CAN TRI-AXIAL ACCELEROMETERS BE USED TO IMPROVE CURRENT CLINICAL MEASURES OF SPINAL MOBILITY IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS?

by © John Charles Snow

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Abstract

Background: Spinal mobility limitation is a characteristic feature in Axial Spondyloarthritis (AxSpA). Current clinical measurements of spinal mobility have shown low criterion-concurrent validity. This thesis sought to determine criterion-concurrent validity for a new, and clinically feasible, measurement of spinal mobility in AxSpA patients using tri-axial accelerometers.

Methods: Two perpendicular upright reference radiographs were taken followed by three flexion trials. For all postures, three measurements were taken: clinical tape, followed immediately by synchronized radiograph and accelerometer at the end ranges of forward and bilateral flexion.

Results: In forward bending, accelerometers ($r=0.590$, $p=0.010$) had a stronger correlation to radiographs than all three tape measures. In lateral bending, the Lateral Spinal Flexion ($r=0.743$, $p=0.001$) and Domjan tape measure ($r=0.708$, $p=0.002$) correlated stronger with radiograph than the accelerometer method ($r=0.556$, $p=0.016$).

Conclusion: The accelerometer measure is superior to current tape measures of spinal mobility in forward bending; but is outperformed in that respect by the LSF and Domjan clinical tests. Further evaluation of accelerometer and tape methods in early stage spinal mobility assessment is warranted.

Key Words: Spinal Mobility, Axial Spondyloarthritis, Tri-axial Accelerometers, Tape Measures.

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List of Abbreviations

ALL	Anterior longitudinal ligament
AS	Ankylosing Spondylitis
ASAS	Assessments of SpondyloArthritis Society
AxSpA	Axial Spondyloarthritis
BASDAI	Bath Ankylosing Spondylitis Disease Activity Index
BASFI	Bath Ankylosing Spondylitis Functionality Index
BASMI	Bath Ankylosing Spondylitis Metrology Index
CMCC	Canadian Memorial Chiropractic College
CRP	C-reactive proteins
DMARDs	Disease-modifying anti-rheumatic drugs
GI	Gastrointestinal
IBP	Inflammatory back pain
ICC	Intraclass correlation
JCS	John Charles Snow
LBP	Low back pain
LLF	Lateral Lumbar Flexion test
LSF	Lateral Spinal Flexion test
LSJ	Lumbosacral joint
MST	Modified Schober's test
MMST	Modified-Modified Schober's test
NSAIDs	Non-steroidal anti-inflammatory drugs
OST	Original Schober's test

PA	Posteroanterior
PLL	Posterior longitudinal ligament
RRT	Registered Radiologic Technologist
SI	Sacroiliac
SpA	Spondyloarthritis
TNFα	Tumor Necrosis Factor alpha

Glossary

Accelerometer – a sensor that measures acceleration and can be used to calculate inclinations with respect to gravity using trigonometric equations

Ankylosing Spondylitis – an inflammatory axial disease of the spine that predominantly affects the sacroiliac and spinal joints (must present with radiographic sacroiliitis according to the Assessment of Spondyloarthritis Society (ASAS) criteria

Annulus fibrosus – tough circular tissue on outer rim of intervertebral disc

Axial involvement – disease involvement of the axial skeleton (longitudinally oriented axis)

Axial Spondyloarthritis - a group of chronic inflammatory rheumatic diseases classified into two subgroups (radiographic AxSpA & non-radiographic AxSpA)

Bone remodeling – process by which bone tissue is removed and new bone tissue is formed

Calcification – the accumulation of calcium salts in the formation of bone or abnormal calcium deposition in soft tissues causing them to harden

Collimation – the narrowing of an x-ray beam to a desired area of interest

Disease-modifying anti-rheumatic drugs – class of drugs that slow the progression of joint damage caused by rheumatoid arthritis

Domjan tape measure test – a method of measuring bilateral spinal mobility using a clinical tape measure (see Appendix F for methodology)

Enthesis – connective tissue between ligament/tendon and bone

Facet joints – a set of synovial joints between two adjoining vertebrae

Goniometer – device used for the measurement of angles

HLA-B27 – Major histocompatibility allele from the B locus that is tested for to help strengthen diagnoses of AxSpA

Inclinometer – device that measures the angle of inclination from a known axis

Intervertebral joint – functional unit comprised of two adjacent vertebrae

Lateral Spinal Flexion test – a method of measuring lateral spinal mobility using a clinical tape measure (see Appendix E for methodology)

Modified Schober's Test – a method of measuring forward flexion spinal mobility using a clinical tape measure (see Appendix C for methodology)

Modified-Modified Schober's Test – a method of measuring forward flexion spinal mobility using a clinical tape measure (see Appendix D for methodology)

Nonsteroidal anti-inflammatory drugs – class of drugs that relieve or reduce pain and inflammation

Non-radiographic AxSpA – a sub classification of AxSpA where there is no evidence of sacroiliitis. This group consists of SpA associated with psoriasis, reactive SpA, SpA associated with inflammatory bowel disease and undifferentiated SpA

Original Schober's Test – clinical tape measure assessment of forward flexion in the lumbar spine (see Appendix B for methodology)

Ossification – the process of hardening of bone in bone remodeling or in soft tissue

Osteoproliferation – the growth of bone

Posteroanterior view – radiographic view where x-ray enters through the back and exits out the front aspect of the subject

Radiographic AxSpA – a sub classification of AxSpA where definitive x-ray evidence of sacroiliitis is present. Also known as Ankylosing Spondylitis.

Sacroiliac joint – joint between the sacrum and the ilium bones of the pelvis

Sacroiliitis – inflammation of the sacroiliac joint

Spondyloarthritic diseases – a group of inflammatory rheumatic diseases of the spine

Syndesmophyte – bony growth occurring inside a ligament, often seen in spine pathologies

Tumor necrosis factor alpha – cell signaling protein released in acute inflammatory response

Tri-axial accelerometer – device that measures acceleration about three orthogonal axes

X-ray scatter – the deviation of x-rays produced by a medium in which an x-ray beam passes through

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Chapter 1: Introduction

1.1 General Introduction

Axial spondyloarthritis (AxSpA) is a term used to classify a group of chronic inflammatory rheumatic diseases of the spine that carry a heavy burden of disease, characterized by pain, stiffening of the vertebral joints and progressive loss of spinal mobility. [1] The predominant symptoms of AxSpA are inflammation and back pain. Radiographic sacroiliitis may or may not also be present. [2] Thus, AxSpA can be subdivided into radiographic AxSpA and non-radiographic AxSpA. When definitive x-ray evidence of sacroiliitis is present, the disease is classified as radiographic AxSpA, more classically known as ankylosing spondylitis (AS). Regardless of the subgroup, AxSpA patients carry a heavy burden of disease, ultimately leading to severe functional limitations. [1] According to a study conducted in 2012 on the prevalence of Axial Spondyloarthritis in the United States, the age-adjusted prevalence of this disease was 1.4%. [3] This corresponded to 2.7 million Americans living with AxSpA at the time of the study. From 1995 to 2010, the age/sex-adjusted prevalence of Radiographic AxSpA in Ontario, Canada, increased from 79/100,000 to 213/100,000 people and the number of new diagnoses continues to grow. [4] This trend of increasing prevalence is likely a result of earlier diagnoses and an increase in years lived with disability within the AS population. AS often goes undetected or undiagnosed over a prolonged period of time. For instance, it has been shown to have a diagnosis delay of five to ten years; this is the longest delay when considering those of all common inflammatory rheumatic disorders. [5] This disease typically manifests in the teenage years or early twenties but due to the current classification criteria, early identification is rare and subsequently, treatment often begins much later than optimal. Previous New York criteria used for AS mandated some radiographic evidence of damage in the SI joint. Since a period of time is required for these

findings to become visible on radiographs, this diagnostic requirement resulted in a delay between the onset of symptoms to diagnosis. It is expected that the new classification criteria for AxSpA, established in 2009 by the Assessments of SpondyloArthritis Society (ASAS), should reduce the diagnosis delay in this patient population by documenting sacroiliitis via MRI or through HLA-B27 positivity and clinical features of SpA. [6,7]

AxSpA is typically associated with back pain, morning and evening stiffness, joint inflammation and proliferative bone formation. [8] Due to the early presentation of signs and symptoms, disease identification and management are imperative to maintaining functional mobility and quality of life in those affected by AxSpA. [8] Disease management in AxSpA focuses on symptom relief and minimizing or avoiding the structural damage responsible for physical and functional impairments. The sacroiliac (SI) and intervertebral joints are of primary focus as the manifestation and progression of the disease occurs largely in these structures. [9]

Clinical measures of spinal mobility are a standard element in the assessment of patients with spinal disease. In AxSpA, these measures are vital both because mobility limitations are an indicator of disease progression and also because there is evidence that they are a predictor of poor outcomes. [10] The ASAS recommends the assessment of spinal mobility for monitoring disease activity and for the assessment of disease-modifying treatment responses. [11] Tape measure methods such as the Schober's tests of forward spine bending range as well as the Lateral Spinal Flexion (LSF) test are commonly used to assess mobility in the clinical follow-up of this population. Rezvani et al. (2012) examined the reliability and validity of these tape measurements to assess sagittal plane spine mobility of AS patients in a controlled clinical study. This study found weak correlation between tape measure methods and radiographic analysis (gold standard), also suggesting low validity of these measures. [12] Further, a systematic review

by Castro et al. (2015) concluded that the spinal mobility tests currently used in clinical practice such as those using a measuring tape, inclinometer or goniometer have low criterion-concurrent validity with poor correlation to a gold standard. [13] Therefore, these measures may not provide an accurate measure of spine motion and may contribute to inadequate disease management. Despite this shortcoming, these convenient measures are currently in routine clinical use worldwide. [13] Thus, there is a need for further research to explore improved clinical measures of spinal mobility that are valid, reliable and simple to apply.

This thesis will explore the use of tri-axial accelerometers as a measure of frontal and sagittal plane spinal mobility in AxSpA. If shown to be more valid than traditional tape measures, these sensors have the potential to improve current monitoring methods for spinal mobility in primary care and with rheumatologists who are interested in the response to biologic therapy. This is important, as early identification of limitations and progression can lead to improved clinical outcomes with earlier treatment in the AxSpA population.

1.2 Objective

The objective of this thesis was to determine the criterion-concurrent validity of spine mobility measurement by accelerometers and traditional tape measures compared to the radiographic gold standard.

1.3 Hypothesis

It was hypothesized that tri-axial accelerometers would provide a more valid measurement of spinal mobility than traditional tape measures. Specifically, it was expected that the use of tri-axial accelerometers would have a stronger Pearson (r) correlation coefficient than

traditional tape measure when compared to the radiographic gold standard measure of spinal mobility.

Chapter 2: Review of Literature

2.1 An Overview of Axial Spondyloarthritis

2.1.1 The History of AxSpA

Axial Spondyloarthritis is a chronic inflammatory disease that affects the sacroiliac (SI) joints and the spine. AxSpA is a relatively new term that has emerged across medical literature in response to a series of studies conducted by the ASAS, addressing the challenges in classifying spondyloarthritis (SpA). [6,7] By definition, AxSpA is considered a form of spondyloarthritis where the predominant symptoms are inflammation and back pain where radiographic evidence of sacroiliitis may or may not be present. [2] This broader definition formed the foundation of the recent classification of radiographic and non-radiographic AxSpA subgroups, thereby resolving the classification issue in cases where progression of the disease are not severe enough to present radiographic changes. When definitive x-ray evidence of sacroiliitis is present, the disease is classified as radiographic AxSpA, more classically known as ankylosing spondylitis (AS). Many clinical cases have presented typical SpA disease factors such as inflammatory back pain (IBP), testing positive for the HLA-B27 gene, and family history but never develop radiographically confirmed sacroiliitis. This subgroup is therefore classified as non-radiographic AxSpA which consists of SpA associated with psoriasis (PsSpA), reactive SpA (ReSpA), SpA associated with inflammatory bowel disease (SpAIBD), and undifferentiated SpA (uSpA).[14] Ankylosing spondylitis accounts for about half of all AxSpA patients and is the most studied and documented form of AxSpA.[15]

At this time, there is no known cure for AxSpA. Experts have drawn associations to genetic markers such as HLA-B27 as a tool to aid with the classification of AxSpA. [10,16] 85-95% of Caucasians of North European ancestry with AS will test positive for HLA-B27, although

only 7-8% of the general population who show HLA-B27 positivity will develop this disease. [3] Further, these prevalence statistics are also variable across ethnic groups; therefore, this biomarker alone is not sufficient for a definitive AxSpA diagnosis. Although there have been advancements in the classification criteria to date, the exact etiology of the disease remains unknown.

2.1.2 Disease Presentation

AxSpA is commonly associated with back pain, inflammation of SI and spinal joints, and proliferative bone formation. [8] This disease typically manifests in the teenage years or early twenties, with clinical features at presentation being generally similar between men and women. [17,18] AxSpA course is variable but can be progressive in nature. The typical symptom profile of this disease includes morning and evening stiffness, low-back pain, and joint inflammation. [8] Early spinal involvement originates at the SI joints progressing upwards through the lumbar, thoracic, and in severe cases, the cervical spine. This pattern remains constant across sex, disease duration, and severity. [19]

Enthesitis and syndesmophyte formation are characteristic progressions that make AxSpA unique amongst the inflammatory rheumatic diseases. [20] Enthesitis is the inflammation of the insertion site of tendons and/or ligaments into the bone. [21] Syndesmophytes occur from progressive bone formation resulting in bony growth within the ligaments of the intervertebral joints. This progressive bridging/fusion across vertebrae is central to the irreversible spinal mobility limitations of the disease. [22] Although it is assumed that cyclic inflammation leads to osteoproliferation at these joints, no direct correlation between these two elements has been established. [8] Spinal deformity correlates with mobility limitations in both mild and severe

disease cases. [23] Mobility restriction increases with increased disease severity thereby emphasizing importance of early diagnosis and treatment to minimize progression before severe limitations occur.

