Keeping a Chin Up in the Face of Adjacent Segment Pathology: A Biomechanical Analysis of Prophylactic Treatments for Proximal Junctional Kyphosis in Adult Spinal Fusions

By:

Damon E. Mar

M.S. Mechanical Engineering, University of Kansas, 2012

B.S. Mechanical Engineering, University of Kansas, 2007

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Chair: Terence E. McIff

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Member: Douglas C. Burton

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Member: Sara Wilson

____

Member: Carl Luchies

____

Graduate Program Representative: Elizabeth Friis

Date Defended: December 6th, 2017

The dissertation committee for Damon E. Mar certifies that this is the approved version of the following dissertation:

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Chair: Terence E. McIff

Date Approved: ______________

Abstract: The use of prophylactic tethers for treatment of proximal junctional kyphosis has been gaining clinical interest in recent years. There is currently no clinical consensus on appropriate technique and little biomechanical data to provide initial guidance. The intent of this work is to provide an improved understanding of the basic techniques relevant to spinal reconstructive surgery and to provide initial biomechanical characterization of basic tethering techniques. Three primary goals are proposed: 1) complete a review of spinal tethering techniques to determine the current state of the art of spinal tethering, 2) conduct a series of mechanical characterizations of basic tethering parameters in order to demonstrate their effects on spine biomechanics, and 3) provide concise engineering commentary and perspectives that help tie study findings to relevant clinical concepts and concerns. A review of the literature on spinal tethering resulted in six common techniques, twelve devices, and only six publications to date focusing on tethering for prophylactic treatments in adult spinal deformity. The review indicated a severe lack in current understanding of biomechanical effects. The characterizations of basic technique parameters was done in a series of four biomechanical cadaveric studies which investigated the effects of tether tension, looping technique, and anchoring methods on segment range of motion, intervertebral disc pressures, spinous process loads, and failure modes. The primary results indicate that tether tension plays a significant role in the effectiveness/effect of a tethering technique and that increased spinous process loads are most critical at the uppermost tethered level. Additional findings indicate that the combination of varying multiple technique parameters allows for great flexibility in treatment strategies. While basic in nature, the results found in this work stand are the first of their kind and provide a basis upon which further investigations may better elucidate the relationship of tethering techniques to clinical outcomes.

Acknowledgements: For as much as a dissertation is about the summary of work and understanding of a single individual, the work presented in this document could not have been possible without the tireless efforts and meaningful contributions of many. While it is simply impossible to express my thanks and appreciation to all that contributed to this work, there are a few that I have chosen to mention in particular:

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List of Common Abbreviations:

AF – Annulus Fibrosis
ANOVA – Analysis of Variance
ASP – Adjacent Segment Pathology
ASD – Adult Spinal Deformity, alternately Adjacent Segment Degeneration
ASDeg – Adjacent Segment Degeneration
ASDis – Adjacent Segment Disease
BMD – Bone Mineral Density
BMI – Body Mass Index
CASP – Clinical Adjacent Segment Pathology
CDC – Center for Disease Control
CH – Chained Looping Method
CL – Cross Link, alternatively Cervical Lordosis
CM – Common Looping Methods
DAI – Disc Angle Index
DEXA – Dual Energy X-Ray Absorptiometry
DDD – Degenerative Disc Disease
DRI – Disc Ratio Index
EZ – Extension Zone
F8 – Figure-Eight Looping Method
FDA – Food and Drug Administration
FEM – Finite Element Model
FSL – Functional Slack Length
FSU – Functional Spinal Unit
ICOR – Instantaneous Center of Rotation
IVD – Intervertebral Disc
LL – Lumbar Lordosis
MANOVA – Multivariate Analysis of Variance
PJK – Proximal Junctional Kyphosis
PJF – Proximal Junctional Failure
PLC – Posterior Ligamentous Complex
PLIF – Posterior Lumbar Interbody Fusion
PSO – Pedicle Subtraction Osteotomy
NP – Nucleus Pulposis
NZ – Neutral Zone
RASP – Radiographic Adjacent Segment Pathology
ROM – Range of Motion
SP – Spinous Process
SPH – Spinous Process Hole
ST – Single Tether Looping Method
TLA – Three Letter Acronym
TK – Thoracic Kyphosis
UIV – Uppermost Instrumented Vertebra
WHO – World Health Organization

1. Chapter 1 - Introduction and Background

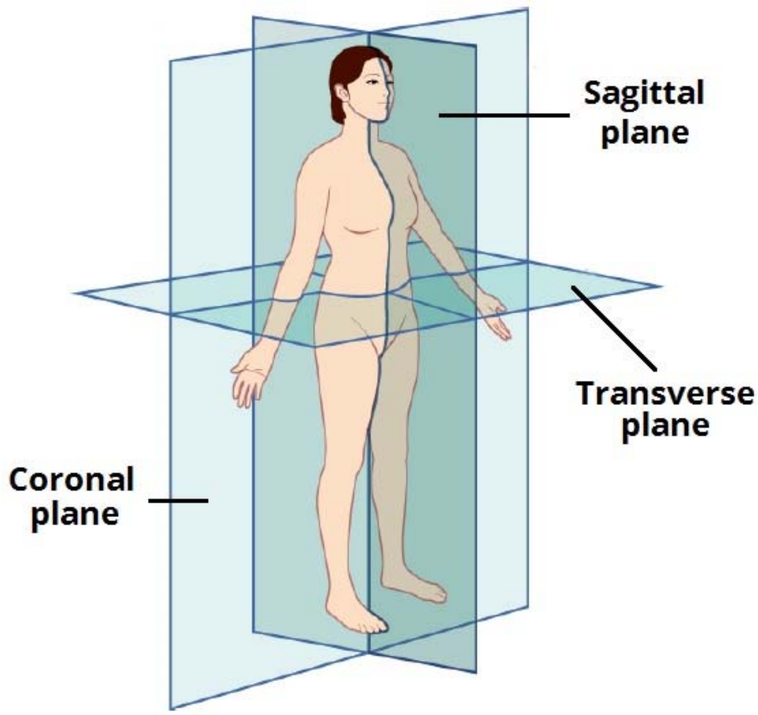
This chapter will begin with a brief overview of human spine anatomy and an introduction to spine biomechanics concepts and terminology. An introduction to adult spinal deformity and adjacent segment pathologies will follow. The chapter ends with a summation of the current needs in surgical treatment strategies for adult spinal deformities and a statement of the primary goals and specific aims of this body of work.

1.1. Spine Anatomy and Terminology

As the core of the work presented in this dissertation lies between clinical technique and biomechanical evaluation, it is necessary to review the common terminology used in each field. First, anatomical terminology will be introduced, both for standard human anatomy and for the human thoracic spine. Second, engineering concepts related to the form and function of the human spine will be introduced. Individuals familiar with any portion of this introductory section may feel free to skip ahead to Section 1.2, the introduction of Adult Spinal Deformity.

1.1.1. Human Spine Anatomy and Terminology

Basic Human Anatomical Terminology: The reference coordinate system used throughout this document will follow standard human anatomical planes: coronal (the plane as viewed from the front of a person), sagittal (the plane as viewed from the side of a person), and axial or transverse (the plane as viewed from the head down of a person) as shown in Figure 1.1.



http://teachmeanatomy.info/wp-content/uploads/The-Anatomical-Planes-of-the-Human-Body-1.jpg

Figure 1.1: Depiction of the three standard human anatomical planes: the coronal plane, the sagittal plane, and the axial or transverse plane.

The terms medial and lateral will refer to closer to and further from the middle respectively (such as the hand position relative to the spine in the coronal plane). In the sagittal plane, the terms anterior and posterior will refer to locations closer to the front and back of the vertebral body respectively. Alternately the term rostral and dorsal may be used respectively. For location of individual spinal levels relative to those above or below, the terms cranial (closer to the head) and caudal (closer to the sacrum) will be used. In certain instances the terms superior (above) and inferior (below) may also be used to represent relative positions within a localized region. Another set of terms used for specifying relative location of spinal levels is proximal, a level above, and distal, a level below.

Thoracic Spine Anatomy: The human thoracic spine is the middle segment of the three regions (cervical, thoracic and lumbar) and is normally comprised of twelve vertebral bodies and the adjoining soft tissues. The most prominent difference between the thoracic spine and the other regions is the presence of the bony rib structure which provides support and protection of the vital organs. In addition, the thoracic spine provides axial support of the head and upper extremities and provides a protected routing for the spinal cord and related nerves to the lower torso and lower extremities. The addition of the rib anatomy results in a spinal region that generally sees lower flexibility compared to the cervical and lumbar regions [1]. Different sections, even within a primary region, may see variations in flexibility and stiffness depending on degree and mode of loading [1-4].

Thoracic Kyphosis: Another primary defining feature of the human thoracic spine is a prominent kyphotic curve which is reciprocal to the lordotic curves of the lumbar and cervical regions in the sagittal plane. The primary anatomical measure of thoracic kyphosis is defined by the kyphotic angle between the superior endplate of T1 and the inferior endplate of T12 as shown in Figure 1.2.

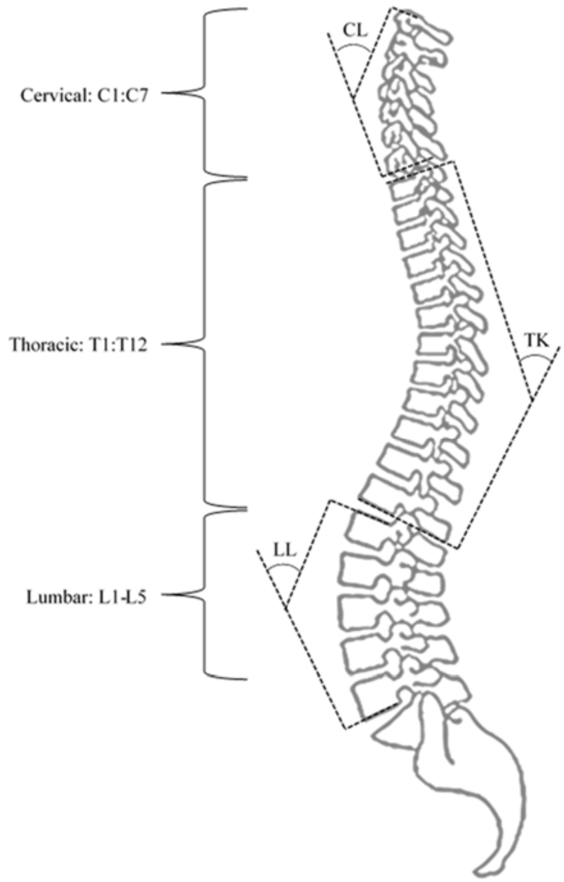


Figure 1.2: Schematic of the human spine with indication of the cervical, thoracic, and lumbar regions. The cervical and lumbar regions exhibit primary lordodic (backward-curving) curves (CL and LL respectively) while the thoracic region exhibits a primary kyphotic (forward-curving) curve, labeled as TK.

Thoracic Vertebral Body: The anatomical structure of the thoracic vertebral body is more similar to lumbar spine than to the cervical; however, there is a gradual change in morphology from T1 to T12. The thoracic vertebra is comprised of an anterior region commonly referred to as the vertebral body (or centrum) and a posterior (or dorsal) region comprised of the pedicles, facets, lamina, and spinous process. An overview of the human thoracic vertebral body is shown in Figure 1.3.

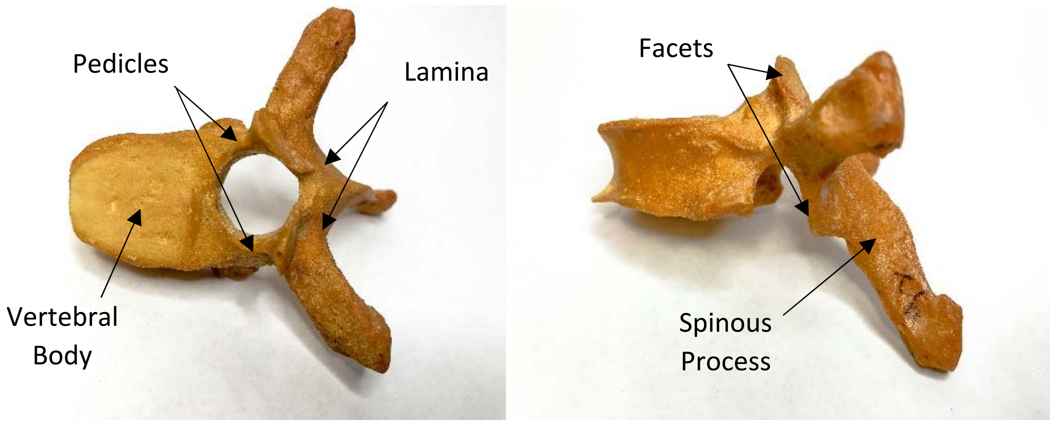


Figure 1.3: Overview of the human vertebral body. Primary features include the vertebral body or centrum, the pedicles, lamina, facets, and the spinous process.

Vertebrae bone morphology follows Wolfe's Law which states that bone structure remodeling responds accordingly to how it is loaded, thus putting the majority of the structure in line with the lines of force acting on it. The vertebral bodies, which form the central, axial weight-bearing column, are predominantly a cancellous structure with vertically oriented trabeculae surrounded by a thick cortical shell. The vertebral endplates are generally thinner than the sides of the vertebral body and show a transition from the cancellous structure into the avascular tissues of the intervertebral disc (IVD). The pedicles, laminae, and spinous processes (SP) are similar morphologically in that they are made up of outer cortical shells surrounding inner trabeculae oriented in primary load bearing directions.

Soft Tissues of the Thoracic Spine: The primary passive soft tissues that work in conjunction with the thoracic vertebral bodies are the IVD and seven primary ligaments which include the anterior and posterior longitudinal ligaments (ALL and PLL), the ligamentum flavum (LF), the transverse ligaments (TL), the facet capsule (FC), the interspinous ligament (ISL), and the supraspinous ligament (SSL). Commonly, the ligaments are grouped into anterior, middle, and posterior complexes. The anterior and middle complexes (ALC and MLC respectively) both include the annulus fibrosis (outer layer of the intervertebral disc) and their respective longitudinal ligament (ALL for ALC and PLL for MLC). The posterior ligament complex (PLC), which will be a primary focus in this work, is comprised of the FC, ISL, and SSL. The ligaments functionally work in tension to resist bending. In flexion, a forward bending of the spine, the PLC is the primary mode of restriction with some additional restriction provided by the MLC. In extension, a backward bending of the spine, the ALC provides the primary mode of restriction along with the facet joints. The complexes work in conjunction to varying degrees for lateral bending and axial rotations of the spine. The IVD is comprised of two primary sections: the outer, lamellar layers that make up the annulus fibrosis (AF), and the inner, gel-like nucleus pulposis (NP). The IVD functions as the primary load transfer and shock absorber in the spine and allows for motion between vertebral levels. The form of the IVD with the outer AF and inner NP also acts as a primary stabilizer when acted on by external loads causing ligament tension. The healthy NP exhibits a net positive pressure causing a natural tensioning of the AF annular fibers. This static preloading combined with upper body weight loading results in non-linear loading profiles as the spine is bent in the anatomical planes. These loading profiles will be introduced and discussed in Section 1.1.2 which covers basic spine biomechanics.

Thoracic Back Muscles: The back muscles serve as the primary control mechanisms and active stabilizers. The primary muscle groups acting on the thoracic spine include the erector spinae, spinalis, and longissimus muscle groups. Muscle weakness has been identified as a common risk factor in the development of ASD [5].

1.1.2. Spine Biomechanics Background & Terminology

From an engineering perspective, the human spine can be viewed as a complex mechanical system comprised of a passive structural framework (vertebral bodies, IVD, ligaments) which is acted on and loaded by a dynamic loading system (the back muscles). The simplest form of a single functional level of a spine, often referred to as a functional spinal unit (FSU), is comprised of a pair of adjacent vertebrae and their adjoining soft tissues which includes the intervertebral disc and the supporting ligaments. An example of a model FSU is shown in Figure 1.4.

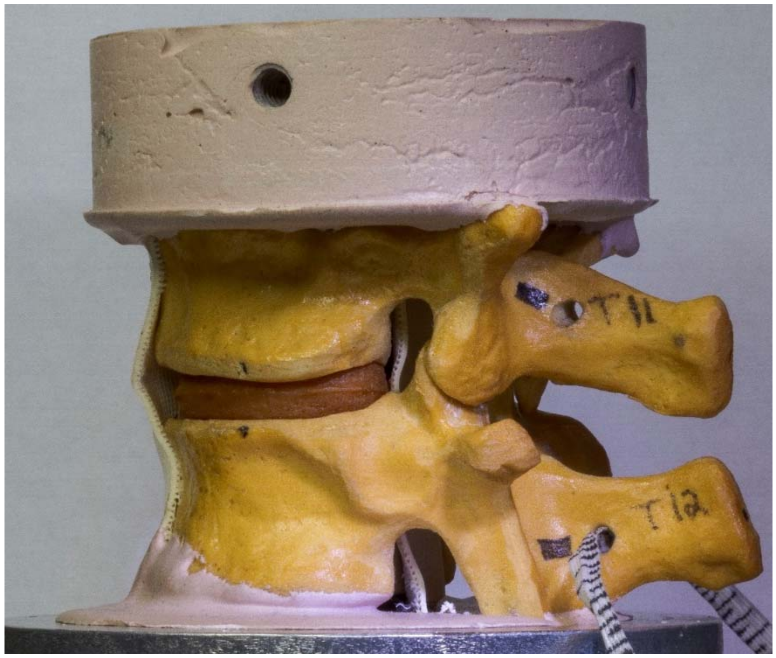


Figure 1.4: Example of a single spinal level, a functional spinal unit (FSU) comprised of two adjacent vertebra, the IVD, and the adjoining soft tissues (not shown).

The primary aspects of the vertebral bodies are related by geometry: distance and position of features relative to each other as defined by the physical size and anatomy. The center of mass for a given vertebral body is located approximately in the posterior third of the midline of the centrum in the midsagittal plane. The instantaneous center of rotation (ICOR) of a given vertebral level varies depending on the region and level within the spine and the degree of loading [6, 7]. In the thoracic spine, the ICOR of a given vertebral body typically lies at approximately the center of the vertebral body below it [7, 8]. The primary aspects of the soft tissues are a combination of both geometry and physical properties: their anatomical positions are the points of attachment to the geometry of the vertebral bodies and their physical properties define and govern how they carry and transfer loads. The physical properties of most soft tissues in the human body exhibit viscoelastic behavior which can be summarized as a non-linear behavior to changes in position or loading that shows dependency on magnitudes and rates of such changes. From a mechanical modeling point of view, viscoelastic behavior can be represented as the spring and dampener components of the classic mass-spring-dampener mechanical model. These aspects are important considerations when evaluations of spinal treatments are made with the acknowledgment that motion or loads may vary in terms of loading rate and range.

Spine Motion: Standard spinal motion evaluation is done in the anatomical planes: flexion-extension bending in the sagittal plane, lateral (side-to-side) bending in the coronal plane, and axial rotation (torsion) in the axial or transverse plane. The resulting nonlinear loading profile is typically divided into two zones: the neutral zone (NZ) of relatively low-stiffness (larger change in angle for a given change in load) at lower loading ranges of motion and the extension zone (EZ) with relatively high stiffness (less change in angle for a given load) at greater loading ranges. A typical bending load profile is shown in Figure 1.5.

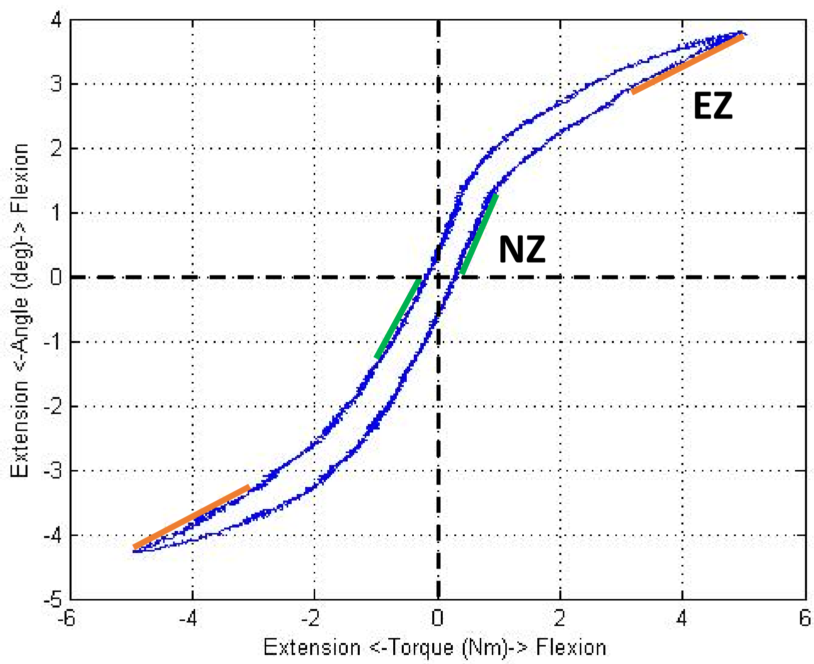


Figure 1.5: Example of a standard range-of-motion profile of a spine segment for flexion-extension bending with indication of the neutral zone (NZ) and extension zone (EZ) stiffness regions indicated by the green and orange lines respectively. The loading path follows a counter-clockwise direction with flexion bending first (to right corner) followed by extension bending (bottom left).

The NZ is primarily defined by IVD stability and health whereas the EZ is defined partially by the IVD, contact of the facets in certain modes, and the primary ligament complex resisting each mode. While the zones are typically easily recognizable, the exact point of transition from NZ to EZ can be difficult to reliably locate. Several methods have been proposed to quantify and define its location mathematically [9-11].

Biomechanical Spine Loading: While a variety of loading methods have been utilized historically for spinal testing, the most common and widely accepted technique is the use of a pure moment system [3, 11-13]. The advantage of a pure moment load is that it allows for equal loading across all levels tested.

Follower Load: In the field of spinal biomechanics, an important testing parameter associated with NZ and EZ stiffness is the degree of simulated bodyweight used during a ROM testing protocol. This load is often referred to as a follower load and is designed to channel a constant compressive load through the vertebral body centers of mass to simulate physiological loads acting on each level and to prevent segmental buckling which can occur at large bending angles as shown in Figure 1.6.

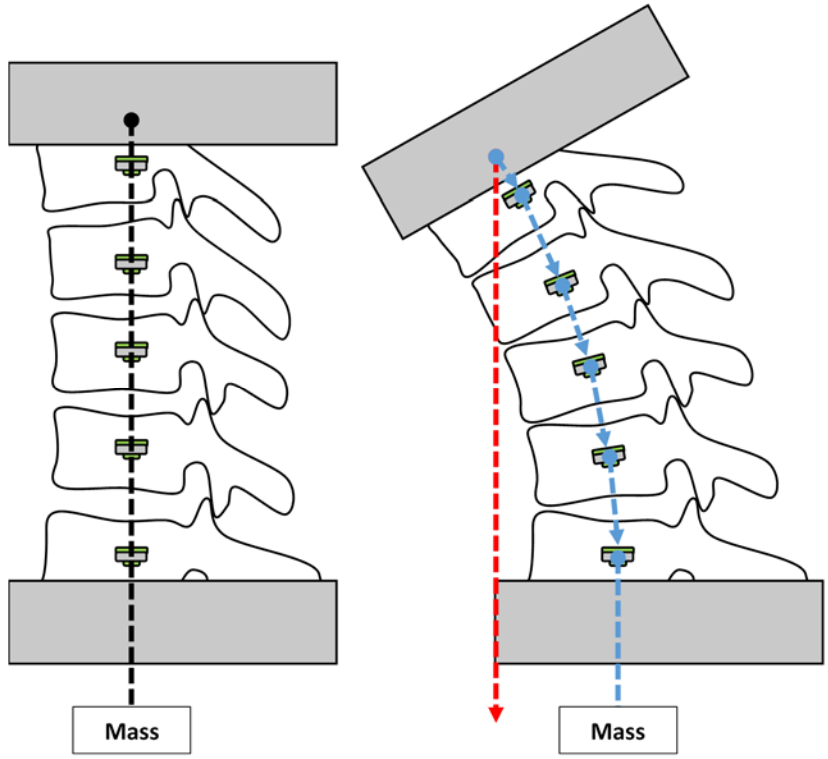


Figure 1.6: Overview of the function of a standard follower load method for segmental spine biomechanics. In the left schematic, a spine segment is shown in a neutral position with the dashed black line indicating the path of a compressive load applied by a mass hanging below the lower fixture which is anchored at the upper fixture block. The force line follows gravity through the centers of mass of each vertebral body. In the right schematic, the spine segment is flexed with the same compressive load applied. In this position, the gravity line of the unguided compressive force travels outside the centers of the vertebrae below it (dashed red line). The follower load guides correct this by channeling the line of the compressive load, shown as the dashed blue lines, through the center of mass of each vertebral body.

