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The Effect of the Duration and Amplitude of Spinal Manipulation Therapy on the Spinal Stiffness of a Feline Model

by

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Abstract

The effect of duration and amplitude of spinal manipulative therapy on the spinal stiffness of a feline model.

Introduction: The purpose of this study was to determine the effect of spinal manipulation therapy (SMT) duration and amplitude on spinal stiffness.

Methods: Simulated SMTs were performed at the L6 spinous process in twenty-two felines. SMTs ranging from 25 to 250 ms duration were performed. Groups 1 and 2 received maximal displacements of 1.0mm to 3.0mm. Groups 3 and 4 received maximal loads of 25% to 85% body weight. Local stiffness was quantified by applying an indentation to the vertebra.

Results: Repeated SMTs caused minimal changes in stiffness. The interaction effect of duration X displacement in Groups 1 and 2, and the effect of duration in Group 3 were significant.

Conclusion: Repeated SMTs cause minimal changes in stiffness thought to be due to the viscoelastic responses of spinal tissues. Some of the changes following select SMT conditions may be the result of an interaction effect between SMT duration and amplitude. No specific threshold condition was identified as causing a greater stiffness change.

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List of symbols and Abbreviations

ANOVA	Analysis of variance
CNS	Central nervous system
CPR	Clinical prediction rules
EMG	Electromyography
FD	Force-displacement
HVLA	high velocity, low amplitude
Hz	Hertz
ICC	Intra class correlation coefficient
K	Stiffness coefficient
LBP	Low back pain
L1 to L5	Lumbar vertebra 1 to 5
MRI	magnetic resonance imaging
mm	Millimetre
ms	Millisecond
N	Newton
N/mm	Newton/ millimetre
PA	Postero-anterior
PMAD	Passive Movement Assessment Device
RCT	Randomized controlled trial
ROM	Range of motion

SD	Standard deviation
SMT	Spinal manipulation therapy
SPAM	Spinal Postero-Anterior Mobilizer
SPS	Spinal Physiotherapy Simulator
TIS	Terminal instantaneous stiffness
V	Volt

Definitions

Biomechanics	Application of mechanics to the analysis of biological systems.
Cavitation	During a SMT, the facet joint gets distracted or gapped, causing the capsule to be pulled in. When the capsule snaps back to its original position, it gets stretched, the intra-articular pressure suddenly drops, and dissolved synovial fluid gases are released causing a cracking sound.
Creep	Viscoelastic tissue property. Increase in strain of a tissue under constant load.
H-reflex	A reflex contraction of a muscle when the skin overlaying the large fibre afferents (nerve) is stimulated. This indicates the excitability (facilitated of inhibited) of the alpha motorneurons (Ia, Ib).
Hysterisis	Mechanical energy dissipated between loading and unloading of viscoelastic tissue. Difference between the rate of deformation and the rate of recovery.
Indentation	Postero-anterior load applied to the spinous process of a vertebra to generate a force-displacement response.
Postero-anterior (PA) pressure	Manual technique used by clinicians to determine the mobility of spinal segments. Involves the application of a dorso-ventral load the spinous process of a vertebra, while assessing the stiffness response.
Spinal stiffness	For the purpose of this thesis, spinal stiffness will refer to the ratio of the change in force to the change in displacement.
Strain	The amount of deformation incurred by an object when a force is applied to it.
Stress	The magnitude of loading, equal to the force exerted divided by the area over which it is applied.
Stress relaxation	Viscoelastic tissue property. Gradual decrease in stress when tissues are loaded to a repeated or constant strain.

Viscoelasticity	Biological materials exhibit viscous and elastic properties when submitted to loading. The stress-strain response of viscoelastic materials is dependent on the rate at which the stresses and strains are developed in the tissues, and the recovery between repeated loads.

CHAPTER ONE

INTRODUCTION

1.1 Overview

Low back pain is an undeniably prevalent and costly condition. Spinal manipulation therapy is one of many conservative approaches used by physiotherapists and chiropractors in the treatment of low back pain. Although it is a common therapy, objective data evaluating the efficacy of spinal manipulation therapy are mixed, as is the case with other frequently used therapies [*Assendelft et al.,* 2003; *Bronfort et al.,* 2004]. Discrepancies in study results are due, in part, to the difficulty in controlling treatment techniques, and the shortage of standardized, quantifiable and relevant outcomes measures [*Bouter et al.,* 1998]. Therefore, in order to better understand the effects imparted by spinal manipulation therapy, further knowledge is needed regarding the different biomechanical parameters used in spinal manipulation therapy provision. Given the above, the objective of this thesis is to determine the effect of spinal manipulation therapy parameters on spinal stiffness. This information will enhance our understanding of the mechanical characteristics of spinal manipulation therapy and their mechanisms of action.

1.2 Background & Rationale

1.2.1 Low back pain prevalence and economic impact

Low back pain (LBP) is an undeniably prevalent and costly condition. In the United Kingdom, approximately 7% of the adult population consulted their general practitioner within a one year period because of LBP [*Wynne-Jones et al.,*

2008]. A United States National Health survey revealed that 26% of respondents reported LBP lasting at least an entire day over the last 3 months [*Deyo et al.,* 2006]. These reports from other countries are consistent with a Canadian study suggesting that the three month prevalence of LBP is about 28%, of which, 11% had been disabled by LBP in the previous 6 months [*Cassidy et al.,* 1998]. In terms of cost, consultations and associated patient care expenses in the United States created total health care costs for back pain in 1998 of approximately $91 billion USD [*Luo et al.,* 2004]. In addition to the significant burden on the health care system, national labor productivity losses were estimated at $28 billion for 1996 in the United States [*Rizzo et al.,* 1998]. Because less than 33% of patients who consult for LBP fully recover after three months and most still have some pain after 12 months, long and/or incomplete recoveries could account for such high morbidity [*Croft et al.,* 1998].