The presentation of syndesmophytes on a radiograph is one of the current methods for evaluating the progression of structural changes in the AS population [24]. These structural changes are directly associated with spinal mobility impairments. [23] In a study investigating the natural disease course prior to the introduction of disease modifying anti-rheumatic drugs (DMARDs), Carette et al. (1983) found that greater than half of AS patients eventually develop moderate to severe spinal motion impairment leading to functional limitations in day to day activities. This investigation found a mean onset of symptoms of 24 years of age in their 142 patient cohort with a mean duration of symptoms being 38 years. [23] Although this chronic disease is progressive, a recent prospective study reported that within a cohort of patients with new-onset non-radiographic AxSpA, only 26% of cases went on to develop AS upon a 15 year follow-up. [17]

2.1.3 Pathophysiology/Pathogenesis of AxSpA

The biological mechanisms contributing to the manifestation and further progression of this disease have been subject to much research in the field of rheumatology. Ossification of the spinal ligaments and/or annulus fibrosus of the intervertebral disc are common developments in this disease. The clinical course involves "quiet" periods of relatively few symptoms and active inflammation "flare-up" episodes with more severe symptoms. When a characteristic flare-up occurs, inflammatory cells increase locally, producing chemical products from cytokines and other bone mediators that can degrade bone. In an attempt by the body to repair the damage, new scar and bone tissues are formed.[25] When this inflammation subsides, the body continues its

repair efforts by producing calcium deposits, which spread to the ligaments and joint capsules of the spine. [25] This proliferative bone formation is directly associated with the mobility limitations affecting this population. [23] It has also been suggested that repetitive biomechanical stress of the entheses may contribute to enthesitis and new bone formation in SpA resulting from the innate immune response to repetitive stress. [26]

Genetic research has been at the forefront in attempting to draw conclusions about the etiology of this disease. There have been associations made between many different genetic biomarkers as predictors of SpA, however their direct roles remain unknown. HLA-B27 has been suggested to contribute to the susceptibility of AxSpA. [27] This HLA class 1 allele is positive in an estimated 80-90% of established AS cases, although its presence is less common (70-75%) in non-radiographic AxSpA patients. [28] Only an estimated 7-8% of Caucasians of North European ancestry who test positive for HLA-B27 will develop AS, [3] further highlighting the ill-defined associations between AxSpA and this biomarker. Regardless of the poor positive predictive value for using genetics as a definitive tool for diagnosis, the use of certain genetic markers remains valuable upon drawing the clinical picture for patients with AxSpA. There are three proposed theories of why HLA-B27 causes spondylitis. The theory of 'molecular mimicry' suggests that a cross-reactive peptide originating from a bacterial pathogen activates T cells that respond to an HLA-B27 associated peptide. [29] This response causes characteristic inflammation. A second theory is based on the reduced folding rate of disease associated HLA-B27 molecules. The increased assembly time in the endoplasmic reticulum (ER) causes a build-up of misfolded HLA-B27 molecules, resulting in ER stress. [30] The third 'HLA-B27 homodimers theory' suggests that randomly formed HLA-B27 dimers that are formed on the surface of the cell will bind killer immunoglobulin receptors and subsequently cause inflammation. [30] These theories are

a result of ongoing research into the pathogenesis of AxSpA and with further research, will likely form the basis for understanding the pathway of this rheumatic disease.

2.2 Impact of AxSpA on the Patient

2.2.1 Inflammatory pain

Back pain in individuals with AxSpA is the subsequent result of inflammation or new bone formation. [31] This pain can impact the life of a patient in a number of ways. While some studies have focused on the psychosocial impacts of inflammatory back pain (IBP), [32] the literature primarily focuses on the influence of IBP on physical function. [33] In a prospective cohort study from Kiltz et al. (2012), similar levels of pain and physical function were reported by AS patients and non-radiographic AxSpA patients. [2] Differentiating between mechanical back pain and inflammatory back pain can pose difficulties and is clinically important in diagnosing suspected cases. Patients with IBP generally report morning stiffness, sudden onset back pain, nocturnal flare ups and buttock pain. As mentioned above, disease management focuses largely on minimizing symptoms, therefore aiming to reduce IBP. This is crucial in maintaining patient quality of life, social participation and occupational contribution. Regular mobility exercises, and medications such as non-steroidal anti-inflammatory drugs (NSAIDs) and biologics are the primary treatment recommendations for inflammatory pain reduction in this population. [2]

2.2.2 Spinal Mobility Impairments

The hallmark progression of spinal motion limitation in AxSpA is a direct result of the intervertebral restrictions caused by inflammation and syndesmophyte formation. [23] Axial Spondyloarthritis has been characterized by bony fusions within the axial skeleton. The anterior

and posterior longitudinal ligaments, responsible for restricting extreme ranges of vertebral flexion/extension, further limit these ranges of motion when increased calcification is present. [34] This process then progresses to affect the intertransverse ligaments and the annulus fibrosus of the intervertebral disc, which further contributes to lateral flexion restrictions in those affected by this disease. The damage to the axial skeleton in this condition is, in general, irreversible unless surgically intervened upon. However, spinal inflammation is reversible. It is important to note that mobility limitations are more influenced by spinal inflammation in early stages of the disease, further emphasizing the importance of early treatment to tackle inflammation, maintain mobility, and to ensure better long-term outcomes. [35] The spinal mobility impairments affecting AxSpA patients typically impact activities of daily living such as dressing and hygiene. [36] Difficulties performing these everyday tasks are not only inconvenient but have been shown to negatively impact the psychological and emotional wellbeing of patients. [37]

2.2.3 Quality of Life

It is well documented throughout the literature that mobility restrictions and disease-related pain affects the quality of life in AxSpA patients. [36] Limitations on physical functioning and independence can influence an individual's vocational role, societal role and activities of daily living, which can negatively impact their emotional well-being. Approximately 66% of AxSpA patients report experiencing fatigue and perceive that nocturnal pain affecting their sleep quality was the primary contributor. [38] Both fatigue and physical limitations are major restrictions impacting the employment status of these individuals. In a study investigating the impact of work limitations in an AS patient cohort, 50% reported experiencing work instability while 15% reduced and/or changed their work as a result of their condition. [39] Treatment costs,

compounded by absence from work, can cause serious financial strain on both the individual and their employer. This economic burden is augmented by the typical early presentation of this condition making for long periods of work instability throughout an individual's working years.

Spinal deformation and postural changes have also been found to negatively impact body image, which has been associated with increased rates of depression and anxiety. [37] In a study comparing AxSpA patients to the general population, rates of depression in women was 80% higher in the disease cohort while depression was 50% more prevalent in male patients. [40] Other factors impacting rates of depression and anxiety in this population are sexual dysfunction, impaired relationships, and intimate dissatisfaction. For example, erectile dysfunction was found to effect 42% of men with AxSpA compared to 18% of the general population. [41] Although AxSpA can have a serious impact on an individual, one can maintain a good quality of life with the appropriate treatment plan.

2.3 Clinical Assessment of AxSpA

2.3.1 Diagnosing AxSpA

Symptoms that are common in this disease are often confused with mechanical or non-inflammatory low back pain. [42] This is a problem as many cases can easily be missed or misdiagnosed as a different condition. For example, when a patient reports widespread peripheral pain concurrently with back pain, the case could become difficult to differentiate from fibromyalgia. [43] The progressive nature of this rheumatic disease makes early and accurate diagnosis critical. However, the delayed onset of AxSpA specific symptoms makes this very difficult. There are many factors that contribute to the inherent diagnosis delay in AxSpA. For decades, patients who presented with the characteristic symptoms of this condition but did not

demonstrate radiographic sacroiliitis would go undiagnosed. The recent changes in nomenclature and classification criteria, discussed above, have been a pivotal step towards tackling the diagnosis delay problem in this population. The difficulty in distinguishing between inflammatory and mechanical low back pain also presents the issue of patients being misdiagnosed as having chronic LBP or other arthritis conditions resulting in patients seeking ineffective therapies. [44] Further, a study that estimated the prevalence of clinically diagnosed AS in primary and secondary care simultaneously, only one-third of patients were managed at the secondary care level. [45] This is a problem as it indicates the majority of diagnosed patients may not be benefiting from additional specialist assessment.

The diagnosis of AxSpA is made when specific classification criteria are met. Distinguishing the presence of sacroiliitis on a radiograph can be difficult causing uncertainty in diagnosing the disease. Generating a clinical diagnosis often involves expert opinion and interpretation from experienced clinicians. As highlighted in Table 1, there is no definitive test to confirm the diagnosis. The classification criteria are based on imaging, clinical and laboratory data. Sacroiliitis as demonstrated on radiographic imaging is a requirement for the diagnosis of ankylosing spondylitis. According to the ASAS, a triad of classification criteria, which includes a positive test for HLA-B27, is sufficient to diagnose a patient with non-radiographic AxSpA.

Table 1. Classification Criteria for Axial Spondyloarthritis according to the Assessments of SpondyloArthritis Society

Ankylosing Spondylitis (radiographic AxSpA)	**Non-radiographic AxSpA**
Sacroiliitis on imaging plus one the following;	HLA-B27 positive plus two of the following;
Dactylitis Psoriasis Inflammatory back pain Good response to NSAIDs Arthritis Elevated C reactive protein Inflammatory bowel disease HLA B27 positive Family history of spondyloarthropathy Uveitis	

Although research continues to investigate and develop more definitive classification criteria, little progress has been made. This emphasizes not only the need to continue this research, but to also improve current clinical measures to optimize disease identification and management.

2.3.2 Importance of Early Diagnosis

For decades, classification criteria mandating SI joint damage in the form of erosions or new bone formation has created a barrier to early diagnosis, and consequently the appropriate management, for those suffering from this disease. With radiographic sacroiliitis being a requirement for AS diagnosis in the past, many patients went undiagnosed for long periods of time because of the late onset of radiographic changes in the disease course. In other words, previous criteria focused the diagnosis on an advanced stage of the disease progression where structural damage is often irreversible. Early diagnosis in AxSpA is paramount and there is evidence for substantial benefit when diagnosed at an early stage. [46] Many studies have found

that reports of pain severity and disability in the early non-radiographic phase are comparable to those with radiographically confirmed disease activity. [31,47] From a clinical scope, this typical diagnostic delay causes patients to miss a critical window for timely and appropriate treatment. Aggarwal and Malavija (2009) concluded that there were statistically significant findings of increased disease severity, functional loss and tissue damage as a result of the typical diagnosis delay in AS. [5] This is important for patients as an early and accurate diagnosis can minimize mobility limitations and pain, while maximizing quality of life. Early diagnosis can also reduce the number of unnecessary diagnostic procedures or inappropriate treatments a patient may experience. Evidence has shown that problems deciphering between inflammatory back pain and mechanical back pain at the primary care level has led to diagnosis delay. [48] Practitioner awareness of inflammatory back pain is therefore critical to early diagnosis. Fortunately, studies have suggested that diagnosis delays are decreasing. [49,50] This is likely due to increased referrals to rheumatology, adoption of less stringent classification criteria (ASAS), and the recent introduction of MRI to assess SI joint inflammation. [50] With recent advancements in effective therapies, early diagnosis is arguably more important than ever, where proper treatment at early stages can significantly improve outcomes.

2.3.3 Plain Film Radiography

Plain film radiography can be used as a means to identify sacroiliitis. [51] This is the primary role of radiography in diagnosis and management of AS patients. These radiological changes present themselves much later in the disease course than initial symptoms such as low back pain. This is because the erosions or new bone formation can take up to 10 years to be visible on an x-ray film,[5] which contributes to the delay in diagnosing radiographic AxSpA. In

AxSpA, radiographic measurement is widely considered to be the gold standard of reference in measuring spinal ranges of motion. [12,52,53] However, spine motion is not typically measured in this way because of feasibility and exposure to ionizing radiation. Using x-ray films, one can identify vertebral bodies and then determine the relative angle between segments of interest. This method can be completed directly on the developed film using a ruler and protractor or digitally using DICOM imaging processing software. Radiographic measurement of lumbar spine mobility is illustrated in Figures 5 and 6 on page 34. The increased risk inherent to ionizing radiation exposure poses both ethical and feasibility issues in using this method at follow up assessments. Radiosensitive regions such as the breast, gonads and thyroid are more sensitive to radiation exposure than other tissues; thus, these areas are shielded with lead during radiographic examinations wherever possible. Similarly, following the ALARA principle (As Low As Reasonably Achievable) by optimizing technique factors to use only the minimum amount of energy necessary as well as narrowing the field exposed through collimation are all strategies used to minimize the risk of this exposure. However, it is recognized that even when adhering to ALARA principle, the risks due to radiation exposure are never eliminated; therefore, surrogate measures such as the tape measure of spinal mobility are typically used. [13]

Previously, an x-ray that was graded as normal would exclude the diagnosis of AS, often leaving individuals undiagnosed for long periods of time or in extreme cases, never being diagnosed. As mentioned earlier, the recent expansion of the ASAS criteria has brought light to this situation by establishing the non-radiographic subgroup of axial spondyloarthritis. It is worth noting that individuals who are classified in the non-radiographic subgroup may progress into the radiographically confirmed disease group. In a review by Boonen et al. (2015), it was estimated that over two years, approximately 10% of non-radiographic patients progress to have

radiographic evidence of the disease, leading to a new diagnosis of ankylosing spondylitis. [54] Another study completed a long-term follow up of 10 years, where they also confirmed that the 75% of patients did not develop radiographic change. [55]

2.3.4 Clinical Tape Measurements

Considering the risk of radiation exposure inherent to successive radiographic imaging, non-invasive methods of lumbar spine mobility measurement are used in clinical follow-ups with the use of standardized tape measures. Since the progressive spinal involvement of this disease results in limitations of spine motion, these measures can be safely taken at periodic follow-up appointments. The Original Schobers test (OST), Modified Schobers test (MST) and Lateral Spinal Flexion (LSF) test (sometimes referred to as lateral lumbar flexion test) are among the most frequently used tape measurements in this clinical population. [12] Both the OST and MST measure the sagittal plane flexion range of motion while the LSF test measures lateral spinal mobility in the frontal plane. [56] The OST is conducted by drawing horizontal reference lines at the level of the lumbosacral joint (LSJ) and 10 cm above the LSJ. With the subject in standing, they are instructed to bend forward at the waist as far as they can where the distance between the lines is re-measured. [12] The MST is conducted by drawing reference lines 5 cm below the LSJ and 10 cm above the LSJ followed by re-measuring the distance between the lines with the subject in maximum forward flexion. [12] A third variation of this test called the Modified-Modified Schober's test (MMST) is conducted by drawing reference lines at the level of the LSJ and 15 cm above the LSJ followed by re-measuring the distance between the lines with the subject in maximum forward flexion. [12] These three forward mobility tape measurements are illustrated in Figure 1 on page 19. Other assessments include measures of chest expansion (sternocostal/costovertebral joint mobility), occiput-to-wall distance (cervical mobility), tragus-

to-wall distance (cervical/thoracic mobility), and intermalleolar distance (hip mobility). [57] However, these secondary clinical measures are unlikely to be affected without decreased spinal flexion measures in the frontal and sagittal planes; commonly impaired by the predominant involvement of the lumbosacral region. [53] These traditional tape measures are inexpensive, noninvasive and easy to use rendering the method an attractive alternative to radiographic measures of spine motion; otherwise considered the gold standard. [13]

The effectiveness of tape measurements of spinal mobility in the sagittal plane has been evaluated in numerous studies, which have raised questions regarding their validity. [12,53,56,58] Rezvani et al. (2012) found a weak correlation in both the OST and MST with reference to the radiographic measure, yielding Pearson (r) correlation coefficients of 0.363 and 0.333, respectively. The MMST was also conducted in their study with researchers concluding that this measure did not reflect spinal mobility. Similarly, a recent systematic review by Castro et al. (2015) concluded that there is a lack of evidence for the criterion-concurrent validity of these tape measures suggesting that they are not an adequate representation of spinal motion. [13] The rationale as to why this measurement method lacks validity has been addressed in the literature. Rezvani et al. found that there was a larger systematic difference at the end ranges of spinal flexion when using the OST. Specifically, as the radiographic angular change increases towards the end ranges of forward bending, the metric changes of the OST do not increase proportionally. [12] Miller et al. suggest that this discrepancy is potentially explained by the relationship of skin distraction to movement of underlying tissues. [58] With application to the AxSpA population, those with greater ranges of motion, who may be in early stages of the disease, will have OST results that will plateau before they reach a true end range of spinal flexion. In follow up appointments, this measure may seem to have not changed when in fact the previously taken

measure was not an accurate reflection of spinal mobility due to the plateau. This can give a false sense of successful symptom management. The lack of criterion-concurrent validity for tape measurement methods presents the need to explore alternative spinal mobility measures.