Of particular importance is the sensitivity of segmental biomechanics to the amount of follower load used. Historically, a variety of studies have shown that both the method of application and amount of load results in significant changes in segmental biomechanics including range of motion and load carrying capacity [13-15]. Additionally, the degree of anatomical dissection for biomechanical testing has also been shown to have significant effects [16, 17]. In most cases, the goal is to preserve as much anatomical structure as reason allows, either bony or soft tissues, in order to better preserve the base characteristics of the in-vivo behavior.

1.2. Spinal Reconstructive Surgery and Adult Spinal Deformity

1.2.1. Spinal Reconstructive Surgery

History of Reconstructive Spine Surgery: Treatment of spinal trauma and deformities date back as early as 1550 BC and has since seen a wide variety of techniques attempted with varying degrees of success [18]. In the earliest developments of surgical techniques for the spine, infection was the primary complication. The earliest reports of the successful use of spinal fusion date to 1911 by Hibbs and Albee with the use of posterior facet fusion techniques [19]. Spinal instrumentation was first introduced in the 1950s by Dr. Paul Harrington primarily out of the immediate need for efficient and effective treatment of post-polio scoliosis [18, 19]. The early instrumentation was comprised of rods with hooks at each end which functioned as either a mechanical support (strut) or compressive element for the correction of side-to-side curvatures common to scoliosis. At the time of its early development, the instrumentation was done primarily without the addition of spinal arthrodesis [19]. Over time however, arthrodesis was adopted as the standard treatment adjunct for corrective surgeries with spinal instrumentation. The use of implants within fusion surgeries increased from 23% in 1980 to 41% in 1990 [20]. Modern techniques for spinal instrumentation commonly include the use of pedicle screws and hooks interconnected with fusion rods spanning the length of the fused levels. Techniques may solely rely on pedicle screws or on a hybrid combination of pedicle screws and hooks. Additionally, interbody fusion devices and autogenous grafting are commonly used as part of an instrumentation and arthrodesis operation.

1.2.2. Spinal Fusion and Adult Spinal Deformity

Incidence and Costs of Spinal Fusion: The combination of spinal fusion and total joint arthroplasty, which includes total knee (TKA) and total hip (THA) replacements, makes up the most common orthopedic reconstructive procedures. In 2013, the total national cost for spinal fusions in the United States was $11.6 billion corresponding to over 405,245 principal procedures [21]. In comparison, the total cost for TKA was $11.6B for 700,740 procedures and for THA $7.9B for 457,195 procedures [21]. Figure 1.7 show the comparison of trends in mean cost per hospitalization for TKA, THA, and spinal fusion from 2000 to 2013 [21].

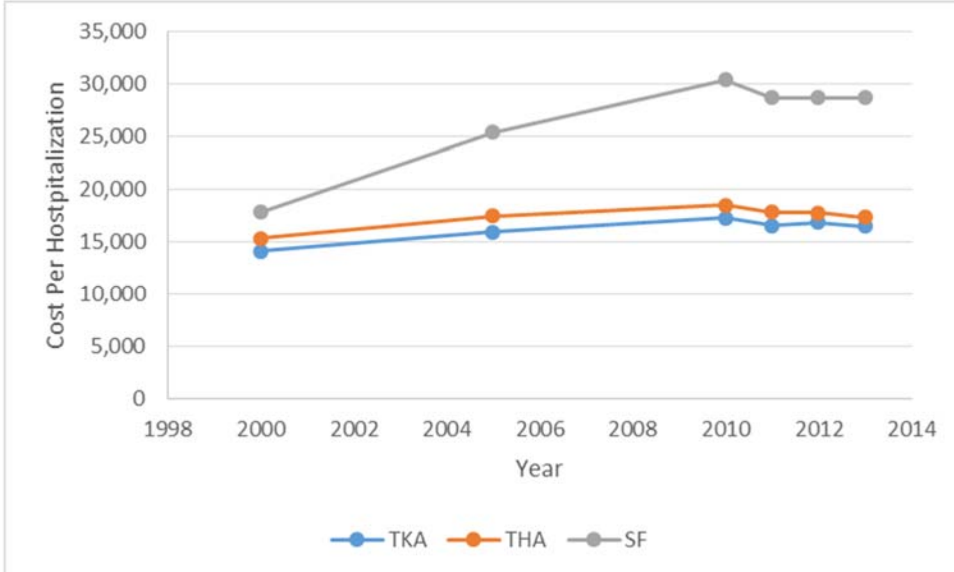


Figure 1.7: Mean cost per hospitalization for total knee arthroplasty (TKA), total hip arthroplasty (THA), and spinal fusion (SF) from 2000 to 2013 in the United States (CDC 2015). Amounts are reported in 2013 US dollars.

While cost increases stabilized in 2010 following the Affordable Care Act, the relative amount for spinal fusion remained at almost twice the cost of TKA and THA. In 2013, McCarthy et al. reported an average direct cost of $72,034 per case for adult spinal deformity (ASD) corrective surgery with a range of $10,768 to $187,458 [22]. The same study also reported average direct costs of $147,613 per case for primary cardiac procedures and $14,670 per case for TKA and THA. Given the relatively high costs and invasiveness associated with ASD corrective surgery, there have been consistent efforts to quantify and justify its value [22-24].

ASD and ASD Treatment: ASD is becoming progressively more prominent in the United States [25-28]. Incidence of ASD among adults has been reported to range from 1.4% to 32% depending on age [29-31]. Rates as high as 68% have been reported at the mean age of 70.5 years [32].

Pathology: ASD conditions are comprised of a variety of planar malalignments including scoliosis, kyphosis, lordosis, and axial rotations [33]. The underlying causes of spinal deformities present in a wide variety of forms. Aging plays a prominent role in the development of ASD by effecting bone integrity, IVD health, and muscle strength [25]. Often ASD occurs as a sequence of degenerations which compound over time leading to greater degeneration and deformity. Common types of degeneration include: degenerative disc disease, ligamentous laxity or failure, arthritis, and progressive abnormal curvatures like scoliosis, kyphosis, or lordosis [25]. Spinal deformity in adults may differ markedly from adolescent spinal deformity as adolescent conditions like adolescent idiopathic scoliosis (AIS) are often painless and are primarily a cosmetic concern [34-37]. For ASD, clinical symptoms are often indicated by pain, such as low back or leg pain, and functional disability [33, 36, 37].

Nonoperative Treatment of ASD: For ASD without progressive neurological deficits or rapid curve progression, treatment often focuses on core strengthening, flexibility, and endurance [38]. The use of analgesics such as anti-inflammatory drugs or nerve stabilizers have been shown to be beneficial in reducing pain [25]. Additionally, local steroid injections or nerve blocks may also be used for certain indications [25]. Other experimental treatments, including IVD biologics and tissue engineered biomaterials, show promise, however are still under development and require complete clinical evaluations. Bracing is normally not indicated for ASD as it has been shown ineffective toward mitigating progressive curves and in reducing pain [29, 38]. Evidence has suggested that better outcomes may be associated with surgical compared to nonoperative techniques [25, 34, 39, 40]. Surgical intervention is however, only indicated after nonoperative techniques have been found to be ineffective.

ASD Surgery Complications: Although modern techniques are considered quite successful for treatment of ASD, rates of complication are often high [29, 35, 38]. A wide variety of complications have been reported, including surgical site infections, neurological injury, implant failure, pseudoarthrosis, and adjacent segment pathologies. Reports of ASD complication rates have ranged from 13% to 71% depending on factors such as age and surgical approach [41, 42]. Rate of revision following primary ASD corrective surgery is 9% at an average of four years following primary correction [43]. There have been reports suggesting that although complications are generally higher for older individuals, the benefits in terms of cost and pain reduction that they see compared to younger individuals makes them better suited for ASD surgery [25, 35].

1.3. Adjacent Segment Pathology and Proximal Junctional Kyphosis

1.3.1. Adjacent Segment Pathology

Since the earliest documentations of spinal fusions over a hundred years ago, the prevalence of undesired effects at the untreated, adjacent levels has been noted [44]. These adverse effects are explained primarily by the abrupt change in motion and loading that occurs which puts increased loads and motion on the adjacent mobile levels. These concentrations can lead to vertebral fractures, accelerate IVD degeneration or failure, and ligamentous laxity or failure. Historically, a variety of definitions and classifications have been proposed to describe these effects. Early definitions included adjacent segment degeneration and adjacent segment disease [45, 46]. Often there were disconnects between conditions that were purely radiographic in nature and those that were purely symptomatic (associated with pain or disability). In 2012, Lawrence et al proposed the term adjacent segment pathology (ASP) to serve as the umbrella term for both clinical (CASP) and radiographic (RASP) effects seen at levels adjacent to fusions [47]. Lawrence et al. reported the risk of developing CASP was between 0.6% and 3.9% following fusion depending on age and other degenerative factors. Risk of developing RASP, in its most basic form, ranges wildly from 5.2% to 100% depending on follow-up time [48]. For the remainder of this document, ASP will refer to CASP unless noted otherwise.

1.3.2. Proximal Junctional Kyphosis

Among the various forms of ASP, one of the most prevalent is proximal junctional kyphosis (PJK), particularly among adults treated for ASD. The most widely accepted definition for PJK was proposed by Glattes et al. in 2005 which defined the condition radiographically as: 1) a sagittal angle of greater than 10 degrees between the inferior endplate of the uppermost instrumented vertebra (UIV) and the superior endplate of the vertebra two levels above it (UIV+2) and 2) a change of ten degrees or more of the same angle from preoperative to postoperative alignment [49]. Incidence of PJK has been shown to be from 13% to 55% [50, 51]. The presentation of PJK may vary from a relatively early postoperative complication up to three months or later [51-53]. Schairer et al reported that among 27 patient readmissions following ASD surgery, PJK accounted for over half (51.9%) of the readmissions due to surgical complications within 90 days [54].

Risk Factors for PJK: Risk factors for PJK are commonly grouped into three distinct categories: surgical, radiographic, and patient-specific factors [55]. Common surgical factors include type of approach used, surgical disruption of soft tissues, number of levels treated, fusion extending distally to the sacrum, and construct rigidity [55-57]. Surgical factors may also be referred to as biomechanical factors [58]. Radiographic factors are normally characterized by preoperative alignment parameters which include a variety of sagittal measurements such sagittal vertical alignment (SVA), T1 pelvic angle, and pelvic incidence to lumbar lordosis mismatch (PI-LL) [59, 60]. Common patient-specific risk factors include age, BMI, bone health, smoking, and presence of other preoperative comorbidities [49, 51, 61, 62].

Proximal Junctional Failure: While PJK is defined by radiographic criteria, proximal junctional failure (PJF) has had a variety of definitions and classifications proposed [63-65]. Generally, the most common definition is the occurrence of PJK with the presence of a structural failure [65]. Incidence of acute PJF is 5.6% with an underlying cause of fracture at a rate of 47% and soft tissue failure at a rate of 44% [65].

Prophylactic Treatments for PJK: Given that ASPs such as PJK and PJF result from a primary surgical intervention, the efforts to reduce them focus primarily on prophylactic treatment methods. Prophylactic techniques for ASPs break down roughly into two categories: vertebral body augmentation and dynamic stabilization. Vertebral augmentation techniques such as vertebroplasty and kyphoplasty have been shown to be effective in reducing the risk of PJF caused by vertebral fractures [66-68]. Several techniques have been well researched and key parameters such as fill volume [69-71], cement type or properties [72], and cement distribution [73] have been refined to improve efficacy and reliability. Clinical studies have backed many of these findings; however, some debate remains as to whether or not rates of PJK are reduced or just maintained with vertebral augmentation [68, 74, 75]. With the assumption that vertebral body strength can be adequately reinforced, the fight to prevent PJK now shifts focus to the health and stability of the soft tissues which includes the IVD and PLC. Given the anatomical limitations and restrictions of accessing thoracic IVD spaces anteriorly, the posterior aspects of the spine and the PLC becomes the logical area of interest for providing ligamentous support to maintain kyphosis. Support of the posterior elements has had great interest in the last decade and a wide variety of techniques and devices have been proposed and tested. Several motion sparing devices have been investigated for ASP prophylaxis, however unlike vertebral augmentation techniques, there has yet to be any clinical results to champion a particular device or technique. In comparison to the progress and current acceptance of vertebral augmentation for PJF due to vertebral fracture, there is a severe lack of both biomechanical characterization of PLC augmentation techniques and clinical results to guide emerging techniques.

1.4. Summary of Current Needs and Statement of Intent

1.4.1. Current Needs in Spinal Tethering

As efforts are made clinically to define and classify ASPs such as PJK in order to improve understanding of underlying causes, risk factors, and standardization of treatment, equal gains need to be made in the biomechanical understanding of the techniques and devices used to treat them. While there is growing interest in the use of spinal tethering for prophylactic treatment of ASP such as PJK, there is a significant deficit in the understanding of which tethering technique parameters and surgical methodologies should be utilized. **There is currently no clinical consensus on prophylactic treatment strategies to prevent PJK due to ligamentous laxity. Additionally, there is no surgical technique or device which has been identified as a starting point for preliminary investigation and development for PJK prophylaxis.** Given the overwhelming need clinically to reduce the prevalence of PJK while simultaneously accounting for increasing number of spinal surgeries and rising costs, the development of novel techniques such as prophylactic tethering must be done in a concise and efficient manner. Without initial characterization at the most basic functional level, advanced tethering techniques will not be adequately manageable and development will go unguided.

1.4.2. Statement of Intent

The intent of this work is to provide initial guidance for surgical tethering techniques for prophylactic treatment of PJK and to advance the engineering understanding of biomechanical effects of tethering.

1.4.3. Primary Goals

The following primary goals are proposed.

1. **Provide a detailed review of spinal tethering techniques to date, to summarize the current state of the art, and to determine the aspects of current tethering techniques that should be considered important for prophylactic treatment of ASP.**
    - **a.** Provide a historical review on the use of tethers in spine surgery.

b. Provide a summary of current techniques and devices utilized in the surgical treatment of ASPs.

2. **Provide the first detailed biomechanical characterization of a tethering technique for prophylactic treatment of PJK.**
   a. Basic biomechanical analysis on the effect of tether tension and relation to tether pull-out or failure loads.
   b. Biomechanical analysis of tether technique parameters on segmental biomechanics.
   c. Demonstration of the effect of tether looping technique on segmental biomechanics.
   d. Demonstration of the effect of a slack tethering technique and range of motion prediction using radiographic measurements.

3. **Provide an engineering perspective on the art of tethering for prophylactic treatment of PJK.** In my view, the surgeons experience with recognizing, documenting, and treating PJK far exceeds the engineers basic biomechanical understanding and proposed functional treatment methods and devices to address it effectively. The goal of providing engineering perspectives throughout the content presented in this dissertation seeks to:
   a. Highlight the mechanical nature and nuance of PJK to better match it to standard biomechanical principles while keeping clinical requirements and strategies paramount.
   b. To compare and contrast the state of clinical understanding and treatment of PJK to that of the engineer's ability to describe and develop methods or devices to meet clinical needs.

1.5. Chapter 1 References

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2. Chapter 2 - Spinal Tethering Techniques

The primary goal of this chapter is to educate the reader on the history of the use of tethers in spinal surgery and to elucidate the current deficits in clinical and biomechanical understanding of emerging tethering techniques for the treatment of ASPs such as PJK.

2.1. Overview of Tethering Techniques in Spine Surgery

2.1.1. Principles of Spinal Tethering

Generally, the goal of the use of tethers in the spine has been to serve as tensile elements which act against the development of curvature in the spine. Commonly this has been for convex curve support in the side-to-side deformity of scoliosis or for posterior support of the spine to fight kyphotic collapse forward due to aging or degeneration caused by fusion. Historically tether materials have been in the form of braided cords or laces and are often used by looping through or around anatomical features such as the lamina, pedicles, transverse process, or ribs and to purpose built devices such as pedicle screws and fusion rods.

2.1.2. Needs In Spinal Tethering

Compared to other surgical techniques or devices used in the spine, tethering has seen limited use in only a few clinical indications. Given this narrow vein of use, research into the biomechanical aspects of tethering and development of tether-based devices has been minimal. Clinical guidance has been driven primarily by limited size case studies and retrospective reviews which has resulted in a largely cautious approach toward tethering being established as a reliable or appropriate technique. With the maturation of spinal arthrodesis techniques and the emergence of motion-sparing implants, new light is being cast on tethering as a potential tool offering unique and novel advantages. The goal of this chapter is to provide a broad review of tethering in the spine both as a technique and as a collection of devices to in order to identify current clinical and engineering needs. Follow-up commentary will discuss possible disconnects between clinical and engineering understandings related to the use and development of spinal tethering techniques.

2.2. Manuscript: Tethering Techniques in Spinal Surgery for Adjacent Segment Pathology: A Review of Techniques, Implants, and the State of the Art

2.2.1. Document Information

Authors: Damon E. Mar[1], Brant S. Ansley[1], Joshua T. Bunch[1] Douglas C. Burton[1], Terence E. McIff[1]

Institution: [1]Department of Orthopedic Surgery, University of Kansas Medical Center, Kansas City, KS

Disclosures: Damon E. Mar (N), Brant S. Ansley (N), Joshua T. Bunch (N), Douglas C. Burton (Royalties for orthopedic device: DePuy/Synthes Spine, consultation for orthopedic device: DePuy/Synthes Spine, Recipient of research funding or institutional support for orthopedic devices: DePuy/Synthes Spine), Terence E. McIff (N)

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2.2.2. Abstract

Introduction: Tethering techniques are increasingly being used in the surgical treatment of adult spinal deformities (ASD). Currently there is a lack of clinical and biomechanical guidance for their use and development. The purpose of this review was to provide an overview of the types of tethering commonly used, to review the types of tethering devices that have been used or proposed for the spine, and a summary of the current tethering techniques that have been discuss for prophylactic treatment of adjacent segment pathology (ASP) and proximal junctional kyphosis (PJK).

Search Criteria: PubMed searches for: Adjacent segment pathology AND Tether, Proximal junctional kyphosis AND Tether, Dynamic Stabilizer AND Tether, plus online searches for tether-based spinal devices.

Tethering Methods: Among all of the techniques identified, the methods were found to include six standard tethering techniques: pedicle, sublaminar, spinous process, centrum, costotransverse foramen, and rib.

Tethering Devices: A total of twelve devices were included in the tethering device list which were separated into three type categories: independent or non-commercial (two devices), commercial (eight devices), and commercial material (two materials). Common fixation methods included pedicle screws, interspinous spacers, and fusion rod. Most devices followed the 510k predicate device regulatory path.

Tethering For ASP: Ten studies were identified which include either direct investigation or discussion of tethering techniques specifically for ASP. Eight were clinical trials, one was a biomechanical study, and one was a combination of clinical trial and finite element model. A majority of the studies used tethering devices in conjunction with posterior lumbar interbody fusion.

Tethering For PJK: Six studies were identified which either directly investigated or discussed the use of tethers for prophylactic treatment of PJK. Four were reviews which provided clinical commentary on the use of tethering for PJK, one was a finite element model, and one was a technical white paper with a case series.

Summary: Although a wide variety of tethering techniques and devices have been used for a variety of spinal conditions and treatments, there is a lack of consensus on appropriate technique for prophylactic tethering of ASP and PJK. There is currently no definitive basis upon which to establish standard technique and indication. Basic biomechanical characterizations are needed for initial guidance.

2.2.3.Manuscript

Introduction:

Background on ASD: In 2005, Schwab et al. reported a drastic increase in the top end of the perceived incidence of adult spinal deformity (ASD) from the previously established range of 1.4% to 32% to a staggering 68% at an average age of 70.5 years [1]. What followed that report became the beginning of the development and understanding of the modern view of ASD and a rush of novel methods to better define, classify, and treat it. Advancements have been made across nearly all fronts of the condition: improved radiographic understanding, refined surgical techniques, and better understanding of disability and patient reported metrics. The attention of ASD treatment strategies has consistently been gaining attention in recent years [2-4]. ASDs covers a wide variety of conditions which includes malalignments in the anatomical planes such as scoliosis, kyphosis, and lordosis in addition to axial rotations [5]. Many deformities are commonly found with the presence of additional degenerative comorbidities such as degenerative disc disease, spondylitis, osteoporosis, and weakened ligamentous structures or musculature [6]. Complications rates associated with ASD corrective surgery have been reported from 13% to 71% depending on a variety of risks factors [4, 7-9]. Revision rates following primary ASD correction are 9% with a mean time of four years following the primary correction [10].

ASD Treatment Costs: The cost effectiveness of ASD surgery is well established against World Health Organization (WHO) standards [11]. McCarthy et al. suggested that ASD corrective surgery is easily justified over a 10 year follow-up, as they calculated the total ASD corrective surgery cost at $80,000 per case which is $60,000 below the 140,000 threshold of responsible health care described by WHO [11]. Even when primary surgical treatment is justified, costs associated with revisions have been shown to be on the order of the primary procedure itself and can lead to substantial economic burdens [12].

Background on Spinal Arthrodesis for ASD: Spinal arthrodesis is the standard of care for ASD patients who have failed nonoperative measures. Current spinal arthrodesis techniques commonly include segmental spinal instrumentation utilizing anchors such as hooks and pedicle screws with rods spanning the treated levels. Alignment correction is achieved through vertebral osteotomies such as Ponte/Smith-Petersen osteotomies, pedicle subtraction osteotomies, and vertebral column resections as well as deformity correction maneuvers facilitated by current spinal instrumentation systems.

Background on ASP: While fusion provides segmental realignment, improved global sagittal and coronal balance, and stabilization, it often has adverse effects on adjacent mobile levels. These effects are rooted primarily in the abrupt change in spinal biomechanics that occur between the uppermost instrumented vertebrae (UIV) and the levels above it [13, 14]. In order for a patient to achieve comparable preoperative range-of-motion (ROM), mobile levels superjacent to the UIV must see increases in individual level motion which in turn results in increases in intervertebral disc (IVD) pressures and vertebral body loading. Often these increases may go beyond what a single level can withstand structurally leading to failures which in turn cause loss of stability and alignment.

ASP Terminology: As advances were made in the understanding of the underlying risks and pathological mechanisms of adjacent level effects, a new vocabulary was needed to convey and describe them. Several attempts were made to classify, define, and differentiate various aspects of adjacent level pathologies. In a 2008 review, Harrop et al. defined adjacent segment degeneration (ASDeg) and adjacent segment disease (ASDis) to differentiate the instances of ASD with clinical symptoms (ASDis) from those that are simply radiographic phenomena (ASDeg) [15]. Lawrence et al introduced the term adjacent segment pathology (ASP) in 2012 as the umbrella term for clinical or radiographic changes that occur at levels adjacent to fusions [16]. In similar fashion to the review by Harrop et al., Lawrence included the definitions of clinical adjacent segment pathology (CASP) and radiological adjacent segment pathology (RASP) to differentiate ASP with clinical symptoms from purely radiographic ASP. Proximal junctional kyphosis (PJK) is a common ASP among ASD with reported incidence rates of 13% to 55% [17-20]. The most widely accepted definition for PJK was proposed by Glattes et al. in 2005 which defines it as a kyphotic angle of greater than 10 degrees between the inferior endplate of the UIV and the superior endplate of the vertebra two levels about it (UIV+2) and a change of more than 10 degrees of the same angle compared to the preoperative angle [20]. Similar to the differentiations of ASD and ASP, PJK has been found to exist as either symptomatic or just as a purely radiographic finding [20, 21]. Proximal junctional failure (PJF) has been recognized as one of the more severe forms often requiring revision surgery and increased likelihood for other comorbidities. Unlike PJK however, a concise definition has yet to be determined, and a variety of definitions and classifications have been proposed [17, 22, 23]. Generally, PJF is referred to as occurrence of PJK with the presence of a structural failure contributing to the kyphotic angulation. Commonly reported structural failures include vertebral body fracture at UIV or UIV+1, posterior ligamentous complex (PLC) failure, and implant pullout or failure.

Treatment Strategies for ASP: While a variety of treatment strategies for ASP have been described and summarized [2, 24, 25], there has yet to be found a definitive technique which consistently and reliably prevents ASPs such as PJK and PJF. The most common prophylactic treatment methods can be grouped roughly into two groups: vertebral body augmentation techniques and motion-sparing devices. Treatments for vertebral body augmentation focus on reinforcement of the vertebral body which primarily includes vertebroplasty and kyphoplasty. Motion sparing devices, often referred to as "dynamic stabilizers," consist of a variety of implants whose function is to provide increased stability while preserving some degree of baseline motion or load transfer. Examples of motion sparing devices include total disc replacements, flexible rod segments, and other elastic materials such as suture or tethers. Among all of the prophylactic methods, vertebral augmentation techniques appear to be the most widely investigated and tested, particularly for prevention of PJF [26-30]. The acceptance of motion sparing implants for ASP prophylaxis is currently less concise. Biomechanical and clinical evaluations have been limited to only a select few devices [31, 32]. The overwhelming consensus to date is that there is limited evidence to support the claim that the use of motion sparing implants is any better than rigid fixation for preventing ASPs [32-36].