1.2.2 Spinal manipulation therapy intervention for LBP

Spinal manipulation therapy (SMT) is one of many conservative approaches commonly used by physiotherapists and chiropractors in the treatment of LBP which is recommended in recent LBP guidelines [*Raspe,* 2008]. It is a passive, high-velocity, low-amplitude thrust applied to a joint eliciting a displacement beyond its physiological limit of motion (active or voluntary range of motion), but within its anatomical limit [*Maitland GD,* 2001]. SMT can be applied manually or mechanically by contacting the overlying skin of the identified vertebra and then applying a rapid force [*Haldeman,* 2004]. Although it is a common therapy, evidence regarding the efficacy of SMT is mixed [*Assendelft et al.,* 2003; *Bronfort et al.,* 2004], as is the case with other frequently used therapies such as massage, acupuncture and modalities [*Raspe,* 2008]. As a result, randomized controlled trials and subsequent systematic reviews investigating the relative effectiveness of SMT and other therapies often lead to non-significant findings. [*Assendelft et al.,* 2004; *Assendelft et al.,* 2003; *Ernst*

and Canter, 2006]. Discrepancies are due, in part, to the complex and heterogeneous nature of LBP disorders, the difficulty in controlling treatment techniques, and the shortage of standardized, quantifiable and relevant outcomes measures [*Bouter et al.,* 1998]. For example, a previously validated clinical prediction rule (CPR) has identified a subgroup of patients who demonstrate significant improvements in pain and function following a specific SMT [*Child et al,.* 2004]. In a subgroup of patients identified by this CPR, Cleland et al. noted greater pain and disability improvements following either of two thrust techniques (SMT) compared to a non-thrust technique [*Cleland et al.*, 2007; *Cleland et al.*, 2009]. This study highlights the likely importance of SMT parameters of application. Therefore, in order to better understand the effects imparted by SMT, further knowledge is needed regarding the different biomechanical parameters used in SMT provision.

1.2.3 Spinal stiffness as a biomechanical outcome

Spinal stiffness is a biomechanical property that is thought to be relevant to LBP. In some cases, spinal stiffness has been associated with severity of LBP symptoms [*Latimer et al.,* 1996; *Colloca and Keller,* 2001], the presence of vertebral degeneration [*Kawchuk et al.,* 2001], paraspinal muscle activity in the presence of dysfunction [*Shirley et al.,* 1999] and likelihood of improvement following SMT [*Flynn et al.,* 2002]. Clinicians who perform SMT and other manual therapy interventions (manual therapists) believe that full postero-anterior (PA) mobility is necessary for normal and painless spinal movements [*Magee,* 2002; *Maitland GD,* 2001].

Given this association, stiffness is commonly assessed by clinicians. Clinically, spinal stiffness assessment is performed by manually applying PA pressures to spinal segments and assessing the perceived force and displacement response. However, the detection of significant spinal stiffness changes can be

problematic. Using manual PA pressure techniques, clinicians have been unable to accurately or reliably perceive changes in the force displacement relationship [*Bjornsdottir and Kumar,* 2003], to judge spinal stiffness [*Maher and Adams,* 1994], and to apply consistent forces [*Simmonds et al.,* 1995]. Consequently, clinicians are unlikely to detect changes in stiffness responses following therapies. To reliably quantify spinal stiffness, investigators have therefore developed various mechanical devices [*Latimer et al.,* 1996; *Edmondston et al.,* 1998; *Kawchuk et al.,* 2006; *Owens et al.,* 2007; *Tuttle et al.,* 2008]. These devices perform automated indentation to simulate PA pressures while collecting force and displacement data. They all offer highly reliable measurements, although none offer sufficiently small components to accommodate small animal model studies or perform both the high and the low loading rates required for SMT and stiffness measurements, respectively.

Many factors causing variations during PA stiffness measurement have been identified; they include intra-abdominal pressure changes due to breathing, muscular response, patient position, and device repositioning error [*Kawchuk and Fauvel,* 2001]. These factors, as well as the heterogeneity of the subjects and LBP disorders, may explain why investigations into the effects of SMT have often been unable to detect significant changes in stiffness, even when assessed mechanically [*Allison et al.,* 2001; *Tuttle et al.,* 2009].

1.2.4 SMT mechanisms behind stiffness changes

Restoration of lumbar mobility by decreasing spinal stiffness is believed to be one of the fundamental mechanisms behind the effects of SMT on LBP [*Maitland GD,* 2001]. Some studies have shown that manual therapy interventions could decrease local stiffness and improve range of motion (ROM) [*Fernández-de-las-Peñas et al.,* 2007] in the presence of hypomobility [*Tuttle et al.,* 2008]. Biomechanical and neurophysiological theories have been proposed to explain

the mechanisms by which SMT affects spinal stiffness. Biomechanically, it is believed that SMT distracts the facet joints and stretches the joint capsule and surrounding spinal tissues through a high rate of loading [*Brodeur,* 1995]. Because of the rate-dependant viscoelastic properties of spinal soft tissues, the fast loading from SMT generates greater tissue strains [*Gal et al.,* 1997; *Ianuzzi and Khalsa,* 2005] which may break adhesions and restore mobility [*Isaacs et al.,* 2002]. Neurologically, the novel strains created by SMT have been found to influence local neural responses [*Colloca et al.,* 2004] leading to altered stimulation of the somatosensory system, the pain processing system, and the motor system [*Pickar,* 2002] (see section 2.8). These various changes in neural response following SMT could contribute to reduction of abnormal muscle activity [*Colloca and Keller,* 2001] and therefore decrease stiffness [*Shirley et al.,* 1999]. Although biomechanical and neurophysiological effects are described separately here, they are thought to interact to cause changes in stiffness. This interaction has made the investigation of the contribution of each of these mechanisms challenging. One outcome from this challenge has been a shortage of clinical evidence supporting these different theories which, given current investigational tools, are best investigated through cadaver and animal models.

1.2.5 SMT parameters

It is assumed that the mechanical characteristics or parameters of SMT application techniques modulate both neurophysiological and biomechanical mechanisms, which lead to changes in spinal stiffness. SMT is typically applied at the end of the physiological range of motion after first preloading the tissues. As a result, greater forces can be effectively transmitted causing greater periarticular tissue stretch. Studies have shown that SMT applied at a greater force produced greater vertebral accelerations [*Keller et al.,* 2006], displacements, and electromyographic (EMG) responses [*Colloca et al.,* 2006]. To investigate the neurophysiological effects of SMT parameters, Pickar and

Kang (2006) used a feline model to measure the neurological potentials evoked by mechanically simulated SMTs. They observed greater discharge frequencies from lumbar paraspinal muscle spindles with SMT durations below a threshold of about 200ms (i.e. faster manipulations) [*Pickar and Kang,* 2006; *Pickar et al.,* 2007]. Patient positioning [*Cramer et al.,* 2002; *Caling and Lee,* 2001], location and direction of loading [*Caling and Lee,* 2001; *Kawchuk and Perle,* 2009] are parameters also believed to affect the outcome of SMT; therefore, they should be measured or controlled to fully characterize SMT application

Although previous research has described various SMT characteristics including preload, force, displacement and duration [*Herzog et al.,* 1993; *Pickar et al.,* 2007; *Pickar and Kang,* 2006; *Snodgrass et al.,* 2006; *Ianuzzi and Khalsa,* 2005; *Colloca et al.,* 2006], no studies have quantified optimal SMT parameters or their specific contribution to these potential mechanisms of effect. A feline model has been previously developed to systematically investigate the effect of SMT loading parameters on neural outputs [*Pickar,* 1999; *Pickar,* 2002; *Pickar and Kang,* 2006; *Pickar et al.,* 2007]; however stiffness outcomes were not measured.