The LSF measure is the recommended tape measurement for the assessment of lateral spinal mobility by the ASAS. This is conducted with the subject in a standing position with their hands at their sides. With their hand on the lateral aspect of the leg, the distance between their middle finger and the floor is measured in upright standing as well as ipsilateral side bending. The difference between upright standing and maximum lateral flexion is recorded. This is conducted on both sides of the body and an average of the two is taken [59] (Figure 2A). A second, more recently adopted measure of lateral spine bending range is the Domjan tape measurement. This is conducted with the participant in standing with their hands by their sides and feet shoulder width apart. The subject is instructed to bend maximally at the waist to the right side, where a horizontal mark is made on the right leg at the level of the ipsilateral middle finger. A second line is drawn during left lateral flexion where the tip of the middle finger of the right hand touches the right thigh. The distance between these two points on the right leg indicates the total range of lateral flexion as a combination of both sides [60] (Figure 2B). The LSF is one of the five widely used tape measure assessments of overall spinal mobility that make up the Bath Ankylosing Spondylitis Metrology Index (BASMI). Although this measure is recommended and used clinically, [59] there is no evidence for the criterion-concurrent validity of the LSF lateral measure compared to the radiographic gold standard. The same applies to the Domjan tape measure test of lateral spinal mobility thereby warranting the investigation of the criterion validity of both of these clinical tests. Collecting two tape measures of lateral bending (Domjan and LSF) did not burden the length of the study or the participant in any way.

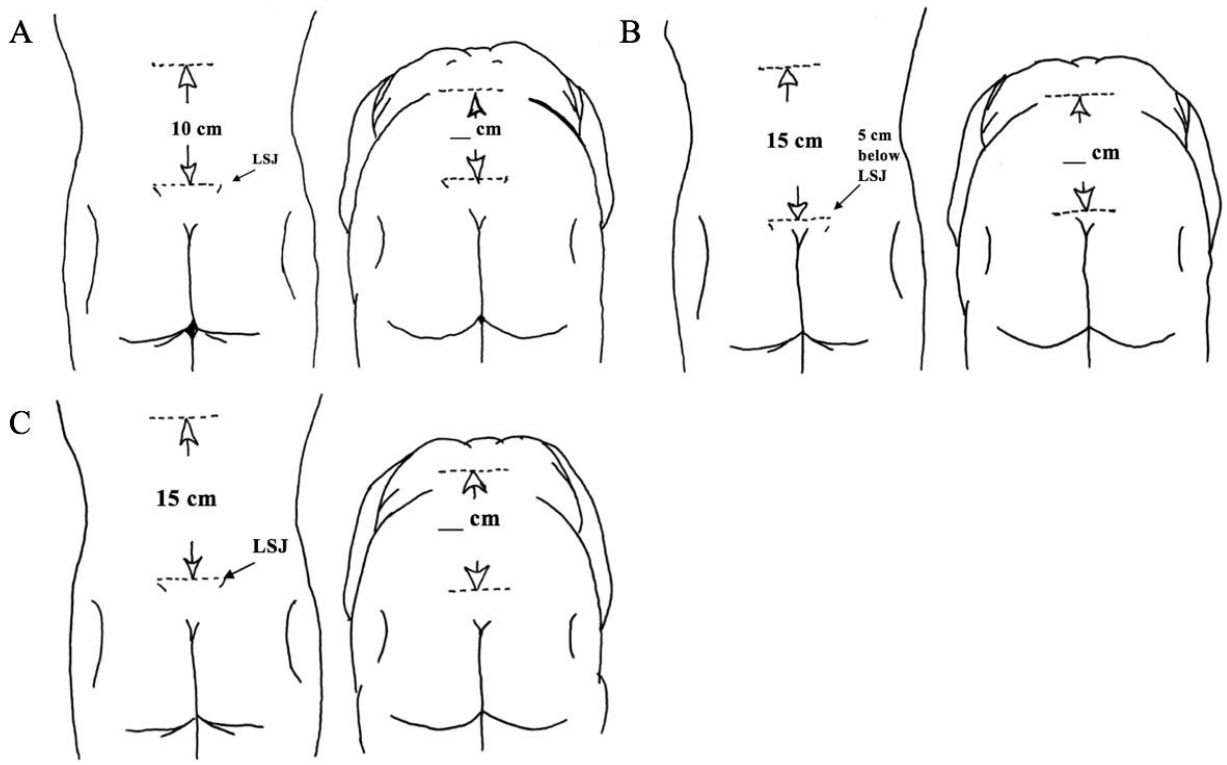

Figure 1. The three forward bending clinical tape measurements. In each panel, the left schematic illustrates the reference lines in upright standing while the right schematic shows the participant in maximal forward bending where the distance between the lines is remeasured. A. Original Schober's Test. B. Modified Schober's Test. C. Modified-Modified Schober's Test. Figure drawn by JC Snow.

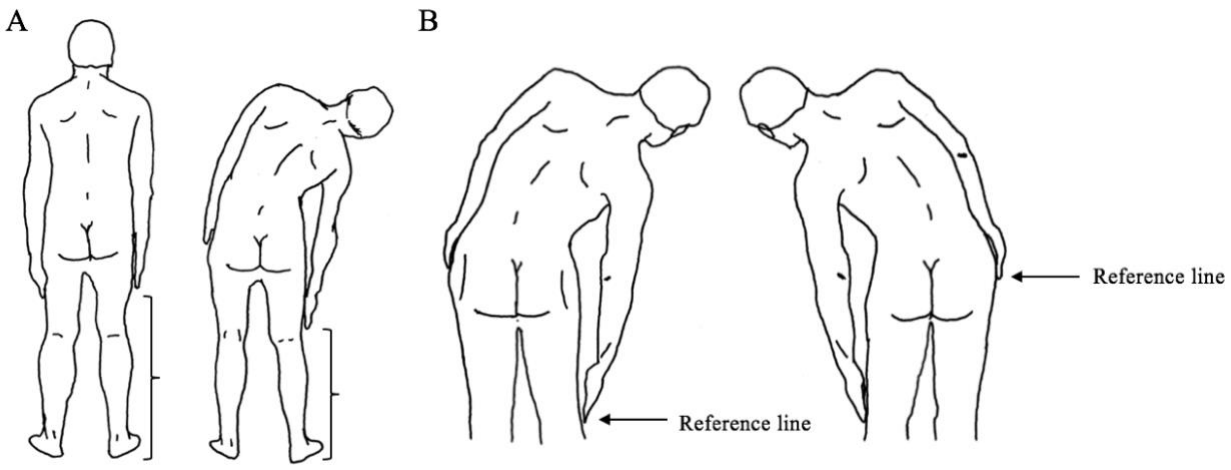

Figure 2. The two lateral bending clinical tape measurements. A. The distance between the middle fingertip and the floor is recorded for upright standing and max lateral bending and the difference is recorded to the nearest mm. This is conducted on both sides of the body and an average of both sides indicates the LSF test. B. With the subject in maximal right lateral bending, a reference line is drawn at the level of the middle finger on the lateral aspect of the right leg. With the subject's hands still on the thigh, they then maximally bend to the left side where another line is draw at the level of the middle finger on the right leg. The difference between these two marks on the leg is recorded to the nearest mm indicating the Domjan measure. Figure drawn by JC Snow.

2.3.5 Tri-axial Accelerometers

The use of accelerometers, sensors that measure acceleration, are prominent in our day-to-day lives. They feature in both industrial and scientific applications together with gyroscopes and are used extensively in everything from our personal devices (phones, laptops, wearable fitness gear) to complex machines such as in vehicle and aircraft navigation systems. Accelerometers have seen a multitude of application in the fields of biomechanics, activity and postural analysis, gait analysis as well as in the assessment of force and impact in concussion research. [53-56] Three studies, conducted between 2010 and 2014, concluded that tri-axial accelerometers offer a valid method of trunk and center of mass acceleration during human gait. [61–63] Since the internal validity of these sensors with reference to a camera motion capture system has been established in the biomechanical analysis of joint angle measurement during human

gait; the potential for expanded application of these sensors is compelling. Further investigation of biomechanical trunk measurement specifically, is of primary interest to this thesis project.

Tri-axial accelerometers provide output in raw data format as voltage in response to a change in acceleration. [64] Upon calibrating these sensors with respect to gravity (see Appendix A), one can then use a conversion factor from calibration trials to acquire a measure of acceleration from a voltage output of a given trial. Then using trigonometric functions, absolute angles of each accelerometer can be extracted from the accelerations present in each axis; thus calculating the inclination of the sensor. Using the absolute inclinations of two sensors, the relative angle between can then be calculated by subtraction giving a measure of spine kinematics. This method of measuring spine angles is very similar to how spine angles are calculated from radiographs (Figures 5 and 6, page 34). Theoretically, this method of spine angle measurement should be correlated with radiographic measures of spine angle making it a valid method of determining spine mobility. The technique of measuring orientations and angles using accelerations from a gravitational field provides great potential for expansion of accelerometer application in the fields of clinical biomechanics and rheumatology.

2.3.6 Accelerometry for Spine Motion Measurement

Various techniques have been previously investigated to measure lumbar spine motion for clinical assessment and/or diagnosis. Many of these have been shown to have limitations or prove to be less than ideal. Radiographic methods are very accurate but are inherently complex and present health risk due to radiation exposure. Optical motion tracking equipment is expensive and time consuming to employ. Clinical tape measures have been proven to have very low criterion validity in measuring spine motion. [12] Consequently, numerous accelerometry

methods have been studied as a way of measuring spinal mobility. One study investigated the use of gyroscopes as an inertial tracking system to measure movements of the lumbar spine. [65] They found that in 19 healthy people, this method of measuring anatomical angles using angular rates of rotation in a three-dimensional coordinate system was a reliable technique in measuring movements of the lumbar spine. The coefficient of multiple correlation in flexion, extension and side bending ranged from 0.972 to 0.991 in three repeated measurements. In another study completed by Wong & Wong (2008), spine posture changes in sitting was compared between tri-axial accelerometers and a 3D motion analysis system. In a small sample of three healthy subjects, the accelerometers were shown to fall within the accepted 5° difference in all four postures (neutral, forward bending, left and right lateral bending) when compared to the motion analysis system. [66] The results of this study verified the feasibility of using accelerometry to detect posture change in seated positions, while reaffirming the potential for using tri-axial accelerometers in the clinical measurement of spinal range of motion. For this thesis study, we were primarily interested in evaluating tri-axial accelerometry compared to current clinical tests in measuring of spinal mobility in the AxSpA population. No study has investigated the true criterion-concurrent validity of tri-axial accelerometers compared to the radiographic gold standard of spinal mobility measurement. The findings from the previous studies above contribute to the rationale for conducting this validation study and drive the hypothesis that accelerometers will correlate stronger than the clinical tape measures when compared to the radiographic measure of spinal mobility.