Prophylactic Tethering for PJK: With vertebral augmentation methods showing promise as effective and reliable means to prevent vertebral fractures leading to PJF and subsequently to PJK, the current focus shifts to the gap among available techniques to provide PLC support left by current motion sparring implants. Recently, there has been growing interest in the use of posterior tethering techniques to provide ligamentous support of the PLC, however there is a severe lack of published data of any kind to provide clinical guidance of their use and development. As there is an equal lack of both clinical experience and basic science research backing these techniques, it is important that a framework first be established to help guide characterization and initial evaluation.

Review Goals: Based on the current evidence at hand, the goals of this review were as follows:

a. First to provide a historical overview of the types of tethering techniques that have been used and developed for spinal corrections.
b. Second to provide an overview of tether-based devices that have been proposed, used, and their apparent success for prophylactic treatment of ASP.
c. Third to show the current extent of published work of tethering specifically for prophylactic treatment of ASP and PJK.
d. Identify deficits in understanding and primary needs for prophylactic tethering techniques for PJK.

Review Search Criteria: PubMed searches were made using key words including: adjacent segment pathology, proximal junctional kyphosis, dynamic stabilizer, and spinal tether. Search results were screened for relevance first by title and then by abstract. Qualified articles were then reviewed for the four individual sub-reviews in this article. For the device searches, additional online searches were done.

Tethering Techniques: Tether techniques have been developed and utilized to either partially or solely address a wide array of commonly encountered spinal diagnoses. Table 2.1 summarizes the targeted uses for various tethering techniques. Techniques and their first descriptions were limited to those employing non-metallic, braided tether materials.

Table 2.1: Summary of tethering techniques used in spine surgery historically.

	Technique	First Described Use	Fixation	Stated Goal
1	Pedicle-Based Tethering	Graf 1992	Tether spanning single or multiple levels with anchoring to pedicle screws.	Retrolisthesis, PLC support.
2	Sublaminar Tethering	Gallie 1939 (wire), Gaines 1979 (polyethylene)	Tether passed through sublaminar space and anchored to a rigid construct such as a pedicle screw or rod.	Retrolisthesis, PLC support.
3	Spinous Process Tethering	Ailon 2015[6]	Tether looped either through or around spinous process of single or multiple levels. Done either with or without anchoring to various instrumentation.	PLC support.
4	Centrum Tethering	Crawford 2010 (human)[37]	Tether spanning single or multiple levels with anchoring to lateral centrum screws.	Lateral realignment and stabilization for scoliosis.
5	Costotransverse Foramen Tethering	Sun 2017 (animal)[38]	Tether passed through costotransverse foramen of multiple levels and anchored to screws at cranial and caudal-most levels.	Lateral realignment and stabilization for scoliosis.
6	Rib Tethering	Braun 2003 (animal)[39]	Tether passed through, looped around, or anchored via screws or hooks across multiple levels of ribs.	Lateral realignment and stabilization for scoliosis.

PLC=Posterior Ligament Complex

A set of six independent tethering methods were identified in the literature. A majority of the techniques (four out of six) involve a posterior approach for tethering. The earliest mention of spinal tethering was reported by Gaines et al. in 1979; however, Gallie et al. first reported on a similar technique in 1939 with the use of a solid metal wire. The rate of introduction of new tethering techniques was relatively low until the mid-2000s. The techniques can be divided equally into two general categories: 1) treatments focusing on retrolisthesis and PLC support, and 2) realignment and stabilization for scoliosis.

Tether-Based Devices: Table 2.2 provides a summary of devices identified in this review that include the use of a tether component for use in spinal surgery.

Table 2.2: Overview of tether-based spinal devices.

Device Type		Device/Company	Site/Fixation Method	Region	Function	Indication/Use	Regulation
Independent / Non-Commercial Device	1	Graf Ligament / Non-Commercial	Pedicle Screw	TL	Limit flexion, allow multi-directional mobility	Degenerative spondylolisthesis, disc herniation, spinal stenosis, degenerative scoliosis.	Patented in 1992
	2	Natural Neutral Concept / Showa Co Ltd	Pedicle Screw	L	Limit flexion, allow multi-directional mobility	Adjunct to lumbar fusion.	First disclosure of use in 1999
Commercial Device	1	Dynesys & Dynesys DTO / Zimmer	Pedicle/Centrum Screw	TL, L, S	Limit flexion and extension independently	Adjunct to Fusion for acute spondylolisthesis with objective evidence of impairment, pseudoarthrosis, adjunct to fusion.	FDA approval in 2002, DTO FDA 510k in 2014
	2	Wallis / Abbot Spine (Gen. 1), Zimmer (Gen. 2)	Interspinous Spacer	TL, L	Limit flexion and extension independently	Discectomy stabilization, DDD, adjacent to fusion.	CE mark in 1986
	3	Viking / Oxford Performance Materials	Interspinous Spacer	TL	Limit flexion and extension independently	DDD, spinal stenosis, spondylolisthesis	NA
	4	Diam / Medtronic	Interspinous Spacer	TL	Limit flexion and extension independently	Adjacent to lumbar DDD.	FDA IDE trial in 2006, FDA recommends against PMA, suggests new PAS in 2016
	5	Universal Clamp / Abbot Spine & Zimmer	Fusion Rod, Laminar Cerclage	TL	Anchor for immobilization, adjunct to fusion	Trauma, reconstruction, adjunct to fusion.	FDA 510k in 2008
	6	Jazz & Jazz Lock / Implanet	Fusion Rod, Laminar Cerclage	C, TL	Anchor for immobilization, adjunct to fusion	DDD, spondylolisthesis, trauma, stenosis, deformity, pseudoarthrosis, tumor, adjunct to fusion.	FDA 510k in 2016
	7	LigaPASS, PASS LP / Medicrea	Fusion Rod, Laminar Cerclage	T, TL, L	Anchor for immobilization, adjunct to fusion	Idiopathic scoliosis	FDA 510k in 2016
	8	Transition / Globus Medical	Pedicle Screw	TL, L	Anchor for immobilization, adjunct to fusion	In conjunction with fusion	FDA 510k in 2009
Commercial Material	1	Mersilene Suture / Ethicon	Lamina, Transverse Process, Spinous Process Cerclage	C, T, TL, L	Anchor for immobilization, adjunct to fusion	Not indicated for spine	First introduced in 1979
	2	Dyneema Purity Polyethylene / DSM	Lamina, Transverse Process, Spinous Process Cerclage	C, T, TL, L	Anchor for immobilization, adjunct to fusion	Not indicated for spine	FDA 510k in 2015

C=Cervical, T=Thoracic, TL=Thoracolumbar, L=Lumbar
DDD=Degenerative Disc Disease
FDA=Food and Drug Administration, IDE=Investigatory Device Exemption, PMA=Pre-Market Approval, PAS=Post-Approval Study

A majority of the devices are designed to work off of or in conjunction with existing pedicle screw and rod-based fusion systems. Another large subset of the devices function as interspinous spacers with the tether acting as a flexion limiter. The range of years of introduction are from 1986 (Wallis) up to the present. Regulatory paths for clearance of use are predominantly 510k. The most commonly referred to material in clinical reviews of spinal tethering, Ethicon Mersilene suture (Ethicon, Somerville, NJ, USA), is not currently indicated for use in the spine.

Tethering Specifically for ASP and PJK: The use of prophylactic tethering for ASP has been a relatively recent advancement among spinal tethering methods. This has been driven largely by the great interest and attention surrounding PJK and the attempts to prophylactically treat it.

Tethering for ASP: A total of 10 articles were identified which mention the use of prophylactic tethering techniques specifically for ASP. Table 2.3 provides an overview of these studies.

Table 2.3: Overview of studies which investigate or discuss prophylactic tethering techniques specifically for adjacent segment pathology.

	Author / Year	Technique / Device	Study Type / Size	Mean Follow-Up	Primary Outcomes / Results
1	Tachibana / 2017[40]	Sublaminar Tethering	Clinical trial / 76 patients	NA	• L4/L5 PLIF vs. L4/L5 PLIF + Tether • L4/L5 PLIF + Tether: Decreased RASP, no significant decrease in CASP
2	Lu / 2015[41]	Interspinous/ Diam	Clinical trial / 91 patients	41mo	• PLIF only: RASP in 20/42, CASP in 9/20, three revision surgeries • PLIF + Diam: RASP in 3/49, CASP 3/3, one revision surgery
3	Zhu / 2015[42]	Interspinous/ Wallis	Clinical review / 45 patients, + FE model	24mo	• No significant efficacy or safety differences in PLIF only vs. PLIF + Wallis • PLIF only: Increased flexion-extension ROM • PLIF + Wallis: Reduced extension ROM • FE results: altered adjacent level stress conduction during flexion-extension bending, reduced IVD pressures and facet forces
4	Lee / 2013[43]	Interspinous / Diam	Clinical trial / 75 patients	24mo	• PLIF only vs. PLIF + DIAM: No significant difference in clinical outcomes • PLIF only: CASP in 24/50, PJK in 3/50 • PLIF + DIAM: CASP in 6/24, no PJK
5	Cabello / 2013[44]	Pedicle / Dynesys	Biomechanical / 6 spines	NA	• Fusion: fusion segment decreased disc pressure 65%, increased adjacent segment (+1) disc pressure 20%, no increase in superjacent (+2) disc pressure • Fusion + Dynesys: fusion segment decreased disc pressure 65%, decreased adjacent segment (+1) disc pressure 50%, increased superjacent (+2) disc pressure 10%
6	Liu / 2012[45]	Interspinous Device	Clinical trial / 67 patients	24mo	• PLIF only: No significant change in adjacent segment disc height, increased adjacent segment flexion-extension ROM • PLIF + Interspinous Device: No significant change in adjacent segment disc height, no significant change in flexion ROM, significant decrease in extension ROM
7	Putzier / 2010[46]	Pedicle / Dynesys	Clinical trial / 60 patients	76mo	• No significant difference in clinical outcomes between SLF and SLF + Dynesys • SLF Only: Progressive ASP in 6/30 • SLF + Dynesys: Progressive ASP in 1/30 • Authors Recommend against Dynesys in asymptomatic ASP because of complication rate
8	Ogawa / 2009[47]	Sublaminar Tethering	Clinical trial / 54 patients	40mo	• Fusion only: Two subsequent surgeries (disc herniation), significant lumbar lordosis decrease, two compression fractures • Fusion + Sublaminar Tether: Decreased adjacent segment ROM and no subsequent surgeries in tethered group, 4/27 developed retrolisthesis, no lumbar lordosis change, no compression fractures
9	Imagama / 2009[48]	Pedicle / Natural Neutral Concept	Clinical trial / 70 patients	24mo	• PLIF only: RASP in 18/35, stenosis in 17/35 • PLIF + NNC: RASP in 4/35, stenosis in 6/35
10	Korovessis / 2009[49]	Interspinous / Wallis	Clinical trial / 50 patients	60mo	• PLIF only: RASP in 6/21, CASP with revision surgery in 3/21 • PLIF + Wallis: RASP in 1/24, no CASP

FE=Finite Element, PLIF=Posterior Lumbar Interbody Fusion, ASP=Adjacent Segment Pathology, CASP=Clinical Adjacent Segment Pathology, RASP=Radiographic Adjacent Segment Pathology, ROM=Range of Motion, IVD=Intervertebral Disc, SLF=Single Level Fusion

Among the ten studies reviewed for tethering of ASP a majority utilize pedicle based anchoring methods. The most common indications are for the use of a device to be done in conjunction with posterior lumbar interbody fusion (PLIF) techniques. The most frequently used loop points include the spinous process, lamina, or purpose-built implants. Korovessis et al. were the first to publish findings on the prophylactic treatment of ASP utilizing tethers in 2009 [49]. Since that point the rate of additional studies has consistently been on the rise to date. Cabello et al. and Zhu et al. are the only groups to report biomechanical data on tethering techniques for ASP [42, 44].

Tethering for PJK: The search for prophylactic tethering techniques specifically for PJK produced six results, all of which were considered relevant to this search and were included for review. Table 2.4 provides an overview of the studies identified which include specific mentions of tethering for prophylactic treatment of PJK.

Table 2.4: Overview of studies which investigate or discuss prophylactic tethering techniques specifically for proximal junctional kyphosis.

	Author / Year	Technique	Study Type	Key Findings / PJK Commentary
1	Safaee M. / 2017[24]	Spinous Process Tethering	Clinical Commentary	• Discussion of ligamentous augmentation technique. • SP tethering with anchoring to fusion rod implants. • Video technique guide.
2	Smith J. / 2017[2]	Spinous Process Tethering	Clinical Commentary	• Discussion of SP tethering for prophylactic treatment of PJK. • Figure depicting a looping technique spanning UIV-1, UIV, and UIV+1 with tether anchoring to rods. • Conclusion: Possible effectiveness requiring further study.
3	Nguyen N. / 2016[50]	Spinous Process Tethering	Clinical Commentary	• Description of SP (UIV to UIV+1) and sublaminar tethering (UIV-1, UIV, and UIV+1) anchored to rods. • Conclusion: Possible effectiveness requiring further study.
4	Bess S. / 2016[13]	Pedicle-Screw-Based Tethering	Biomechanical Finite Element Model (FEM)	• FEM used to demonstrate ability to create ROM transition zone across tethered levels superjacent to UIV. • Decreased IVD pressures and increased screw forces • Conclusion: Suggested clinical utility but requires further study
5	Zaghloul K. / 2016[51]	Spinous Process and Pedicle Screw-Based Tethering	Technique White Paper and Case Series	• Description and discussion of tethering materials and multiple techniques. • Case series: 18/18 patients (mean age 63yr) tethered did not develop PJK at mean follow up of 11.9mo. • Conclusion: Possible effectiveness requiring further study.
6	Ailon T. / 2015[6]	Spinous Process Tethering	Clinical Commentary	• Mentioning of spinous process tethering with Mersilene for prevention of PJK. • Conclusion: Possible effectiveness requiring further study.

SP=Spinous Process, UIV=Uppermost Instrumented Vertebra
FEM=Finite Element Model, ROM=Range of Motion
IVD=Intervertebral Disc, PJK=Proximal Junctional Kyphosis

Of the six studies reviewed for this search, four were clinical review-based articles, one was a finite-element biomechanical study, and one was a technical white paper combined with a case series. Ailon et al. were the first to discuss tethering as part of a prophylactic treatment strategy specifically for PJK [6]. All of the studies were published in the last two years. Zaghloul et al. is the only group to report on clinical outcomes of prophylactic tethering for PJK and showed promising outcomes [51]. Bess et al. is the only study to present biomechanical data on the effects of tethering specifically for PJK prophylaxis [13]. Not a single study to date has directly investigated specific tether looping techniques, tether tensioning, comparison of tether materials and relation to posterior ligament complex tissues, or failure mode analysis of any kind related to prophylactic treatment of PJK. All studies consistently suggest additional investigation is required to better understand the efficacy of tethering for prophylactic treatment of PJK.

Discussion of Tethering for ASP and PJK:

Summary of Spinal Tethering: While tethering has seen much less attention in terms of basic biomechanical research and clinical trials compared to fusion techniques, it has seen consistent attention for more specialized cases and situations. Tethers have been applied to every region of the spine and with a variety of anchoring methods and tether materials. Indications include both individualized use at localized levels or as part of larger arthrodesis construct systems. The focus of tethering for prophylactic treatment of ASP has been gaining interest over the last decade and is now at its greatest with a majority of the focus lying on PJK and PJF. The majority of techniques rely on posterior approaches and attachment to posterior elements of either fusion instrumentation or bony structures such as the pedicles or spinous process. In nearly every case, the primary goal is to function as a tensioned support for preventing loss of sagittal plane correction and limiting ROM in flexion. While a majority of the methods or devices developed for spinal tethering have been shown to be biomechanically functional through basic bench science and modeling, there is a general lack of clinical validation to support their efficacy. As with many other motion-sparing implants, the patient cohort who meets indications for use often becomes quite small and represents a rather limited population of patient’s seeking spinal care.

Tethers as a Unique Class of Dynamic Stabilizers: The class of devices and materials that constitute tethering systems appear to represent a unique class of devices within the more-broad category of dynamic stabilizers. Tethering systems in particular show a tendency of being more open-ended in terms of technique and are rarely indicated for more precise/specific conditions that are more common with dynamic stabilizers. There are distinct subgroups of tethering devices as well, particularly with systems that are designed to work in conjunction with modern fusion rods and screws and those that are purely independent such as the use of sutures or other plain tethering materials.

Prophylactic Tethering for PJK: The rise of prophylactic tethering techniques appears to have followed in the footsteps of the advances made in better understanding and defining ASPs like PJK. A large portion of the understanding of tethering techniques to date has been done after the initial recognition and definition of PJK by Glattes et al. in 2005 [20]. Initial reports of tethering methods for PJK prophylaxis show promise as a novel means of supporting ligamentous laxity. In comparison to various motion sparing implants, these new techniques show potential advantages with reduced invasiveness, lest risk for surgical complications, and simplified surgical technique [2, 24].

Prophylactic Technique by Region: Clinical understanding of PJF has begun to identify that different regions of the spine may have different risk factors associated with PJF. In 2013, Hostin et al. reported that PJF due to PLC failure is more likely in the upper thoracic region than in the thoracolumbar region [52]. This hints at the possibility that with time and further characterization of tethering techniques, location and spinal pathology may more effectively guide when a given tethering construct or device is best utilized. A study by Theologis et al. has already provided cost estimates by region and showed that upper thoracic revision following ASD surgery were significantly higher compared to the thoracolumbar region [12]. Future investigations will undoubtedly provide greater insight and understanding into indication and method of prophylactic treatment strategies.

State of Prophylactic Tethering Techniques: While many advancements have been made in understanding and treating PJK, the current evidence at hand indicates that there is still a major lack in ability to control and prevent it. Debate continues over various aspects of PJK prophylaxis including surgical invasiveness, degree of correction, location of the UIV, and the use of specialized implants. Regardless however, there is clearly an immediate need for review of preliminary clinical outcomes and further basic characterization of specific techniques. Characterization should fully consider the technical aspects of the materials or devices used in addition to the biomechanical and physiological functions associated with it. Additionally, there is a need for characterizations to be done in a way to allow for evaluation of individual effects of each tethering parameter that is available to the surgeon for a given method to insure a proper baseline understanding of how they contribute to the overall function. As the understanding of PJK, PJF, and other forms of ASP have been developed and refined over time to more adequately match surgical treatment for at risk patients, a similar pathway should be charted for the development and refinement of prophylactic tethering techniques.

Conclusion: While tethering in the spine has had limited use historically, there has been a consistent cohort within specific ASD patient populations that have benefited from its use. Emerging tethering techniques appear to show promise as a new horizon for corrective spinal techniques which can both stand on their own and supplement and enhance existing methods. There is currently a deficit in the understanding of how these new techniques function biomechanically when used in conjunction with spinal fusion for deformity correction. Action should be taken to both improve the understanding of biomechanical function and to define, classify, and monitor current clinical tethering practices for prospective and retrospective evaluations.

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2.2.4. Commentary

Difficulties in Summarization of Techniques: This was a somewhat difficult review to put together as the jump from all spinal tethers to tethering specifically for ASP or PJK is quite large. Given the relatively recent growth in prophylactic treatments for ASP like PJK, there is currently very little published information on the techniques and a severe lack of initial guidance. While the review of devices was somewhat arbitrary, our goal was to provide a reasonably wide view of the variety of devices that have been proposed, tested, or marketed for use in the spine. There is clearly going to be an influx of many more new devices incorporating tethers as interest grows in their utility for motion-preservation indications. Likely many will follow in the usual 510k regulatory pathway and provide only menial changes or improvements compared to existing products. If the history of dynamic stabilizers as a class of devices teaches us anything, it may be that without a clear framework of basic functional understanding either put forth by the surgeon or a reflected understanding by the engineer, development will be slow, ambiguous, and ultimately the techniques may rarely be indicated.

Lack of Tether References: Related to the difficulty in summarizing the current state of the art of spinal tether is simply the lack of published data on the concept. In particular, the lack of biomechanical studies related to spinal tethering is eye opening. From an engineering perspective, even the most basic aspects of tethering such as tension and loop technique have had essentially no investigations of any kind. This makes a clear argument for undertaking the immediate characterization of these basic aspects in order to respond to the large clinical interest.

2.3. Discussions on the State of the Art of Spinal Tethering

2.3.1. Tethering Techniques

The use of tethers in spinal surgery has clearly been a niche within the full scope of surgical techniques and devices. In particular, there seems to be a clear differentiation of tethering used solely on its own or as an adjunct to fusion. For the former, the most commonly reported techniques appear to focus on transverse process or rib tethering for lateral stabilization of scoliosis in adolescent idiopathic scoliosis (AIS). The clear advantage to this indication is for consideration of growth and major realignment of the spine in a child. The apparent success of these techniques is however limited and for only a narrow band of indications.

2.3.2. Tether-Based Devices

The development of spinal tether devices has largely been done "on the side" of standard fusion devices. While a variety of forms and functions have been proposed, only a select few devices have seen clinical use and review. Among these, the predominant FDA clearance route has been through the 510k pathway. This has resulted in a field of devices that are more similar than different to each other and to the predicate devices (primarily fusion devices) they are based on. Very few radical advancements, if any, have been made in the field of spinal tethers. Personally, I find it interesting that the current attention in posterior tethering for PJK has come primarily from the off-label use of standard orthopedic sutures. While commercial device design is now following close behind with the proliferation of new devices which work directly with existing fusion instrumentation, the fundamental reasoning and understanding of their targeted function appears unclear. Current engineering seems to be focused more on the ability to build upon existing fusion devices which do not directly address the clinical problems surgeons are facing related to PJK. Current tether-based device development is missing the due diligence of fundamental biomechanical characterization to truly address the clinical needs being set forth by spine surgeons and the conditions they are treating.

2.3.3. The Future of Spinal Tethering

It seems clear that as the clinical understanding and further classification of ASP conditions is further refined, there will be a variety of new opportunities for novel indications of new surgical techniques. In my mind, spinal tethers, at least as they are currently envisioned, seem to nicely fit in the historically persistent gap crated by motion sparing implants and traditional fusion instrumentation. Tethering seems a less precise, however more utilitarian, tool in the spine surgeons armamentarium. The wide variety of parameters associated with tethering allow for flexibility in intended use and function, however this leads to confounding any clear effect a particular technique has and in turn makes it difficult for the surgeon to be able to infer the degree of success or failure. With time however, I believe that tethering may become a much more defined and understood technique which will may be better integrated as a common tool in standard spinal fusions. An interesting technique that seems to be missing from current standard surgical spine instruments is the use of tethers as a means of leveraging for reorientation or realignment rather than just as part of the surgical construct.

3. Chapter 3 – Biomechanical Analysis of Spinous Process Tethering Techniques

This section will introduce spinous process-based tethering techniques and provide a detailed investigation of the techniques through a series of four biomechanical studies.

3.1. Introduction to Spinous Process Tethering for PJK

3.1.1. Spinous Process Tethering

The review of tethering techniques from Chapter 2 provided an overview of the wide variety of methods that both have been proposed and used. Among the handful of techniques that have been proposed for ASP and PJK prophylaxis, a majority include the technique of looping the tether through a hole drilled laterally in the spinous process (SP), particularly at the uppermost tethered vertebra (UTV). This technique takes advantage of the girth of strong cortical bone at the intersection between the lamia and the SP, the spinolaminar junction. An important aspect of this junction is that it provides adequate dorsal clearance from the spinal cord and provides anatomical references for dorsal location of the hole. The typical height of the SP at the spinolaminar junction also provides a range of possible points to locate the hole superiorly or inferiorly. Varying this location allows for more or less cortical bone to be used structurally to resist pull-out. Not a single study to date has shown any basic biomechanical data on this technique.

3.1.2. Goal of Biomechanical Characterizations

The primary goal of the work included in this chapter seeks to provide a solid basis for understanding the underlying principles of tethering techniques proposed for prophylactic treatment of PJK. To achieve this aim, a series of biomechanical characterizations of fundamental tethering techniques are presented. The studies will evaluate a variety of parameters, both independently and in combinations. A secondary goal of this chapter is to conduct the basic characterizations in a manner to be equally guided by both biomechanical methodology and clinical applicability and relevance. All of the individual parameters and techniques tested in these studies were chosen based on current clinical practices. Discussions are oriented toward linking biomechanical effects of the parameters to intraoperative considerations as much as possible. Commentary following each manuscript provides a more detailed engineering perspective on the significance of the biomechanical results and their relation to clinical relevance. Section 3.6 provides a master summary and consolidation of the key points identified across all of the studies.