1.3 Definition of the Problem

Although it is believed that stiffness changes produced in response to neurophysiological and biomechanical mechanisms are central to the SMT paradigm, the impact of the various parameters which make up SMT application are not understood fully. There is a clear need to systematically measure the effect of SMT loading parameters on an outcome related to SMT that can be quantified such as spinal stiffness. Although clinical trials can determine the impact of interventions on clinical outcomes, clinicians are unable to provide adequate control over each SMT parameter and various factors (described in section 2.5) affecting spinal stiffness cannot be controlled in human subjects. In

light of these facts, SMT parameters must be individually controlled and their impact on spinal stiffness must be mechanically assessed in controlled in-vivo conditions.

1.4 Significance of Study

It is essential to enhance our understanding of the mechanical characteristics of SMT and their impact on stiffness. This information will contribute to defining the systems affected by SMT and quantifying optimal loading parameters. Findings from this study could also provide a rationale for imposing control over specific aspects of SMT interventions in future trials which could lead to improved therapeutic outcomes.

1.5 Objectives

The objectives of the current research are to adapt Pickar et al.'s feline model and SMT device to perform reliable PA stiffness measurements, and to investigate how SMT parameters influence the segmental stiffness response. The specific aims of this thesis are as follows:

Aim 1: Adapt Pickar et al.'s SMT device to quantify PA stiffness and establish its reliability.

Aim 2: Determine the effect of SMT duration and displacement on spinal stiffness of a feline preparation.

Aim 3: Determine the effect of SMT duration and force on spinal stiffness of a feline preparation.

1.6 Hypotheses

The research hypotheses in relation to the aims described above are based on current knowledge from a review of the literature. The hypotheses are as follows:

Hypothesis 1: A device capable of providing indentations using variable application rates of force or displacement will be successfully adapted to provide highly reliable [*Portney and Watkins,* 2008] postero-anterior stiffness measurements during repeated tests of inanimate objects expected to have linear stiffness behavior.

Hypothesis 2: A threshold SMT duration and displacement approximating those values applied clinically will result in a maximal change in spinal stiffness in the presence or absence of a preload.

Hypothesis 3: A threshold SMT duration and force approximating those values applied clinically will result in a maximal change in spinal stiffness in the presence or absence of a preload.

1.7 Thesis Overview

This thesis is comprised of four chapters. A focused literature review is presented in Chapter 2; its topics include: anatomy and function of the lumbar spine, relationship between stiffness and LBP, issues with SMT research, measurements of stiffness, analysis of stiffness data, theories of mechanisms of effect of SMT, and mechanical parameters of SMT. These topics are discussed within the context of how they relate to SMT research, SMT parameters and spinal stiffness. Chapter 3 addresses Aim 1 and has been constructed around a manuscript that has been accepted for publication. Finally, Chapter 4 addresses Aims 2 and 3 and has been constructed as a manuscript to be submitted for publication. This chapter will also include a discussion of the strength and limitations of the project as well as the future investigations likely to evolve from this work.

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CHAPTER TWO

LITERATURE REVIEW

The objective of this thesis is to investigate how SMT parameters influence the local biomechanical response by adapting Pickar et al.'s feline model [*Pickar,* 1999] and SMT device to perform reliable postero-anterior (PA) stiffness measurements. The following is a contextual review, guided by the aims of this thesis. The topics presented are therefore discussed in relation to SMT research, SMT parameters and spinal stiffness.

2.1 Anatomy and function of the lumbar spine

Panjabi proposed that spinal structures could be divided into three subsystems that interact to regulate the stability of the human spine: 1) the passive subsystem composed of the ligaments and vertebrae, 2) the active subsystem composed of muscles and tendons, and 3) the neural control subsystem composed of receptors, nerves and the central nervous system [*Panjabi,* 1992]. These are represented in Figure 2.1. The components contained within each of the three subsystems will be defined, highlighting their contribution to spinal stability.

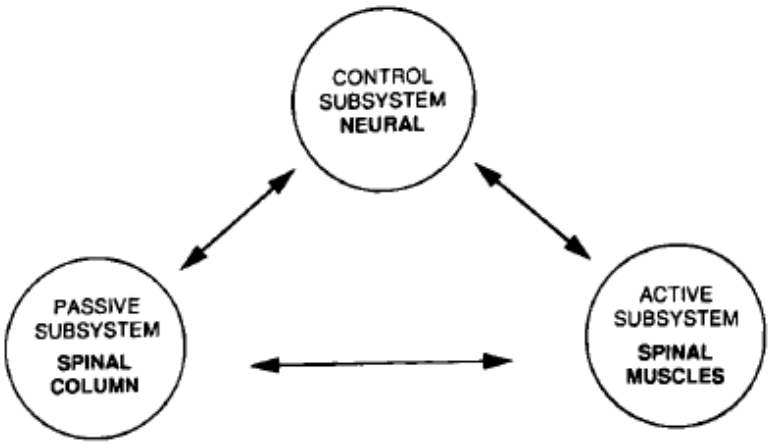

Figure 2.1 The spinal stability system consists of three subsystems: passive spinal column, active spinal muscles, and neural control unit, which interact to regulate the stability of the spine [*Panjabi,* 1992]**.**

2.1.1 Passive subsystem

Passive or non-contractile structures provide the base of support for other spinal components. Discs and ligaments connect five lumbar vertebrae, and together they provide rigidity while passively guiding movements of the lower trunk. Major passive components of the lumbar spine are shown in Figure 2.2 [*Adams MA et al.,* 2002]. The anterior elements of the bony spine are the vertebral bodies. They are separated by discs, which transfer the weight of the upper body between them, and allow movement to occur. The annulus is made up of collagen fibers organized to resist each spinal movement [*Adams MA et al.,* 2002]. Injury to the disc can initially lead to an increase in motion and an inflammatory reaction [*Goel et al.,* 1986; *Zhao et al.,* 2005], which would later lead to degeneration [*Kaigle et al.,* 1998; *Kawchuk et al.,* 2001].

