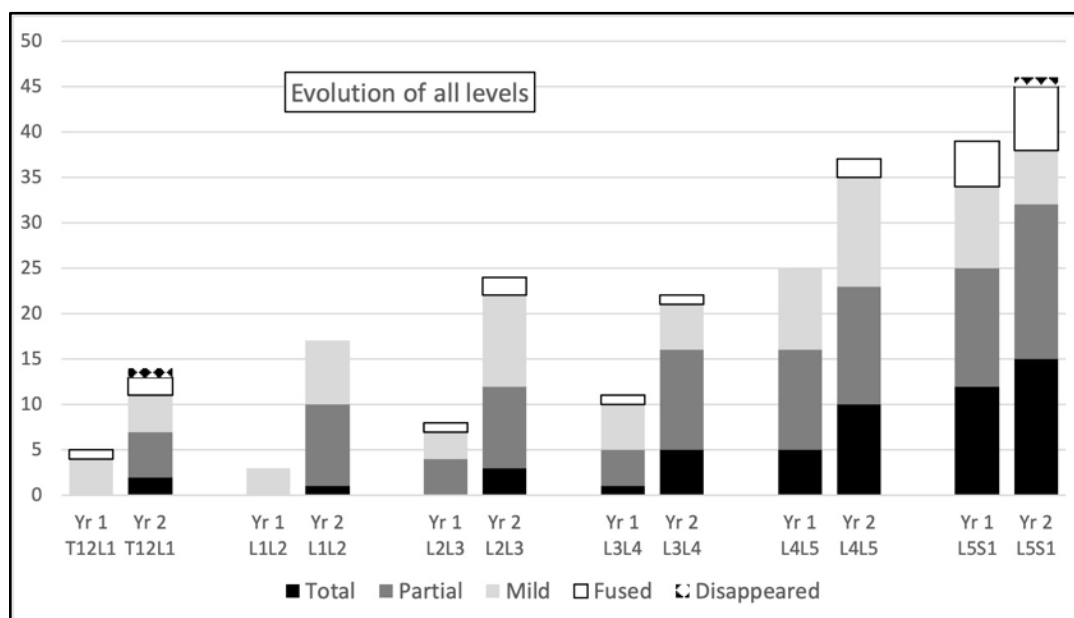


Figure 5.1: Evolution of IDVP at all levels over 10.3 years: Comparisons of IDVP from T12-S1, identifying progression of severity and incidence at each level.

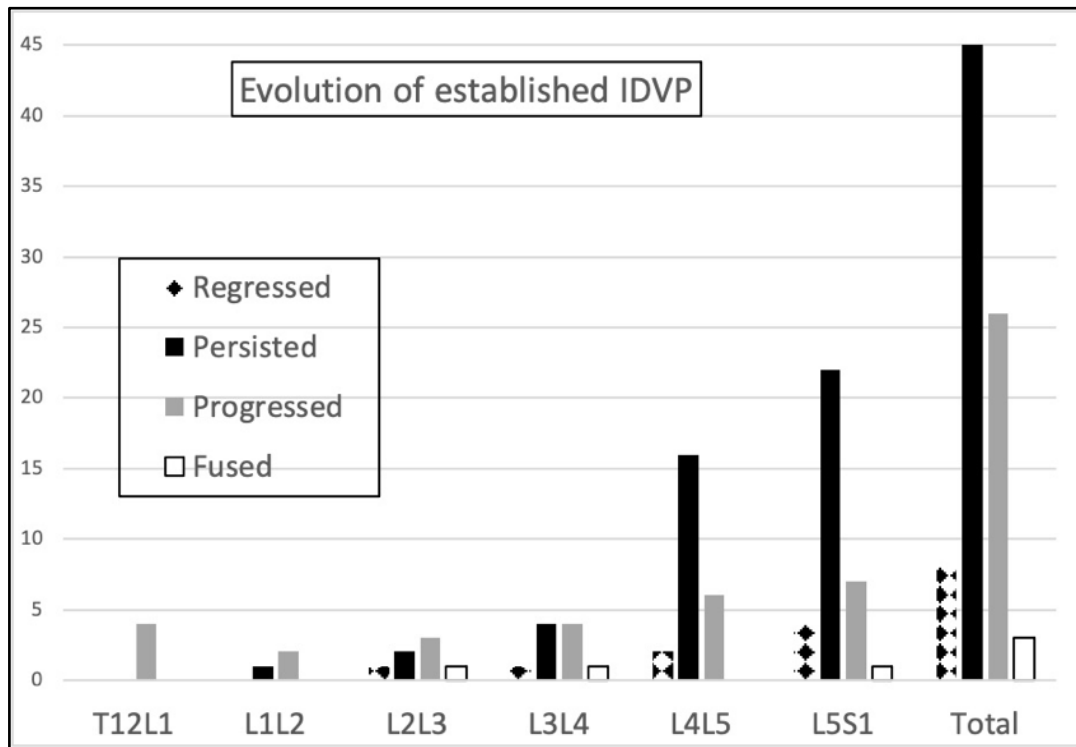


Figure 5.2: Evolution of IDVP at established levels detected on the index scan, identifying persistence of the same severity in most cases.