3.2. *Manuscript:* Characterization of Spinous Process Tethering Tension and Pull-Out Forces for Prophylactic Treatment of Proximal Junctional Kyphosis

3.2.1. Document Information

Authors: Damon E. Mar[1], Steven J. Clary[1], Douglas C. Burton[1], Terence E. McIff[1]

Institution: [1]Department of Orthopedic Surgery, University of Kansas Medical Center, Kansas City, KS

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3.2.2. Abstract

Introduction: Proximal junctional kyphosis (PJK) is defined as a kyphotic angle of 10 degrees or more between the inferior endplate of the uppermost instrumented vertebrae (UIV) and the superior endplate of the vertebrae two levels above it (UIV+2). PJK is one of the most common complications of Adult Spinal Deformity (ASD) surgery. The use of tethering techniques to reinforce ligamentous structures above the UIV have begun to gain favor clinically. However, there is no consensus on appropriate tethering techniques and little biomechanical data exists regarding the effects on the tethered levels. The goal of this study was to demonstrate the effect of tether tie-off tension on functional spinal unit (FSU) flexion range-of-motion (ROM), spinous process (SP) strain, and intervertebral disc (IVD) pressure. We hypothesized that higher tie-off tensions would result in greater reductions in ROM, increases in SP strain, and reductions in IVD pressures. A second goal of this study was to provide suture pull-out data and compare the values to maximum SP forces generated during flexion ROM. We hypothesized that SP strain values seen during standard flexion ROM conditions would be significantly below pull-out failure loads.

Methods: Nine T11-T12 cadaver FSUs (mean age 66.1yrs, range 54-85yrs, 5 female, 4 male) were potted in Bondo to allow for mounting onto test fixtures. Each ROM test was comprised of five cycles of +/-5Nm of flexion-extension bending at 0.5deg/sec with a constant 50N axial follower load. Moments were applied with a pure-moment spine testing machine. A motion capture system was used to measure T11 motion kinematics. SP tethering was done by passing a 5mm polyester suture through lateral holes drilled just dorsal of the spinolaminar junction of each SP. A single uniaxial strain gage was applied at the base of each T11 SP adjacent to the tether hole. Two pressure sensors were inserted into the anterior and posterior thirds of each IVD in the mid-sagittal plane. Data analysis was done on the third loading cycle of each test. Baseline ROM tests were performed first without tethering. Tethering was then tested at five different tie-off tensions: 0, 22, 44, 66, and 88N. Tensioning force was measured with a hand-held force gauge. For 0N, the tether was set to the point where no slack was visible and no tension force was registered on the force gage. Once tensioned, the tether loop was clamped in place with a needle driver. After ROM testing, each FSU was dissected into individual vertebrae with all soft tissues removed. Suture pull-out testing was then done on each vertebra by mounting the vertebra in a clamp and then pulling a loop of suture axially out of the SP hole in each level’s anatomical loading direction: inferior for T11 and superior for T12. Pull-Out testing was

done using a hydraulic load frame at a rate of 0.5mm/sec to failure. During the pull-out testing of T11 levels, SP strain data was recorded during the test to calibrate the ROM test SP data. Univariate repeated-measures ANOVAs were used to test for effects of suture tension on ROM, SP strain, and IVD pressures. Paired t-tests were used to compare pull-out forces to maximum SP forces generated during flexion ROM.

Results: With increasing tether tie-off tension, flexion ROM reduced significantly ($p<0.001$), SP force increased significantly ($p=0.04$), and IVD pressures decreased significantly (both $p<0.001$). A significant flexion ROM reduction (8%) was seen even at 0N of tie-off tension ($p=0.03$). The rate of flexion ROM reduction as related to increasing tie-off tension was 0.4%/N or approximately 0.02deg/N. The average maximum SP forces generated during flexion ROM were significantly below the lowest pull-out forces for each specimen ($p=0.01$ for T11 and $p=0.006$ for T12) with an average of 66% below pullout with a range of 77% to 19%. Six pull-out tests resulted in tether failure (four T11 and twoT12) with an average failure force of 100N.

Discussion: The results show that increasing tether tie-off tension reduces flexion ROM, increases SP loading, and reduces IVD pressure. Even minimal tie-off tension produced a significant reduction in flexion ROM. Given the strong correlation between tensioning and flexion ROM reduction, tie-off tension should be considered an integral factor in the overall effect of the technique. Even though SP forces generated during flexion were below the pull-out forces, there should still be concern for SP failure, particularly in the presence of poor bone quality. Additionally, the results indicate that tether failure should be considered a possible failure mode. As with most cadaveric studies, a low sample size is a limitation to this study along with only a single level being tested and at only one loading range. Future studies are planned to further optimize this technique including attention to hole-placement, effects of cyclic loading, and more physiological failure modes. Findings from the present study may have implications beyond just SP-specific techniques to any tethering technique that allows for control over tie-off tension.

Significance: SP tethering with any amount of tie-off tension will reduce flexion ROM and IVD pressure at the cost of increased SP loading. This study is the first of its kind to relate flexion ROM loading values to tether pull-out forces. Maximum SP forces generated during the flexion ROM range tested were significantly less than SP pull-out forces. Tether tie-off tension is likely an integral factor in the effectiveness of a prophylactic tethering strategy for PJK and should be monitored clinically.

3.2.3. Manuscript

Introduction:

Adult Spinal Deformity: Incidence of adult spinal deformity (ASD) has been reported to be 2% to 32% among adults and as high as 68% among the elderly [1]. Surgical treatment strategies often include multilevel fusions which may span multiple regions of the spine including to the sacrum. The impact of these large fusions often has a drastic impact on overall spine biomechanics, particularly at the levels superjacent to the uppermost instrumented vertebra (UIV).

Adjacent Segment Pathology & Proximal Junctional Kyphosis: Adjacent segment pathology (ASP), is the umbrella term used to describe the adverse effects of fusion on adjacent levels [2]. The risk of developing ASP after primary surgical treatment of ASD is reported to be 0.6% to 3.9% and is greatest for individuals over the age of 60 [2]. Proximal junctional kyphosis (PJK) is one of the most common forms of ASP with an incidence of 13% to 53% [3-6]. Despite identification of risk factors and attempts to mediate PJK, it remains a challenge to prevent and manage [5, 7-11]. Prophylactic vertebroplasty has been shown to be effective in reinforcing vertebral body strength to avoid proximal junctional failure (PJF), one of the most common causes of PJK [7, 12-14], there is however still a need to provide support for posterior ligamentous laxity. Preservation and reinforcement of the posterior ligament complex (PLC) has been shown to be a critical factor in segmental stability and may play an important role in prevention of PJK [12, 15-17].

Spinal Tethering: Tethering techniques at the levels superjacent to the UIV have been gaining clinical interest recently for prophylactic treatment of PJK [12, 15, 18-21]. The primary goal of posterior tethering is to reduce joint flexion ROM and to more widely distribute load concentrations in the adjacent vertebra and intervertebral discs (IVDs). Bess et al. demonstrated that the use of tethering across multiple levels adjacent to UIV can be used to create a transition zone to alleviate load and motion concentrations that normally occur above UIV [18]. While the discussion highlighted the theoretical benefits, there are still many details regarding tethering technique that need to be addressed. There is currently no consensus on appropriate tethering techniques specifically for prophylactic treatment of PJK. Additionally, there has been no characterization of potential failure modes for posterior tethering.

Among the most basic factors of any tethering technique is the amount of tension put into the tether at the time of tying off the tether loop. There have been few studies that have investigated any form of tether tensioning to date [22, 23], and none that have addressed the relation of varied tension to dynamic segmental biomechanics and relation to failure modes.

Goals and Hypotheses: The primary goal of this study was to demonstrate the effect of tether tension on flexion range-of-motion (ROM), spinous process (SP) force, and intervertebral disc (IVD) pressure using an in-vitro cadaveric functional spinal unit (FSU) model using a SP tethering technique. We hypothesized that higher tether tensions would result in greater reductions in flexion ROM, increases in SP force, and reductions in IVD pressure. The second goal of this study was to provide tether pull-out failure data and to compare them to tether forces generated during maximum flexion ROM. We hypothesized that tether pull-out forces would be significantly greater than maximum forces generated during peak flexion ROM.

Methods:

Specimen Preparation: Nine fresh-frozen cadaveric spines were included in this study: five female and four male with a mean age of 66.1yrs and a range 54yrs to 85yrs. A ll spines were inspected fluoroscopically for arthritis and other bony defects which might affect ROM. Qualified spines were scanned using DEXA to determine L1-L4 T-scores and individual level BMD values. T11-T12 functional spinal units (FSUs) were dissected out of each spine. Care was taken to preserve as much soft tissues as possible including the PLC.

A 5mm braided polyester suture was used for tethering (Ethicon, Somerville, NJ, USA). For tether looping, a 2.5mm hole was drilled laterally through the base of each SP just dorsal of the spinolaminar junction. The holes were located at approximately one third in from the superior and inferior edges of the SP bases for T11 and T12 respectively. A uniaxial strain gage (Omega Engineering, Stamford, CT, USA) was applied anteriorly adjacent to the SP hole on each T11 SP. The superior endplate of T11 and the inferior endplate of T12 were cleared of all soft tissues and potted in Bondo (3M, Maplewood, MN, USA) for attachment to loading fixtures. The potting depth line for each vertebra was set so that only the facets were embedded and not the SP in order to not artificially increase baseline SP rigidity. Specimens were covered in saline-soaked gauze and stored at -20°C when not in use and thawed at room temperature for 24hrs prior to testing. Before testing, two custom-made pressure sensors (Precision Measurement Company, Ann Arbor, MI, USA) were inserted into the anterior and posterior thirds of the IVD at the mid-sagittal plane. Figure 3.2.1 shows an example model of a prepared FSU specimen for ROM testing.

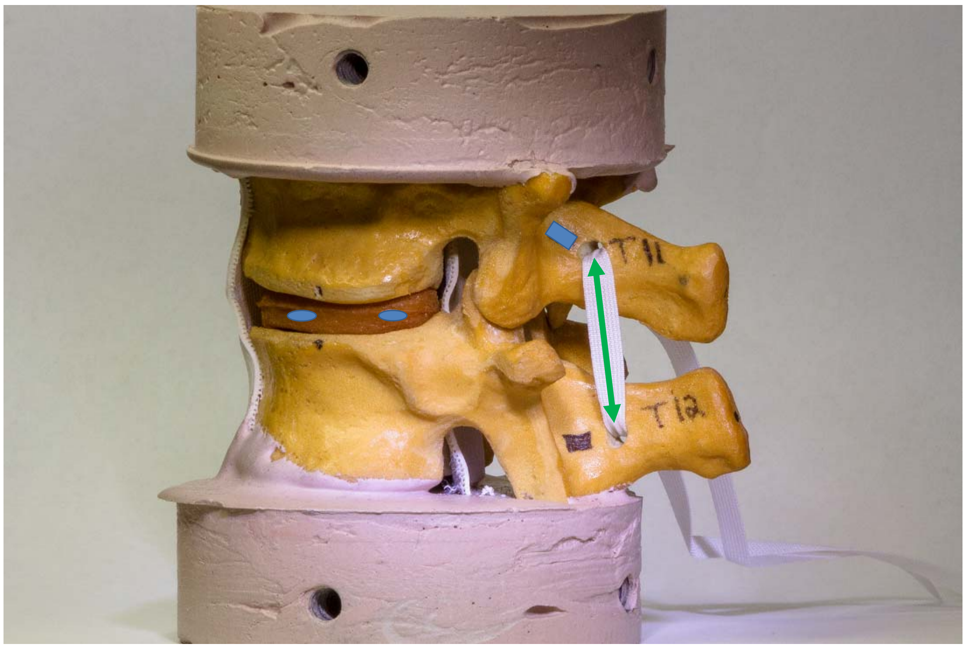

Figure 3.2.1: Example model showing a prepared T11-T12 functional spinal unit for range-of-motion testing indicating hole and tether location (green arrow), strain gage placement (blue box), and pressure sensor locations within the intervertebral disc (blue ovals).

ROM Testing: Loading was done using a pure-moment mechanical testing machine (Applied Test Systems, Butler, PA, USA). Each test consisted of five cycles of +/-5Nm of flexion-extension bending applied to the potting of T11 at a rate of 0.5deg/sec in angular control with a constant 50N axial compressive load applied. An Optorak Certus motion-capture system (Northern Digital, Waterloo, Ontario, CAN) was used to record motion kinematics of T11. Two preconditioning tests were done prior to ROM testing. ROM testing included an initial baseline test without tethering followed by five tethered tests with the tether looped through the SP holes set at the following tensions: 22N (5lbf), 44N (10lbf), 66N (15lbf), 88N (20lbf), and a test with the tension set approximately at zero which is referred to as the minimum or "0" tension. The order of the tension tests were randomized across specimens. Tether tensioning was done using a hand-held force gauge (Mark-10, Copiague, NY, USA). The tension was set by clamping the tether loop at the target tension using a needle driver as shown in Figure 3.2.2.

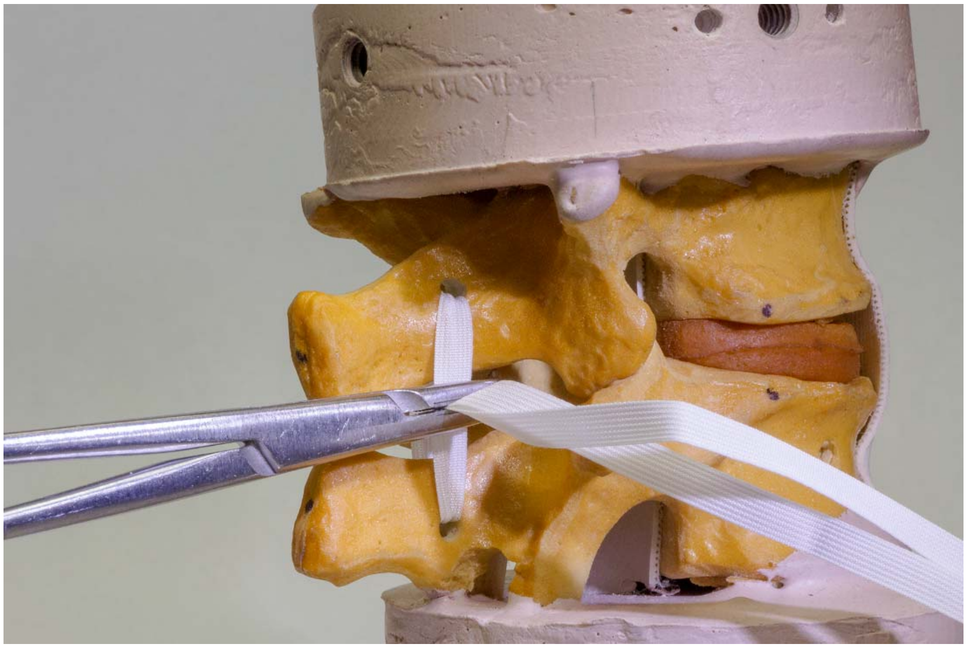

Figure 3.2.2: Example picture showing spinous process tethering with clamp placement for tensioning.

For each ROM test, the initial values of the FSU angle, SP force, and IVD pressures were recorded to determine if there were any neutral (unloaded) position offsets relative to the baseline values cause by the tensioning of the tether. Data analysis of the loaded state was done on the third loading cycle of each test and only for the flexion portion of the loading cycle. Data was acquired using Labview hardware and software (National Instruments, Austin, TX, USA) and analyzed using Matlab (The MathWorks, Natick, MA, USA) and Excel (Microsoft, Redmond, WA, USA).

Univariate ANOVAs were used to test for effects of tension on flexion ROM reduction, SP force, and IVD pressures. All statistical analysis was done using IBM SPSS software (IBM, Armonk, NY, USA).

Tether Pull-Out Testing: After ROM testing, each FSU was dissected into individual vertebrae devoid of all soft tissue including the IVD. Tether pull-out testing was done with a MTS 858 MiniBionix II hydraulic load frame

(MTS, Eden Prairie, MN, USA). Each vertebra was loaded into a fixture which axially constrained the exposed endplate of each potted vertebra. A tether was then looped through the SP hole and pulled to failure at a displacement rate of 0.5mm/sec in the anatomical loading direction of each vertebra: inferior for T11 and inferior for T12. An example of a pull-out test is shown in Figure 3.2.3.

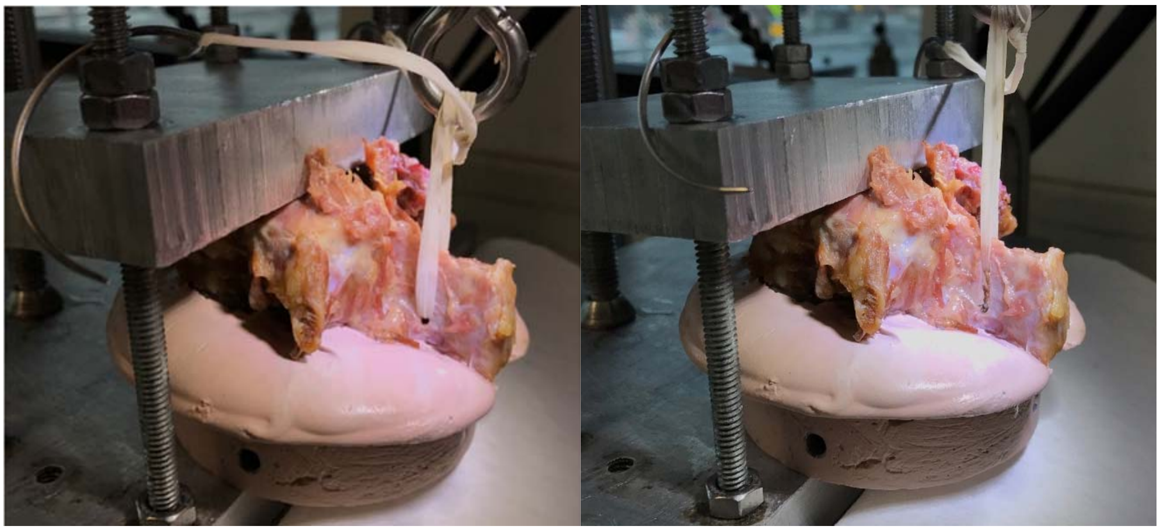

Figure 3.2.3: Example of a specimen before (left) and after (right) tether pull-out testing. This specimen exhibited failure of the spinous process bone rather than tether failure.

Failure was determined using a peak detection method by identifying the first peak followed by a 10% drop in tensile force. Additionally, the mode of failure was divided into two categories: SP bone failure or tether failure. SP strain was recorded during T11 pull-out failure testing and calibrated to tether tension force (and therefore SP force) after testing. Data was analyzed using another Matlab program and Excel.

Paired t-tests were used to compare failure averages by level and failure averages to calibrated maximum flexion forces generated during ROM testing. Pearson correlations were calculated to determine any relationship between failure load and bone quality (level BMD).

Results: Demographics for all specimens included in the study are shown in Table 3.2.1.

Table 3.2.1: Specimen demographics for cadaveric T11-T12 functional spinal units.

Specimen	Gender	Age (years)	L1-L4 T-Score	BMD (g/cm^3)	
				T11	T12
1	F	59	1.104	0.955	0.870
2	M	85	1.217	1.126	1.088
3	M	54	1.003	0.826	0.738
4	F	66	1.111	0.921	0.953
5	F	58	1.150	0.967	0.885
6	F	66	1.280	1.232	1.091
7	M	70	1.442	1.230	1.070
8	M	72	0.963*	1.211	0.898
9	F	65	0.988*	0.640	0.721
	Average	66.1	1.140	1.012	0.924
	Range	54-85	0.963-1.442	0.640-1.232	0.721-1.091

* Indicates osteopenia

ROM Testing: Percentage of baseline averages for peak flexion ROM reduction, SP strain change, and IVD pressure changes are shown in Figure 3.2.4.

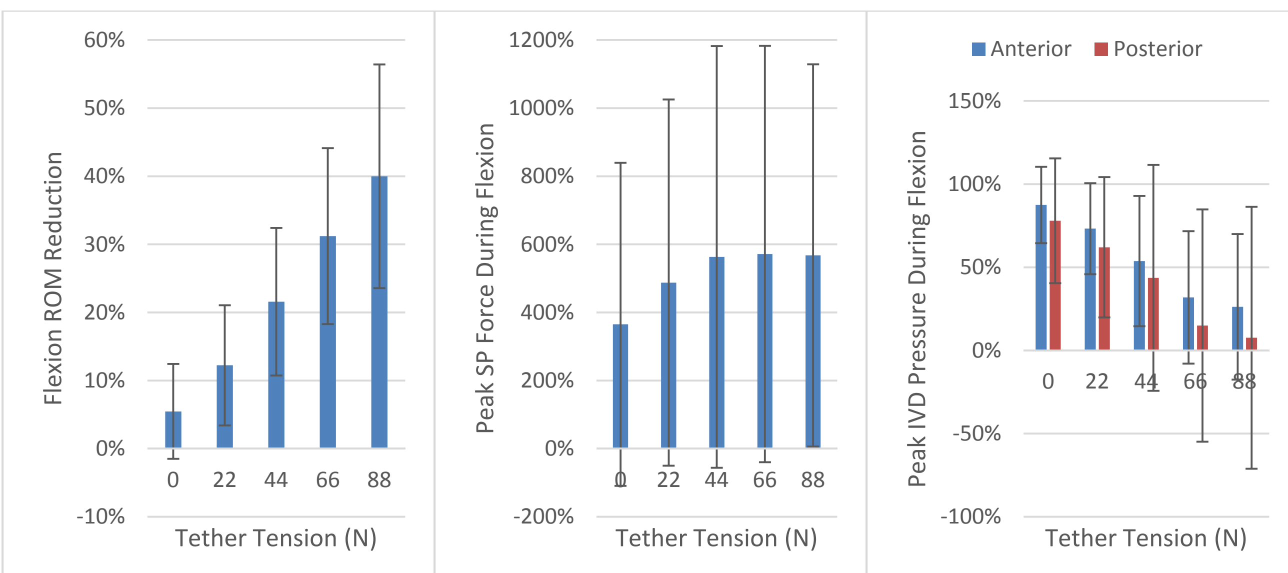

Figure 3.2.4: Percentage of baseline (untethered) peak averages for flexion range-of-motion (ROM) reduction (left), spinous process (SP) strain (middle), and intervertebral disc (IVD) pressures (right) with increasing tether tension. Note that the "0" tension test is still tethered but with just minimal tension set in the neutral (unloaded) position. Error bars indicate +/- one standard deviation.

With increasing tether tension, flexion ROM decreased significantly ($p<0.001$), SP force increased significantly ($p=0.018$, $n=7$), and both IVD pressures decreased significantly (both $p<0.001$). All tether tensions including the minimal tension significantly reduced flexion ROM (all $p<0.05$). The relationship between tether tension and % flexion ROM reduction was highly linear (average of each individual $R^2=0.99$) with an average slope of 8.8% reduction per 22N (5lbf) of tension or 0.4%/N (1.76%/lbf). In terms of FSU angulation, this corresponds to approximately 0.02deg/N (0.1deg/lbf). One specimen exhibited SP bony failure during tensioning at 88N and was excluded from SP force analysis and pull-out testing.

Pull-Out Testing: Tether pull-out test results for each specimen are summarized in Table 3.2.2.

Table 3.2.2: Tether pull-out test results and comparison to flexion range-of-motion (ROM) forces.

	Pull-Out Force (N)		Maximum SP Force Generated During Flexion ROM @5Nm by Tether Tension (N)				
Specimen	T11	T12	0N	22N	44N	66N	88N
1	453.7*	197.3	NA	NA	NA	NA	NA
2	278.9	197.1	18.2	29.5	43.7	58.8	81.9
3	271.5	187.0	81.0	108.4	125.0	142.4	151.0
4	227.8	139.5	8.8	21.1	33.9	40.5	52.9
5	242.7	225.8	56.7	70.9	91.8	105.4	121.7
6	407.0*	224.0	NA	NA	NA	NA	NA
7	417.0*	530.0*	21.7	38.7	52.0	77.5	94.1
8	550.0*	319.0*	38.9	46.9	68.6	74.5	89.9
9	117.0**	207.0	NA	NA	NA	NA	NA
	Average		37.5	52.6	69.2	83.2	98.6
	Std. Dev.		27.2	32.3	34.1	36.1	33.9

*indicates tether failure
**SP bone failure during ROM testing
NA indicates SP force exclusion due to complication or failure

Among the nine vertebrae pairs (18 individual tests), six pull-out tests resulted in tether failure (four T11 and two T12). The average tether failure force was 446.2N (100.3lbf) with a standard deviation of 85.4N (19.2lbf). The average SP pull-out force was 255.2N (57.4lbf) with $n=4$ for T11 and 196.8N (44.2lbf) with $n=7$ for T12. The average maximum SP force generated during flexion (at 88N tension) was significantly below the average of the lowest pull-out force for each specimen ($p=0.045$ for T11 and $p=0.006$ for T12). The average failure margin for peak flexion SP force was 66% below pull-out with a range of 77% to 19%.