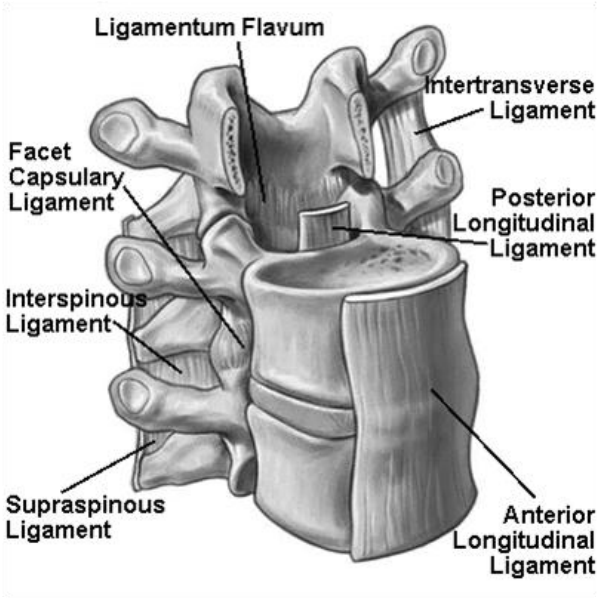

Figure 2.2 Lumbar ligaments. Discs and ligaments connect five lumbar vertebrae, and together they provide rigidity while passively guiding movement of the lower trunk [*Vertical Health*]**.**

The pedicles and laminae join with the vertebral body posteriorly to form the vertebral canal that houses the spinal cord. Inferiorly and superiorly, each lamina gives rise to articular facets (Figure 2.3). These articular facets play a critical role in guiding and limiting physiological movements. The inferior facets face antero-laterally to interlock with the postero-medially facing superior facets of the vertebra below. Although the shape of articular facets may vary, their curve and angle are conceived to limit forward translation. During extension, the inferior facets of the top vertebrae will glide downward onto the superior facets of the bottom vertebra. Further extension is stopped once the articular process impacts the lamina below [*Adams MA et al.,* 2002]. A joint capsule surrounds each facet joint and contributes to stability. Connective tissue rims, adipose tissue pads and fibro-adipose meniscoids are contained within the intra-articular space. It is believed that these intra-articular structures can break loose or get entrapped causing pain and limiting mobility [*Evans,* 2002].

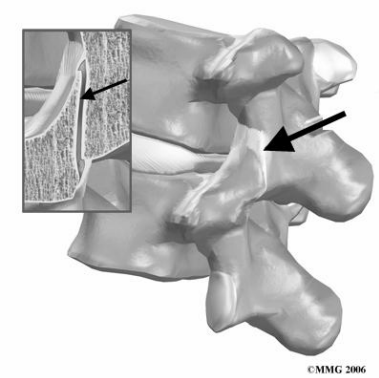

Figure 2.3 Lumbar facet joint. Articular facets play a critical role in guiding and limiting physiological movements. A joint capsule surrounds each facet joint and contributes to stability [*eOrthopod*]**.**

In addition to the disc and joint capsule, many other ligamentous structures provide support to the spinal column [*Adams MA et al.,* 2002]. The different components of the passive subsystem are engaged during specific spinal movements according to their shape and orientation to provide stability to the spine.

2.1.2 Active subsystem

Active or contractile tissues of the lumbar spine have been classified into two subgroups: the deep local muscles that attach directly on the vertebrae, and the larger, superficial global muscles that attach indirectly to the spine (Figure 2.4). These two muscle subgroups are believed to work together to provide control to the spine by generating forces which can limit motion [*Cholewicki et al.,* 1997; *Richardson C et al.,* 2004].

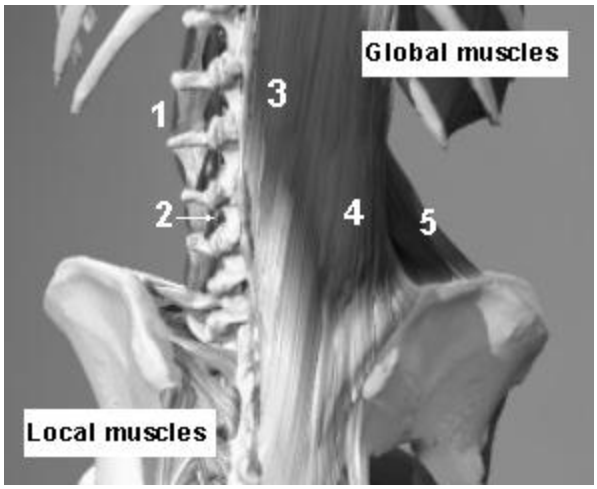

Figure 2.4 Posterior lumbar muscles. Contractile tissues of the lumbar spine have been classified into two subgroups: the deep local muscles (left) that attach directly on the vertebras, and the larger, superficial global muscles (right) that attach indirectly to the spine [*anatomy.tv*]**. Numbers 1, the intertransverse, and 2, the interspinous, are examples of deep local muscles. Numbers 3, the longissimus, 4, the iliocostalis, and 5, the quadratus lumborum, are examples of the global muscles.**

The deep, segmental attachments of the local muscles provide proprioceptive information which is relayed and processed by the neural system to provide motion control essential to the stability of the spine [*Panjabi,* 1992]. The intervertebral muscles, the multifidus, the transversus abdominis, the diaphragm and the pelvic muscles are proposed members of the local muscle group. The intertransverse muscles attaching to the transverse processes and the interspinales muscles attaching to the spinous processes are too small to generate relevant forces, but their dense concentration in mechanoreceptors suggests that they provide important proprioceptive information [*Adams MA et al.,* 2002]. The diaphragm and pelvic floor muscles are also proposed as components of the local system because of their role in modulating intra-abdominal pressure [*Hodges et al.,* 2003; *Richardson C et al.,* 2004]. The multifidus and transverse abdominis are important components of the local system. It is proposed that the transversus abdominis can increase spinal stiffness by increasing tension on the thoraco-lumbar fascia or by increasing intra-abdominal pressure [*Hodges et al.,* 2003]. The multifidus is also believed to

play an important role in regulating spinal stability and significantly decreasing extension range of motion (ROM) [*Wilke et al.,* 1995]. Although the multifidus has been shown to atrophy [*Hides et al.,* 1994; *Barker et al.,* 2004] and lose its ability to control the spine in the presence of pain [*Kong et al.,* 1996]; some studies have shown an increase in their electromyographic (EMG) activity with nociceptive stimulation of the disc and facets [*Idahl A et al.,* 1995].