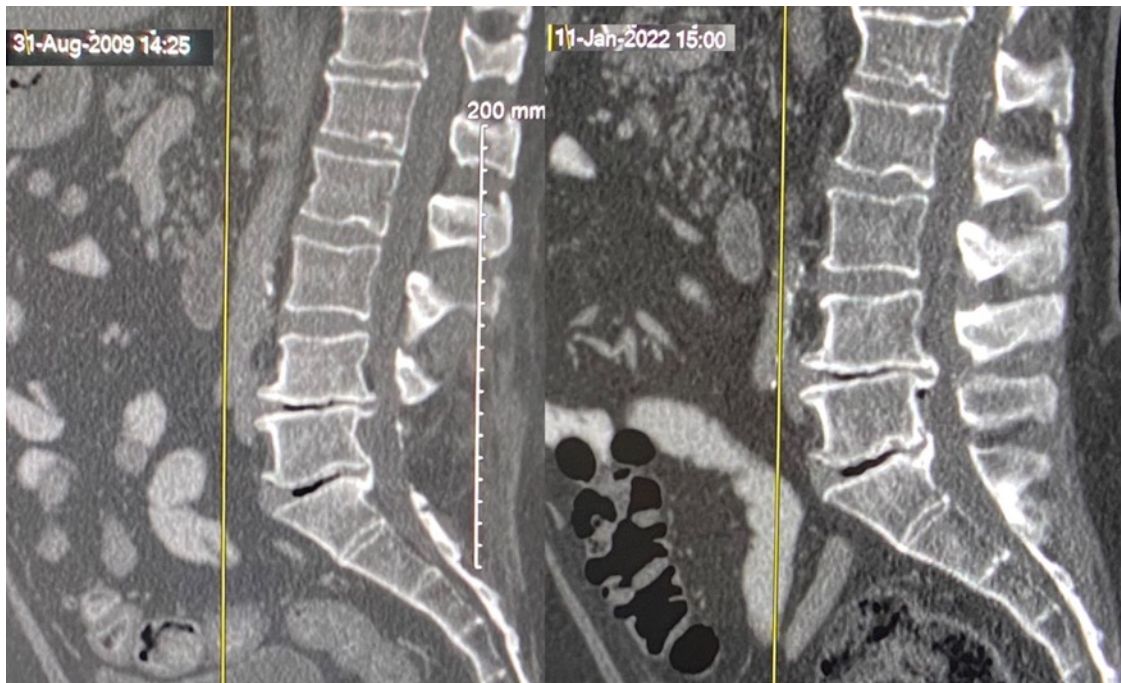


Figure 5.3 Persistence of IDVP. 60M, IDVP at L45 and L5S1 at 13 years.

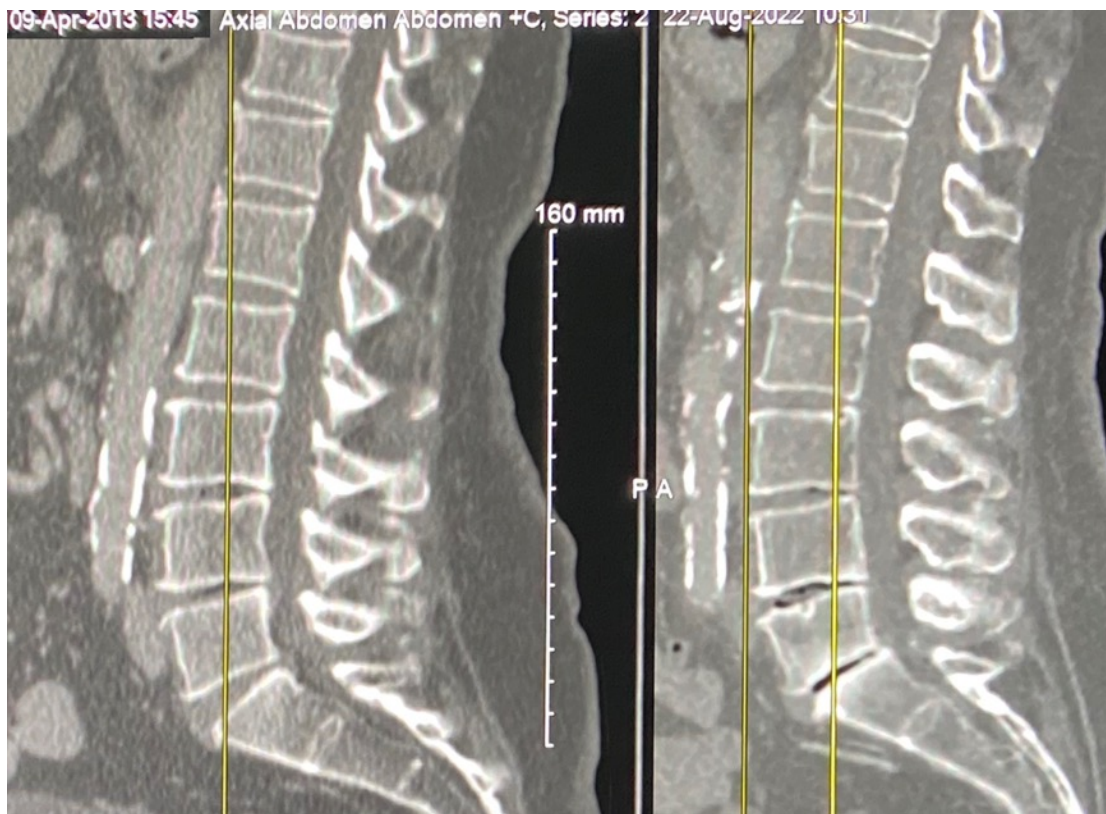


Figure 5.4: Progression of IDVP. 75F, IDVP at L3L4, L4L5 with new IDVP at L5S1 after 9 years.