Pearson Correlations: BMD was not found to significantly correlate with pull-out force for either level (p=0.698 and p=0.901 for T11 and T12 respectively).

Discussion:

Effect of Tension on Flexion ROM: All tensions including the minimum resulted in a significant reduction in flexion ROM which indicates that the presence of tether tension in the neutral position is not a requirement to achieve a functional effect. Rather, as long as the tether loop length is set such that it engages at some distance within the full baseline flexion, the ROM will still be reduced. This study did not examine an increasing amount of slack beyond the minimum tension, however the results demonstrate that a tether can be used in a way to preserve neutral-zone stiffness and provides a basis for further investigation.

Risk of SP Failure: The primary concern of utilizing higher tensions is the increase in SP loading. The selection of tension becomes a balance of achieving a desired reduction in flexion ROM and related reduction in IVD pressures while incurring increased SP force and risk of failure. Unloading of the IVD provides potential benefits not only for disc pressure but also the adjoining vertebral endplates. By shifting more load transfer through the SP and facets, the risk of vertebral wedge fracture leading to PJF and subsequently PJK could theoretically be reduced.

Tether Pull-Out and Relation to Tension: Maximum SP forces generated during flexion ROM were less than pull-out failure forces for both levels which suggests that there can be a degree of headroom possible for increased SP loading in order to achieve ROM reduction. The amount of headroom is however dependent on bone strength, integrity of supporting ligaments, and actual in-vivo load magnitudes. While the average headroom was 66% below the lowest pull-out force, the high end of the range was only 19%. This suggests that there is likely an elevated risk for failure with consideration of true in-vivo loads and that a factor of safety may be necessary when determining an appropriate tension. One specimen did exhibit SP cortical bone failure during ROM loading at the highest tether tension. The specimen coincidentally had the lowest BMD value and was considered the most-likely to fail. Clearly bone quality of is one of the upmost concerns for an SP-based tethering technique. Ideal preoperative planning would include consideration of lumbar T-Score or individual level BMD to help guide tensioning. Site preparation should include careful placement and creation of the hole in order to provide the strongest possible support for the tether and to avoid unnecessary damage to the cortical bone. While significant correlations were not found between BMD and SP failure force, we believe that it is still a critical indicator and that the lack of significance is likely due to a low sample size and confounding effects such as SP bone geometry which was not measured.

Risk of Tether Failure: The Mersilene failure values from this study are in agreement with previously reported values by Harrell et al. 2003 of 461N (104lbf) [24]. It is important to note that in this study, tether failure mechanisms may have included stress concentrations caused by sharp edges in the SP cortical bone created during drilling. Care was taken to keep the suture flat and even as possible while setting the suture knots during pull-out testing however no control was used during SP hole drilling to account for edge sharpness. Both modes of stress concentrations should be considered potential contributors to failure of any similar tethering technique that passes through drilled bone.

Variability in Tension: Given the significance tension has on flexion ROM, it is clear that variability in one's ability to accurately set a tension will translate to a variability in the resulting reduction. The accuracy of tensioning done within this study was approximately within 5N which equates roughly to a 2% variance in flexion ROM reduction. The ability of a surgeon to accurately set a desired tension intraoperatively relies on their own abilities and the tools available. Purpose-Built devices designed for tether tensioning would provide the ideal mechanism for reliably and accurately setting tension. It may be reasonable however for surgeons to be able to determine an approximation of their own variability in tensioning. We feel that efforts should be made to standardize, if not directly monitor and control, tensioning of tethers intraoperatively to serve as a quantifiable or categorical record as part of the complete treatment course.

PJK Prophylaxis: Tethering done in conjunction with prophylactic vertebral augmentation provides a robust basis for reduction of risks for developing PJK. Vertebral augmentation provides support for increases in load transfer between the IVDs and adjoining endplates however without the addition of posterior support, increased loading of the PLC may result. The addition of the tether addresses this issue and can take advantage of mechanical leverage depending on the hole-placement dorsally. There is of course a limit to how much leverage can or should be utilized. Tether tension plays a part in this as do other factors like hole-placement and SP bone morphology. Assuming the combined prophylaxis is successful, the remaining biomechanical concerns shift to disc health, the abruptness of the transition from arthrodesis to untreated levels, and the healing processes. Bess et al. demonstrated the functional ability of a tethering technique to create a tapered transition zone above the UIV to reduce motion and load concentrations [18].

Healing Characteristics & Long Term Stability: The healing characteristics of the SP and PLC with the tether are not currently known. If there is fibrous tissue ingrown, the long-term tension in the tether may go up. Alternatively, if soft tissue interaction with the suture is minimal and if there is SP bone compaction due to cyclic loading, the long-term tension may actually be below what is set intraoperatively. All of these factors may contribute to possible failure mechanisms and future clinical studies are needed to monitor tethering success and failure rates.

PLC Augmentation: The importance of the contribution of the PLC to segmental stability has been well documented [13, 16, 17, 25]. Many studies have demonstrated and discussed the benefits of minimum disruption of posterior ligaments and musculature [4, 6, 7, 9, 11, 26, 27]. There have been recent reports however, which suggest that pedicle screw-based minimally invasive techniques may not solely reduce the incidence of ASP [28]. There may be potential benefits to using a technique such as SP tethering which preserves the pedicles at the adjacent levels.

Cadaveric Study Limitations: Primary limitations of this study include a limited sample size, only single motion level was tested, and only a single mode of loading was evaluated. Additionally, only one technique of SP tethering was used. Tether looping at the lowest level can be done a variety of ways in addition to looping through a hole, such as under the SP or around implants including pedicle screws, rods, or rod cross-links. Further investigation is needed to evaluate mode and magnitude of failure for these alternate techniques.

Facet Force: Facet force was not measure during ROM testing due to concerns of compromising the facet capsules and adjacent tissues for force sensor insertion. Papp et al demonstrated the tether tension required to lock the facet joints in lumbar FSU motion segments with a pedicle based tethering system [23]. Their results suggested that facet locking resists further angular flexion. There may be a potential benefit to using higher tether tensions to increase facet interaction/load transfer and thereby improve resistance to extreme flexion. The health and stability of the facet joint spaces in addition to the IVD likely are critical factors for the effectiveness of this particular strategy. It is not clear whether this finding will translate to thoracic levels. Future study of tether tension related to facet joint loads and IVD compression capacity are necessary to validate this theory.

Level Failure vs. FSU Failure: The failure testing for this study was isolated to a uniaxial pull-out force for each individual vertebra to provide a comparable loading scheme between specimens. True in-vivo failure would likely manifest as a combination of factors and not necessarily be linked to just a single acute failure. In the present study, we sought to avoid a multifaceted failure mode which would confound our ability to report tether pull-out or tether failure values.

Conclusions: This study has demonstrated the effect of increasing tension on local FSU biomechanics and related tether pull-out forces to SP forces generated at peak flexion. The results indicate that increasing amounts of tension, significantly reduce flexion ROM and that tension should be considered an integral factor of any stabilizing technique that involves a tether. The benefits achieved with this potentially low-cost, pedicle-preserving technique should be considered an effective option for supporting ligamentous laxity which may in turn reduce the risk of developing PJK. While SP forces generated during flexion ROM did not exceed tether pull-out failure forces, use of higher tensions should be done with caution and with consideration of bone quality and integrity. Tether failure should be considered a possible mode of failure, particularly among individuals with healthier bone and higher anticipated physiological loads.

Summary: The results of the present study, while basic in nature, provide a necessary first step towards understanding the relationship of tether tension and segmental biomechanics and provides a framework for more detailed studies of clinically relevant tethering techniques and development of novel tethering instrumentation. Future studies will investigate multi-segment regions of the spine and the effects of cycling loading on long-term stability.

Key Points:

- Any amount of tether tensioning will reduce flexion ROM and IVD pressure at the cost of increased SP loading.
- The relationship between percentage flexion ROM reduction and tether tension for the T11-T12 FSU was found to be approximately 0.4%/N (2%/lbf) or 0.02deg/N (0.1deg/lbf).
- Average tether pull-out values were 255.2N (57.4lbf) and 196.8N (44.2lbf) for T11 and T12. Average maximum SP forces generated during flexion ROM was 66% below pull-out forces for the loading range of 5Nm.
- Tether failure occurred in a third (6/18) of the pullout tests and should be considered a possible failure mode, particularly for individuals with strong, healthy bone.

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3.2.4. Commentary

ICOR Discussion: In the original study design, instantaneous center of rotation (ICOR) was included as one of the main set of dependent variables. The measure was separated into three related values: anterior-posterior translation, superior-inferior translation, and total translation magnitude. Previous studies have described typical ICOR behavior [1-3] as a posterior shift with increasing flexion. With the use of motion sparing devices, a variety of path changes can be seen [1]. In the present study, the hypothesis for ICOR was that a posterior shift in location and a reduction in magnitude relative to untethered behavior would be seen. The statistical results showed no significance which we attribute mostly to low sample size. Consideration of ICOR modification is likely an important aspect of the overall functionality of a tethered level. Local stabilization is highly dependent on ICOR which is essentially a measure of the center of the balance and motion. ICOR is commonly used as a measure for comparison of dynamic stabilizer devices to untreated states. While we were unable to provide meaningful data on shifts in ICOR in this study, future investigations should strive to better characterize the relationships between particular tethering techniques and their related changes in ICOR.

Tensioning Intraoperatively: This study does not address how tether tensioning is achieved nor how it could be controlled in vivo. Several current tether-based devices allow for control of tension either manually (by hand) or via a purpose-built device that provides a tension indicator. In the most basic form, monitoring intraoperative tension may be simply reduced to an attempt to consistently use a certain tension, such as “relatively light” or “relatively high” tension. A slightly more quantifiable method could be to use a simple traction gauge that provides some tension force reading. Ultimately a purpose-built device designed for this application would serve as the most useful and reliable means for setting loop tension.

Relation of Tension to Increased Risk of Failure: Analysis of the relationship between SP force generated during flexion ROM and the applied moment highlighted a dependence of likelihood of failure to tether tension. While it should be obvious that higher tensions should correspond to an increased risk of failure, it is important still to recognize this in the event that tension becomes a measure of degree of support required. As was discussed previously, a balance must be achieved between desired ROM reduction and increased SP loading.

Use of Tethering For Realignment vs. Support: Guidelines for previous tethering techniques and systems stated that they should not be utilized for sagittal realignment however these were mostly based on indication and used primarily in the lumbar region [4]. It is less clear in situations where risk of ASP is extremely high whether emerging tethering techniques should still follow the same guidelines. The results of this study have demonstrated the baseline angulation offset can be achieved at higher tension. There is however a need for further investigation and clinical validation of whether this should be considered appropriate when including other considerations beyond the scope of this study.

Technical Challenges: A challenging aspect of studying tether tension during dynamic loading was how to measure and set the various tensions tested. The use of a needle driver and the hand-held force gage allowed for a fairly simple and repeatable means for setting the loop tensions however it likely differs some from similar tensioning set with a standard surgical knot. During testing, there were two instances of clamp placement affecting SP strain measurement requiring them to be excluded from strain and calibrated force analysis.

Effect of Viscoelastic Creep and Relaxation: Another lesson learned from this study was that viscoelastic relaxation following tether tensioning may be present immediately after setting the tension. This relaxation highlights several questions related to the overall effect of the particular tension used and to long-term stability of the technique. Depending on the time taken to tension the loop, a measureable amount of extension may be induced in the FSU. For this study, we chose to simply set the tension as quickly as reasonably possible and to then start the test as consistently as possible after tensioning. Since dynamic loop tension was not known until after failure testing and SP strain calibration was done, we were unable to see if static loading initially dropped prior to the start of the test. Since the completion of this study, we have developed a new method for measuring loop tension directly and dynamically over the course of the entire test. We hope to use this method to evaluate in-vitro tension relaxation in full human cadavers to provide more insight into this matter.

Effect of Hole-Placement: Another important factor that was considered beyond the scope of this study was hole-location. Placement within each SP and location relative between the two levels can change the loading direction of the tether and in turn, likely changes its effect on the biomechanical measures. Relative to the typical ICOR (or ICOR path), the further dorsal the hole is located, the greater the leverage arm they have and, in turn, the less tension the tether may need to provide adequate support. This would however put more load over a longer dorsal length of the SP. Bone morphology and health of individuals would dictate whether this would be tolerable or not. Future studies are planned to investigate the effect of hole-placement both in terms of functional ROM reduction and on relation to changes in load distribution and failure.

Failure Modes: Finally, the failure mode examined in this study was idealized to provide the simplest loading mode to allow for comparison between levels. Ideally the specimens could have simply been flexed to failure intact, however this would introduce the possibility of a variety of confounding events such as vertebral body fracture, IVD herniation, facet failure, or multiple pull-out failure. While the determination of the initial instance of any individual or combination of these failures could be useful, it would not be definitive for the pull-out forces that we sought to demonstrate in the present study. Such data would be helpful for other considerations of the intact FSU and such tests are planned for future studies.

Cost Benefit: In addition to a less invasive technique, the use of the standard orthopedic suture may be a cost-competitive means of providing the ligamentous support and ROM reduction compared to alternative techniques that employ dynamic stabilization implants with increased costs and surgical complexity. The particular suture is commonly chosen for tethering as it is one of the largest and strongest sutures currently used in orthopedic procedures. Use of other sutures or materials could provide increased control over both tether stiffness and ultimate strength which could allow for more detailed stabilization.

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3.3. *Manuscript:* Biomechanical Characterization of Posterior Tethering Techniques for Prophylactic Treatment of Proximal Junctional Kyphosis in Adult Spinal Deformity Constructs

3.3.1. Document Information

Authors: Damon E. Mar[1], Steven J. Clary[1], Douglas C. Burton[1], Terence E. McIff[1]

Institution: [1]Department of Orthopedic Surgery, University of Kansas Medical Center, Kansas City, KS

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Publications:

Abstract Presentation: North American Spine Society 2017 Annual Meeting, Poster P20

3.3.2. Abstract

Background Context: The use of spinous process (SP) tethering techniques above the uppermost instrumented vertebra (UIV) for prophylactic treatment of proximal junctional kyphosis (PJK) has begun to gain favor clinically. However, there is little understanding of how basic technique parameters impact segmental biomechanics and no consensus on appropriate technique. While basic demonstrations have shown effectiveness of tethering to reduce segmental range-of-motion (ROM), there has been no complete biomechanical characterization of clinically relevant SP-based tethering techniques.

Purpose: The goal of this study was to demonstrate the effect of level-inclusion, UIV attachment method, and tether tension on flexion ROM (FROM), SP strain, and intervertebral disc (IVD) pressure for SP-based tethering techniques.

Study Design/Setting: Cadaveric biomechanical study.

Patient Sample: NA

Outcome Measures: Flexion ROM, SP strain, IVD pressure.

Methods: Six T6-T10 cadaveric motion segments were tested to 5Nm in flexion-extension ROM. UIV was set at T9 using standard pedicle screws and rods. For UIV attachment, direct looping through a UIV SP hole (SPH) was compared to looping under a standard cross-link (CL). For level inclusion, tethering was done across a single level (SL) from UIV to UIV+1 or double level (DL) from UIV to UIV +1 and UIV+2. For tensions, 5lbf and 15lbf were tested. Test measures included segmental FROM, SP strains, and IVD pressures across all configurations. SP holes were drilled just dorsal of the spinolaminar junction in UIV, UIV+1, and UIV+2. A 5mm polyester suture was used for tethering. Initial baseline instrumented ROM tests were run without tethering. Each specimen was then tested across each combination of loop level, UIV attachment, and tension. Tensioning was done with a hand-held force gauge.

Results: Tension had a significant effect across all tethering techniques (p=0.01). The greatest change in SP strain occurred in the highest level tethered. While the use of the CL attachment reduced UIV SP strain, it caused an increase in UIV+1 and UIV+2 SP strain compared to UIV SP attachment. The combination of DL and CL attachment provided the greatest reductions in FROM with the least amount of increase in SP strain at either UIV or UIV+1.

Conclusions: This data provides initial guidance for SP tethering in the TL spine with the goal of providing adequate ROM reduction with minimal SP strain increase. Tension had a significant effect across all measures and should be considered an important factor in the overall success of a tethering technique. The present finding may have implications beyond just SP-based tethering techniques to any which allow control over tension. This improvement in understanding of tethering techniques has the potential to decrease PJK caused by ligamentous laxity. Future studies should study the effect of cycling loading and long-term stability of tethered segments above UIV. Additionally, characterization of the upper thoracic spine is needed to elucidate any differences in sensitivity of technique.

3.3.3. Manuscript

Introduction: Adjacent segment pathology (ASP) is a common complication following adult spinal deformity (ASD) corrective surgery, with an incidence of 0.6% to 3.9% and is most prevalent with individuals over the age of 60 [1]. Proximal junctional kyphosis (PJK), with incidence rates of 13% to 55% [2-5], is one of the most prevalent ASPs and has yet to be fully understood and managed. PJK was defined by Glattes et al. as the presence of a radiographic angle of greater than 10 degrees between the inferior endplate of the uppermost instrumented vertebra (UIV) and the superior end plate of the vertebra two levels above it (UIV+2) and additionally an equal change of the same angle between the preoperative and postoperative angle [5]. There has been great interest in recent years with improving the understanding of underlying pathologies, risk factors, and preventative treatment strategies associated with PJK. Commonly reported risk factors include BMI, number of levels fused, fusion extending to the sacrum, and age [2, 6-8]. Current treatment strategies for PJK focus primarily on prophylactic methods of structural reinforcement of the vertebral body and the posterior ligamentous complex (PLC). Prophylactic vertebral augmentation such as vertebroplasty is a common method for providing vertebral body support to reduce the risk of vertebral wedge fractures at and adjacent to UIV [9-11]. The use of spinous process (SP) tethering techniques above the UIV has been gaining interest recently to provide support for PLC laxity or failure. Recent studies have begun to investigate the effectiveness of posterior tethering to reduce the risk of developing PJK. Bess et al. investigated the ability of multiple level tethering to create a transition zone for flexion ROM, screw forces, and IVD pressures using a finite element model [12]. Zaghloul et al. reported the first case series on prophylactic treatment of PJK with tethering showing promising results [13]. Recent reviews of ASD treatment methods have made mentions of tethering techniques for PJK prophylaxis as well with various tethering methods proposed [14-17]. Amidst all of this attention however, very few of these reports have provided concrete biomechanical data regarding the effects of tethering technique. There is still little understanding of how basic technique parameters impact segmental biomechanics and no overarching consensus on appropriate technique. To date, there has been no complete biomechanical characterization of clinically relevant SP-based tethering techniques.

Goals: The goal of this study was to demonstrate the effect of level-inclusion, UIV attachment method, and tether tension on flexion ROM, SP force, and intervertebral disc (IVD) pressure for SP-based tethering techniques.

Methods:

Specimen Preparation: Six fresh-frozen cadaveric spines were included in this study. Each spine was prescreened using fluoroscopy to identify and exclude any segments which might have motion inhibited by the presence of osteophytes, arthritis, or other bony defects. Each spine was then dissected down to a T6-T10 motion segment taking care to preserve as much soft tissues as possible. UIV was designated at T9 and standard pedicle screws and fusion rods (DePuy-Synthes, Raynham, MA, USA) were implanted using standard technique. The fusion rods were cut to be even with the inferior endplate of T10. The superior endplate of T6 and inferior endplate of T10 were cleared of all tissue and were then embedded in Bondo (3M, Maplewood, MN, USA) for mounting the specimens to test fixtures. Braided 5mm polyester suture was used for tethering (Ethicon, Somerville, NJ, USA). For tether looping, transverse holes were drilled in the SP of UIV, UIV+1, and UIV+2 (T9, T8, and T7 respectively) using a 2.5mm drill just dorsal to the spinolaminar junction. Eyelet screws with custom guide bushings were inserted laterally into UIV, UIV+1, and UIV+2 vertebral bodies for follower load application. Uniaxial strain gages (Omega Engineering, Stamford, CT, USA) were placed anteriorly adjacent to each SP tethering hole and were used as a relative measure of force acting on each SP by the PLC and tethering. Custom pressure sensors (Precision Measurement Company, Ann Arbor, MI, USA) were inserted into the nucleus pulposis of the UIV/UIV+1 and UIV+1/UIV+2 intervertebral disks using a cannula prior to testing. Figure 3.3.1 shows an example of a prepared specimen.

Figure 3.3.1: Model showing an example of a prepared T6-T10 segment. Pressure sensors are indicated by the blue ovals at UIV/UIV+1 and UIV+1/UIV+2 intervertebral discs, and spinous process strain gages are indicated by the blue rectangles at UIV, UIV+1, and UIV+2.

ROM Testing: To evaluate each test parameter, the specimens were loaded to 5Nm of flexion-extension bending using a pure moment testing machine (Applied Test Systems, Butler, PA, USA). A constant 400N follower load was applied during testing to simulate body weight. Each test was comprised of five cycles of loading and analysis was done on the third. Specimens were preconditioned with two untethered tests followed by a third test to serve as the baseline. Following the baseline test, a series of tests were run to evaluate the combinations of each of the three tethering parameters. To compare the effect of level inclusion, tethering was done either with a single level (SL) from UIV to UIV+1, or with a double level (DL) between UIV to UIV+1 and UIV to UIV+2. To compare the effect of tension, tests were done at both 22N (5lbf) and 66N (15lbf) of tensioning. Loop tensioning was measured using a hand-held force gage (Mark-10, Copiague, NY, USA) and then set in place with a needle driver prior to testing. For the DL tests, each loop was set independently and was always done first at UIV/UIV+1 and then UIV/UIV+2. To compare UIV tether attachment method, looping at UIV was done either through the SP hole (SPH) or under a standard rod cross-link (CL) which was placed just inferior to the pedicle screws spanning the rods (DePuy-Synthes, Raynham, MA, USA). A total of eight tethered tests were run to evaluate all combinations of each of the three techniques considered. The order of each test was randomized between specimens however all SPH tests were run prior to CL tests as partial removal of UIV SP bone was required for CL placement. During each test, ROM data was measured at UIV, UIV+1, and UIV+2 using a motion capture system (Northern Digital, Waterloo, Ontario, CAN). Strain and pressure data was measured using a data acquisition system (National Instruments, Austin, TX, USA). Data analysis was done using Matlab (The MathWorks, Natick, MA, USA) and Excel (Microsoft, Redmond, WA, USA) software.

Statistical Methods: Repeated measure multivariate and univariate ANOVAs were used to test for significance of effects of level inclusion, UIV attachment method, and tension on flexion ROM, SP forces, and IVD pressures. Post-Hoc paired t-tests were used to make individual comparisons between techniques. Statistical analysis was done using SPSS (IBM, Armonk, NY, USA) software.

Results:

Specimen Demographics: The average specimen age at death was 59.5yr with a range of 35yr to 85yr. The study included four females and two males.

ROM Test Results: Average test results for flexion ROM, SP force, and IVD pressures are shown in Figures 3.3.2, 3.3.3, and 3.3.4 respectively.

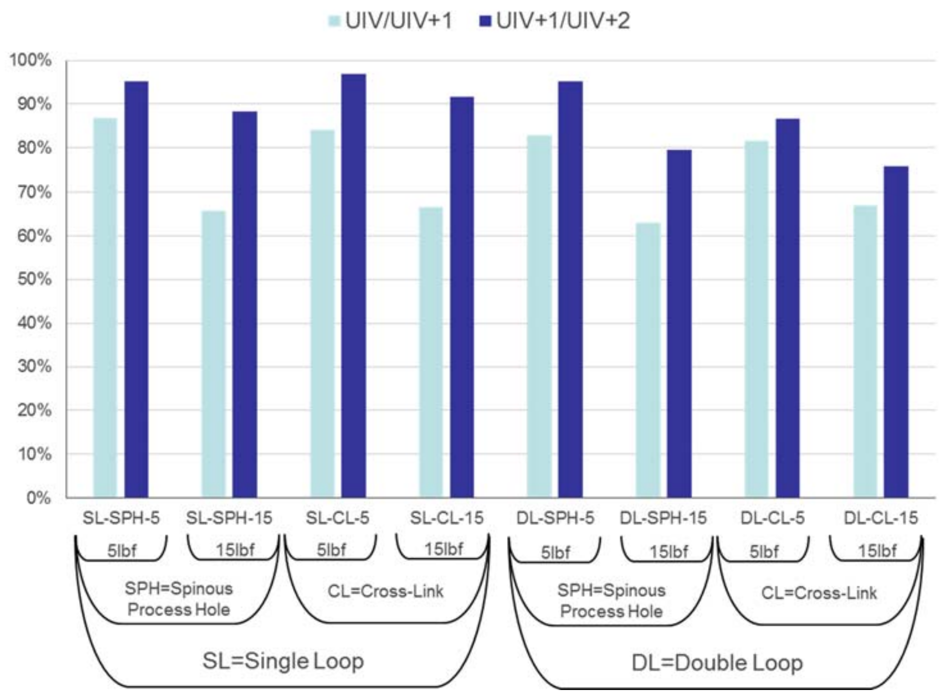

Figure 3.3.2: Average flexion ROM for each technique combination reported as percentage of baseline values.