2.4 Clinical Treatment and Management of AxSpA

2.4.1 Patient Management/ Treatment Recommendations

The management of AxSpA is similar between radiographic and non-radiographic subgroups. This is important as those who do not present radiographically confirmed AxSpA, still receive appropriate therapy. Treatment goals are largely focused on reducing symptoms as early as possible to maintain spinal mobility, reduce functional limitation, and maintain patient quality of life. [11] Optimal disease management combines two modalities: patient controlled lifestyle factors and pharmacological therapies. The goal of treatment such as pain reduction or increasing mobility should be established though communication between the patient and rheumatologist. Low impact mobility exercises as well as physical therapy are usually recommended by rheumatologists and have proven to be beneficial in reducing disease activity and improving functional status. Group physical therapy participation comprising of active, passive and relaxation therapies were found to be better than home-based exercises in terms of physical function and mobility outcomes. [67] Occupationally, individuals are recommended to alternate between sitting and standing to avoid exposure to prolonged postures, which may exacerbate stiffness and pain in the affected areas. [11] Changing other lifestyle factors such as smoking or drinking habits has been shown to improve outcomes. [68] Smoking is a known cause of inflammation and will therefore further contribute to the inflammatory pain inherent to AxSpA. [69] Eating habits can have either a positive or negative impact on the individual. Due to the association of SpA and osteoporosis, it is important to maintain a healthy diet rich in calcium. [16] The use of pharmacological therapy concurrently with the standard non-pharmacological recommendations above provide great potential for optimal quality of life in this population. [11]

2.4.2 Pharmacological therapies

According to the Assessments of SpondyloArthritis Society (ASAS) guidelines, non-steroidal anti-inflammatory drugs are the primary drug treatment as they have been proven to reduce both the pain and inflammation inherent to the disease. [70] Some studies have suggested that regular use of NSAIDs have a beneficial effect on structural damage of the axial skeleton. [71] Response to this line of treatment must be monitored closely because contraindications in the gastrointestinal (GI) tract and/or kidneys may occur in some cases. [72] If this is the case and pain remains severe, other opioid-like drugs may be warranted. [11] Also used in the management of AxSpA is the family of disease-modifying antirheumatic drugs (DMARDs), particularly among patients with concomitant peripheral arthritis. In a systematic review by Zochling et al. (2006) investigating the effects of different drug treatments in AS patients, the use of the traditional DMARD, Sulfasalazine, was found to show significantly improved morning stiffness but was unable to improve back pain and physical function. [73] This review also highlighted that common adverse effects of these agents included GI and hepatic manifestations such as enzyme imbalances due to toxicity of the drug. [73] In the same review, the utility of Tumor Necrosis Alpha (TNFα) inhibitors was documented. They highlighted evidence for therapeutic benefit with TNFα inhibitors, Infliximab and Etanercept, producing significant reductions in spinal pain and improved physical function. [73] The benefits of these TNFα inhibitors were considered rapid with a long therapeutic effect although treatment must be monitored to ensure a response to the drug. [68] Recently, the routine use of the anti interleukin-17A monoclonal antibody, Secukinumab, has been found to be a viable alternative to TNFα inhibitors in AS patients who are resistant to NSAID therapy. [74] In the randomized control trial conducted by Baeten et al. (2013), the efficacy and safety of Secukinumab was investigated in a cohort of 30 patients with

moderate-to-severe AS. This research concluded that treatment with Secukinumab induced a clinically significant reduction of disease activity in active AS patients with significant improvements as early as six weeks post initiation of treatment. [74]

2.4.3 Monitoring Disease Progression

The response to the treatments prescribed to AxSpA patients is central to monitoring of disease progression. The frequency of follow up appointments is determined on a case-by-case basis considering symptoms, severity and response to treatment. [11] Disease monitoring should also focus on patient characteristics such as functionality, disease activity and pain as reported by questionnaires, clinical parameters, laboratory tests and imaging. [11] Non-invasive assessments such as the Bath Ankylosing Spondylitis Functionality and Disease Activity Indices (BASFI and BASDAI) compose a series of patient reported measures that are used in monitoring progressions in follow up assessments. The Bath Ankylosing Spondylitis Metrology Index (BASMI) is composed of five measures used to assess spinal mobility in patients with AxSpA. Assessing spinal mobility is an accepted method of progression monitoring, where improvements from treatment response correlate to decreased inflammation and pain response, while increasing spinal ranges of motion. These measures are followed over time. [75] C-reactive proteins (CRP) are biomarkers in the blood that elevate in response to inflammation. Laboratory testing for CRP levels can provide information on patient responses to anti-inflammatory drugs upon clinical follow up. Radiographs are used to assess progression of fusion and/or new bone formation. Frequency of radiographic assessment is made on a case-by-case basis according to patient outcomes. [59] Similarly, medication dosing is monitored and modified according to response to the drug. If response to treatment brings about sustained remission, tapering of biologic

DMARDs should be considered. [11] The physician, usually a rheumatologist, will consider the overall health of the patient using the above assessment to make a prognosis and subsequent treatment recommendations.

2.5 Conclusion

This chronic form of inflammatory axial disease predominantly affects the spine and sacroiliac joints causing pain, stiffening of joints, and mobility limitations. These symptoms ultimately lead to functional impairment often causing limitations in the lives of AxSpA patients. The measurement of spinal mobility is clinically used as an indicator of disease progression and treatment response in this patient population. The literature presents evidence that does not support the criterion-concurrent validity of current tape measurement methods of spinal mobility. The identification of symptoms in this population is crucial to the clinical management of AxSpA patients. This population will benefit from a more valid measure of spinal mobility where, early identification of signs and symptoms will provide the framework for timely and appropriate therapy for optimal disease management in AxSpA.

Chapter 3: Methods

3.1 Ethics statement

The Canadian Memorial Chiropractic College and the Newfoundland Health Research Ethics Board approved this study. Subjects provided informed consent prior to participation in this study.

3.2 Participants

Fifteen individuals diagnosed with AxSpA were recruited from disease-specific interest groups and rheumatology practices in the Greater Toronto Area. All participants were required to be older than 18 years of age and have a confirmed diagnosis of AxSpA. Potential participants who were occupationally exposed to radiation as well as women who were or might be pregnant were excluded.

3.3 Collection procedure

After completing the informed consent process, the participant was instrumented with accelerometers and landmarks were made for the tape measurements. The two tapes were instrumented beneath the accelerometers so that the accelerometers did not impede the tape measurement methods, which minimized the time taken between tape, accelerometer and radiographic measures (Figure 3). To synchronize the measures as much as possible, accelerometer data were simultaneously collected during each radiographic exposure via a thumb switch trigger initiated by the Registered Radiologic Technologist (RRT) as the exposure switch was engaged. Lateral and PA reference upright standing radiographs were taken first in a randomized order. Then, the following trials were collected in a randomized order: maximal

forward flexion (OST, MST, MMST), maximal right lateral flexion, maximal left lateral flexion [Lateral Spinal Flexion (LSF) test] and bilateral flexion (Domjan test). For these trials, the corresponding clinical tape measurements were taken first as the participant held the end range position immediately followed by the synchronized accelerometer data and radiographic exposure. The participant held each position for approximately six to seven seconds, while all three methods were measured. To minimize errors, all tape and accelerometer measures were taken by John Charles Snow (JCS).

3.4 Instrumentation

Prior to the commencement of the data collection, JCS palpated the lumbar spine region for purposes of landmarking anatomical reference points for the instrumentation of the tape measures and accelerometers.

3.4.1 Tape measures

With the subject in an upright standing position, JCS located the 12th thoracic vertebrae by palpating the inferior aspect of the last rib and tracing inwards to its articulation with the 12th thoracic vertebrae. Individual vertebral levels were counted by tracing down the spinous processes of the lumbar vertebrae until reaching the inferior endplate of the 5th lumbar vertebrae, which established the lumbosacral joint (LSJ). A horizontal reference line was marked with pen at the level of the LSJ. While a tape measure was help firmly to the skin, three more horizontal reference lines were drawn with the subject in upright standing: 10 cm above, 15 cm above, and 5 cm below the reference line made at the LSJ. Two tape measures were affixed to the participant prior to collecting data: one that ran underneath the fixed accelerometer atop the 1st

lumbar vertebrae for the MMST measure and one that ran underneath the accelerometer fixed atop the sacral base for the OST and MST measures (Figure 3).

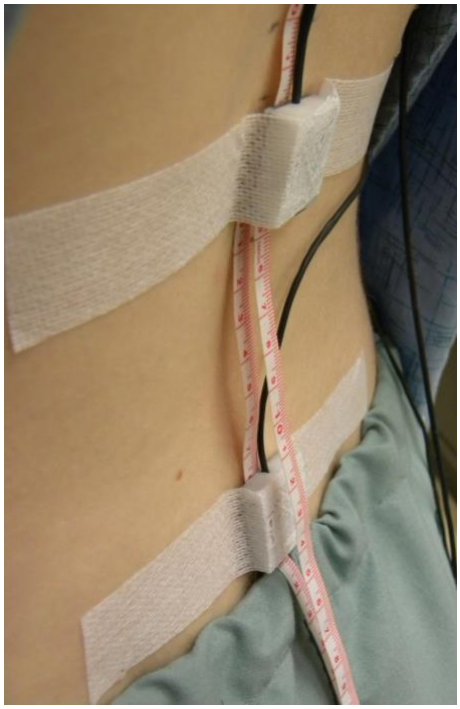

Figure 3. Visual representation of two tape measures lying underneath the L1 and S1 accelerometers.

3.4.2 Accelerometer measures

Two tri-axial accelerometers (ADXL335, Analog Devices, Norwood, MA, USA) were calibrated in relation to gravitational acceleration. JCS located the 12th thoracic vertebrae via surface palpation as described above. Tracing down one spinous process established the 1st lumbar vertebrae (L1) where a horizontal reference line was made with a pen. Using the previously established reference line at the level of the LSJ, JCS traced down one spinous process to establish the first sacral vertebrae (S1) where another horizontal reference line was marked. The subject was then instrumented with two accelerometers fixed atop the L1 and S1 reference lines using double sided tape in the + y down orientation. Figure 4 illustrates a tri-axial accelerometer and the accelerometer encased in protective plastic in a +y down orientation.

Fabric tape (Soft Cloth Tape, 3M, St. Paul, MN, USA) was placed atop each accelerometer to ensure there was no sensor movement relative to the skin throughout range of motion trials.

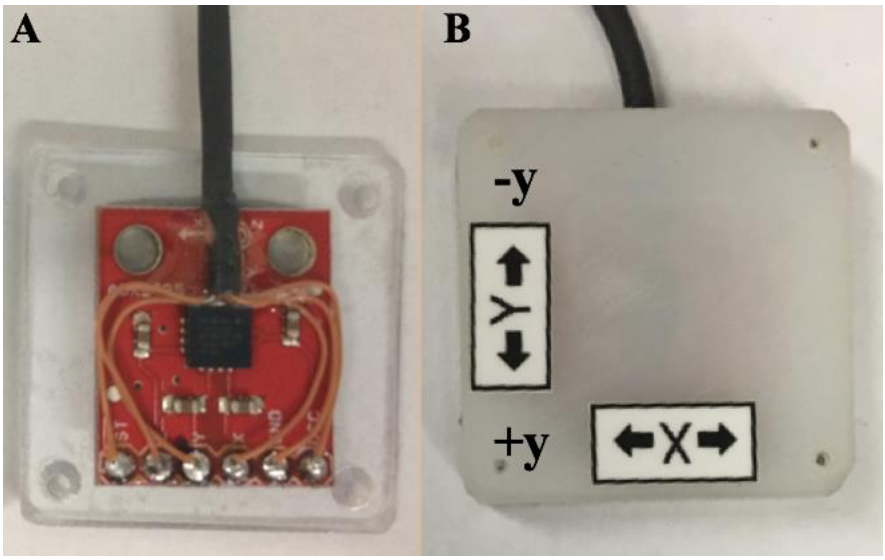

Figure 4. A. Tri-axial accelerometer. B. Tri-axial accelerometer encased in plastic in a +y down orientation as instrumented on the participant.

3.4.3 Radiographic measures

Radiographic technique factors were set based on the torso thickness measurement in both the sagittal and frontal planes for each participant. Subjects were fitted with thyroid and gonadal shielding to protect radiosensitive tissues from x-ray scatter.

3.5 Data Collection

3.5.1 Tape Measures

Forward lumbar spine flexion range was assessed using the OST, MST and MMST. The OST was conducted using the two reference lines at the level of the LSJ and 10 cm above the LSJ as established during instrumentation. With the legs shoulder with apart, the participant was

instructed to bend forward reaching their fingertips to the floor. The distance between the two reference lines was then measured at maximum forward flexion. The distance between the lines in forward flexion minus 10 cm (distance between lines at upright standing) indicated the OST measure to the nearest mm. [12] The MST was conducted using the two references lines that were drawn 5 cm below the LSJ and 10 cm above the LSJ as established during instrumentation. With the subject in the same maximally forward flexed posture as described for the OST measure, the distance between these two reference lines was measured. The distance between the lines in forward flexion minus 15 cm (distance between lines at upright standing) indicated the MST measure to the nearest mm. [12] The MMST was conducted using the two references lines that were drawn at the level of the LSJ and 15 cm above the LSJ as established during instrumentation. With the subject in the same maximally forward flexed posture as described for the OST measure, the distance between these two lines was measured. The distance between the lines in forward flexion minus 15 cm (distance between lines at upright standing) indicated the MMST measure to the nearest mm. [12] All three Schober's variations are illustrated in Figure 1 on page 19. Lateral spine bending range was assessed using the lateral spinal flexion (LSF) test and Domjan test. The LSF test was conducted with the subject in a standing position with their feet shoulder with apart and hands at their sides. With their right hand on the lateral aspect of the leg, the distance between their right middle finger and the floor was measured in upright standing. The subject was then asked to maximally bend to the right, keeping the trunk in the frontal plane and maintaining feet in contact with the floor. The distance from the right middle finger and the floor was then measured at maximum lateral bend. The difference between the measures at upright standing and maximum lateral flexion was recorded to the nearest mm. This was then conducted on the left side of the body and as instructed by the ASAS guidelines, an average of

the two sides indicated the LSF measure. [59] The Domjan measure of bilateral spine bending was taken as the measurement (nearest mm) between two horizontal lines as marked on the participant's right leg during right and then left side bending. Specifically, the first horizontal line was marked with a pen on the person's skin at the point where the tip of right middle finger touched the lateral side of the leg at end range right lateral flexion. The second horizontal line was drawn during left lateral flexion where the tip of the right middle finger touched the right thigh. The distance between these two marks on the right leg indicated the total range of side flexion, as a combination of both sides. [60] Each measure was taken once, read out loud by JCS and recorded by a research assistant. Both lateral spinal mobility tests are illustrated in Figure 2 on page 20.

3.5.2 Radiographic Measures

For all views, collimation was set superiorly to include the vertebral body of T12, inferiorly to include the vertebral body of S3. Two upright standing reference films were taken: posteroanterior (PA) lumbar and lateral lumbar. This was followed by three end range flexion films: lateral lumbar view of forward flexion, PA lumbar view of right lateral flexion and a PA lumbar view of left lateral flexion. All films were taken with the feet shoulder width apart. For each film, breathing instructions were given by the radiographic technologist such that the film was taken on suspended expiration in order to minimize superimposition of the diaphragm over the upper lumbar vertebral bodies. To control for the effect of arm position on lumbar spine angle, participants were instructed to have their arms crossed over their chest for all trials. [76] All films were taken with a diagnostic x-ray high voltage generator machine (HFQ-12050P, Toshiba,

Bennett X-ray Technologies Inc., Copiague, NY, USA) by an experienced (42 years of practice) RRT with a 36 by 43 cm film size using 400 speed screen digital cassettes.

3.5.3 Accelerometer measures

Two upright standing accelerometer measures were taken concurrently with the posteroanterior and lateral lumbar radiographs. This was followed by three measures taken in forward end range flexion, left lateral end range flexion and right lateral end range flexion.