The muscles of the global system (superficial) cross multiple segments, their main function is to move the spine, although they can co-contract to stabilize the spine without creating movement [*Richardson C et al.,* 2004]. The muscles of the global system can be grouped according to their location in relation to the spine. The anterior group includes the psoas major, quadrates lumborum and abdominal muscles; the posterior group includes the extensors [*Adams MA et al.,* 2002].

In addition to their active function, spinal muscles also limit mobility through their passive length or extensibility. Muscles that are immobilized or shortened for a prolonged period will further restrict mobility, because the number of sarcomeres (titin) they contain will decrease and the bonds (actin and myosin) that connect them increase [*Lundy-Ekman,* 2002].

2.1.3 Neural subsystem

The neural subsystem consists of various sensory receptors (e.g. mechanoreceptors) located in the ligaments, muscles and tendons, and of the peripheral and central nervous system (CNS) [*Panjabi,* 1992]. The peripheral nervous system begins where the nerve roots split off from the spinal cord to enter the intervertebral foramen formed by the pedicles of adjacent vertebrae. The dorsal and ventral nerve roots merge to form the spinal nerve, which contains both sensory and motor fibers. The nerves will further divide and

combine to supply spinal muscle compartments lower limb structures, and ligaments. The outer third of the intervertebral disc, the facet joint capsule and the segmental intervertebral muscles are richly innervated by local nerve plexus [*Adams MA et al.,* 2002]; they can therefore elicit pain responses and provide proprioceptive information.

The nervous system receives and analyses proprioceptive and nociceptive information from the mechanoreceptors contained within ligaments and muscles. Feedback responses are sent back to the active subsystem, which adjusts the position of the spinal column through the level and pattern of muscle activation. In a healthy and functional stability system, the joint-ligament complex allows full ROM and provides feedback to the neural system, which regulates muscle activation, allowing full, controlled motion of the spine to occur (Figure 2.5) [*Panjabi,* 1992; *Panjabi,* 2006].

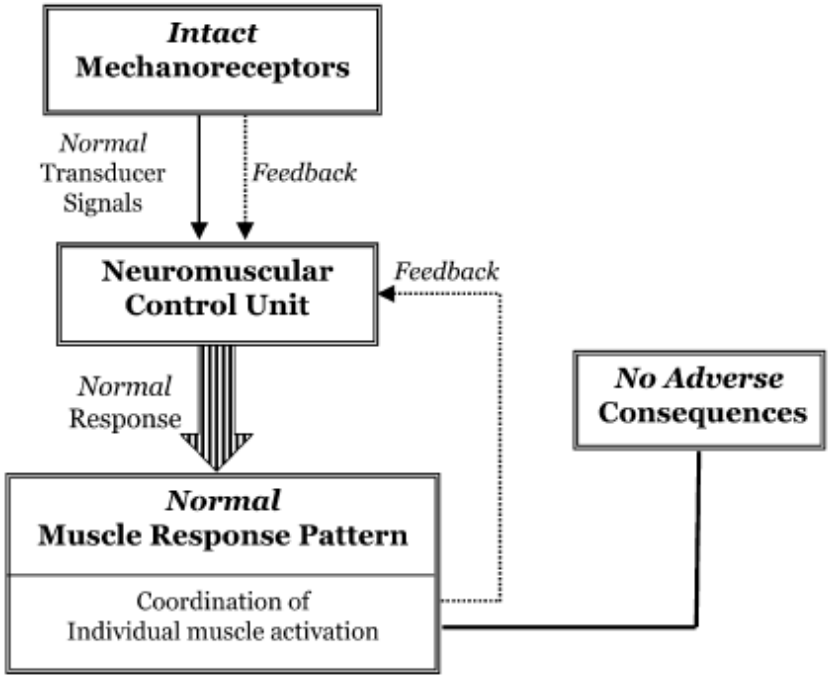

Figure 2.5 Normal spinal system. The intact mechanoreceptors send signals to the neuromuscular control unit for analyses. Signals are sent back to coordinate the activation response of individual spinal muscles. There is feedback from the muscle spindles and golgi tendon organs of the muscles and mechanoreceptors of the ligaments to the neuromuscular control unit. Under normal circumstances there are no adverse consequences [*Panjabi,* 2006]**.**

2.1.3.1 Effect of injury on the spinal stability system

In the presence of pain and injury, the spinal unit becomes dysfunctional. Injury to the passive subsystem may initially create excessive and abnormal segmental mobility [*Abumi et al.,* 1990; *Goel et al.,* 1986] through disruption of proprioceptive input or decreased ligamentous support [*Panjabi,* 2006]. In an attempt to decrease movement and loading of injured structures, the neural system will increase global muscle activation [*Silfies et al.,* 2005; *Panjabi,* 2006], potentially producing excessive, misdirected forces [*Richardson C et al.,* 2004] which contribute to degeneration and fatigue [*Elfving et al.,* 2003]. Nociceptive signals can also disrupt proprioceptive information sent to the neural system [*O'Sullivan et al.,* 2003; *Solomonow,* 2009] resulting in inadequate feedback information to the muscle control system [*Leinonen et al.,* 2003; *Leinonen et al.,* 2002] and subsequent levels and patterns of adjustments (Figure 2.6) [*Brumagne*

et al., 2000]. Passive, active and neural subsystems interactions are therefore crucial in providing adequate regulation of spinal stability [*Panjabi,* 2006].