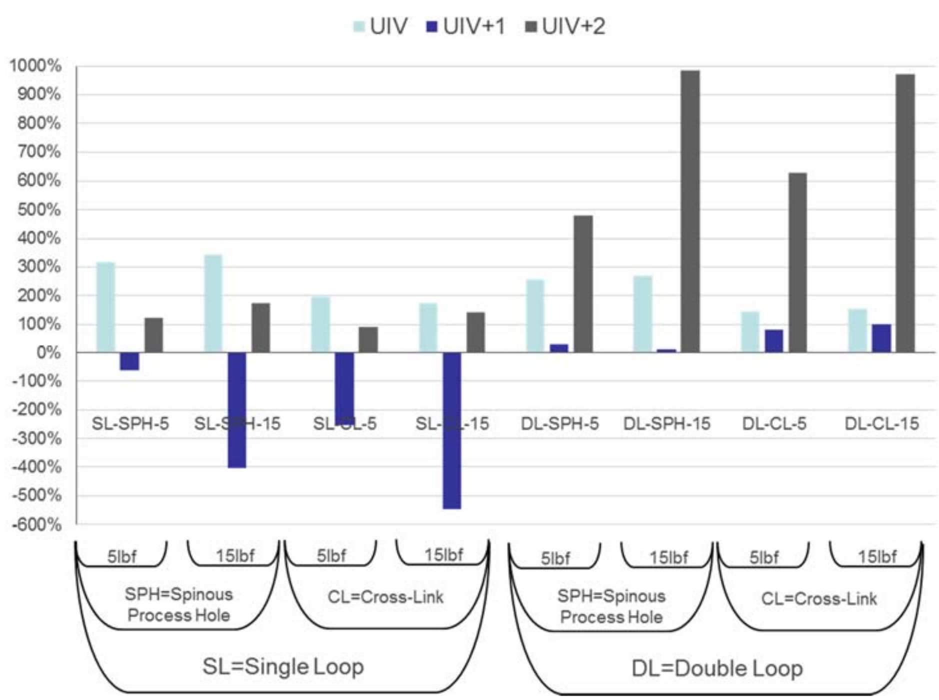

Figure 3.3.3: Average SP forces for each technique combination reported as percentage of baseline values.

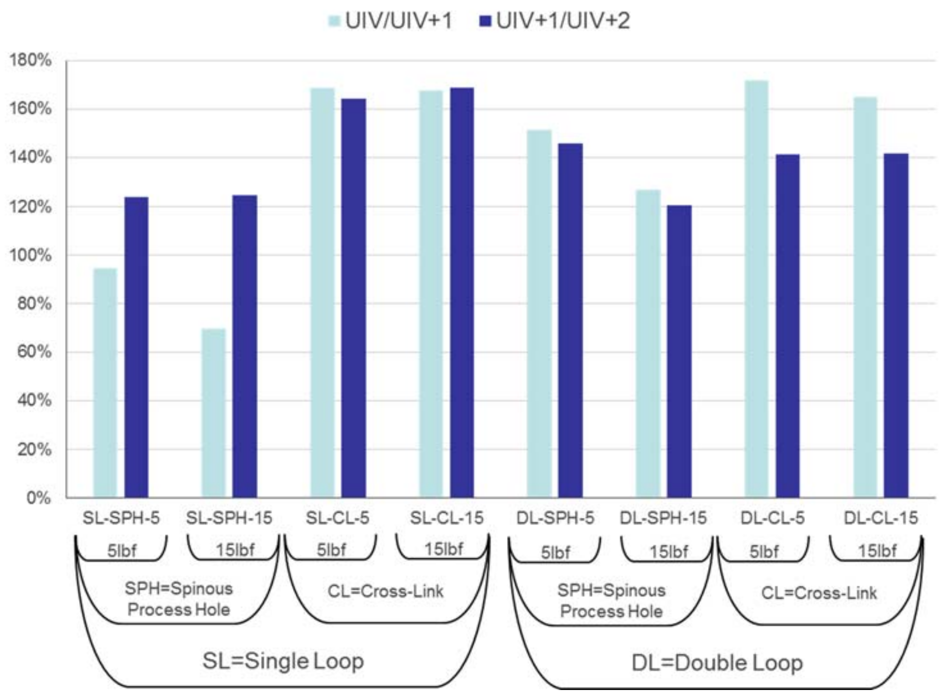

Figure 3.3.4: Average IVD pressures for each technique combination reported as a percentage of baseline values.

Level Inclusion Results: There were significant differences found in flexion ROM (p=0.01) and SP forces at UIV+1 and UIV+2 (p=0.01 and p<0.001 respectively). There was a consistent trend in the uppermost tethered level seeing the highest change in SP force.

UIV Attachment Results: There were no significant effects at either the multivariate or univariate level for use of SPH compared to the CL. The use of the CL did however, significantly decrease the SP force at UIV as expected (p=0.04). The use of the CL showed increases in SP force at UIV+1 and UIV+2 compared to SPH looping.

Tether Tension Results: Tension showed a significant multivariate (p=0.003) and univariate effects for flexion ROM at both UIV/UIV+1 and UIV+1/UIV+2 (p<0.001 and p=0.003 respectively).

Descriptive Results: The combination of DL and CL attachment provided the greatest reductions in flexion ROM with the least amount of increase in SP force at either UIV or UIV+1.

Discussion: This study evaluated the effects of multiple tethering technique parameters on a thoracolumbar motion segment. Tension showed the greatest effect among the three parameters on flexion ROM reduction. The effects of level inclusion and UIV attachment had lesser effects and were more localized to specific levels.

UIV Attachment Method: Considerations of UIV attachment method likely is a multifaceted choice that includes consideration beyond simply just whether the UIV SP has the capacity for increased loading. A variety of attachment methods and sites have been discussed in previous investigations [12, 13, 15]. A method of utilizing SPs below UIV such as UIV-1 or UIV-2 have been mentioned however were not tested in the present study. Proposed benefits include improved load sharing across more levels and reduced invasiveness superiorly. Additionally, methods of attaching to other points on the fusion construct such as the pedicle screws themselves or to clamps on the fusion rods have been mentioned which may change how forces are directed and translated to the tethered levels. Generally speaking, the focus of UIV attachment seems to be on avoidance of overloading UIV posteriorly and on ease or convenience of looping.

Risk of SP Failure: In terms of failure, the primary focus for SP tethering is on SP bone quality and degree of loading. Presence of osteopenia or osteoporosis are among the key risk factors for PJF and subsequently PJK [6, 18, 19]. Reduced bone quality would theoretically correspond to reduced load capacity and in turn a reduced functional benefit of ROM reduction. The question arises whether osteoporotic patients should even be considered for posterior tethering directly to bony features such as the SP. Ultimately clinical outcomes may provide the best data for guidance. Additional study of failure modes and correlation to BMD or T-scores may provide some insight however. Alternatively, individuals with relatively healthy bone but presence of IVD degeneration may stand to gain the most benefits from posterior tethering.

Discussion of Peak SP Forces: A consistent trend was seen in the uppermost tethered level seeing the greatest change in peak SP force. This phenomenon was also found in the results reported by Bess et al. [12]. This corresponds to the uppermost tethered level seeing the greatest total flexion ROM relative to UIV. In the case of DL looping, UIV+2 sees angular flexion of UIV/UIV+1 and UIV+1/UIV+2 referenced to UIV so therefore it is always greater than UIV/UIV+1 alone. This effect may indicate that a potential benefit of using a DL method to UIV+2 is to provide shielding of SP loading at UIV+1 which would otherwise see comparable increases in SP force. The leveraging of two levels effectively provides greater SP force dissipation which may provide improved risk of avoiding SP pullout failure. It is important to note however that the present study did not find significant differences between UIV+1 and UIV+2 SP forces when comparing them as the uppermost tethered level. Further study is needed to know whether or not a true dissipation is seen rather than just a simple translation of equal force to the superjacent level.

Limitations: A primary limitation to this study is the limited sample size particularly for the number of effects tested, the number of dependent measures included, and the number of tests done. Another concern related to specimen relaxation is the notion of tether settling and segment reorientation during cyclic loading. Tether tension was only measured during tensioning and SP force was not measured until the start of each test, so it is difficult to know what sort of relaxation, primarily by the IVDs, might be occurring. Some drift or change in peak values from cycle one to cycle five were seen for particular specimens which indicate that settling occurred. The selection of the analysis of the third cycle was chosen primarily based on standard testing methodology however future investigation likely suggests that a greater number of cycles may provide a better picture of how stable the tension is. Greater tensioning effectively puts a tethered level into a static extension offset however it is not clear what might happen in-vivo after tens or hundreds of cycles of loading. Future investigations are required to determine the clinical presence and long-term effect. Another limitation is that only a single spinal region and a single UIV location was used for evaluation. Location of the tethering holes were standardized as much possible to provide a consistent basis for technique comparisons; however, alternate placements most likely leads to changes in how load is transferred and how motion is constrained. Facet joint forces were not monitored. The primary issue with this was the need to preserve as much soft tissue structure as possible to not adversely affect the baseline behavior. Anderson et al. provided insight into the importance of posterior tissue preservation [20]. Papp et al. showed the effect of tether tension on facet loading and eventual locking in lumbar motion segments [21].

Conclusion: The results from this study provides initial guidance for SP tethering in the TL spine with the goal of providing adequate ROM reduction with minimal SP force increase. Tension had a significant effect across all measures and should be considered an important factor in the overall success of a tethering technique. The present finding may have implications beyond just SP-based tethering techniques to any which allow control over the parameters tested and to emphasize the importance of their utilization. This improvement in understanding provides a basis for further development and evaluation of tethering techniques which may provide improved support for ligamentous laxity or failure to reduce the risk of developing PJK. Future studies should study the effect of cyclic loading and long-term stability of tethered segments above UIV. Additionally, characterization of other spinal regions such as the upper thoracic spine are needed to elucidate any differences in sensitivity of the parameters.

Key Points:

- Tension had a significant effect on flexion ROM.
- The greatest change in SP force occurred at the uppermost tethered level.
- The combination of the use of a CL at UIV for tether attachment and DL inclusion resulted in the greatest flexion ROM reductions with the least amount of SP force increases.

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3.3.4. Commentary

Effect of Neutral Offsets: With the current data on hand, it is difficult to discern the importance of static neutral offsets. Biomechanically, static offsets introduce an issue with how to locate the reference point for data analysis. Should the neutral position be based on the preliminary, untreated positioning regardless of repositioning caused by tethering, or should the neutral point be based on the static positioning following a particular treatment? It can be relatively easy to establish a strict standard for this from a biomechanical testing point of view however, clinically there may be differences of functional effect and ultimate success based on these assumptions.

Effect of Mode of Loading: Related to the issue of defining the true neutral position is the effect of the mechanical loading mode on segmental biomechanics. Displacement (or angular) control and load (or moment) control results in different mechanical endpoints. Often the choice of control mode is directed by ease of implementation and control. The choice, however becomes more than just a matter of convenient consistency and ultimately can affect outcomes with consideration of what true zero or neutral position is for in-vitro biomechanical testing. In this study, we chose to reference values of flexion angle, SP strains, and IVD pressures based on the static positioning prior to each individual test which means that the full flexion-extension ROM may have been proportionately shifted. Ultimately a true understanding of the exact modes of loading in-vivo is near impossible. Additionally, testing methodology should not be excluded simply because it cannot be precisely defined to meet perfect in-vivo behavior. In my view, the most important factor is that clinical views need to be taken into account equally with the engineering assumptions made for a particular protocol.

Technical Issues with IVD Pressures and Strain: Chronologically this study served as a pilot for most of the other studies in Chapter 3. Several discoveries were made during the course of testing for this study that ended up impacting our methodologies for the other studies that followed. The first discovery was that our pressure sensors were not staying in place as well as we had thought after preliminary testing. Sensor slipping caused issues with the relation of tethered test values to baseline values. Ultimately, we feel that pressure data found in this study is likely unrepresentative of true pressure changes due to the parameters tested. There are a few individual comparisons that may provide reasonable relative comparisons in magnitude, but overall the larger multivariate and univariate trends are likely inaccurate. The second discovery was that there were several confounding issues associated with the analysis of our SP strain data. The biggest issue and limitation was that we only used uniaxial strain gauges which cannot provide a direction component that a triaxial gauge would have provided. While this is not an issue for simply testing one linear variable like tension, it ultimately confounds effects that cause changes in loading direction such as the use of the CL. Based on these discoveries, several changes and improvements were made to the protocol used in the succeeding study in Chapter 3, Section 3.4.

3.4. *Manuscript:* Comparison of Posterior Tether Looping Techniques for Prophylactic Treatment of Proximal Junctional Kyphosis in Adult Spinal Deformity Surgery

3.4.1. Document Information

Authors: Damon E. Mar[1], Douglas C. Burton[1], Terence E. McIff[1]

Institution: [1]Department of Orthopedic Surgery, University of Kansas Medical Center, Kansas City, KS

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Manuscript Publication: Spine Deformity, SRS (tentative)

3.4.2. Abstract

Summary: Biomechanics of 4 spinous process (SP) tether looping methods were evaluated using T1-T4 motion segments. Significant differences in biomechanical effects were seen between the methods.

Hypothesis: Different looping methods will significantly alter flexion range-of-motion (FROM), intervertebral disc (IVD) pressure, and peak loop tension. The use of a common (CM) anchored method will more greatly reduce FROM and IVD pressure compared to chained (CH) or figure-eight (F8) methods.

Design: Biomechanical study.

Introduction: Prophylactic tethering for proximal junctional kyphosis (PJK) is gaining interest for long fusions in adult spinal deformity (ASD) surgery. Consensus on appropriate technique has yet to be established and there is a lack of biomechanical data to provide initial guidance. The goal of this study was to determine the effect of tether looping method on FROM, IVD pressure, and tether force.

Methods: Nine T1-T4 cadaveric motion segments were tested in flexion-extension to 5Nm. The uppermost instrumented vertebra (UIV) was placed at T3 using standard pedicle screws and fusion rods. A crosslink was placed inferiorly of the pedicle screws. Motion kinematics were recorded by a motion capture system. Custom IVD pressure sensors inserted into the nucleus pulposis of T1-T2 and T2-T3. 5mm braided polyester suture was used for tethering. The tether was looped under the crosslink at UIV, and through lateral holes drilled dorsal of the spinolaminar junction at UIV+1 and UIV+2. An untethered test was used for baseline values. Tethered test included: single level (SL) from UIV to UIV+1, double level (DL) from UIV to UIV+1 and UIV to UIV+2 (CM), DL from UIV to UIV+1 and UIV+1 to UIV+2 (CH), and DL from UIV to UIV+1 and UIV+2 (F8). Loops were tensioned to 22N prior to testing. Tension was recorded using custom loop tension sensors.

Results: SL resulted in significant reductions in FROM at UIV/UIV+1 ($p=0.001$) but not at UIV+1/UIV+2 ($p=0.052$). For FROM, the univariate effect of method was significant at UIV/UIV+1 ($p=0.004$) but not at UIV+1/UIV+2 (0.14). For IVD pressure, the univariate effect of method was significant at UIV/UIV+1 ($p<0.001$) but not at UIV+1/UIV+2 ($p=0.311$). For DL methods, the average peak tether force occurred at the uppermost tethered level. CM yielded the most reduced FROM and IVD pressures with the lowest peak tether tensions compared to CH or F8.

Conclusion: Tether looping method significantly alters segmental biomechanics. New understanding of loop method effects may provide improved ability to reduce PJK caused by ligamentous laxity.

3.4.3. Manuscript

Introduction:

Proximal Junctional Kyphosis: Proximal junctional kyphosis (PJK) is a common postoperative complication in adult spinal deformity (ASD) corrective surgery with a reported incidence of 13% to 53% [1-4]. The underlying mechanics of the development of PJK has and continues to be studied with scrutiny and increasingly there have been attempts to differentiate and classify PJK. The most widely accepted definition of PJK was proposed by Glattes et al. is the presence of a sagittal Cobb angle of greater than 10 degrees between the inferior endplate of the uppermost instrument vertebra (UIV) to the superior endplate of the vertebra two levels above it (UIV+2) and an angle of at least 10 degrees greater than the preoperative angle [4]. In the last decade, several additional definitions and classifications have been made [1, 3, 5]. Yagi et al. devised a classification system for the severity of the kyphotic angulation and categorized modes of failure including disc or ligamentous failure, bone failure, and bone/implant interface failure [3]. Hart et al. provided the first subcategorization of proximal junctional failure (PJF) with classification based on three failure types associated with PJK: vertebral fracture at UIV or UIV+1, posterior ligamentous complex (PLC) disruption, or instrumentation failure [5]. In 2014, Lau et al. provided a detailed review of the current understanding and classification of PJK and PJF [1]. Across all of the systems proposed to better define the particular forms of PJK and PJF, there has been a consistent recognition that both vertebral body failure and PLC disruption or failure are key factors for the underlying pathologies.

Prophylactic Treatment of PJK: A great deal of attention has been given to prophylactic treatment strategies to avoid structural failures to reduce the risk of PJK. To date, a majority of the efforts have sought to address the risk of vertebral fracture with the utilization and development of vertebral augmentation methods. Common techniques include vertebroplasty or kyphoplasty which have been shown to be effective both in in-vitro testing [6, 7] and with clinical outcomes [8, 9]. Much less attention has been given to strategies to address PLC disruption or failure up until very recently. Several biomechanical studies have demonstrated the contributions of the PLC to segmental stability and emphasized their importance [10-12]. While there have been recent discussions of PLC augmentation methods for PJK prophylaxis [13-16], there remains only a handful of studies that provide any biomechanical data

[17] or clinical evidence [18] to support its use and efficacy. The present understanding does not convey a complete understanding of PLC augmentation and that there is currently no consensus on appropriate tethering techniques for the prophylactic treatment of PJK. Among the various tethering techniques proposed, none have provided any biomechanical analysis of method of tether looping used.

Goal: The primary goal of this study was to elucidate differences in the effects of different spinous process (SP) tether looping techniques on flexion range-of-motion (ROM), intervertebral disc (IVD) pressures, and SP loading using cadaveric T1-T4 spine segments. We sought to answer the following questions: 1) Is there a significant difference in effect of tethering technique on segment biomechanics when using a consistent tether tension, and 2) Are there differences in IVD pressure changes and peak tether tension (corresponding to SP loading) between the techniques and if so, which have the most or least desirable effects compared to the degree of flexion ROM reduction?

Hypotheses: The following hypotheses were proposed:

- We hypothesize that relative to the untethered state, all tethering methods will result in a significant reduction in flexion ROM.
- In comparison of three different double-level techniques, we hypothesize that there will be a significant effect of technique on segmental ROM, IVD pressures, and SP loading.
- We hypothesize that a common anchoring method will result in the greatest flexion ROM reduction compared to a chained anchoring method or a figure-eight loop method.

Methods:

Specimen Preparation: This study included nine fresh-frozen cadaveric spines which were prescreened using fluoroscopy. Exclusion criteria included presence of endplate or facet arthritis and any other bony defects which might affect segmental ROM. Qualified spines were dissected down to T1-T4 motion segments with T3 designated as the UIV. Care was taken to preserve as much soft tissues as possible. Pedicle screws (DePuy-Synthes, Raynham, MA, USA) were inserted into the T3 pedicles using standard free-hand placement technique and rod segments were attached such that they extended inferiorly even with the inferior endplate of T4. The superior endplate of T1 and the inferior endplate of T4 along with the fusion rods were embedded in Bondo (3M, Maplewood, MN, USA) for mounting the specimens to testing fixtures. A standard fusion rod cross-link (DePuy-Synthes, Raynham, MA, USA) was sized and placed just inferior of the pedicle screw receivers. For tethering at T2 (UIV+1) and T1 (UIV+2), 2.5mm holes were drilled laterally through each spinous process just dorsal of the spinolaminar junction. The T1 hole was located at a third down from superior edge of the total height of the SP. For T2, the hole was located at the mid-point of the total height of the T2 SP. Custom follower load guide screws were inserted laterally into the T2 and T3 centrums positioned midway between each bodies' endplates and at the posterior third in the sagittal plane. Custom pressure sensors (Precision Measurement Company, Ann Arbor, MI, USA) were inserted into the UIV/UIV+1 and UIV+1/UIV+2 IVDs using a cannula. The sensors were positioned to be within the center of the nucleus pulposis in the mid-sagittal plane. Motion capture markers were mounted the test fixtures at the base and at UIV+2 and to the vertebral bodies of UIV and UIV+1 using custom cancellous screws. A schematic overview of a prepared specimen is shown in Figure 3.4.1.

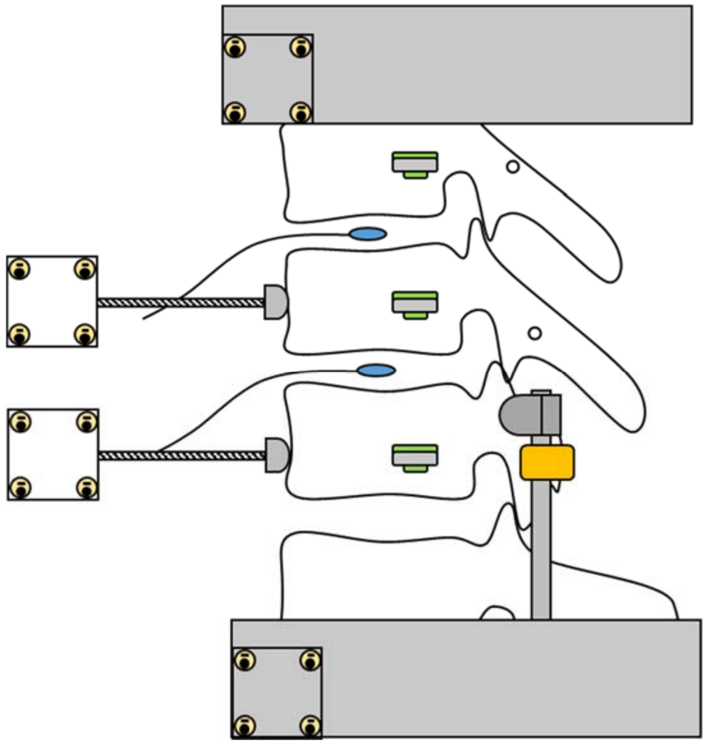

Figure 3.4.1: Schematic overview of a prepared T1-T4 motion segment for range-of-motion testing. Measurements include vertebral kinematics of the base fixture, UIV, UIV+1, and UIV+2 (squares with four circles) and IVD pressure at UIV/UIV+1 and UIV+1/UIV+2 (blue ovals). Additional instrumentation includes the follower load guides (green bushing), pedicle screws, rods, rod cross-link, and base fixtures.

ROM Test Setup: Testing was done using an MTS MiniBionix II hydraulic load frame (MTS, Eden Prairie, MN, USA) with custom fixtures to create a pure-moment loading system. The pure moment loading was applied to the upper potting base of T1. The potting base of T4 was used as the point of reference for ROM measurements. A constant 100N follower load was applied using chords attached to UIV+2 (T1) which passed through UIV+1, UIV, and UIV-1 (T4) via the guide screws to weights hung below with pulleys.

Test Sequence: Each ROM test was comprised of five cycles of flexion-extension (FE) bending to 5Nm in angular control with a constant static 100N compressive follower load. Analysis of each test was done on the third loading cycle. An initial set of two tests were first done for preconditioning followed by a third to serve as the baseline (B). Following the baseline test, the single tether (ST) test was done with a tether looped from UIV to UIV+1. After the

ST test, a series of three double level tests were done: common (CM) with two independent loops looped from UIV to UIV+1 and UIV to UIV+2, chained (CH) with two independent loops looped from UIV to UIV+1 and UIV+1 to UIV+2, and figure-eight (F8) were a single loop was looped in a figure-eight pattern through UIV, UIV+1, and UIV+2. Examples of the four looping techniques are shown in Figure 3.4.2.