3.6 Data Processing

3.6.1 Accelerometer measure

For all accelerometer measurements, the RRT used an external trigger to time synch the radiographic exposure to the accelerometer measure. For all accelerometer data, an average value of the 1-1.5 seconds that the RRT held down the trigger was taken. From the calibration trials, conversion factors were calculated using voltage output from the accelerations in +1 g, -1 g and 0 g (where g = -9.81m/s^2) and the sensitivity of each axis (Equation 1). The arctan function was then applied to the accelerometer values to give the absolute inclination of both sensors respectively (Equations 2, 3). Relative lumbar spine angles were then calculated between the top and bottom sensor (Equation 4). In theory, this relative lumbar spine angle is analogous to the radiographic measure as calculated from the x-ray image (Figures 5, 6). For each trial, the difference in relative lumbar angle from upright standing to end range bending was used to calculate range of motion (ROM) in degrees. An average of left and right lateral bending was computed to indicate the accelerometer measure of lateral spine flexion range of motion. Accelerometer data were collected with a 16-bit analog-to-digital conversion board at a sample

rate of 32 Hz (NiDAQ, National Instruments, Austin, TX, USA) using custom written data acquisition software (Matlab version 2015b, The MathWorks Inc., Natick, MA, USA).

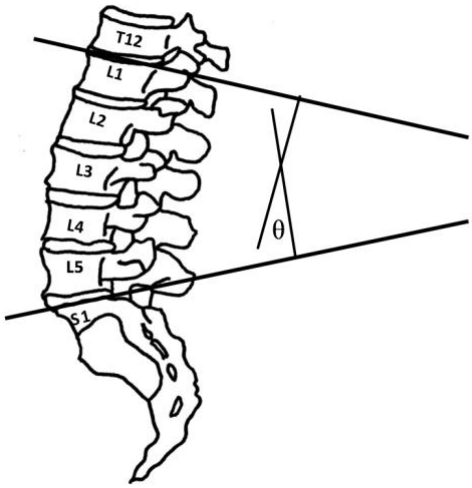

Figure 5. The radiographic method of calculating the lumbar spine angle from a lateral projection radiograph film. [77] *Horizontal lines are drawn parallel and through the superior endplate of L1 and the superior endplate of S1. Perpendicular lines are drawn from the two original lines and the large angle at their intersection is measured. Figure drawn by JC Snow.*

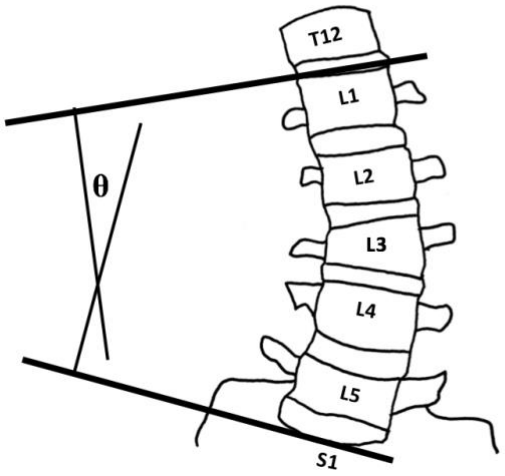

Figure 6. Method of calculating the lumbar spine angle from posteroanterior plain radiograph. [77] *Horizontal lines are drawn parallel and through the superior endplate of L1 and the superior endplate of S1. Perpendicular lines are drawn from the two original lines and the large angle at their intersection is measured. Figure drawn by JC Snow.*

Equation 1. Accelerometer calibration equation for an axis. Using the + X_{up} calibration trial as an example of converting voltage to acceleration. Where V/g is sensitivity of the accelerometer.

$$\text{Acceleration}_{\text{Xup}} = \left(\frac{\text{Voltage}_{\text{output}} - \text{Voltage}_{\text{gravity}}}{\frac{\text{V}}{\text{g}}} \right)$$

Equation 2. Calculating the absolute angle of an individual accelerometer. This gives an angle of rotation for forward flexion about the x-axis (forward bend). Where A is acceleration of a given axis.

$$\theta_{\text{abs}} = \tan^{-1} \left(\frac{A_X}{\sqrt{A_Y^2 + A_Z^2}} \right)$$

Equation 3. Calculating the absolute angle of an individual accelerometer. This gives an angle of rotation for forward flexion about the z-axis (lateral bend). Where A is acceleration of a given axis.

$$\theta_{\text{abs}} = \tan^{-1} \left(\frac{A_Z}{\sqrt{A_x^2 + A_Y^2}} \right)$$

Equation 4. Calculation of the relative lumbar spine angle between the top (L1) and bottom (S1) accelerometers.

$$\theta_{\text{rel}} = \theta_{\text{abs of top accel}} - \theta_{\text{abs of bottom accel}}$$

3.6.2 Radiographic measure

Radiograph angles were calculated from the digital films by JCS using the Horos DICOM software (Horos v2.4.0, Pixmeo SARL, Geneva, Switzerland). All films were randomized and blinded prior to being measured.

Lumbar angles of forward flexion were calculated from the lateral view radiographs according to the commonly used method presented in Figure 5. Specifically: a line was drawn

through and parallel to the superior endplate of the first lumbar segment and a second line was drawn through and parallel to the superior endplate of the first sacral vertebra. Perpendicular lines were drawn from both original lines and extrapolated. The large angle at their intersection was measured to give the relative lumbar angle. [77] The difference between the relative lumbar angles from upright standing to maximum flexion was then used to represent the forward bending range of motion (Equation 5). The range of lateral bending was measured from the PA radiographs as follows: a line was drawn through and parallel to the superior endplate of the first lumbar segment and a second line was drawn through and parallel to the superior endplate of the first sacral vertebra. Then, erected perpendicular lines were drawn at right angles to both original lines. The angle at which these lines intersect was then measured [77] (Figure 6). Range of motion in lateral bend was calculated bilaterally by the difference in relative lumbar angles from upright standing to end range lateral bend (Equation 6).

Equation 5. Calculation of the Forward flexion range of motion (ROM) for radiographic measurements.

$$\text{Forward Flexion ROM } (^\circ) = \theta_{\text{relative of max forward flexion}} - \theta_{\text{relative of upright stand}}$$

Equation 6. Calculation of lateral flexion range of motion (ROM) from upright standing to maximum lateral flexion posture.

$$\text{Lateral Flexion ROM } (^\circ) = \theta_{\text{relative of max lateral flexion}} - \theta_{\text{relative of upright stand}}$$

3.7 Statistical analysis

Corresponding measures of spine flexion motion from the tape measure and accelerometer were analyzed alongside the radiograph data using a scatterplot. Pearson's correlation coefficients (r) were used to assess the correlation between both measurements

(clinical tape and accelerometer) with reference to the radiographic data. Interclass Correlations (ICC) were calculated to observe the level of agreement between the accelerometer and radiographic measures. A Bland-Altman analysis was completed to further test for the presence of proportional bias between the accelerometer and radiograph data. A Bland-Altman analysis could not be completed between the tape measure and radiographic data because they have different units of measurement. Statistical significance was taken at $p < 0.05$ and correlation coefficients at $|r| > 0.20$. To assess intra-rater reliability, JCS performed repeat measures of the radiographic angles from two sets of films: PA view upright standing and lateral view forward bending radiographs of all fifteen participants. These measures were taken at the same time of day on three consecutive days. Inter-rater reliability was assessed by comparing the measures made by a second trained rater to those originally made by JCS for the two sets of films as indicated above. Intraclass correlations were calculated to measure the inter- and intra-rater reliabilities of radiographic measures. Means and standard deviations were calculated for all measures. All statistics from this analysis were completed using SPSS software (SPSS Statistics 23, IBM Software, Armonk New York).

Chapter 4: Results

4.1 Participant Demographics

Table 2 presents the demographic and anthropometric characteristics of the study population.

Table 2. Participant Characteristics

Sample Size (n)	Sex	Mean Age (year)	Mean Height (cm)	Mean Weight (kg)	Diagnosis	Mean Time Since Diagnosis (year)
15	9F, 6M	45.93 ± 15.14	167.11 ± 9.38	85.41 ± 17.84	15 Radiographic AxSpA	11.65 ± 9.35

4.2 Forward Bending

Table 3 presents correlation data for all forward bending spinal mobility tests. Figure 7 presents a graphical summary of the results from the measurement tests in forward bending. Pearson's correlations between OST, MST and MMST tape measurements to radiographic gold standard were very weak (r=0.195, p=0.243), weak (r=0.295, p=0.143), and moderately strong (r=0.414, p=0.063) (Figure 8) respectively. The accelerometer measure displayed a significant (p=0.010), moderate-strong correlation (r=0.590) (Figure 9), compared to the gold standard radiographic values. Interclass correlations between the accelerometer and radiographic measures indicated a fair level of agreement (ICC=0.583, p=0.009). A Bland-Altman analysis comparing the radiographic and accelerometer measures was conducted to test for the null hypothesis that there was no proportional bias between the two measures (Figure 10). A t-score of 0.717 and a significance level of p=0.486 was computed. This t-score was not significant and

therefore we accepted the null hypothesis indicating that there are no systematic differences between the accelerometer and the radiograph at a particular range of values.

*Table 3. Summary correlations for spinal mobility tests in forward bending. * indicates statistical significance at an alpha level of 0.05.*

Measurement Tests Compared	**Pearson Correlation Coefficient (r)**	**p-value (p)**	**Strength of Correlation**
OST vs. Radiograph	0.195	0.243	Very Weak
MST vs. Radiograph	0.295	0.143	Weak
MMST vs. Radiograph	0.414	0.063	Moderate
Accelerometer vs. Radiograph	0.590	0.010*	Moderate

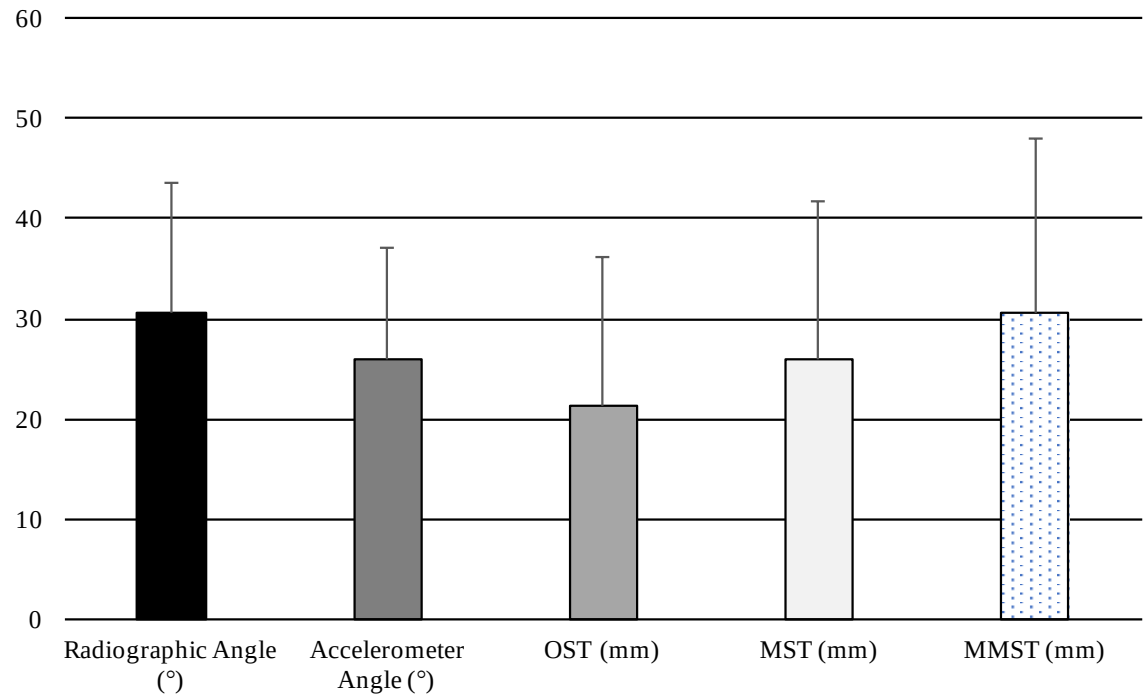

Figure 7. Mean results (S.D.) for spinal mobility tests in forward bending. Radiograph and accelerometer angles are presented in degrees (º). Tape measurements are presented in millimetres (mm).

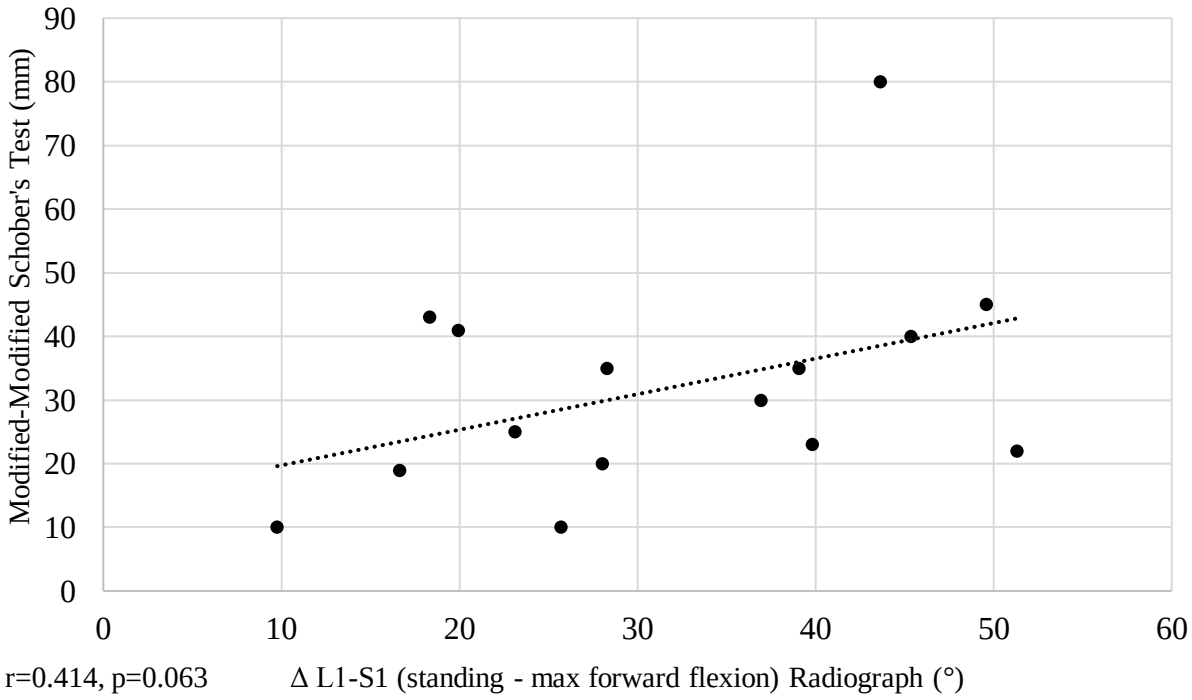

Figure 8. A scatterplot presenting the change in radiographic L1-S1 angles (º) from upright standing to maximum forward bending (x-axis) compared to the Modified-Modified Schober's Test (mm) scores for each participant. These two measures had a moderate Pearson's correlation coefficient of r=0.414, p=0.063.