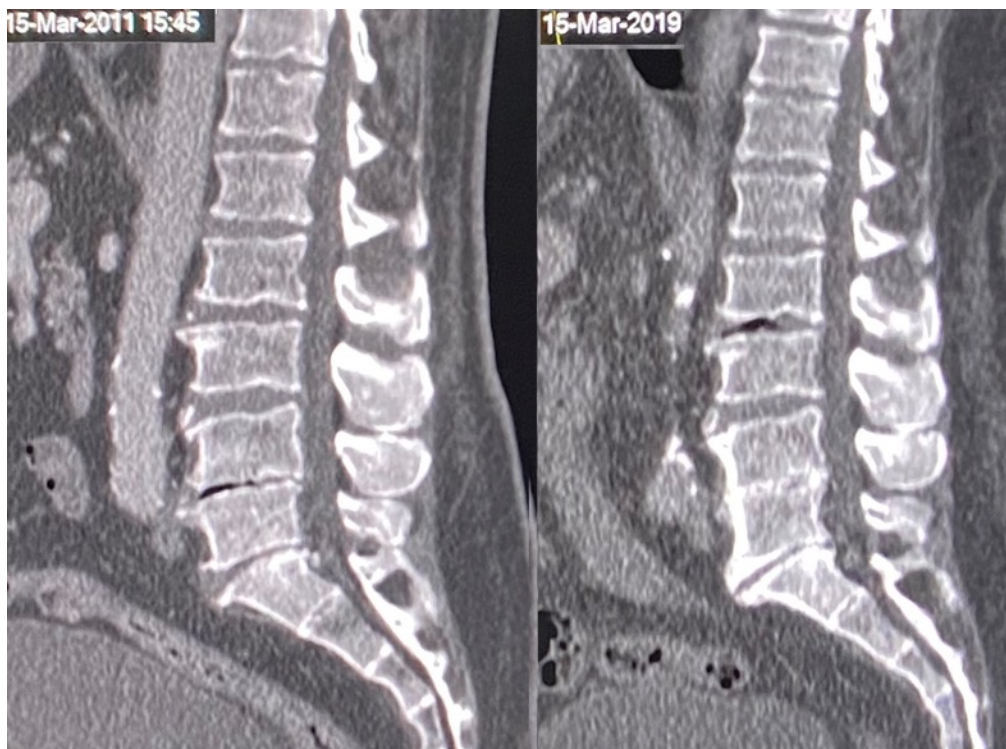


Figure 5.5: Autofusion of IDVP. 61M, with disappearance of IDVP at L4L5, new IDVP at L23, persistent disc degeneration at L5S1, over 8 years.

5.4 Conclusion

This study of subjects over 60 years of age, all chosen with an incidental diagnosis of at least one IDVP on an index CT abdomen scan, has shown that on analysis over 10 years, almost 90% of IDVP persist or progress and almost 75% will display additional IDVP at another level. These are new findings, previously unreported. This complements the findings of Chapter 3 which outlines the distribution of IDVP with disc degeneration and associated diagnoses. Findings of Chapter 4, which focus on degenerative scoliosis would not reflect a significant proportion of the population with disc degeneration and therefore would not correlate with the typically natural history.

It is expected that with increasing age, comes increasing disc degeneration, particular with more caudal disc levels. However, in most cases, the affected level will display the same severity of IDVP 10 years later, most likely plateauing of progression at a partial-to-total severity of IDVP. Furthermore, while a significant number progress in severity, very few IDVP progress to autofusion (4% (3/82)-3% (10/360)).

As a surrogate marker for movement, IDVP signifies persistent movement in the presence of advanced degeneration. With increasing severity of IDVP, there was a corresponding reduction of disc height. The reported re-stabilisation of degenerate discs therefore encompasses the reduction in disc height as well as the increased severity of IDVP.

Cadaveric analysis has shown that at a histological level, there is evidence of cleft progression within the degenerate disc^{44,45}. Posterior concentric tears are first to appear, with radial and perinuclear tears coalescing to become transdiscal tears. Similar to previous works, there is ingrowth of vascularized reparative tissue and while minor cracks may be filled by scar formation, complete healing of large tears is not possible owing to constant motion between the tear margins. Similarly, albeit not specifically measured, it was noted that IDVP morphology did not vary over the time period, and while compressible, is not a mobile bubble as potentially perceived (Figure 4).

Evidence of spontaneous autofusion of lower lumbar spondylolisthesis is seen in 20% when followed over a long period⁶¹. The exact pathophysiology of autofusion remains unclear, but it is likely to be like other osteogenic processes including immobilization, inflammation, vascularization and decortication. Some of the autofusions originated in partial and some from an originally IDVP negative disc. None of the autofusions originated from Total IDVP. As neither age nor length of scan interval was significant, it is evident that progression to autofusion is not necessarily a time dependent factor.

6. Correlation of Lumbar Spine Disc Degeneration on MRI with Intra-Discal Vacuum Phenomenon on CT scanning.

6.1 Introduction

Intra-Discal Vacuum phenomenon (IDVP) is associated with advanced disc degeneration, as shown in previous chapters, representing a surrogate marker for persistent intra-segmental movement. MRI is by far the most common imaging modality used to investigate this. It demonstrates disc degeneration as disc height loss, intradiscal hypo-intensity and distinction loss between nucleus and annulus, but not as reliably delineating IDVP as with CT. With advanced changes on MRI, observer agreement is reduced, largely because of poor signal from the dehydrated disc and sclerotic end plates¹⁶. CT is not well documented as an imaging study for degenerative conditions or deformity, even since digital sagittal reconstructions have been made possible. By encompassing sagittal plane CT evaluation along with MRI, our objective is to identify correlative features of IDVP in disc degeneration, including upper versus lower lumbar distribution and why it may be absent.