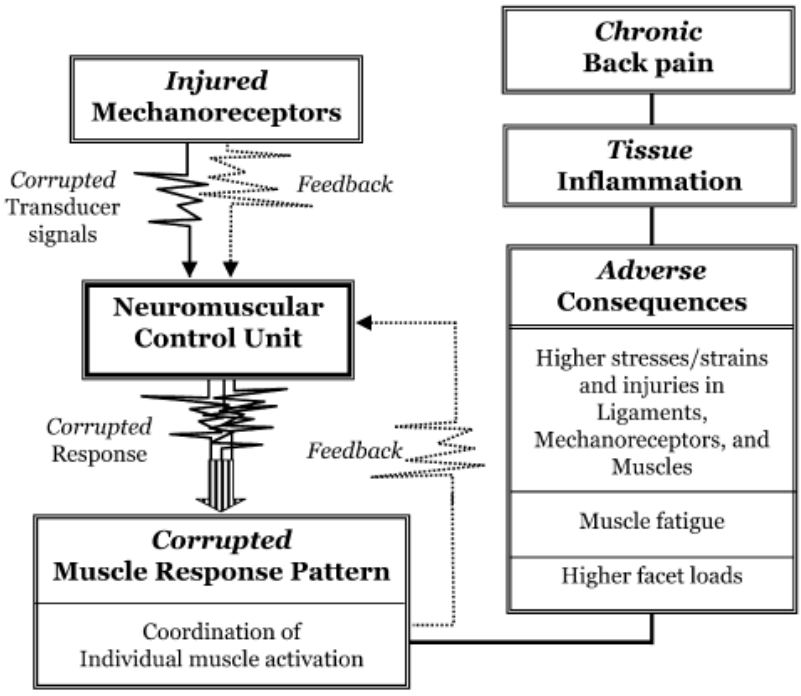

Figure 2.6 Injuries of the ligaments. The injured mechanoreceptors send out corrupted input signals to the neuromuscular unit. As a result, the neuromuscular system sends a corrupted response, which can produce excessive misdirected forces. There are adverse consequences: higher stresses, strains and even injuries to the ligaments, mechanoreceptors, and muscles [*Panjabi,* 2006]**.**

2.1.3.2 Relation between the integrity of the spinal stability system and spinal stiffness

Spinal stiffness is the resistance generated by spinal components to restrict spinal displacement. Although spinal rigidity is essential to protect the integrity of spinal structures, excessive rigidity resulting from improper feedback-control will limit mobility and may lead to dysfunction. Injury at any level of the spinal system can alter the stiffness of the spine and contribute to spinal pathology [*Kong et al.,* 1996].

2.2 Relation between stiffness and low back dysfunction

Panjabi's model highlights the integrated function of each subsystem in providing mobility and stability to the spine, as well as the impact of any level of disruptions on this function. Increased stiffness was found to be a measurable outcome associated with low back pain (LBP) symptoms, relevant to classification into appropriate treatment approaches [*Flynn et al.,* 2002; *Fritz et al.,* 2005], and subject to change following intervention [*Tuttle et al.,* 2008; *Fernández-de-las-Peñas et al.,* 2007]. The following section presents the evidence linking low back dysfunction and stiffness.

2.2.1 Stiffness and LBP

Spinal stiffness has been associated with LBP symptoms. Latimer et al. noted that patients experiencing LBP presented with higher PA stiffness compared to when their pain had resolved by more than 80% [*Latimer et al.,* 1996]. Colloca et al. obtained similar results; patients with frequent and consistent LBP symptoms presented with greater PA stiffness when compared to patients with infrequent intermittent symptoms [*Colloca and Keller,* 2001]. Tuttle noted greater variations in stiffness on tender sides than on control sides of a cervical segment. Force displacement (FD) curves from tender sides were also significantly different from control sides [*Tuttle et al.,* 2009]. Although these studies had small sample sizes ($n<30$) they show a link between spinal stiffness and patient symptoms.

2.2.2 Stiffness and pathophysiology

A more direct relationship between spinal stiffness and spinal pathology is demonstrated in Kawchuk et al.'s study. Increased postero-anterior (PA) stiffness was associated with degeneration caused by surgically induced injury to the disc in a porcine model [*Kawchuk et al.,* 2001]. This suggests that scar tissues, adhesions and degeneration can form in injured or dysfunctional tissues,

increasing stiffness [*Kawchuk et al.,* 2001; *Kaigle et al.,* 1998]. Conversely, an alteration in spinal mobility can induce pathological changes. Cramer et al. immobilized facet joints in a rat model, which induced degenerative changes [*Cramer et al.,* 2004]. Immobilization leads to many detrimental changes of articular tissues: shortening of collagen fibers, periarticular fibrosis, and articular cartilage atrophy [*Herzog,* 2000]. Furthermore, hypomobility of one segment due to improper muscle recruitment or passive limitation can overload adjacent segments and pose further risk to the spine [*Little et al.,* 2004]. Stiffness is therefore an integral part of the LBP, pathophysiology, and dysfunction cycle.

2.2.3 Abnormal muscle activation among LBP patients

In contrast with passive structures, the involvement of muscle activation levels in LBP pathophysiology and stiffness is less clear. Abnormal paraspinal muscle activation or spasms have been observed in some patients with LBP in static and in dynamic positions. Fryer et al. recorded EMG activity in the deep thoracic paravertebral muscles of LBP patients. Higher mean EMG activity was detected at sites reported as tender compared to normal (non-tender) sites with patients in different positions [*Fryer et al.,* 2006]. Ambroz et al. also measured EMG signals of lumbar spinal muscles. EMG levels in chronic LBP patients were three times higher during static standing and two times higher during flexion and re-extension compared to those of matched controls [*Ambroz et al.,* 2000]. In healthy subjects, the paravertebral muscles are typically silenced during flexion, a phenomenon called the flexion-relaxation response. A stretch inhibition reflex is believed to cause relaxation of the paravertebral muscles transferring the extension moment to the passive structures. Mak et al. also noted decreased sitting flexion-relaxation response in LBP patients compared to healthy subjects [*Mak et al.,* 2010]. These findings suggest improper muscle relaxation during trunk flexion in addition to higher muscle activation in static postures, which can contribute to lumbar PA stiffness [*Shirley et al.,* 1999; *Hu et al.,* 2009].

A few theories have been proposed to describe the mechanism behind abnormal muscle activation. Studies by Idahl et al. and by Solomonow et al. suggest that dysfunction of paraspinal structures could elicit a protective reflex muscle activation [*Idahl A et al.,* 1995; *Solomonow et al.,* 1998]. Johansson and Sokja proposed another hypothesis to explain the pathophysiological mechanisms behind the origin and perpetuation of muscle pain and activation in chronic musculoskeletal pain syndromes. They suggested that increased activity of the muscle afferents (group III and IV) was induced by the presence of metabolites (e.g. lactic acid) formed by static muscle contractions (spasm). This increased activity would lead to increased stretch sensitivity, therefore, further muscle activation (through gamma-motoneuron activation) and metabolite production, perpetuating a pain/spasm/pain cycle [*Johansson and Sojka,* 1991]. To study the spindle sensitization hypothesis, Pedersen et al. injected bradykinin (a chemical promoting the inflammatory response) into feline splenius and trapezius muscles. They found increased static stretch sensitivity of the muscle spindle afferents [*Pedersen et al.,* 1997]. In contrast, two studies later failed to substantiate the theory of chemically induced muscle spindle sensitivity [*Kang et al.,* 2001; *Zedka et al.,* 1999]. The authors suggested that pain elicited a guarding behavior which could be voluntarily overcome by patients to allow normal movements to be performed [*Zedka et al.,* 1999]. However, the ligamentous structures in these studies remained intact, no injury was created, therefore no protection was required.