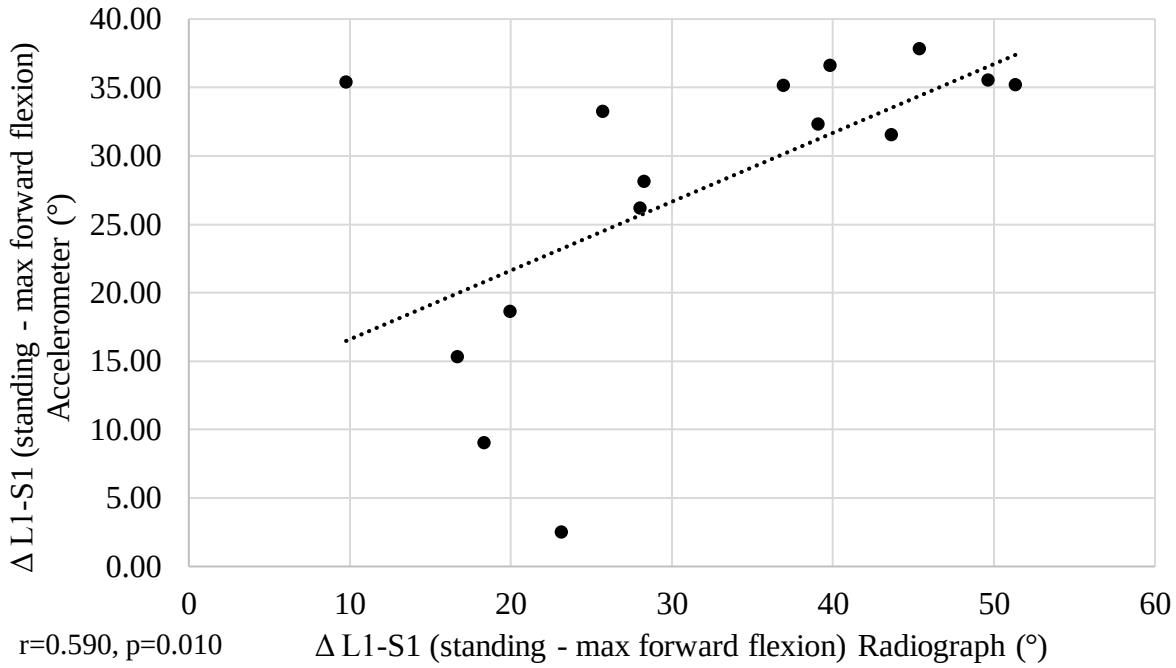

Figure 9. A scatterplot presenting the change in radiographic L1-S1 angles (º) compared to the change in accelerometer L1-S1 angles (º) from upright standing to maximum forward bending (x-axis) for each participant. These two measures had a moderate-strong Pearson's correlation coefficient of r=0.590, p=0.010.

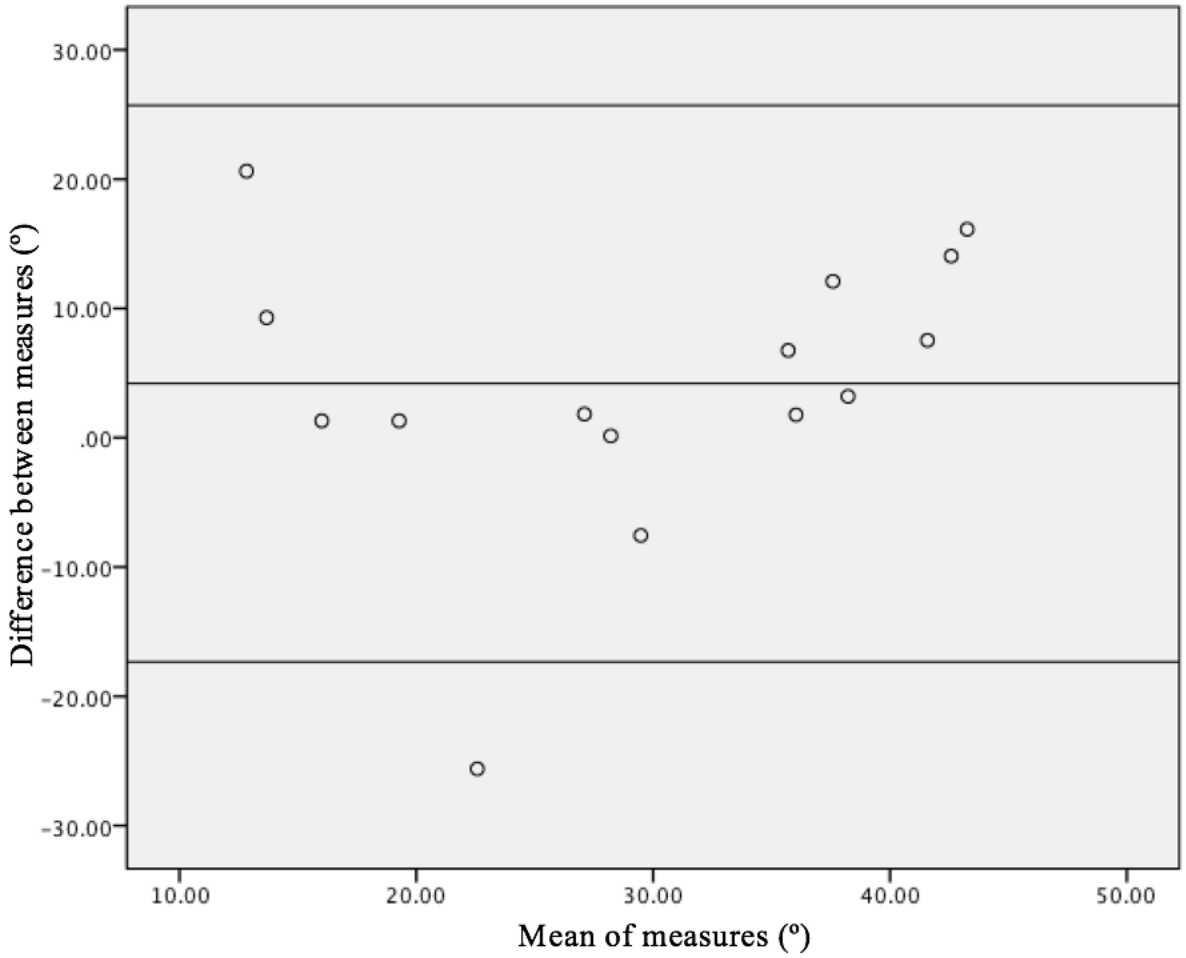

Figure 10. A Bland-Altman plot comparing the accelerometer and radiographic measures of forward bending. The Bland-Altman analysis indicated that there were no systematic differences between the two measures at a particular range of values.

4.3 Lateral Bending

Table 4 presents correlation data for all lateral bending spinal mobility tests. Figure 11 presents a graphical summary of the results from the measurement tests in lateral bending. Measurements from the LSF test were reported as an average of left and right lateral ranges of motion. The LSF test had a significant (p=0.001), strong correlation (r=0.743) (Figure 12) compared to radiographic measures. The Domjan method of bilateral flexion also presented a significant (p=0.002), strong correlation (r=0.708) (Figure 13) to the radiographic gold standard

of spinal mobility measurement. The correlation between accelerometer and radiographic measure of lateral bending was found to be moderately strong (r=0.556, p=0.016) (Figure 14). Pearson's correlation coefficients were also individually observed for right and left lateral bending measures. In comparing left lateral flexion measure to the radiographic measure, the tape measure was found to be moderately correlated (r=0.529, p=0.021), while the accelerometer had a weak correlation (r=0.303, p=0.136). In right lateral bending, the tape measure showed a strong correlation (r=0.727, p=0.001) while the accelerometer also had a strong correlation (r=0.670, p=0.003) to radiographic reference standard.

*Table 4. Summary correlations for spinal mobility tests in lateral bending. * indicates statistical significance at an alpha level of 0.05.*

Measurement Tests Compared	**Pearson Correlation Coefficient (r)**	**p-value (p)**	**Strength of Correlation**
LSF vs. Radiograph	0.743	0.001*	Strong
Domjan vs. Radiograph	0.708	0.002*	Strong
Accelerometer vs. Radiograph	0.556	0.016*	Moderate

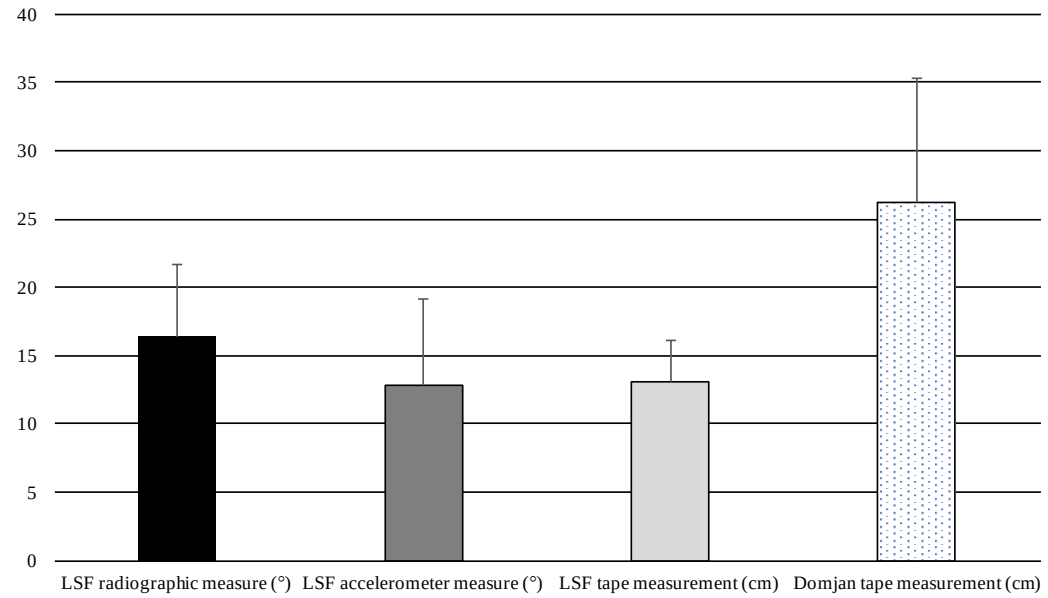

Figure 11. Mean results with standard deviations for spinal mobility tests in lateral bending. Radiograph and accelerometer angles were calculated as an average of left and right lateral bending and presented in degrees (º). The LSF test was calculated as an average of left and right lateral bending while the Domjan test was calculated as a sum of left and right lateral bending. Tape measurements are presented in centimetres (cm).

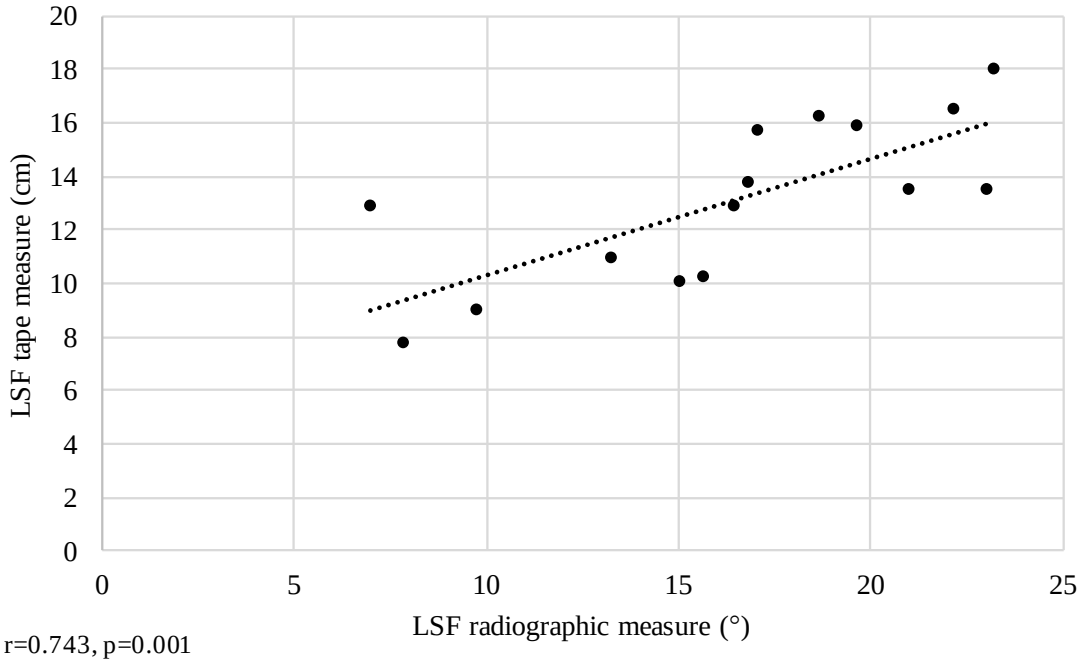

Figure 12. A scatterplot presenting the LSF radiographic measure compared to the LSF tape measure. The radiographic ranges of motion were calculated as a change in radiographic L1-S1 angles (º) from upright standing to maximum lateral bend for both sides. Both measures are presented as an average of left and right lateral bending ranges of motion. These two measures had a strong Pearson's correlation coefficient of r=0.743, p=0.001.