6.2 Methods

As per previously, this study was designed using retrospective data, using the national medical imaging platform. All patient data was pseud-anonymised at source, then image interpretation data were collected in a secure database. Randomisation was performed through inclusion of all subjects, over 60 years of age, over a historic three-month period (2014) with complete imaging. An over-60s population random sample of 65 subjects (29M, 36F) with low back +/- leg pain was isolated, who had

- MRI of the lumbar spine,
- but who separately had a CT abdomen within 9 months

All scans were assessed using Change Healthcare™ software across scanners from eight hospitals. CT scans were performed on multiple 64-MDCT scanners (Figure 1), with the subject in a supine position, with slice thickness of 1mm, as part of an abdominal protocol. MRI data were acquired with a 1.5-T imaging system with a maximum gradient strength of 30 mT/m, without intravenous contrast. Selected scans had full visualisation of L1/L2 to L5/S1. CT and MRI scans were simultaneously assessed by two clinicians (with at least two-year post qualification experience), who underwent IDVP-specific training in a consensus reading for the presence, location and severity of intervertebral IDVP, and repeated at six weeks.

This totalled an evaluation of 325 levels. Exclusion criteria were those with insufficient quality or detail, non-degenerative or destructive spinal pathology (tumour or infection), previous neuromodulation or previous spine instrumentation, throughout the study period. Categorisation of IDVP was followed as previously.

Given the known association of advanced disc degeneration with IDVP, disc levels were also selected out with Pfirrmann grade 4 or 5, with reductions in disc height, who did not display IDVP as part of their pathogenesis, to investigate why some degenerate levels do not display IDVP.

The reliability of the CT & MRI evaluations was estimated using agreement percentage and kappa statistics within raters (intra-observer reliability) and between raters (inter-observer reliability). The presence and severity of IDVP (none, mild, partial, total) was modelled using ordinal logistic regression to investigate associations with age (years), gender (male, female), disc height (%) and Pfirrmann grade.

6.3 Results

49/65 (74%) of subjects, including 94/325 (29%) of levels displayed IDVP. For every increase in Pfirrmann grade⁵, the odds of IDVP severity increased by 17 (OR 17.2, 95% CI 9.4-31.5; $R^2=0.6$, $p<0.001$, Figure 6.1). For every 1% decrease in disc height, the odds of IDVP progression increased by 7% (OR 0.93, 95% CI 0.93-0.94; $R^2 = 0.5$, $p<0.001$, Figure 6.2). Affected IDVP levels within the L123 region displayed similar Pfirrmann grade (4.1 v 4.3) and disc height (0.52 v 0.51) compared to the L45S1 region but with greater severity of IDVP in the latter (1.5 v 1.98, $p<.002$). 22/118 (19%) levels with Pfirrmann Grade 4 or 5, with accompanying reduction in disc height, did not display IDVP, with a significantly higher risk of adjacent IDVP (17 of these had adjacent IDVP(s), 2 had adjacent fractures, 3 without explanation).

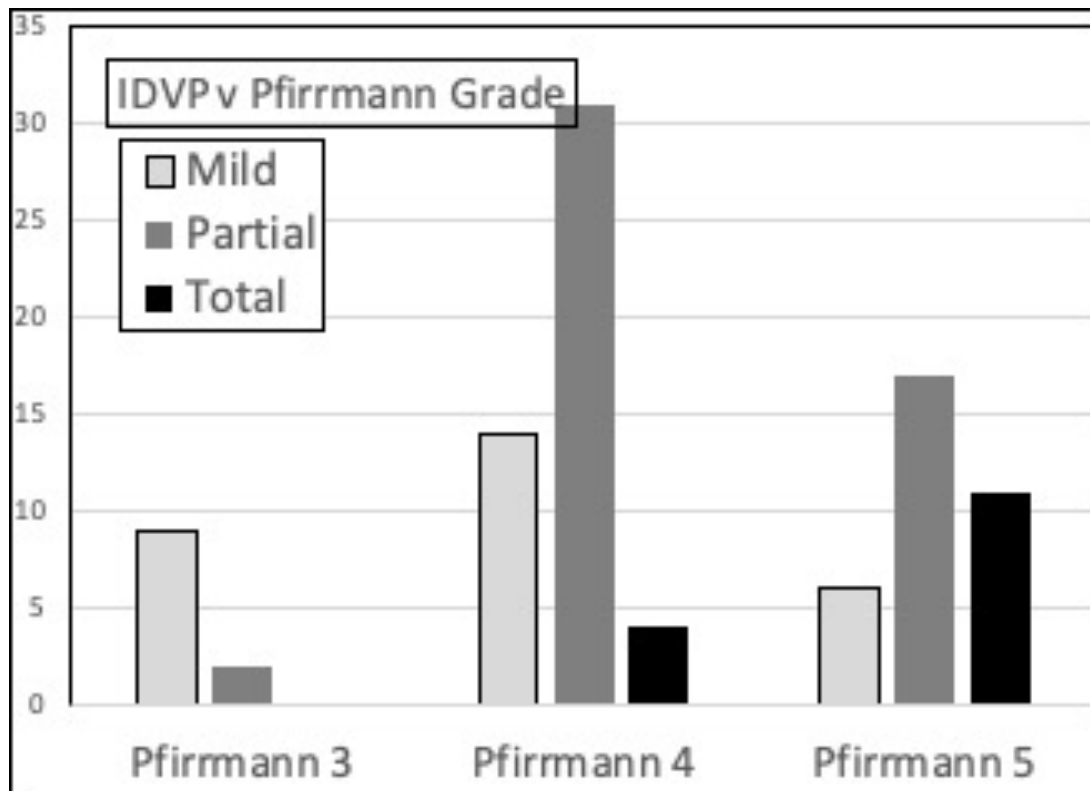


Figure 6.1: Severity of IDVP compared with Pfirrmann grades.