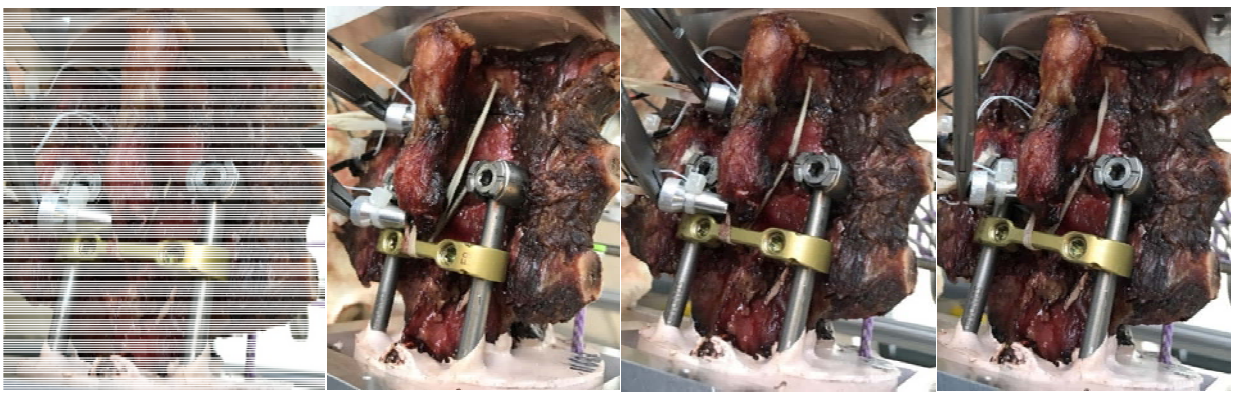

Figure 3.4.2: Examples of the four tethered tests: A) Single Tether (ST) at UIV/UIV+1, B) Common (CM) with two independent loops spanning UIV/UIV+1 and UIV/UIV+2, C) Chained (CH) with two independent loops spanning UIV/UIV+1 and UIV+1/UIV+2, D) Figure-Eight (F8) with a single tether looped through both UIV/UIV+1 and UIV+1/UIV+2 in a figure-eight.

For tether tensioning, each tether loop was passed through a custom tension sensor device and tensioned to 22N (5lbf) using a hand-held force gauge (Mark-10, Copiague, NY, USA) and then clamped in place with a needle driver prior to each tethered test. For double tether techniques, each loop's tension was set independently and was done at UIV/UIV+1 first, then UIV+1/UIV+2 when applicable. The routing and clamp placement of each technique was standardized across all specimens for consistency. The order of the double-level tethering techniques was randomized across specimens to reduce potential effects of test order. During each test, UIV, UIV+1 and UIV+2 motion kinematics were monitored using a motion capture system (Northern Digital, Waterloo, Ontario, CAN). IVD pressure and loop tension data were recorded using data acquisition hardware and software (National Instruments, Austin, TX, USA). Data analysis was done with custom Matlab (The MathWorks, Natick, MA, USA) and Excel programs (Microsoft, Redmond, WA, USA).

Statistical Methods: Paired t-tests were used to compare ST test results to baseline. Repeated-Measure multivariate and univariate ANOVAs were used to test for effects of double-level tether techniques on flexion ROM and IVD pressures followed by post-hoc paired t-tests for individual technique comparisons. A repeated-measure univariate ANOVA was used to test for the effect of double-level tethering technique on tether tension at maximum flexion for UIV/UIV+1. A paired t-test was used to compare CM and CH tether tensions at maximum flexion for UIV+1/UIV+2. Statistical analyses were done using SPSS (IBM, Armonk, NY, USA) and Excel (Microsoft, Redmond, WA, USA) software.

Results: The average flexion ROM and IVD pressure results reported as percentages of baseline values are shown in Figure 3.4.3.

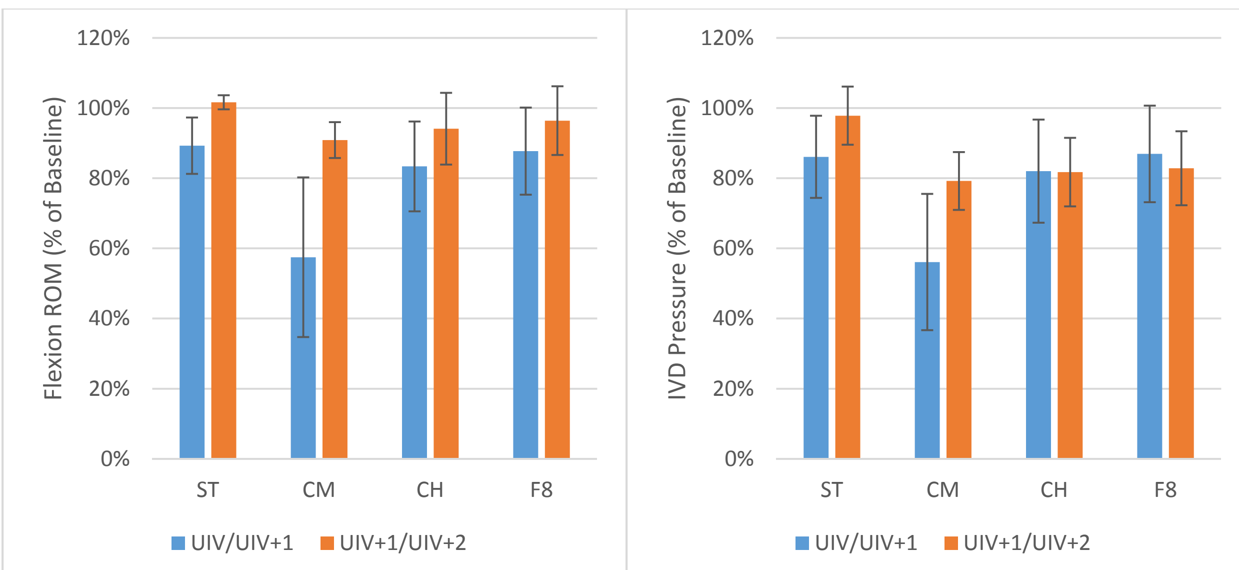

Figure 3.4.3: Average percentages of baseline behavior for flexion ROM (left) and IVD pressures (right) by level. Error bars indicate +/- one standard deviation. ST=single tether, CM=common, CH=chained, F8=figure-eight.

ST Technique Results: ST resulted in a significant decrease in flexion ROM compared to baseline at UIV/UIV+1 ($p=0.007$) but not at UIV+1/UIV+2 ($p=0.052$). ST resulted in a significant decrease in IVD pressure compared to baseline for both UIV/UIV+1 ($p=0.007$) and UIV+1/UIV+2 ($p=0.002$).

Double Level Technique Results: The effect of selection of double level technique resulted in a significant effect on flexion ROM reduction for consideration of both levels (multivariate p=0.02) and for UIV/UIV+1 (univariate p=0.004) but not for UIV+1/UIV+2 (univariate p=0.14). Post-Hoc pairwise comparisons between the techniques for UIV/UIV+1 flexion ROM were as follows: CM was significantly lower than CH (p=0.004), CM was significantly lower than F8 (p=0.005), and CH was significantly lower than F8 (p=0.049). For the effect of double level technique selection on IVD pressures, there was no significant effect found for consideration of both levels (multivariate p=0.077) or for UIV+1/UIV+2 (univariate p=0.311). There was however, a significant reduction in IVD pressure found at UIV/UIV+1 (univariate p<0.001). Post-Hoc pairwise comparisons between the techniques for UIV/UIV+1 IVD pressure were as follows: CM was significantly lower than CH (p=0.003) and F8 (p=0.0.003), and there was no significant difference between CH to F8 (p=0.139).

Peak Tether Tension Results: Average tether tension force at maximum flexion for each tethering technique are shown in Table 3.4.1.

Table 3.4.1: Average tether force (N) at 5Nm of flexion for each technique by level (± one standard deviation).

Level	ST	CM	CH	F8
UIV/UIV+1	31.9±21.1	16.2±7.1	34.5±19.9	23.1±15.8
UIV+1/UIV+2		53.3±24.2	55.6±31.1	

ST=Single Tether
CM=Common
CH=Chained
F8=Figure-Eight
UIV=T3, UIV+1=T2, UIV+2=T1

The univariate effect of double-level technique on peak tether tension at maximum flexion was significant (p=0.036) for UIV/UIV+1. Post-Hoc pairwise comparisons for UIV/UIV+1 peak tether tensions are as follows: significant different between CM to CH (p=0.034) and CH to F8 (p=0.006) but not for CM to F8 (0.264). The difference between UIV+1/UV+2 peak tether tension was not significantly different between CM and CH (p=0.73).

Descriptive Statements: CM resulted in the greatest flexion ROM among all the techniques and additionally created the most even taper among the double-level techniques. CM also resulted in the greatest reductions in IVD pressures at both UIV/UIV+1 and UIV+1/UIV+2. The greatest increases in SP loading were seen with ST and CH at the uppermost tethered level.

Discussion:

Primary Results Summary: The results of this study demonstrated the effect of four different SP tether looping methods on in-vitro segmental biomechanics. The results show that tethering of the SP across any number of levels does have a significant reduction in flexion ROM and IVD pressures while increasing SP loading. Additionally, the results indicate that with consistent tensioning, choice of looping technique does have a significant impact on segmental biomechanics.

Comparison of Double-Level Techniques Discussion: Among the three double-level techniques tested, CM yielded the greatest flexion ROM and IVD pressure reductions with the least increase in peak tether tensions compared to CH and F8. CH resulted in the greatest tether tension at UIV+2 at 55.6N although this was not significantly different than UIV+2 with CM. Clinically, CH done with equal tensioning as in this study, may not be considered logical. Its effect is more or less only a slight change in the baseline ROM behavior but with increased SP loading. With consideration of unequal tensioning between loops however, a taper could easily be achieved. It is unclear as to whether this would be more or less desirable than CM with equal tensioning. Ultimately, allowing multiple technique parameters such as loop method and tension to vary together results in a complex system that has many modes of utility but also increased likelihood of confounding effects. While surgically this suggest that posterior tethering may provide a great deal of opportunities and flexibility for tailoring the technique to each individual patient, it also highlights the importance for preliminary characterization to be done at the most basic levels.

Selection of Basic Looping Techniques for Study: Selection of the three double-level techniques included in this study was primarily based on identifying the most basic forms of the various, more complex methods discussed in the literature. Each essentially represents the most basic form of possible categories for tether looping methods. We felt that it was important to characterize the basic forms of these methods prior to evaluating more complex but possibly more clinically desired. For the case of F8, given the slightly reduced accuracy in tensioning the UIV+1/UIV+2 level since additional clamps would be necessary for maintaining tension, the relative lack of difference of effect compared to CH can be expected. The inclusion of F8 was based primarily on the number of proposed looping methods that utilize more complex weaving patterns found in the literature. In this study, it effectively resulted in a slightly attenuated effect of the CH method. While the present results do not completely rule out the effectiveness of CH or F8 methods (or more complicated versions of either), it does raise the question whether more investigation should consider the CM method clinically.

Comparison of Results to Bess 2016: To date, Bess et al. are the only authors to report biomechanical data on posterior tethering for PJK prophylaxis [17]. Table 3.4.2 shows the comparison of results reported by Bess et al. to the present study.

Table 3.4.2: Comparison of single level (ST) and double level (CM) tethering effects reported by Bess et al. and the present study (Bess 2016). Values are compared as percentage of the instrumented, untethered states for each study respectively.

Variable	Bess et al. 2016 UIV/UIV+1, UIV+1/UIV+2	Present Study UIV/UIV+1, UIV+1/UIV+2
ST F-ROM	84%, 98%	89%, 102%
CM F-ROM	56%, 69%	57%, 91%
ST IVD Pressure	88%, 100%	86%, 98%
CM IVD Pressure	69%, 81%	56%, 79%

Bess Study: UIV=T11, UIV+1=T10, UIV+2=T9, Present Study: UIV=T3, UIV+1=T2, UIV+2=T1
ST=Single Tether
CM=Common Method (Double Tether)
F-ROM=Flexion Range-of-Motion
IVD=Intervertebral Disc
UIV=Uppermost Instrumented Vertebra

Trends in flexion ROM reduction and IVD pressure reduction are remarkably similar between levels relative to UIV even though they represent different segmental regions of the spine. In addition to similarities in flexion ROM reduction and IVD pressures, the data reported for pedicle screw force, which we equate relatively to SP force (via tether tension) in the present study, indicated a trend of the uppermost tethered level exhibiting the greatest peak tether forces during flexion (excluding screw forces at UIV for Bess' data).

Greatest Tension at Uppermost Tethered Level: The characteristic that most logically describes the relation of tension to ROM is simply that tension appears to be proportional to the magnitude of ROM of a level relative to UIV; a greater ROM is seen at the UIV+2 level relative to UIV compared to UIV+1 relative to UIV. This behavior may have potential benefits as a method of shielding the UIV+1 SP from increased loading by more widely distributing SP load increases. The maximum SP load seen at UIV+1 with the CM technique was roughly half of the force that was seen at UIV+1 with the ST technique. It is important to note however that the maximum SP load at UIV+2 for the CM technique was 21.4N greater than the maximum SP load for the ST technique. This indicates that the inclusion of UIV+2 did not simply more evenly distribute the same SP loading over more levels.

Tether Stiffness: An important parameter in the mechanical effect of a tethering technique is the stiffness of the tether itself and the resulting "tether construct" stiffness. Harrell et al. compared the mechanical stiffness and ultimate tensile strength of different tether or suture materials [19]. In addition to comparing individual sutures, they also tested different numbers of loops of sutures to show how equivalent stiffness or tensile strength could be achieved between different materials. When this is taken into consideration with the results from this study in mind, it becomes clear that a wide range of possible methods could be used to change and modify the effects of any particular technique. The dependency of resulting tether stiffness on looping method may have important implications clinically. Several proposed methods of looping in the literature have depicted complex weaving patterns with multiple loops or overlaps of the tether [13, 14, 18]. None of these sources however make any discussion on the net effect of tethering stiffness. With the current lack of biomechanical data regarding tethering, it is unclear what stiffness is adequate or necessary. This suggests that clinical documentation of tethering technique, among other possible tethering parameters, will be necessary for evaluation of clinical outcomes.

Level Inclusion Discussion: While a primary goal of posterior tethering has been to achieve a redistribution of motion and load concentrations which occur at and above UIV, it is unclear how many levels are necessary to include. Depending on the method of tether attachment, the addition of more superjacent levels may result in greater invasiveness which possibly further disrupts PLC integrity and may ultimately increase the risk for developing PJK. It is unclear whether the increased invasiveness can be muted by the fact that the tether serves as a PLC replacement and ultimately provides greater stability than the otherwise undisturbed, but possibly degenerated, PLC may have provided. The increases in loads seen at the uppermost tethered level with greater number of levels tethered does suggest that bone health should be a consideration. A balance must be achieved between greater load distribution and individual level load increases, particularly at the uppermost tethered level.

UIV Tether Attachment: The use of the CL at UIV was chosen for this study to improve consistency between looping techniques and between specimens. The CL provides a much greater stiffness compared to the SP and thus was expected to help increase differences seen due to stiffness at UIV+1 and UIV+2. It could be expected that the use of looping through the UIV SP would result in lower peak loading at UIV+1 and UIV+2 levels. Clinical discussions have taken this into account, and often there is utilization of tethering below UIV to UIV-1 or UIV-2 to help reduce the concentration that occurs at the lowest tethered level [13, 14].

PLC Integrity: Among all factors that are currently believed to contribute to the incidence of PJK, the integrity of the PLC remains one of the most challenging and yet unaddressed issues. A majority of studies attempting to investigate the relation of the PLC to PJK incidence have focused on intraoperative disruption of the PLC and its resulting integrity postoperatively [20]. The evidence at hand regarding the effects of surgical disruption on incidence of PJK is however currently debated [21]. While biomechanical studies have provided insight into PLC contribution to segmental stability [11, 12], additional studies are needed to relate these findings to their impact on PJK.

Study Limitations: Primary limitations of this study include a relatively low sample size, only a single mode and magnitude of loading was evaluated, and only a single region was tested. The segmental region tested was chosen primarily based on findings reported by Hostin et al. that the upper thoracic region is more likely to see PJK due to ligamentous laxity or failure compared the thoracolumbar region [22]. The total number of looping techniques included in this study were intentionally limited to just the most basic in form to reduce the risk of results being affected by viscoelastic creep and relaxation inherent in the repeated testing of cadaveric specimens.

Neutral Position Reorientation: Another important consideration that should be noted is that given the viscoelastic nature of human soft tissues, a degree of tethered level relaxation and neutral positon reorientation may occur. Such mechanism may include a rebalancing or relocation of the center of rotation, tether stretch or knot settling, and bone compaction at loop points through SP bone. The tests used in the present study only included five cycles as this is common practice for in-vitro cadaveric testing. The effects of cyclic loading over time are left unknown. Additional testing is needed to determine what the degree and rate of settling may be. Clinically this has an important impact on what is actually being achieved compared to what is expected and being used as a guide for a tethering strategy.

Conclusions: The overall findings of this study suggest that with consistent tension, the choice of tether looping technique does have a significant effect on segmental biomechanics. All tethered levels saw significant effects on flexion ROM and IVD pressures however at the cost of increased SP loading. Among the double-level techniques tested, CM provided the greatest flexion ROM and IVD pressure reductions with the lowest increase in peak tether forces compared to CH and F8. CM may provide the best "natural" taper with consistent tensioning however each technique may be drastically changed with varied tensioning. It is important to note that even when viewed in its most basic form, posterior tethering constitutes a variety of technique parameters that ultimately all may have comparable effects on segmental biomechanics and when considered in combination will become confounding. With that said, we feel that basic characterizations of the techniques, such as what was investigated in this study, are necessary to be done first in order to provide a reference of understanding as more sophisticated or possibly clinically relevant techniques are evaluated and developed.

Key Points:

- With equal tensioning, tether looping technique does have a significant effect on segmental biomechanics.
- The CM technique produced the greatest reductions in flexion ROM and IVD pressures compared to CH and F8.

- The greatest increase in SP loading occurred at the uppermost tethered level and the force seen at UIV+2 for the double-level techniques was greater than the force seen at UIV+1 for the single-level technique.

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3.4.4. Commentary

Lack of Tether References: As mentioned previously, the amount of detail that is currently missing in the literature related to biomechanical effects of spinal tethering is astounding. This is particularly concerning in light of the amount of clinical discussion and interest that is proliferating around its use for novel prophylactic treatments of ASPs like PJK. Fortunately, from a biomechanical testing standpoint, evaluation can follow standard testing protocols and does not require much additional technology or analytical methods. As a dynamic treatment however, there are new issues that arise related to the functional effects of the techniques that appear to require more sophisticated analysis and discussion. An example is the relationship between dependent factors like change in SP magnitude and direction simultaneously. The basic nature of this study aims to provide an initial footing for additional study and evaluation to follow.

Discussion of Alternative Modes of Loading: Only a single mode of loading was used for evaluation. While the tethering methods currently presented are tailored to function in sagittal plane motion, there is likely some effect in other modes of bending such as right-left bending and axial rotation. The current state of understanding of PJK and PJF have not yet reached the point of identification of any coronal or axial plane contributions that may be tied to incidence rates. Biomechanical stability differences can be postulated, particularly for methods of looping to UIV at the pedicle screws or rods which may create a wider base compared to the inline direction with use of the SP itself or under a cross link that might results is more lateral stability. This is beyond the scope of the present study however and future investigations are needed to determine if these effects exist or if they have clinical implications.

3.5. *Manuscript:* Spinous Process Tethering with Neutral Zone Preservation for Prophylactic Treatment of Proximal Junctional Kyphosis in Adult Spinal Deformity Surgery

3.5.1. Document Information

Authors: Damon E. Mar[1], Steven J. Clary[1], Douglas C. Burton[1], Terence E. McIff[1]

Institution: [1]Department of Orthopedic Surgery, University of Kansas Medical Center, Kansas City, KS

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Abstract Presentation: North American Spine Society 2018 Annual Meeting (tentative)

Abstract Presentation: Orthopedic Research Society 2019 Annual Meeting (tentative)

Manuscript Publication: Spine Deformity, SRS (tentative)

3.5.2. Abstract

Summary: Biomechanical evaluation of nine T11-T12 cadaver functional spinal units (FSU) to determine amount of functional slack length (FSL) which can be added to a tether loop and still have a functional reduction in flexion range-of-motion (ROM). Correlation of radiographic intervertebral disc (IVD) measurements to flexion ROM and FSL.

Hypothesis: Flexion ROM and FSL can be predicted by radiographic IVD measurements.

Design: Biomechanical study.

Introduction: Tethering of mobile segments above long adult spinal deformity (ASD) fusions is gaining clinical interest as a method to reduce the risk of developing proximal junctional kyphosis (PJK). There is no basic biomechanical data to provide initial guidance for clinical use of posterior spinous process (SP) tethering. The goal of this study was to determine if radiographic IVD measurements can be used to predict flexion ROM and maximum FSL.

Methods: Nine T11-T12 FSUs were radiographed and then tested to 5Nm of flexion-extension bending using a pure moment testing machine. A 5mm braided polyester tether was looped through lateral holes drilled just dorsal of the spinolaminar junction of each SP. Flexion ROM tests were repeated with reducing FSL until tension was required to set the loop length. Radiographic measurements included anterior and posterior disc heights (ADH and PDH respectively), T11 endplate length (EPL), and two calculated indexes: disc angle index (DAI) and disc ratio index (DRI).

Results: Average flexion ROM was 5.4 degrees with an average FSL of 5.5mm. Significant Pearson correlations to flexion ROM were found with DAI and DRI. Pearson correlations to FSL were significant for EPL, DAI, and DRI.

Conclusion: Radiographic IVD measurements correlated with flexion ROM and FSL. The calculated indices may be useful for predicting flexion ROM and FSL as part of the preoperative planning for ASD corrective surgery to reduce the risk of developing PJK.

3.5.3.Manuscript

Introduction:

Adult Spinal Deformity and Proximal Junctional Kyphosis: Incidence of adult spinal deformity (ASD) is 2% to 32% among healthy adults [1-3] but has been reported to be as high as 68% among the elderly [4]. Adjacent segment pathology (ASP), is a common complication associated with ASD surgery. The primary characteristic of ASP is the adverse effects that occur at the mobile levels adjacent to the uppermost instrumented vertebra (UIV) in fusion constructs. Proximal Junctional Kyphosis (PJK) is one of the most challenging forms of adjacent segment pathologies (ASP) associated with surgical treatment for ASD. The incidence of PJK has been shown to range from 17% to 53% [5, 6]. Risk factors for PJK include age, BMI, bone quality, numbers of levels fused, and fusions extending distally to the sacrum [5-10].

PJK Prophylaxis: Prophylactic techniques to treat PJK have focused primarily on vertebral augmentation techniques such as vertebroplasty to reduce the risk of vertebral fracture at UIV or UIV+1. While these methods are showing promise at reducing the likelihood of PJK due to PJF [11-14], there is still a need to address ligamentous laxity believed to be caused by degeneration or by surgical disruption. Recently there has been a growing clinical interest in the use of posterior tethering techniques to address ligamentous laxity that may contribute to PJK. A variety of reviews on the current state of the art of classifying and treating PJK have proposed or discussed several tethering methods [15-18]. There has been however, only limited reports of basic biomechanical data on the effectiveness of the techniques to address issues relevant to PJK [19]. Only one report to date has been published on any clinical results [20].

Current Needs in PJK Tethering: There is currently a lack of clinical consensus on appropriate tethering technique and a need for biomechanical investigations to help guide its development. Often the goal of spinal tethering is to achieve a balance between motion preservation and range-of-motion (ROM) reduction. A sister study to the present (see Ch3, Section 3.2) showed that tether tension plays a significant role in the effect of flexion ROM reduction. It is not clear however, whether higher tension, if any, is necessary to provide adequate posterior ligament complex (PLC) support or flexion ROM reduction. In particular, there has been no demonstration to date of the effect of minimal or "slack tensioning" for limiting segment motion at extreme flexion. It has not been shown whether such a technique is functionally possible when done utilizing a spinous process (SP) tethering method. Additionally it is not clear whether one could estimate the amount of functional slack length (FSL) that could be varied and still result in a flexion ROM reduction at peak loading.

Goals and Hypotheses: The primary goal of this study was to determine if radiographic measurements of a thoracic IVD can be used to predict: 1) flexion ROM, and 2) the amount of possible FSL that would result in flexion ROM reduction. A secondary goal was to determine a coefficient value for the average amount of flexion ROM reduction gained or loss per unit of length of FSL. We hypothesized that a proposed IVD dimensional index calculation will significantly correlate with both functional spinal unit (FSU) flexion ROM and with the magnitude of FSL for a given specimen.

Methods: The testing for this study was done in conjunction with a sister study that evaluated the effect of increasing tether tension on the same dependent measures (see Ch3, Section 3.2).