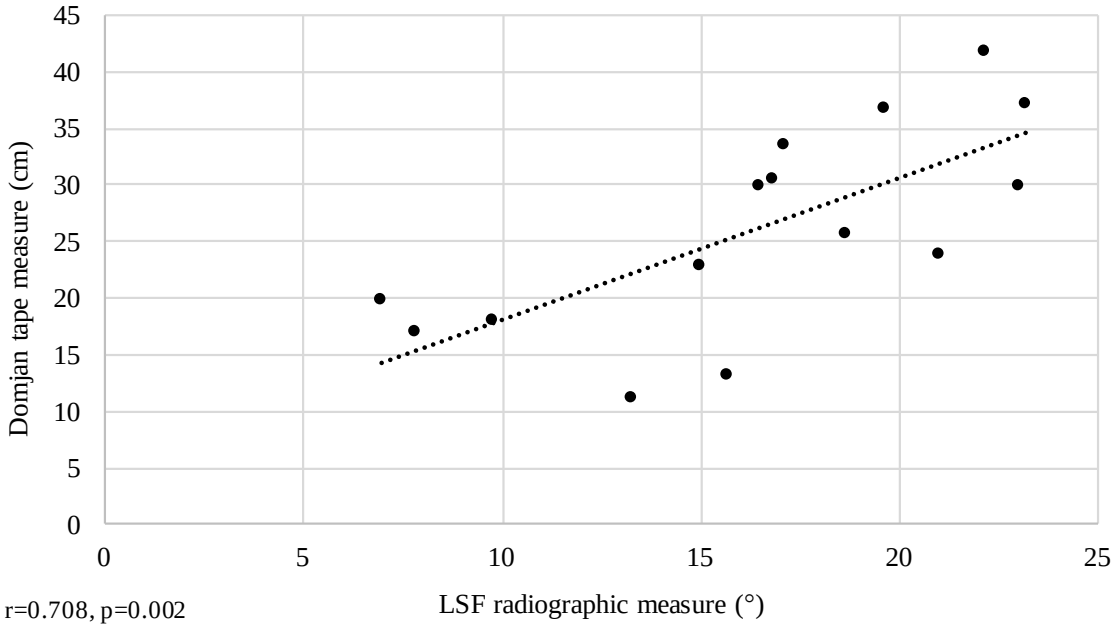

Figure 13. A scatterplot presenting the LSF radiographic measure compared to the Domjan tape measure. The radiographic ranges of motion were calculated as a change in radiographic L1-S1 angles (º) from upright standing to maximum lateral bend for both sides. The radiographic measure is presented as an average of left and right lateral bending ranges of motion. These two measures had a strong Pearson's correlation coefficient of r=0.708, p=0.002.

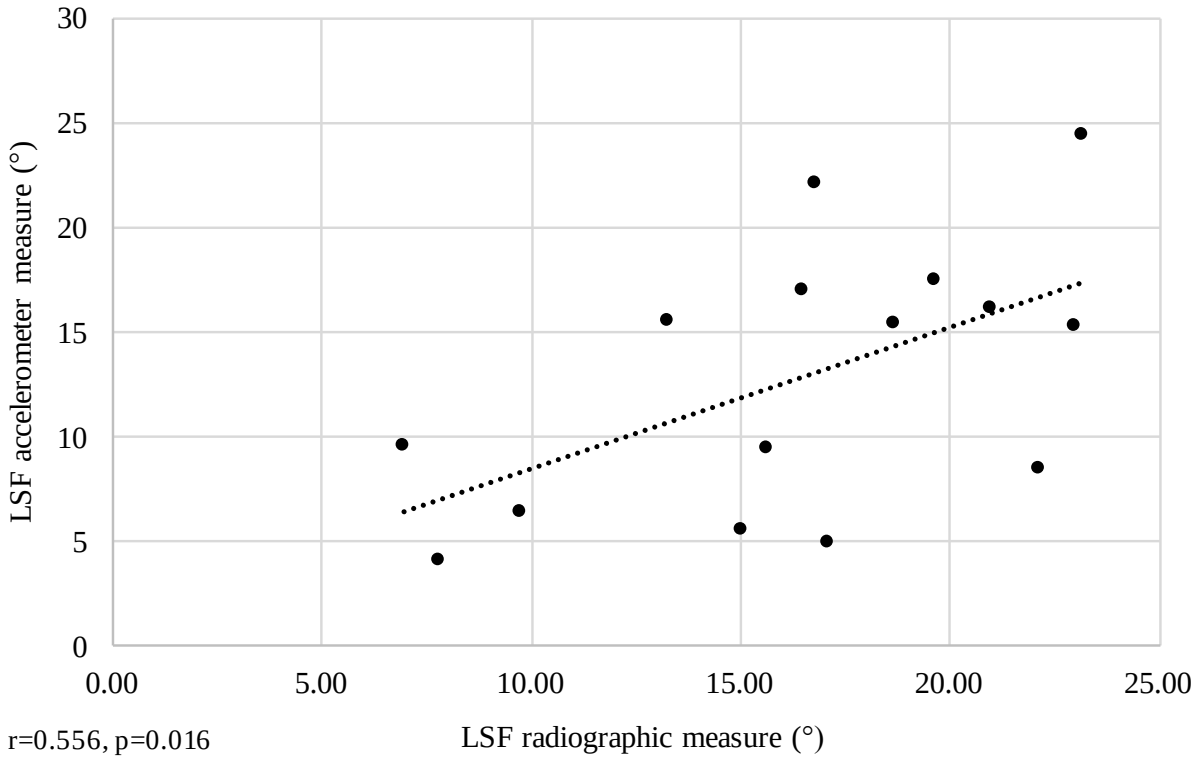

Figure 14. A scatterplot presenting the LSF radiographic measure compared to the LSF accelerometer measure. Ranges of motion were calculated as a change in L1-S1 angles (º) from upright standing to maximum lateral bend (z-axis) for both sides. Both measures are presented as an average of left and right lateral bending ranges of motion. These two measures had a moderate Pearson's correlation coefficient of r=0.556, p=0.016.

4.4 Intra-rater/ Inter-rater Agreement of Radiographic Measure

There was an excellent level of agreement (ICC=0.966, p<0.000) observed when testing the inter-rater reliability between JCS and a second trained rater. Intra-rater reliability also presented an excellent level of agreement (ICC=0.982, p<0.000) for radiographic measurements made by JCS.

Chapter 5: Discussion

In this chapter, the results of the thesis will be further explored in the context of the primary research question. The strengths and limitations of the study will be considered and future directions for this work will be identified. The overall goal of this thesis was to investigate an alternative method of spinal mobility measurement in forward and lateral bending using tri-axial accelerometers. Specifically, to determine the extent to which the accelerometers compare to traditional tape measurement methods in terms of criterion-concurrent validity using the radiographic measure as a reference standard. Previous literature has suggested that the current clinically used tape measurements in sagittal bending are not a valid measure of spine motion [12,53,56,58]. Therefore, it was hypothesized that the range of spine motion calculated from the tri-axial accelerometers would be a more valid measure of spinal mobility than the tape measurement methods. The monitoring of spinal mobility limitations in AxSpA patients provides a snapshot of disease progression and treatment responses. Thus, by exploring a potentially improved method of spinal mobility measurement it may be possible to improve the ability to identify symptoms and monitor its progression; ultimately improving the clinical management and quality of life of this patient population.

5.1 Forward Bending

Accelerometry was superior to clinical tape measure in measurement of forward spine flexion. We confirm that the use of tri-axial accelerometers correlate stronger with the radiographic measure in forward flexion, thereby suggesting that it is a better alternative to the current Schober's test measures. The accelerometer method used in our study yielded a Pearson's correlation coefficient of r=0.590, with a p-value of 0.010 in forward bending mobility

measurement. This significant, yet moderately strong correlation reflects spinal mobility better than its tape measurement counterpart, while still providing an inexpensive, easy to apply and potentially feasible method of measuring spine motion. In this stronger measure of spinal mobility, a relative angular measurement is extracted from two individual accelerometers, which is not dependant on the elastic properties of the skin. The Schober's tape measure variations produce measures that rely on the stretching of the skin when evaluating forward spinal flexion mobility. Research has reported large systematic differences at end ranges of spinal flexion when using current clinical tape measures. [58]At larger ranges of flexion the skin begins to slide across the underlying tissues rather than continuing to stretch, thereby causing disproportional changes to the Schober's measurement. [58] This may explain the stronger correlations to radiographic gold standard in the accelerometer measure compared to the three Schober's tests. At large ranges of motion where the skin stretching transitions to skin sliding across the tissues beneath the accelerometers, this may introduce a minor measurement bias. However, the results of the Bland-Altman analysis confirmed that there was no proportional bias between the radiograph and the accelerometer measures so we can be confident that this risk of bias is small. In theory, the accelerometers will still capture an angle that is methodologically analogous to the radiographic measure as presented in Figure 5. Consequently, accelerometers may present an increased benefit in assessing patients in the early stages of the disease, where larger spinal ranges of motions are more likely and tape measures are likely more susceptible to disproportional changes. Although the accelerometer correlated stronger to the radiographic measure than the tape measures in forward flexion, we could assume that this difference in correlational strength between measures would be more pronounced in a sample with a smaller disease duration and in turn, greater spinal ranges of motion. Upon completing spinal mobility assessment of this patient sample, it is

evident that their range of motion was limited by their disease activity. An Original Schober's test indicating a change of less than 50 mm can be interpreted as a positive test for spinal mobility limitations. [11] In our sample of 15 AxSpA patients the mean OST score was 22.97 mm ± 15.09 mm while the average duration since diagnosis in this sample was 11.65 yr ± 9.35 yr. In contrast, the 50 patient cohort from the Rezvani study that evaluated forward bending tape measures had a mean OST score of 40.7 mm ± 18.8 mm with a mean time since diagnosis of 3.90 yr ± 4.44 yr. Relatively speaking, our 15 patient sample had a much longer duration since diagnosis and, accordingly, their spinal mobility in forward bending was far more limited. We could not accurately approximate the time since initial presentation of symptoms associated with AxSpA, therefore, this time since diagnosis does not account for diagnosis delay between onset of symptoms and clinical diagnosis. Since previous research in spine motion measurement has proven that the use of accelerometry is a reliable technique in the repeated measurement of forward bending lumbar spine movement in a healthy population [65], we can be confident that accelerometers are a good measure of spine motion. It may just be that in our current population, the decreased range of motion limited the difference of correlation strength between accelerometer and tape measure. Specifically, if our sample had included an early diagnostic group with a larger range of motion, we could hypothesize that lower correlations would be observed in the tape measure, further favoring the accelerometer measure of forward bending spinal mobility. The results from our investigation suggest that the tri-axial accelerometers have potential to improve the clinical measurement of forward bending spinal mobility in AxSpA and our findings should be expanded on through future work within this clinical population.

We confirm that tape measure methods have overall poor concordance with gold standard radiography when assessing forward flexion. The results of the forward bending trials in this

study, using the OST, MST and MMST are in accordance with the methodologically similar study from Rezvani et al. (2002), which was considered to be high quality according to the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) assessment tool. Their study established a weak correlation to the radiographic measurement for the OST (r=0.363, p=0.018) and MST (r=0.333, p=0.018) measures in patients with Ankylosing Spondylitis. Similar weak correlations for OST (r=0.195, p=0.243) and MST (r=0.295, p=0.143) were found in our analysis. We are unable to compare our results for the MMST; as the Rezvani team did not report this measure as they concluded that the measure did not reflect spine mobility. There is very limited evidence regarding the criterion-concurrent validity of MMST with reference to the radiographic gold standard of spinal mobility measurement in AxSpA patients. The MMST was originally designed for spinal mobility measurement in patients with AS, but has largely been used to measure ROM in the general population. This has limited the conclusions regarding the validity of this measure in the originally intended AxSpA population, who typically have a smaller lumbar spine ROM. [19] The one other study that has reported results regarding the validity of MMST compared to radiographic gold standard was completed in a cohort of LBP patients, rather than in the AxSpA population. [53] Although this study reported Pearson's correlation coefficient of 0.67, it was not regarded as high quality (QUADAS) in the systematic review by Littlewood and May [78] because the observers were not blinded from the MMST results when interpreting the radiographic measures. In our study, all films were duplicated, blinded, and graded in a randomized order using the Horos DICOM Software. The LBP cohort had a mean MMST measure of 63.00 mm ± 14.00 mm where as our AxSpA had a mean MMST measure of 31.87 mm ± 17.47 mm. This contrasting result illustrates the evident mobility differences between a LBP and an AxSpA cohort, further weakening the generalizability of their findings to

the intended population. In our investigation in AxSpA patients, MMST held the largest correlation of the three forward bending tape measures to the radiographic gold standard. MMST moderately correlated (r=0.414) to the radiographic measure and was not statistically significant (p=0.063). As mentioned above, all three Schober's tests rely on the stretching of the skin to produce a measure representative of forward bending spinal mobility. Research has shown the disproportional changes in tape measure tests at larger ranges of forward bending. [58]Additionally, a study looking at structural deformation of skin in response to spine posture changes found that individuals with greater subcutaneous fat/fascia were associated with greater skin structural deformation in forward flexion. [79] In other words, skin stretching is not proportional to the true spinal range of motion and consequently, tape measures of forward spinal mobility are confounded by the body type of the individual. In summary, none of the forward bending clinical tape measures used in this study performed adequately. This warrants the need of further research into the use of alternative methods of sagittal plane spinal mobility measurement, such as but not limited to accelerometers, which have potential to be a clinical feasible, easy to use assessment tool.

5.2 Lateral Bending

The ASAS recommends the use of the BASMI as a way to assess spinal mobility in AxSpA. [59] This is a compound index that combines five clinical measurements that reflect axial mobility. For example, the Modified Schober's test is used to assess forward spinal bending ROM, while the Tragus-to-Wall test measures cervical and thoracic spine mobility. The Lateral Spinal Flexion test, as evaluated in this study, is included in this index as an assessment of lateral

mobility of the spine. It is a common misconception that these five individual measures are in fact valid measures of spinal mobility in AxSpA patients. Although the individual tests that make up the BASMI have been shown to have construct validity in predicting disease factors such as structural damage [34,80], there is very limited evidence for the criterion-concurrent validity of these individual tests and an accepted reference standard. [13] Without confirmed evidence of concurrent validity, it cannot be assumed that the LSF test is a truly adequate measure of its intended use, which is to provide a measure of lateral spinal range of motion. For the LSF test specifically, this was the first study to evaluate the criterion-concurrent validity of the test with reference to the widely accepted radiographic gold standard. There has been no study that has validated the commonly used Lateral Spinal Flexion tape measurement test with comparison to the radiographic gold standard measure of spinal mobility. A study completed by Moll et al. found a correlation coefficient of r=0.79 when compared to radiographic measures for a methodologically different lateral tape measurement test, however, the results came from pooled data from a sample of AS patients (n=18) and a larger sample of healthy controls (n=36). To our knowledge, our study is the first to investigate the criterion-concurrent validity of the ASAS recommended clinical LSF tape measure.