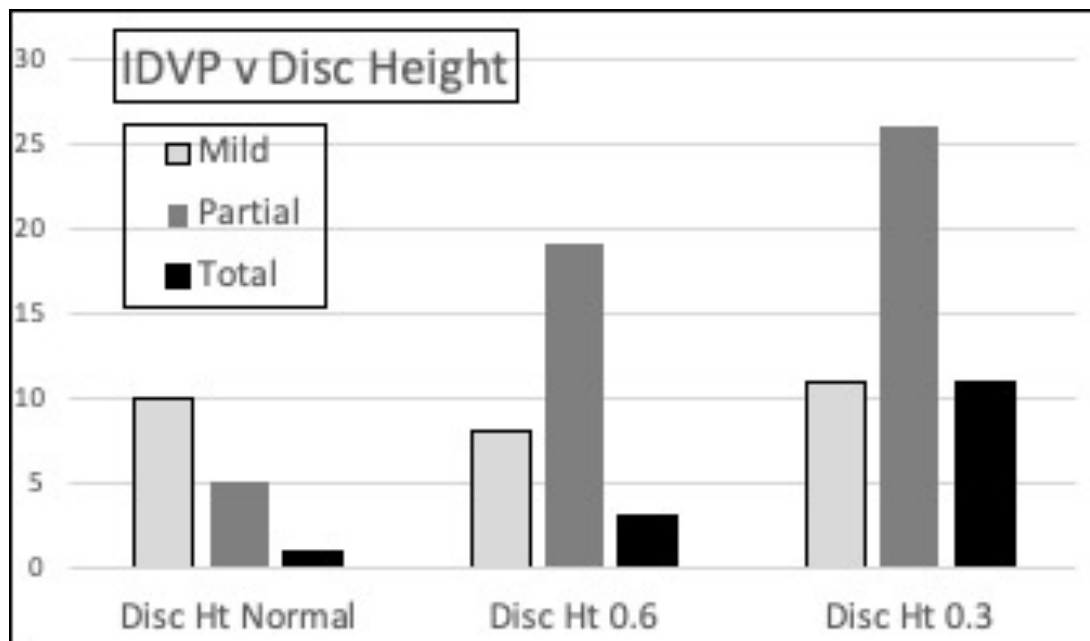


Figure 6.2: Disc height categories and IDVP.

Figure 6.3: L4/5 L5/S1 levels with hyperresonance of IDVP on MRI, with 0.3 disc height at both levels yet Partial IDVP.



Figure 6.4: Multilevel lumbar disc degeneration with greatest severity of IDVP in the lower lumbar region.

Figure 6.5: IDVP absent at L34 with adjacent IDVP at L45 and L23.



6.4 Conclusion

This is the first study to investigate correlations of findings of disc degeneration between MRI and CT, identifying a 29% prevalence of IDVP in all lumbar levels in symptomatic subjects over 60 years of age. With each increase in Pfirrmann grade, IDVP severity increased by a factor of 17 and with a 1% decrease in disc height, there was a 7% increased severity of IDVP. IDVP is integral to advanced disc degeneration as it was observed in 81% of discs with reduced height and advanced degeneration. In the remaining 19% without evidence of IDVP, there was a higher prevalence of adjacent IDVP than in those with IDVP without adjacent IDVP. When comparing upper and lower lumbar regions, accepting a greater incidence of disc degeneration in the latter, affected IDVP levels showed similar Pfirrmann grades and disc heights, but with greater severity of IDVP in the L4/5/S1 region. Previous work identified sagittal patterns that influence the pattern of IDVP, such as pelvic incidence, adjacent to a previous fracture, isthmic spondylolisthesis or suprajacent to a lumbosacral transitional vertebra.

The evolution of IDVP matched the Pfirrmann progression of disc degeneration, particularly where it highlighted Pfirrmann 3 as an inflection point where IDVP first starts to appear. This is of particular interest where IDVP provides further discriminating information on progression of disc degeneration, where the Pfirrmann classification displays high inter-observer disagreement⁵. The MRI progression on this classification identifies an unclear differentiation of *nucleus* and *annulus*. Differentiation between air and disc material is much easier, as shown in this research, thus lending increased clarity to MRI evaluation of disc degeneration.

Prevalence of IDVP was greatest as Pfirrmann 4, with Partial IDVP being most common, even in discs displaying Pfirrmann 5. These were similar to findings by Murata et al⁴³, who analysed the intra-discal

shape and distribution of IDVP, showing that discs with linear and island shaped IDVP had a significantly higher proportion of Pfirrmann 5 discs, particularly where an IDVP involved both the central but also the anterior aspect of the disc.

The radiological finding of IDVP bears some resemblance to histological evidence of intra-discal cleft progression with advanced degeneration. As discussed in Chapter 2, posterior concentric tears are first to appear, with radial and perinuclear tears coalescing to become transdiscal tears⁴⁴, which as shown in Chapter 5, do not autofuse but persist.

Cadaveric studies of range of motion of degenerate discs demonstrate an increase in segmental motion (widening of the neutral zone) in moderate disc degeneration but with a restabilisation with severe disc degeneration- increased movement up to grade IV and decrease with grade V degeneration⁴⁹. The pathogenesis first encounters a period of hypermobile instability followed (in most cases) by a reduction of disc height, dehydration of the disc, osteophyte proliferation and in some cases, autofusion.