Panjabi's model integrates these different mechanisms. He suggests that injury to the spine would corrupt the proprioceptive input from the mechanoreceptors, resulting in mismatched interpretation and response from the neuromuscular system, causing improper muscle recruitment patterns and level of activation, further disrupting mechanoreceptor input (Fig 2.6) [*Panjabi,* 2006]. Different

methodologies, subjects and injuries could explain the lack of agreement on the exact mechanism responsible. However, there is evidence to support the presence of abnormal increases in paraspinal muscle activity following injury [*Mak et al.,* 2010; *Idahl A et al.,* 1995] capable of altering lumbar PA stiffness [*Shirley et al.,* 1999; *Hu et al.,* 2009].

2.2.4 Summary

Divergent evidence has been presented in this and the prior section. Altered muscle recruitment patterns including both increased and decreased muscular activity has been observed in the presence of LBP and dysfunction [*Silfies et al.,* 2005], as well as hypermobility, atrophy, and instability. Although these observations appear to contradict our premise that increased stiffness is a crucial component of spinal dysfunction, they simply reflect the complex and heterogeneous clinical presentation of LBP. Hyper and hypomobility can coexist within one patient [*Fritz et al.,* 2005], or characterize different subgroups of patients [*Brennan et al.,* 2006], although evidence suggests a greater prevalence of hypomobility (71% vs 11%) [*Fritz et al.,* 2005].

2.3 Issues in research on SMT for LBP

The literature has identified numerous structures from which LBP can originate [*Bogduk,* 1995], and an equal abundance of diagnostic terms [*Spitzer,* 1987; *Bernard and Kirkaldy-Willis,* 1987]. Yet, pain and dysfunction etiology often remain unspecified because, among other things, clinical findings are not corroborated by diagnostic imaging [*Boden et al.,* 1990; *Jensen et al.,* 1994; *Peterson et al.,* 2000]. Bouter et al. reviewed and discussed some of the methodological issues relating to LBP research. They attributed previous failures to lack of definition for low back pain, the pooling of heterogeneous groups of

patients, the difficulty in controlling or measuring confounders and treatment techniques, and the shortage of sensitive and valid outcomes measures [*Bouter et al.,* 1998]. Similar issues are encountered in clinical trials and randomized controlled trials of SMT for LBP [*Jüni et al.,* 2009; *Hancock et al.,* 2007]. These issues, which frequently contribute to inconclusive findings, will be discussed in this section.

2.3.1 Heterogeneity of LBP patients

Patients with different characteristics will respond differently to SMT [*Brennan et al.,* 2006]; therefore, appropriate inclusion of homogenous patient groups is crucial for clinical trials. Delitto criticized RCTs published between 1995 and 2005 that failed to isolate subgroups of LBP patients, compromising the ability to determine the effectiveness of specific interventions [*Delitto,* 2005], and to identify key patient characteristics that determine suitability for treatment. Subgrouping according to patho-anatomic diagnosis is difficult because of the many structures from which LBP can originate [*Bogduk,* 1995], and the lack of corroboration of clinical findings with diagnostic imaging [*Boden et al.,* 1990; *Jensen et al.,* 1994]. Additionally, discrepancies in the definition of chronicity [*Cedraschi et al.,* 1999], in the determination and report of progression, and the unpredictable natural history of LBP invalidate classifications based on duration of symptoms [*Hestbaek et al.,* 2003]. These disparities and the use of cohorts of patients at diverse stages in their recovery limit the comparisons between trials.

Symptom and treatment based classifications have been proposed to overcome this issue and provide a simpler and clinically useful alternative [*Spitzer,* 1987; *Werneke and Hart,* 2001; *Flynn et al.,* 2002; *Brennan et al.,* 2006]. Detailed clinical prediction rules (CPR) for matching patients with SMT specifically were developed earlier by Flynn et al. [*Flynn et al.,* 2002]. Patients presenting with non radicular LBP were thoroughly assessed and then underwent a standardized

SMT. Five assessment variables predictive of success with SMT were identified: symptom duration <16 days, low fear avoidance beliefs, >35^{o} hip internal rotation ROM, no symptom distal to the knee, and hypomobility of one or more lumbar levels. This CPR was later validated; patients fitting the CPR who received SMT early in the course of an acute LBP episode required fewer treatments and presented with transient, less severe symptoms [*Fritz et al.,* 2006; Childs, 2004].

2.3.2 Treatment parameters

SMT techniques are defined by the manner in which they are applied; amplitude, speed, duration, position, range, and location are among the primary parameters. As for other treatments, it can be assumed that the dosage and parameters of application of SMT impacts its potency mediated by its mechanisms of action. SMT should be dosage and technique specific in order to optimize the treatment effect on different patient conditions [*Maitland GD,* 2001; *Isaacs et al.,* 2002]. For example, Haas et al. found that patients receiving a greater number of SMT treatment sessions (greater dosage) had greater pain improvements, suggesting a potential dosage response [*Haas et al.,* 2004]. Cleland et al. noted greater pain and disability improvements following either of two thrust techniques (SMT) compared to a non-thrust technique in a subgroup of patients identified by the CPR as potential responders to SMT [*Cleland et al.,* 2007; *Cleland et al.,* 2009]. These studies highlight the likely importance of SMT parameters; however, in depth investigations providing complete control over the amplitude and duration of each parameter, which could not feasibly be controlled clinically, are needed to quantify their individual roles in affecting patient outcomes. A thorough discussion into SMT parameters will be presented in Section 2.8.