Specimen Preparation: Nine cadaveric spines were initially screened with a fluoroscopic evaluation to identify signs of arthritis, IVD degeneration, or other body defects which might affect ROM. A T11-T12 functional spinal unit (FSU) was dissected out of each spine with special care to preserve as much soft tissues as possible. Prior to potting, a lateral radiograph was taken of each FSU for measurement analysis. Measurements were made using Illustrator (Adobe, San Jose, CA, USA) and included the anterior and posterior heights of the IVD (ADH and PDH respectively) and the inferior endplate length (EPL) of T11. All measurements were made by a single observer experienced with radiographic spine measurements. The disc angle index (DAI) was calculated as the angle formed between the line of the inferior T11 endplate and the line from the posterior point of the EPL line to the inferior point of the ADH line. The disc ratio index (DRI) was calculated as the ratio of the EPL divided by the ADH. An example of a radiograph with measurements is shown in Figure 3.5.1.

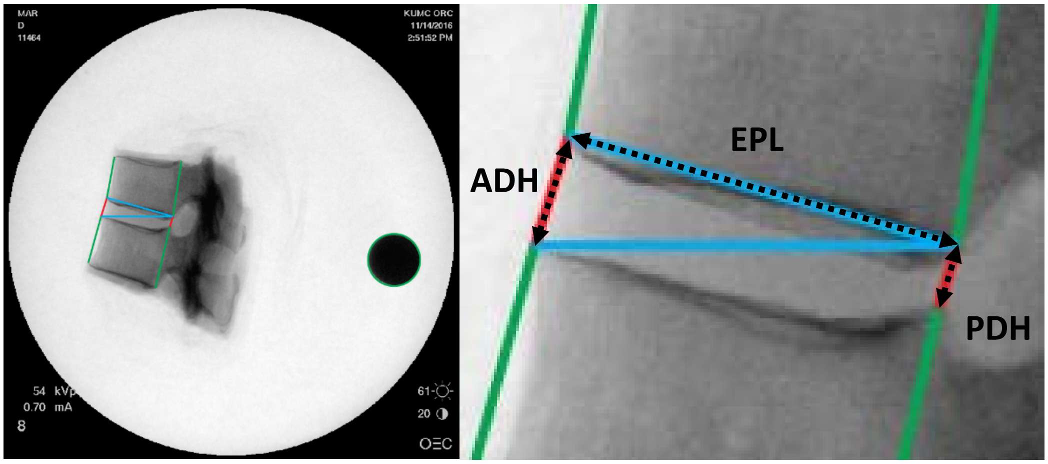

Figure 3.5.1: Example radiograph (left) of a dissected T11-T12 functional spinal unit showing geometric measurements (right) which included: anterior and posterior disc heights (ADH and PDH respectively), T11 end plate length (EPL), and the diagonal line from the posterior edge of the inferior endplate of T11 and the inferior edge of the anterior disc height line. A coin was used for length calibration (green circle in left image).

The superior endplate of T11 and the inferior endplate of T12 were cleared of IVD tissue and were then embedded in Bondo (3M, Maplewood, MN, USA) for mounting to testing fixtures. The potting level was set so that the only the endplates and facets were embedded and so that the loading of the SPs were not affected by the potting. A lateral hole was drilled in each SP using a 2.5mm drill. The holes were located at approximately a third from the superior and inferior edges of T11 and T12 SP bases respectively. Tethering was done using 5mm braided polyester surgical suture (Ethicon, Somerville, NJ, USA). The tether was marked to indicate 2mm increments along its entire length.

ROM Testing and Tethering Technique: Specimen loading was done with a pure-moment testing machine (Applied Test Systems, Butler, PA, USA) which applied a pure moment load to the potting of T11. Each test included five cycles of 5Nm of flexion-extension bending at an angular rate of 0.5deg/sec in addition to a constant 50N axial compressive load to simulate body weight. Each specimen was preconditioned with two tests (ten cycles) of loading untethered. After conditioning, a third untethered test was run to establish baseline behavior. Following the baseline test, the maximum FSL was determined by first loading and holding the specimen at 5Nm of flexion and then pulling the tether loop to the point where it just registered a tension above zero. A need driver was used to set the loop length in place and then the specimen was unloaded back to its neutral position. During loop setting, a hand-held force gage (Mark-10, Copiague, NY, USA) was used to measure tether tension. A depiction of the FSL setting technique is shown in Figure 3.5.2.

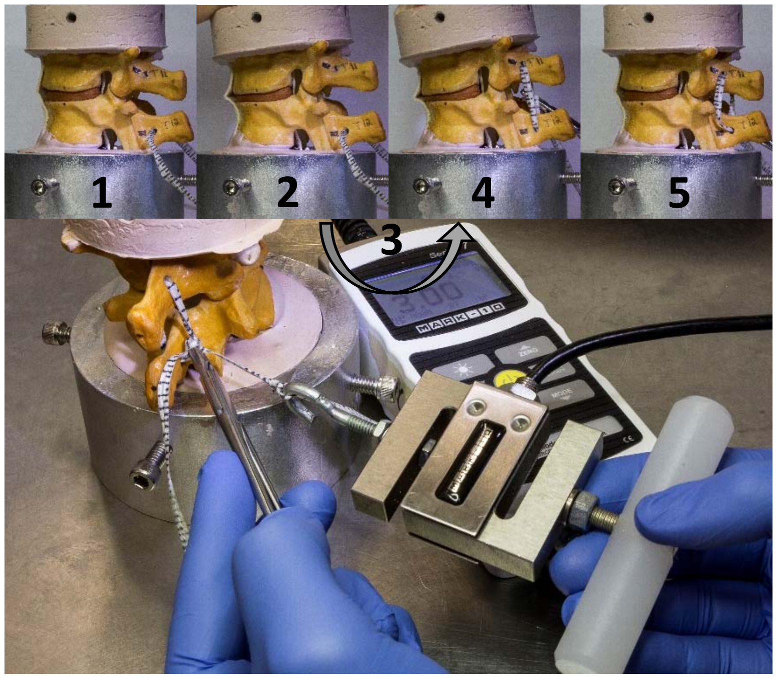

Figure 3.5.2: Demonstration of steps used to determine and set the maximum functional slack length (FSL) prior to range-of-motion (ROM) testing using a model: 1) load specimen to 5Nm in flexion, 2) hold in place, 3) loop tether through T11 spinous process and tension just to a force above zero using a hand-held force gage, 4) clamp the loop in place with a needle driver, and 5) unload the specimen back to its neutral position with the clamped in place.

After setting the maximum FSL, a series of ROM tests were run where the FSL length was reduced 2mm between each test until a tension force of more than 22N (5lbf) was required to reduce the length to the next 2mm increment. T11 motion kinematics were monitored using an Optotrak Certus motion capture system (Northern Digital, Waterloo, Ontario, CAN). Data analysis was done using Matlab (The MathWorks, Natick, MA, USA) and Microsoft Excel (Microsoft, Redmond, WA, USA) software.

Statistical Methods: Pearson correlations were used to test for significance in the relation of flexion ROM to DAI and DRI. Additionally, Pearson correlations were used to test for significance in the relation of maximum FSL to the radiographic disc measurements (ADH, PDH, and EPL), the disc calculations (DAI and DRI), and to maximum flexion ROM. Statistical analysis was using SPSS software (IBM, Armonk, North Castle, NY, USA).

Results: Specimen demographics, radiographic measurements, and baseline flexion ROM values are summarized in Table 3.5.1.

Table 3.5.1: Specimen demographics, radiographic measurements, calculations, and baseline flexion ROM data for the nine T11-T12 functional spinal units tested.

Demographics			Disc Measurements (mm)			Disc Calculations		F-ROM
Specimen	Gender	Age (years)	ADH	PDH	EPL	DAI (°)	DRI (%)	@ 5Nm (°)
1	F	59	9.2	5.3	32.4	15.9	3.5	7.3
2	M	85	6.8	3.4	42.6	9.0	6.3	3.3
3	M	54	8.4	5.3	31.4	14.9	3.7	4.8
4	F	66	8.4	5.0	35.7	13.2	4.3	3.6
5	F	58	6.2	3.3	27.5	12.6	4.4	5.9
6	F	66	7.6	6.3	33.0	12.9	4.3	6.1
7	M	70	8.7	4.8	40.5	12.2	4.7	5.0
8	M	72	9.3	5.9	33.9	15.4	3.6	7.0
9	F	65	6.8	3.8	29.0	13.3	4.3	5.5
	Average:	66.1	7.9	4.8	34.0	13.3	4.3	5.4
	Range:	54-85	6.2-9.3	3.3-6.3	27.5-42.6	9-15.9	3.5-6.3	3.3-7.3

ADH=anterior disc height, PDH=posterior disc height
DAI=disc angle index, DRI=disc ratio index
F-ROM=flexion range-of-motion

The ratio of average flexion ROM angle to DAI angle was 2.6 with a range of 2.1 to 3.7. Pearson correlations of flexion ROM to DAI and DRI were both significant (p=0.029 and p=0.036) with correlation coefficients of 0.718 and -0.698 respectively. Results of the Pearson correlation tests for FSL to the radiographic measurements are shown in Table 3.5.2.

Table 3.5.2: Pearson correlation coefficients and significance values for FSL to radiographic disc measurements, calculations, and flexion ROM.

FLS Correlation to:	ADH	PDH	EPL	DAI	DRI	F-ROM
Pearson Coefficient	0.381	0.542	-0.720	0.851	-0.890	0.675
p-value	0.311	0.132	0.029*	0.004*	0.001*	0.046*

* indicates significance at $p<0.05$

Among the five disc measurement parameters, EPL, DAI, and DRI all showed significant correlations to FLS. DRI showed the strongest correlation among the three although DAI was more similar compared to EPL. Percentage of flexion ROM reductions for each specimen by 2mm loop lengthening increments are shown in Table 3.5.3.

Table 3.5.3: Summary table of flexion ROM reduction at minimum FSL, maximum FSL (point of no flexion ROM reduction), and ratio of flexion ROM reduction to maximum FSL for each specimen.

Specimen	% F-ROM Reduction @ FSL=0	Maximum FSL to no F-ROM reduction (mm)	% F-ROM Reduction / Max FSL (%/mm)
1	19.0%	6	3.2
2	0.0%	2	0.0
3	8.7%	6	1.5
4	11.4%	6	1.9
5	18.6%	6	3.1
6	27.3%	6	4.6
7	12.1%	4	3.0
8	12.9%	8	1.6
9	0.2%	6	0.0
Average:	12.2%	5.5	2.1
Range:	0.0%-27.3%	2-8	0.0-4.6

F-ROM= flexion range-of-motion
FSL=functional slack length

On average, a FSL of 5.5mm could be added to the minimum loop length (to just taut) before flexion ROM reduction was lost. The average slope of the percent flexion-ROM reduction per length of tether slack added was 2.1% per mm.

Discussion: The results of this study relate radiographic disc measurements to functional tether length for prophylactic tethering to reduce the risk of developing PJK due to ligamentous laxity. The results indicate that several of the radiographic parameters, including both direct and calculated, do significantly correlate with FSL. This suggests that such measurements or calculations may provide a reasonable estimate of FSL from a standard sagittal radiograph used during preoperative planning. The relationship seen between slack amount and resulting flexion ROM reduction indicates that slack tensioning can produce an effect on reducing maximum flexion ROM.

Accuracy of FSL: It is difficult to discern with the present data to what degree of measureable FSL can realistically be utilized as a technique intraoperatively. Without a purpose-designed device to monitor or measure the amount of slack present in a tether loop, it may likely be difficult to measure increments at or better than the level tested in the present study. No intra-observer evaluation was done on reliability of consistency in reading and setting loop length as a method for measuring accuracy was unavailable at the time of testing. The 2mm increment used in the present study was chosen primarily as the smallest increment that was reasonable to visually mark and to read during testing. If a purpose built device or technique could allow for resolution as good as 2mm, it is plausible that the results found may be achievable. The primary functional concern with utilizing a slack tether strategy is going beyond FSL. No data, clinical or biomechanical to date, exists that indicates what the minimum desirable effect would be for such a technique or what the maximum loading range should be. While it may theoretically be possible to relate effects of neutral zone stiffness and stability to tensioning, the ultimate guidance is likely inherent in each individual case which may range from difficult to impossible to discern.

Relation of FSL to PLC Integrity: It is also difficult to discern the relation of PLC integrity to the degree of support needed by a tether. The stiffness of the native PLC and the tether are quite different and may be difficult to relate in order achieve some sort of tension sharing during flexion loading. In the most conservative method of only utilizing the greatest FSL, the PLC would hold all tension generated during flexion right up to a point before peak loading at which point the tether would engage and protect the PLC. That point of “on/off” engagement of the tether is likely difficult to set and identify given the complexity of tether stiffness, loop geometry, knot settling, and other factors related to the tether loop. In the full scope of tether strategies for PJK, one possible application for slack tensioning may be for its use at levels above other tethered levels tensioned to greater tensions which could produce a theoretical tapering effect depending on looping technique. Such effects have been demonstrated and discussed by previous studies [19, 21]. Future study would be needed to validate and develop such a technique.

Study Limitations: An important limitation of the study is that the baseline IVD measurements were made in the unloaded state. The geometric values for the IVD heights are likely affected by true in-vivo loading caused by upper body weight. Likely the IVD height measurements would be reduced in value when taken from a standard standing radiograph, which in turn would result in a reduced sensitivity of measurement or calculations involving ADH and PDH. However, among the three significant correlations found for FSL, EPL would be independent of physiological loading and would simply require a clear lateral view of the endplate. While not as well correlated as the calculated parameters that took ADH into account, its independence of loading suggests it may be the most feasible measure to use. Another important limitation of this study is that the SP hole-placement was not standardized beyond basic relation to anatomical features and that it was not measured radiographically. It is not clear what effect repositioning of the holes may have on either the effectiveness of the tether to reduce flexion ROM or on the ability to accurately predict the FSL. Geometrically, the further dorsal the holes are located, the greater the change in length between them will be at maximum flexion and thus, a greater FSL may be seen. With anatomical considerations however, there are limits to how far dorsal the holes can be placed with concerns for adequate SP bone strength. Normally a more anterior location, as used in this study, would be preferred for maximizing bone support and reducing extra bending force on the SP. Another important consideration is the relation of IVD health and resulting ROM to the radiographic measurements. The only qualification of IVD health was done indirectly as a measurement of the angulation of the FSU at full flexion. While this is not a direct quantification of IVD stiffness, we feel that it is a reasonable proxy with the use of loading to a fixed moment as opposed to a fixed angle. It is clear however that an overly stiff or extremely lax disc can likely exist which could confound the present results. Additional study is required to determine if radiographic measures and IVD stiffness can be correlated. Other study limitations include limited sample size, only a single level was tested, and only a single mod and range of loading was evaluated. Consideration of viscoelastic creep and relaxation limit the total number of tests and as a result number of test modes or conditions that can be included.

Conclusion: The results of this study show that slack tethering technique can be used to provide flexion ROM reduction which may be a valuable technique for reducing the risk of PJK caused by ligamentous laxity. Additionally, this study has shown that radiographic measurements of the IVD may be a useful tool for estimating FSL as part of the standard preoperative planning strategy. This technique may hold promise for indications for prophylactic tethering in the presence of relatively healthy IVD or PLC which may require only slight support rather than drastic pretension which my only accelerate degeneration.

Key Points:

- The average FSL for the T11-T12 FSUs tested in this study was 5.5mm.
- Both DAI and DRI correlated with flexion ROM.
- EPL of T11, DAI, and DRI all correlated with FSL.

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3.5.4. Commentary

Impact of Slack Method on Neutral Zone Stability: The results of the present study have shown that FSL can be used as a means of utilizing a tether without preloading the tethered level and in turn not affecting baseline neutral zone stiffness. It is not clear what impact this has clinically. Several studies have indicated the importance of neutral zone stability and its relation to segmental stability and pain [1, 2]. This seems to be an area of study worth further investigation. If relations of IVD health and neutral zone stability could be better described biomechanically, it may be easier to understand and indicate particular tether techniques, particularly those with greater, lesser, or lack of tension for prophylactic techniques for PJK.

Role of Tension on Neutral Zone Stiffness: It is clinically unclear what effect preloading a degenerated disc might have on segmental stability and long-term outcomes. The prevalence and association of degenerative disc disease to ASPs like PJK are well established [3-5]. A variety of consequences can be imagined related to over tensioning causing accelerated degeneration or possibly the opposite, of under-tensioning not adequately supporting the segment and in turn causing greater IVD damage and degeneration. The difficulty in determining this relationship is that clinical outcomes are needed to describe this multifaceted effect. Ultimately the goal should be to determine whether tension of any kind solely improves outcomes or if it is possible that varying degrees of tension will be required for individual treatments.

Relation of Disc Health to ROM: Currently disc health is an area of interest, particularly as a measure of preoperative planning. In 2015 Healy et al. indicated that there is currently no quantifiable way to measure the extent of IVD degeneration which can be used to predict segmental ROM in the thoracic spine [6]. The results found in the present study may serve as an important first step towards correlating radiographic measurements to in-vivo ROM. Obviously there needs to be further investigation to relate the in-vitro results to the in-vivo behavior. The particular measures and calculations used in this study, while considered relevant measures, are less important specifically compared to just the identification of any parameter that can be used to help predict segmental ROM as part of preoperative planning.

Commentary References:

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3.6. Discussion of Biomechanical Characterizations

3.6.1. Summary of Key Findings

The four studies presented in this chapter represent the most detailed biomechanical characterization of basic tethering parameters for prophylactic treatment of PJK to date. A summary of the key findings of each study are summarized in Table 3.6.1.

Table 3.6.1: Summary of key findings from biomechanical studies in this chapter.

Study	Methods	Key Findings
Section 3.2: Effect of Tether Tension on FSU Biomechanics	• Specimens: Nine T11-T12 FSUs • Independent Controls o Tether tension from 0 to 88N. • Dependent Measures o Flexion ROM o IVD Pressure o SP Force o SP Pullout Force	➢ All tensions reduced flexion ROM and IVD pressures while increasing SP loading. ➢ 0.4% flexion ROM reduction per N of tension. ➢ SP forces generated during max flexion ROM were 66% below tether pull-out forces. ➢ Tether failure occurred in a third (6/18) of the tests.
Section 3.3: Effect of Tethering on Segmental Biomechanics	• Specimens: Six T6-T10 Motion Segments • Independent Controls o Tether tension: 22N or 66N o UIV Attachment: SPH or CL o Level Inclusion: SL or DL • Dependent Measures o Flexion ROM o IVD Pressure o SP Force	➢ Tension reduced flexion ROM. ➢ The greatest SP force occurred at the uppermost tethered level. ➢ Use of CL at UIV and DL inclusion reduced flexion ROM the most with the least amount of SP force increase.
Section 3.4: Evaluation of Loop Method on Segmental Biomechanics	• Specimens: Nine T1-T4 Motion Segments • Independent Controls o Single Loop: ST o Double Loop: CM, CH, and F8 • Dependent Measures o Flexion ROM o IVD Pressure o Tether Tension	➢ Tether looping technique significantly effects segmental biomechanics. ➢ CM produced the greatest flexion ROM and IVD pressure reductions compared to CH and F8. ➢ The greatest tether tension occurred at the uppermost tethered level.
Section 3.5: Evaluation of Functional Slack Length on FSU Biomechanics	• Specimens: Nine T11-T12 FSUs • Independent Controls o FSL • Dependent Measures o Flexion ROM o Radiographic IVD measurements: ADH, PDH, EPL o Disc calculations: DAI, DRI	➢ Average FSL was 5.5mm. ➢ DAI and DRI correlated with flexion ROM. ➢ EPL, DAI, and DRI correlated with FSL.

FSU=Functional Spinal Unit, ROM=Range of Motion, IVD=Intervertebral Disc, SP=Spinous Process, SPH=Spinous Process Hole, CL=Cross Link, SL=Single Level, DL=Double Level, ST=Single Tether, CM=Common Method, CH=Chained Method,
F8=Figure-Eight Method, FSL=Functional Slack Length, ADH=Anterior Disc Height, PDH=Posterior Disc Height, EPL=Endplate Length,
DAI=Disc Angle Index, DRI=Disc Ratio Index

In total, the studies covered four segmental levels within the thoracic spine, included analysis of eight independent technique parameters, quantified effects on six biomechanical measures and four radiographic measures, and ultimately found thirteen key findings. Among the key findings, two consistent trends were found: 1) tension plays a significant role in reducing flexion ROM and IVD pressures, and 2) the peak tether tension (and thus SP loading) occurs at the uppermost tethered level. Both of these effects were validated between two or more of the studies at different spinal levels or with different amounts of tension. In addition to showing the effect of tension, two of the studies (Sections 3.3 and 3.4) provide initial insight into the effect of tether looping techniques. The key finding from these studies is that loop technique does play a primary role in the overall functional effect that is achieved. With regards to the variety and complexity of tethering techniques currently being proposed in the literature, this indicates that further characterization of each technique is required individually to fully understand its effect on segmental biomechanics. The results presented in Section 3.5 are the first of their kind and provide a novel means for predicting segment flexion ROM and FSL. This may serve as a new tool in preoperative planning with consideration of the amount of ROM desired at UIV/UIV+1.

3.6.2. Summary of Commentary on Biomechanical Characterizations

Through the course of the four studies included in this chapter, a new level of understanding was not only gained in the biomechanical effects of the tethering techniques, but also in the methodology used to evaluate them. The nuance and complexity of IVD pressure and SP strain data were appreciated in the early studies. Through trial and error, techniques were improved throughout the course of the investigations, and the resulting testbed is the most robust and thorough we have had to date. A consistent point to be made across all of the studies is that there remains a large gap between the understanding provided by the biomechanical characterizations and current clinical needs. Some results are more easily translatable than others, but ultimately clinical outcomes through prospective and retrospective reviews are needed for validation. Efforts must be made to insure that advancement of prophylactic tethering technique is done equally with regards to clinically relevant and concise engineering-based methodologies.

4. <u>Chapter 4 – Master Summary and Conclusions</u>

This chapter provides a review of the primary goals proposed in Chapter 1 and a master summary of conclusions.

4.1. Review of Primary Goals

The intent from Chapter 1 was split into three primary goals. A review each goal and the significance of the findings from the individual chapters are as follows:

1. *Provide a detailed review of spinal tethering techniques to date, to summarize the current state of the art, and to determine the aspects of current tethering techniques that should be considered important for prophylactic treatment of ASP.*

   The purpose of this initial goal was to simply establish an understanding of the current state of the art of spinal tethering techniques before moving on the details biomechanical characterizations. The intent was to cover the state of the art both in terms of surgical technique as well as device technology. The background material provided in Chapters 1 and 2 provide a complete overview of surgical techniques, both with and without tethering methods, to establish a baseline understanding in surgical techniques. The manuscript from Chapter 2, Section 2.2 provides a detailed review of tether-based techniques and implants. This manuscript also provides a concise summary of the current techniques that have been proposed for prophylactic treatment of ASPs such as PJK. The review of prophylactic treatments indicated that the current state of understanding is based primarily on technique discussion and with extremely limited experimental data of any kind and no clinical data.

2. *Provide the first detailed biomechanical characterization of a tethering technique for prophylactic treatment of PJK.*

   The intent of this goal was to provide a series of biomechanical characterizations to serve as the initial baseline guidance for the understanding of the effects of basic tethering technique parameters. The series of four studies were designed to cover a wide range of techniques, spinal regions, and clinical concerns related to prophylactic tethering for PJK. The sum of the studies provides the first complete biomechanical characterization of clinically relevant parameters for spinal tethering. The key findings provide directly translatable results to clinical practice and additionally opens the discussion of several new, previously undescribed aspects of prophylactic tethering techniques.

3. *Provide an engineering perspective on the art of tethering for prophylactic treatment of PJK.* While more general and basic in nature, the intent of this goal was to make sure that through the course of the review and the biomechanical investigations, that technical details relevant to each section were provided and discussed in order to advance the engineering understanding of prophylactic techniques for PJK. The background of Chapters 1 and 2 in addition to the review of Section 2.2 indicated a severe lack in technical understanding on the side of the tether as a surgical device. Through discussion of study findings, complication, and limitations, a wide variety of topics relevant to clinical treatment of PJK were brought to light. The hope is that these points of discussion, while potentially outside the scope of the individual studies as manuscripts, may simply spur curiosity and awareness for future investigations towards reducing the risk of developing ASPs like PJK.

4.2. Summary of Biomechanical Characterizations

4.2.1. Summary of Tether Technique Effects

This work, in its entirety, serves as the first step in describing and understanding the biomechanical effects of clinically relevant tethering techniques for the prophylactic treatment of PJK. This attempts to bring current engineering understanding of the condition closer to that of the surgeon's ability to treat it. While a natural ebb and flow is to be expected between advancements in surgical technique and development of the technical means to treat it, the hope of this work is to keep these advances closer to the heels of one another.

4.2.2. Discussion of Future Needs for Spinal Tethering Techniques

From here, a great deal of work lies ahead in continuing the characterization of remaining basic tethering parameters and their effects on spinal biomechanics. Once a solid basis for fundamental understanding is achieved, clinical outcomes will provide the next step of guidance for improving and refining the technique.