Our study demonstrated reductions of disc height with increasing severity of IDVP, with severity plateauing at Partial-Total IDVP. For disc collapse and restabilisation to occur, it does not necessitate a Total IDVP.

While Pfirrmann grading and disc heights were similar, IDVP progression in the lower lumbar region was more severe. Previous work has shown two distinct entities of disc degeneration, as previously described in the upper versus lower lumbar spine, with endplate-driven disc degeneration in the upper and annulus-driven degeneration in the lower lumbar spine⁶². There may be a greater role for the compensatory effects of IDVP-associated movement, ie. extension moment on IDVP discs in the lower lumbar spine, prompting increased severity of IDVP.

The absence of IDVP was investigated and found to be 19%. Kanna et al maintained that not all degenerate discs or listhesis develop IDVP¹⁹. The presence of an adjacent IDVP, or non-contiguous IDVP was the most common explanation for this. Movement nearby may allow quiescence of the degenerate disc with reductions in height but without persistent movement, accepting the cascade of disc degeneration in a cephalad fashion. While some Pfirrmann 4 discs did not display IDVP, it may have been too early in disease progression, prompting exclusion of discs with normal height. This is particularly relevant in surgical decision making, where the focus is often on the worst disc, yet it may be adjacent to a more mobile and more symptomatic disc. Furthermore, where intra-discal correction is employed, the extent of IDVP can signify intersegment instability and conversely, correctability. End-plate sclerosis (and therefore integrity) is also a key marker for intra-discal cage suitability.

7. Cement Discoplasty

Cement discoplasty (CD) is an emerging technique in spine surgery involving filling of the empty degenerate disc space with polymethylmethacrylate (PMMA) cement. A typical disc endures 70-80% of the body weight through the spine. As the disc degenerates, it overloads the facet joints which can cause pain and arthritis. Injecting cement into the vacuum can restore anterior column loading. It can enhance vertical stability, offload a painful facet joint or compressed nerve root and reduce sagittal and/or coronal spinal deformity.

While cement acts best in compression, the concept of stabilising but not fusing the spine in such cases lacks certainty and clarity as to its clinical effectiveness. Nonetheless, publications on clinical series are increasingly evident despite the technique not being widely known. For this reason, we introduce the concept of “motion attenuation”. Motion attenuation as a concept has not been prevalent in spine surgery, whereas motion preservation is prominent, largely including disc arthroplasty techniques. Motion attenuation may be observed in cases of post-instrumentation asymptomatic pseudarthrosis, where relative or sufficient spinal stability has been achieved.

The current evidence for CD is based on our current knowledge of IDVP. Endplate sclerosis, which has been outlined above as an accompanying factor with IDVP, is a key guide for suitability for CD. This is because of strength and integrity of the endplate to tolerate the additional load on an otherwise empty disc space. Thus a literature review was conducted to investigate this novel technique.

Furthermore, given the author’s experience with CD, technical aspects were also detailed.

The techniques of CD are also an adjunct to cementation techniques for existing loose instrumentation in salvage cases. Symptoms are that of pain with biomechanical instability. These are cases, like elderly CD patients, who would not tolerate extensive revision surgery. An affiliated publication was also published on this subject⁶³.



Figure 7.1: Cement Discoplasty for disc degeneration, IDVP and kyphosis. 72 year old woman with severe arthritic back pain, bilateral (L5) neurogenic leg pain, hamstring fatigue, poor mobility, high BMI and diabetes. After initial rehabilitation and attempted weight loss, she was treated with L34 & L45 decompression and cement discoplasty (CD) at L23, L34 & L45. No peri-operative or early complications. A: Pre-operative mid-sagittal MRI image displaying multilevel disc degeneration & stenosis. B: Mid-sagittal CT image indicating large abdominal girth and multilevel intradiscal vacuum phenomenon (IDVP) and sclerotic endplates. C: Follow-up post-operative radiograph with preservation of lumbar lordosis. VAS improved from 8/10 (constant) to 4/10 (episodic) back pain and 0/10 leg pain, and Oswestry Disability Score (ODI) improved from 76% pre-operatively to 36% after two years.



Figure 7.2: Cement Discoplasty for adjacent segment degeneration. 84-year old man with back pain 7/10 and leg pain 5/10, with kidney transplant, early dementia and low BMI, walking-frame reliant, having received L4L5S1 fusion over 15 years previously. Had percutaneous CD. A: Pre-operative radiograph. B: Intra-operative fluoroscopy with trocar in situ at L34 mid-cementation, small cement leak (not in spinal canal or foramina). C & D: Two-year post-operative radiographs. No peri-operative or early complications. VAS had improved to 2/10 in his back, no leg pain, walking stick reliant. ODI had improved from 72% to 28%.