Tape measure tests have strong concordance with radiographic measurement in lateral spine flexion. Upon comparing both the LSF test and the accelerometer method of measuring lateral spine flexion range of motion, the tape measure had a strong correlation (r=0.743, p=0.001) to radiographic measures while the accelerometer had a moderate strength correlation coefficient (r=0.556, p=0.016). It can therefore be suggested that the LSF tape measure is a valid measure of lateral spinal flexion in the intended AxSpA population. The methodology of the LSF test does not require landmarking of anatomical reference points such as surface palpation and

pen marking that is required for the placement of accelerometers. This minimization of measurement bias may explain the differential benefit of the tape measure versus the accelerometer in measuring lateral spine bending range of motion. It is important to note that the LSF measure is taken from an average of both sides. When collecting experimental data, repeating a measure and taking an average decreases the variability of the measure, thus increasing the reliability and accuracy. This may explain the strong correlations occurring in this measure. This raises the question that if the time was taken to collect multiple forward flexion measures and average them, would they present stronger correlations? The following conclusions are important from a clinical assessment stand point as the values were the result of a clinically used test, which averages both left and right flexion ranges to represent lateral spine mobility as a whole. From a basic science standpoint, comparing the measures of left and right side bending for the tape and accelerometer measures could be a more direct representation of the measure's validity. In both individual side-bending measures, the tape measure (left: $r=0.529$, $p=0.021$; right: $r=0.727$, $p=0.001$) had a stronger correlation to the radiographic gold standard than the accelerometer measure (left: $r=0.303$, $p=0.136$; right: $r=0.670$, $p=0.003$). These findings further suggest that the tape measurements are a more valid measure of spinal mobility when measuring lateral ranges of motion. The tape and accelerometer measures in right lateral bending both correlate strongly to the radiographic measure. This finding may indicate that with further research, the accelerometer may prove to be a valid measure of lateral spinal mobility but does not warrant the use of this method in place of the tape measure at this time. However, we are interested in further investigating the validity of both the accelerometer and the tape measurement of lateral spinal range of motion in AxSpA. There was a difference in the strength of correlations between left and right side bending for both measurements methods. The

literature presents no evidence for predominant disease related spinal mobility restrictions in left lateral bending versus right lateral bending in this patient population. There was no statistically significant difference ($p=0.849$) between left and right lateral bending radiographic measures. Therefore, the difference in correlation strength between sides in this population cannot be explained by a larger ROM in one side versus the other. This discrepancy of correlations between left and right sides raises questions and further justifies the designing of a study that will expand on this sample to investigate the validity of both tape and accelerometers in measuring spinal mobility in this population. The Domjan tape measure of bilateral spinal bending correlated strongly ($r=0.708$, $p=0.002$) to the radiographic measure proving to also out-perform the lateral flexion accelerometer measure. Although this method had a slightly smaller correlation compared to the LSF test ($r=0.743$, $p=0.001$), this relatively new test can be conducted and analyzed quicker in a clinical setting. This test requires the participant to perform two postural movements (maximum lateral bending on both sides) and requires the clinician to report only one measure between two markings on the patient's leg. From a conducting perspective, this is quick and easy as opposed to the four measures that are taken for the LSF test, which requires subtraction and averaging of multiple measures to arrive at a test result. It is also important to note that this test does not average multiple measures as the LSF test does. As we know, averaging multiple measure decreases the variability of a measure, thereby improving accuracy and reliability. This suggests that the results of the Domjan measure may be stronger in nature than the averaged measure presented by the LSF test. This test is ultimately quick and easily implemented in a clinical setting. Our findings confirm that tape measure, whether using the LSF or Domjan technique, is valid for assessing lateral spine flexion.

5.3 Strengths and Limitations

The Domjan and LSF tape measurement tests are currently being used clinically with the assumption that they are a true valid measure of spinal range of motion. This was the first investigation to evaluate the criterion-concurrent validity of the LSF and Domjan clinical tape measurements compared to the radiographic gold standard of spine motion measurement. This is the most objective way of assessing the true validity of a clinical measurement. [81] We confirmed that both the Domjan and LSF tests were valid measures of lateral spinal mobility. This study was also the first to examine the criterion-concurrent validity of tri-axial accelerometers in the measurement of spinal mobility in the very relevant AxSpA patient population. The findings of this study highlight the potential for tri-axial accelerometers in measuring spine motion, warranting further research into the application of these cheap, easily implementable sensors. There were also several limitations to this study. Although we used a multitude of recruitment outlets including the Canadian Spondylitis Association, clinicians from the Canadian Memorial Chiropractic College and disease specific interest groups in the Greater Toronto Area, we did not reach our desired sample size of thirty AxSpA patients. We therefore used convenience sampling to reach a small sample of fifteen patients, which was ultimately a limitation to the power of this study. The data for this study could not be collected at Eastern Health in St. John's, Newfoundland due to barriers in accessing radiographic equipment for research purposes. Evaluating the criterion-concurrent validity of these two methods against the widely accepted radiographic gold standard of spinal mobility measurement required JCS to travel to North York, Ontario to gain access to the radiographic equipment at the Canadian Memorial Chiropractic College. Another limitation, which affected the sample size, was the expenses associated with this imaging study. The budget for this research could not accommodate for the wages of the

RRT, as well as living expenses in Toronto for longer than three months. Consequently, data collection was concluded after three months, where JCS returned to NL to continue analyzing the data from fifteen AxSpA patients. It was originally assumed that three months would be sufficient to collect the desired sample size, however, recruitment barriers became an unforeseen limitation. Recruiting from a patient population can pose problems, especially when participation involves commuting to the collection site, as it did in this study. The AxSpA population typically deals with inflammatory 'flare ups', which restricted two potential participants from participating. Another limitation to this study was that our convenience sample yielded only AxSpA patients from the radiographic/AS subgroup. This may be due to our inclusion criteria requiring a confirmed AxSpA diagnosis from a rheumatologist. Without definitive radiographic evidence, the diagnosis of non-radiographic AxSpA patients becomes increasingly subjective and can cause patients to be misdiagnosed or undiagnosed. [44] Because of this, many non-radiographic patients may not even know they have AxSpA. This may explain the absence of non-radiographic cases in this study. This would reduce the generalizability of our results to the non-radiographic subgroup. To overcome this, our future work will not only focus on the earlier stage and non-radiographic cohort, but also prepare for a longer study period to ensure we reach a desired sample size.

Another limitation inherent to landmarking by surface palpation is the potential for measurement error caused by misplacement of the accelerometers and tape measures. To mitigate this risk, palpation and instrumentation of accelerometers and tape measures was completed by the same trained investigator for all participants. In this study we were able to confirm the actual location of accelerometers with respect to the vertebral landmarks on the radiographs. The bottom accelerometer was consistently placed over the sacrum and the top

accelerometer was never off by more than one vertebral level. Since the L1/L2 intervertebral disc angle only accounts for a small proportion of the lumbar lordosis angle, we are confident that errors in placement would contribute minimally to errors in the accelerometer measure. The placement of the tape measures could not be confirmed via radiograph because the vinyl material of the tape measure is not detected on a radiographic image.

5.4 Future Direction

The findings from this study gave light to a method of assessing spinal mobility in the AxSpA population using tri-axial accelerometers. This method presented more criterion-concurrent validity than the three variations of Schober's tape measures in forward bending measures. Although this may not warrant a change of practice at this stage, it does justify a follow up study that validates our findings in a larger sample set. Establishing which method of spinal mobility measurement is superior is imperative to the monitoring of this susceptible disease cohort.

The future direction of this research also pertains to the further development of the tri-axial accelerometers used in this investigation. The current accelerometers are wired and involve an instrumentation protocol that takes 4-5 minutes. This is not clinically feasible from both a utilization and a time perspective. Future work needs to be done to develop these sensors into a wireless, more user-friendly device that can be set-up in a simple and timely manner by a primary healthcare provider. Once these accelerometers are developed into a more feasible method of measurement, a series of studies should be done to expand upon the applications of these sensors.

As mentioned previously, the accelerometer measure has great potential for increased benefit in assessing early stage AxSpA patients with greater spinal mobility. Designing a study that evaluates the criterion-concurrent validity of these spinal mobility measures in individuals with a disease duration of less than two years can offer evidence as to whether accelerometers are a significantly more valid assessment tool at early stages of this disease.

Research has investigated the use of clinical tape measures as a way of monitoring disease activity, both in patient follow up and to measure treatment response in clinical trials. [68,82] Going forward, to enhance the applications of accelerometry in AxSpA, studies should assess the accelerometer's responsiveness to change in pre- and post-biologic therapy. This will quantify the ability of these sensors in detecting clinically important changes over time, providing additional insight regarding the reliability and construct validity of this measurement tool.

LBP is often characterized as being mechanical or inflammatory in nature, although there have been very limited attempts to distinguish between these groups based on clinical symptoms. Back pain accompanied with stiffness that worsens with immobility is often associated with inflammatory LBP. [15] Future work should involve evaluating spinal mobility using both tape measures and accelerometers in patients who report LBP to see if they can be used to differentiate between mechanical and inflammatory LBP. If these measures of spinal mobility can identify mobility changes in clinical follow-up, this can influence a physicians' decision when attempting to distinguish the underlying cause of the back pain. This will then not only help provide basis for appropriate clinical management going forward, but also recognize inflammatory LBP as potential early stage spondyloarthritis allowing for earlier screening in suspected cases.

5.5 Impact of work

This study was the first to investigate the criterion-concurrent validity of tri-axial accelerometers for measuring spinal mobility in the very relevant AxSpA population. This stronger measure of forward bending spinal mobility presents novel insight into developing improved non-invasive clinical assessment tools. The accelerometers used in this study are lightweight, inexpensive and an easily implementable method of measurement. With future studies validating the findings from this sample, there holds potential for important applications in the field of telemedicine, where they could be used at the primary care level as a method of disease monitoring. In a society where a fair portion of the population lives rurally, it is not always feasible for patients to commute into an urban area for their assessment. With a more objective, valid, and easily implementable assessment tool for measuring spinal mobility, barriers to patient accessibility can be mitigated by incorporating this improved method of measurement into local primary care clinics.

Our study was also the first to investigate the criterion-concurrent validity of the ASAS recommended clinical LSF tape measure as well as the more recent Domjan measurement of bilateral spinal mobility. The correlations that were found for both lateral spinal mobility measures with reference to the radiographic measure suggest that these are valid measurement methods and can continue to be used in clinical follow up. The findings discussed in this thesis will direct further research into the measurement tools that are being used clinically. This work has advanced the knowledge surrounding the clinical application of both tri-axial accelerometers and clinical tape measures in measuring spinal mobility, whilst warranting further development in tri-axial accelerometer technology.

Conclusion

The variability across the literature regarding the criterion concurrent validity of tape measurements of sagittal lumbar spine flexion has raised many questions, although seemingly few solutions. Results from this study suggest that with further development, the accelerometer could be a clinically useful tool to assess forward flexion spinal mobility in the AxSpA population. For patients who have been previously diagnosed, this method of monitoring the spinal mobility limitations inherent to this disease can give a more accurate snapshot of the progressions of spinal involvement. With a more valid assessment tool, clinicians can have greater certainty when evaluating an individual's response to treatment, thereby optimizing and improving clinical management. The criterion-concurrent validation of the Domjan and Lateral Spinal Flexion tape measurements provides novel and clinically relevant insight into the monitoring of lateral spine mobility limitations. Our results for the three variations of the Schober's tests were in accordance with the inconclusive evidence for the validity of these measures. In conclusion, accelerometers have great potential to be developed into a clinically useful measurement tool, but only in terms of forward bending ranges of motion. The stronger correlations from the two lateral tape measurements suggest that the appropriate assessment tool is dependent on which range of motion is being assessed. In AxSpA, spinal mobility correlates strongly with disease duration, function and general health, [33,34] and is a core domain in monitoring disease activity. Clinicians often use spinal mobility measures as a way to see how well a patient is responding to therapies. [11] For example, if a patient's spinal mobility is found to be decreasing upon follow-up assessment, this warrants the consideration of alternative therapies. Disease outcome is therefore reliant on the validity of spinal mobility assessment tools. Finding from this study indicate the potential for further improvements to the clinical

assessment of mobility in AxSpA. Developing up-to-date clinical guidelines is critical to disease management and this study has paved the way for future work in designing improved guidelines for spinal mobility assessment in AxSpA.

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Appendices

Appendix A. Accelerometer Calibration protocol

To calibrate the accelerometer against gravity:

1. The accelerometer is attached to a square calibration block using double sided tape such that the sensor is parallel to the edge of the block.

2. Six trials are collected flipping and rotating the block on a level surface such that data is recorded for +1g, -1g and 0g for each of the three axes. This will give a voltage output from the accelerations that is then used to calculate conversion factors.

Appendix B. Original Schober's Test protocol

This test is used to assess lumbar spine forward flexion mobility as follows:

1. A horizontal mark is made at the level of the lumbosacral joint (LSJ) found via surface palpation. A second mark is made 10 cm above the original mark (measured with a clinical tape measure).

2. The patient is instructed to maximally flex forward without bending their knees, at which time the examiner measures the distance between the two marks using the clinical tape measure.

3. 10 cm is deducted from this measured distance to give the Original Schober's Test value to the nearest millimetre.

Appendix C. Modified Schober's Test protocol

This test is used to assess lumbar spine forward flexion mobility as follows:

1. A horizontal mark is made 5cm below the level of the lumbosacral joint (LSJ), which is found via surface palpation. A second mark is made 10 cm above the LSJ (measured with a clinical tape measure).

2. The patient is instructed to maximally flex forward without bending their knees, at which time the examiner measures the distance between the two marks using the clinical tape measure.

3. 15 cm is deducted from this measured distance to give the Modified Schober's Test value to the nearest millimetre.

Appendix D. Modified-Modified Schober's Test protocol

This test is used to assess lumbar spine forward flexion mobility as follows:

1. A horizontal mark is made at the level of the lumbosacral joint (LSJ) found via surface palpation. A second mark is made 15 cm above the original mark (measured with a clinical tape measure).

2. The patient is instructed to maximally flex forward without bending their knees, at which time the examiner measures the distance between the two marks using the clinical tape measure.

3. 15 cm is deducted from this measured distance to give the Modified-Modified Schober's Test value to the nearest millimetre.

Appendix E. Lateral Spinal Flexion Test protocol

This test is used to assess lateral spine flexion mobility as follows:

1. With the patient's heels and back up against a wall and arms by their side, measure and record the distance between the middle fingertip and the floor.

2. The patient is instructed to maximally flex laterally without trunk rotation. Measure distance from fingertip to the floor on the same side as previously measured. Record the difference between these two measures

3. Repeat this on the opposite side and the average of the two sides is recorded as the Lateral Spinal Flexion Test value to the nearest millimetre.

Appendix F. Domjan Test protocol

This test is used to assess lateral spine flexion mobility as follows:

1. With the patient's heels and back up against a wall and arms by their side, a horizontal mark is drawn on the participant leg at the level of the ipsilateral third finger at end range right lateral flexion.

2. Mark another line at the level of the same finger on the same leg in end range left lateral flexion.

3. Measure the distance between these two marks with a clinical tape measure to indicate the Domjan Test value to the nearest millimetre.