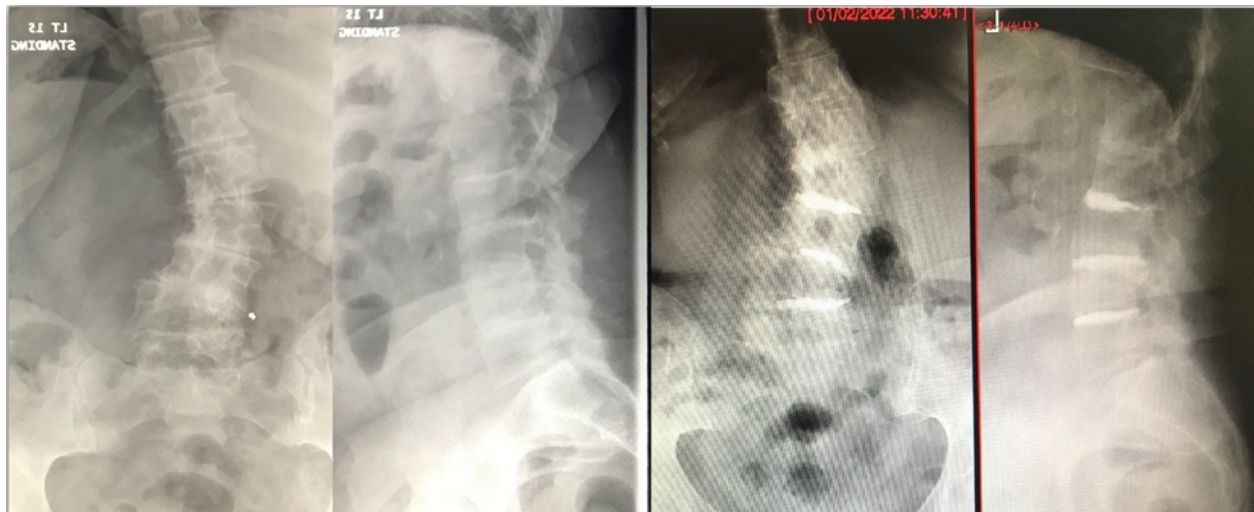


Figure 7.3: Cement Discoplasty for degenerative scoliosis. 78-year old lady with degenerative scoliosis, back pain 5/10 and leg pain (R L34 dermatome) 9/10. Had L34 extra-foraminal decompression and open CD, percutaneous CD at L23 and L45. No peri-operative or early complications. A & B: Pre-operative radiographs. C & D: Two-year post-operative radiographs with restoration of disc height at affected levels, stabilisation of the scoliosis. VAS was 3/10 and ODI was 22%.

8. Discussion

The function of the intervertebral disc is to act as an energy converter with its rotation-counterrotation ability to allow the trunk to help propel the legs, and secondarily as a shock absorber. The fibrous ring around the disc allows constrained movement of the disc and the incarcerated jelly-like *nucleus pulposus* allows compression. The vacuum in IDVP forms where the nucleus is no longer present, through biochemical degradation or herniation, invariably evident in degenerate discs. Our hypothesis was that the IDVP, identified as a nitrogen bubble, forms part of the **function** of the degenerate disc, with degenerative intra-discal changes that occur by design at a molecular level, allowing it, albeit sub-optimally to retain some of the function of the disc.

Central to the hypothesis of function is that IDVP is a marker for intra-discal movement. However, it is recognized that this work was based on static imaging only but supported by previous histological and cadaveric research. Non-reparative degenerative trans-discal clefts are the **histological** equivalent of IDVP. Cadaveric analyses have confirmed this, displaying an increased neutral zone with advanced degeneration, and increases in intra-discal motion with advanced degenerative disease (Pfirrmann 3 and 4 grades)^{48,49}. However, there is a notable cessation of motion at the end-stage Pfirrmann 5 grade, which this work has shown as an uncommon and unlikely end-point. Instead, there is a plateauing of progression of IDVP, most of partial-total severity and mostly as Pfirrmann 4 and some persistent movement.

Most IDVP is in the anterior aspect of the disc, seconded by central-anterior⁴³. We had previously postulated that it most likely corresponds with the area of greatest negative pressure. This may also correspond with the inverse findings by McNally et al where on stress profilometry, discogenic pain was found to be associated with anomalous loading of the posterolateral annulus and nucleus⁶⁴. Similarly in scoliosis, high hydrostatic pressures are seen with asymmetrical stresses from concave to convex sides⁶⁵.

Given the stoop that **aging** confers (sagittal based deformity), this is a manifestation of a spine where the discs degenerate, lose height and lose lordosis, the natural dip in the bottom of the back. 50% of spines in those over 60 years displayed IDVP as part of that degeneration, increasing in prevalence towards the lumbosacral junction. This pattern of degeneration was particularly evident in narrow pelvis cases (low PI) where IDVP was highly prevalent at L5S1. This is a known risk factor in disc degeneration but additional factors that give rise to symptoms of pain in the lower back were also identified as correlating with IDVP, including isthmic spondylolisthesis, degenerative listhesis, prior lumbar fracture, lumbosacral transitional vertebrae.

While the analysis was not done at a microscopic level, the macroscopic visibility on the lumbar spine afforded a broader approach. This work has therefore shown that IDVP allows the degenerate disc to function, perhaps to allow spinal extension to straighten up, in the initial phases of walking, as reflected in the supine position for performing a CT scan. It can also rotate to facilitate walking or for example, to collapse when sitting. The **natural history** of IDVP shows that progression to autofusion is rare over a 10-year period but instead increases in severity, and with additional levels of involvement. It therefore explains why, in most subjects, IDVP persists indefinitely.

Degenerative changes to the disc are best depicted on sagittal imaging⁵, which is a recent function of CT, since digitalisation. This innovation post-dates MRI, which is otherwise the most popular spinal imaging modality, but one that poorly evaluates IDVP. Study of IDVP thus far has been without structural or functional implications. Radiography has further developed, with the benefit of mathematical/computed projections to include full body postural analysis (EOS) which demonstrates where deformity occurs along the kinetic chain⁶⁶. However, this does not highlight IDVP. Erect CT would be the best imaging modality for this but which does not currently exist (although technically possible). Using retrospective CT spine cases for this study was not considered wise as most CT spine scans are either indicated for trauma evaluation or for pre-surgical planning, both of which would skew results. New imaging trends include low-dose CT instead of radiography, SPECT (Single-photon emission computed tomography) for evaluating sources of back pain. These modalities may displace MRI as the preferred imaging modality and the rate of diagnosis of IDVP is likely to increase.

A recurrent question in spinal literature is why asymptomatic aging cohorts display such high prevalence of MRI-based advanced disc degeneration. IDVP displays patterns that mirror known biomechanical causes of disc degeneration and **correlate** with increased severity of degeneration on MRI. The inner nucleus pulposus disappears, with a loss of disc turgidity and instead exchanged for IDVP. It is beyond the remit of this work to identify how, like the function of the intact disc, the IDVP functions in posture and gait, but it may allow for compression, extension, rotation and lateral flexion. Previous studies of disc degeneration through MRI identify increased inter-observer variation between Pfirrmann grades 3 and 4, where MRI-based intra-discal moderate changes appear whereas CT allows use of a highly discriminatory tool, that outlines the inflection point at grade 3, where IDVP starts to appear.

While highly prevalent in disc degeneration, the absence of IDVP in a small minority of degenerate discs is as telling as its presence. They are adjacent to an IDVP level in most cases, suggesting a coupling of movements, where an adjacent **level** may allow quiescence in a more degenerate level. The lower lumbar spine behaves differently to the upper lumbar spine with increased severity of IDVP in the former despite similar Pfirrmann grading of disc degeneration. Given the greater sagittal alignment implications in discs of

the lower lumbar spine, IDVP may allow greater intra-spinal correction, at least as a temporary measure when walking or standing.

Alternatively, upper lumbar spinal IDVP is particularly relevant in the **scoliotic** subject, with coronal S-shape curves in most cases. The patterns identified here reflect multilevel contralateral IDVP, where most likely a pre-existing lower lumbar asymmetric IDVP led to upper lumbar levels of IDVP on the opposite side. All IDVP occurred in the concavity of the disc, reflecting an asymmetric degenerative pattern on one side of the disc, but which maintained flexibility. Further characteristics were identified in association with this, including disc osteophytes- a manifestation of micro-fracturing of bone, “plant-like” bone growth and A disc herniation and the associated sciatica is known to cause flexible asymmetric gait abnormalities with both sagittal and coronal adaptations, which when prolonged are most likely to manifest as a more structural degenerative scoliosis with the development of upper lumbar IDVP. The flexibility that these allow afford a coronal correction so that spinal balance is maintained.

Symptom evaluation was not a focus for this study. There is an expectation of symptom correlation, prompting the research team to evaluate for symptoms based on the clinical notes. This was sufficient to exclude subjects with a prior history of spinal instrumentation, neuromodulation, destructive lesions such as infection or tumour or with an acute fracture. The MRI-CT correlation study only contained subjects with symptoms of back and/or leg pain. The natural history study did not show symptom differences in those who had IDVP progression versus those who did not. Whether symptoms were present or not, it is impossible to differentiate symptoms of IDVP from disc degeneration, particularly as it is shown by these studies that IDVP is present in almost all degenerate discs.

Thus IDVP when evaluated on CT depicts fascinating structural patterns which contribute to the function of the degenerate disc. These insights may inspire clinico-radiological investigations with regard to IDVP. Nonetheless, drawing on existing knowledge of disc degeneration and ensuing spinal deformity, a number of **treatment concepts** can be inferred from these findings, where symptoms predominate. Intra-discal devices have already shown improved deformity correction and fusion rates since posterior lumbar interbody fusion was originally described over 50 years ago⁶⁷. Yet, autofusion is invariably an unnatural outcome. It is well established that where extensive instrumentation aims to fuse a degenerate lumbar spine, pseudarthrosis with failure of fusion is a not-uncommon outcome. Motion-preserving treatments (disc arthroplasty) where necessary would fit this motion concept but have insertional limitations, particularly with anatomical access challenges, in elderly patients and whose proven benefit over fusion are demonstrated in a small minority of younger patients. Cement discoplasty may however prove a worthy treatment which involves cement injection into the disc. This is not strictly a fusion procedure, but it can

correct or at least stabilize IDVP and its associated deformity through a minimalist approach as it acts in compression. We have included a review of cement discoplasty and its relevance to IDVP.

Degenerative disc disease has shown huge increases over the last 50 years, largely influenced by an increasingly sedentary lifestyle^{3,12,13}. The information yield by MRI, considered the gold standard imaging modality is incomplete at best, without depiction of IDVP, and which is evident on CT in most degenerate discs. In addition to the histologic and cadaveric analyses that have complemented our understanding of disc degeneration, bringing a further perspective from CT imaging adds a new dimension of observation and provokes thought.

9. Future Direction

Elderly patients who suffer with back pain may have a broad spectrum of causes for pain. Disc degeneration manifests as a stoop, with facet joint overload, chronic muscular overload with fatigue, associated nerve compression with leg pain or imbalance causing recurrent falls. It is imperative to identify how much the IDVP contributes to this. In cases where IDVP is evident and correlating with symptoms, then elimination of the vacuum may have benefit.

Cement discoplasty (CD) has been mentioned in the literature review as a technique with increasing popularity for elderly patients. A prospective clinical series of patients with IDVP, treated with CD is currently under evaluation. These patients broadly represent degenerative scoliosis, facet arthrosis and proximal adjacent segment degeneration with varying degrees of back and/or neurogenic leg pain.

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