2.3.3 Outcome measures

Scales and measurement tools are used to quantify patient response to treatment such as pain, function and ROM. These outcome measures are designed to determine baseline levels, progress and, ultimately, effectiveness of intervention. The different methods which are used to measure the outcomes of SMT can also produce variable findings. There are currently over a hundred different measurement tools and scales to assess SMT and LBP outcomes, but lack of validity or responsiveness may hinder their ability to detect changes [*Boyling JD and Jull GA,* 2004]. As described in section 2.2, stiffness is a valid LBP outcome [*Colloca and Keller,* 2001; *Latimer et al.,* 1996; *Kawchuk et al.,* 2001]. Stiffness can also be accurately assessed by mechanical devices [*Latimer et al.,* 1996; *Edmondston et al.,* 1998]. Furthermore, the presence of spinal hypomobility was found to have a strong predictive validity for success following SMT as part of a set of clinical prediction rules and independently [*Fritz et al.,* 2005; *Flynn et al.,* 2002]. Specific stiffness testing instruments and their respective reliability and sensitivity will be described in section 2.4.

2.3.4 Systematic reviews of SMT trials

The pooling of heterogeneous patients, techniques and outcomes in research reports through systematic reviews frequently provides little evidence to the relative efficacy of SMT and other therapies [*Assendelft et al.,* 1996; *Ernst and Canter,* 2006]. The issues presented previously are carried over and new ones are introduced. For instance, Assendelft et al. concluded in a meta-analysis that SMT presented moderate effectiveness that was not superior to other therapies [*Assendelft et al.,* 2003]. Conversely, Bronfort et al. argued that a case by case approach to select and critique papers should be employed. They reviewed RCTs that included 10 or more subjects per group who received SMT or mobilizations, were assessed using patient oriented primary outcome measures, and met criteria for validity and statistical significance; they concluded that there was

moderate evidence favoring the use of SMT over other therapies in the treatment of LBP [*Bronfort et al.,* 2004]. As the results from these systematic reviews demonstrate, there are a number of limitations in the development, generalization and application of evidence from reviews in LBP disorders. Inconsistencies and lack of consensus offer little guidance for clinical practice.

2.3.5 Summary

Though existing SMT evidence may be controversial, there is a moderate body of evidence supporting its use. Using less stringent methodologies, authors have shown improved patient satisfaction, pain and disability from SMT of the lumbar, thoracic and cervical spine [*Hertzman-Miller RP et al.,* 2002; *Koes et al.,* 1992; *Haas et al.,* 2004; *Cleland et al.,* 2005; *Cleland et al.,* 2007]. However, the studies by Flynn et al. described earlier, which used a CPR to identify patients suited for SMT, offer some of the strongest evidence favoring SMT [*Flynn et al.,* 2002; *Fritz et al.,* 2006; *Cleland et al.,* 2009]. Because of the numerous issues involving clinical trials and their inability to provide insight into the "active ingredient", reductionist models (basic science research) should be considered to further investigate treatment mechanisms.

2.4 Methods of assessing spinal stiffness

2.4.1 Manual methods of assessing spinal stiffness

Clinicians commonly assess spinal stiffness when investigating complaints of LBP. They do so by applying a manual PA force to the spine with the patient lying prone. The resulting amount of movement indicates the presence of hypo or hyper- mobility or the spinal stiffness [*Riddle,* 1992]. These PA forces are used to assess accessory movement or joint play, small movements that can only be performed by a passive glide of the interveterbral joints. Manual therapy

approaches advocate that full accessory movement is necessary for normal painless spinal movement [*Magee,* 2002], and that the assessment of intervertebral mobility is central to identifying the need for mobilization/manipulation interventions [*Magee,* 2002; *Maitland GD,* 2001]. Manual PA stiffness assessments have proven to be useful to locate hypomobile segments [*Fernández-de-las-Peñas et al.,* 2005] and assign patients to appropriate treatment groups [*Fritz et al.,* 2005]. Experts agree that general manual mobility ratings are useful and valid for diagnostic and treatment planning [*Bullock-Saxton J et al.,* 2002; *Humphreys BK et al.,* 2004]; however, manual grading of specific spinal stiffness values is not sensitive enough to detect small treatment effects.

Maher and Adams reported that judgments of stiffness had poor reliability with intra class correlation coefficient (ICC) values for PA stiffness estimates of the lumbar spine ranging from 0.03 to 0.37 [*Maher and Adams,* 1994]. Simmonds et al. reported that clinicians were also unable to accurately apply force and perceive resultant displacements [*Simmonds et al.,* 1995]. Nicholson et al. suggested that the poor reliability in manual stiffness assessments of *in vivo* tissues may be due to the difficulty in judging viscoelastic soft tissues which exhibit rate-dependent loading responses, and creep [*Nicholson LL et al.,* 2003]. Therefore, indentations applied at different rates would yield different stiffness values and repeated indentations would cause fluid losses, which would also cause stiffness values to increase [*Lee and Evans,* 1992; *Nordin and Frankel,* 2001].

As a result, others have attempted to standardize manual PA stiffness assessments to improve reliability and accuracy. Bjorndottir and Kumar demonstrated that a spinal model and an oscilloscope could be used as training tools to significantly improve the accuracy of displacement perception because

clinicians were unable to accurately or reliably perceive changes in the force displacement (FD) relationship [*Bjornsdottir and Kumar,* 2003]. Binkley et al. used a 9 point mobility assessment scale so that stiffness could be rated objectively, but mobility ratings had poor reliability (ICC: 0.25) [*Binkley J et al.,* 1995]. Chiradejnant et al. developed a reference device to provide 11 standard comparison points against which spinal stiffness could be matched [*Chiradejnant et al.,* 2003]. This resulted in increased reliability with a reported ICC of 0.74. Fritz et al. proposed rating the entire lumbar spine as hyper or hypomobile instead of rating individual segments, which also improved reliability [*Fritz et al.,* 2005].

The statistical effect size following SMT is typically small [*Boyling,* 2004]. Without the ability to accurately and reliably detect small stiffness differences, clinicians may not be sensitive enough to perceive changes caused by SMT. Better accuracy in quantifying PA stiffness is necessary so that significant differences in stiffness conditions can be detected.

2.4.2 Mechanical methods of assessing spinal stiffness

Various mechanical PA stiffness testing devices have been developed to enhance the objectivity of PA spinal stiffness assessments. These devices perform automated indentation to simulate PA pressures while collecting force and displacement data. Their performance has been established by measuring the stiffness of beams, cadaveric spines, and live subjects.

Specifically, Lee and Svensson developed the Spinal Physiotherapy Simulator [*Lee and Svensson,* 1990] (SPS) which they reported as having a ICC of 0.88 for stiffness coefficients calculated from the linear portion of the FD curve obtained in asymptomatic subjects. The validity of the SPS was also evaluated by determining its ability to assess the true stiffness of an aluminum beam, which

confirmed stiffness values to be within 1% of the true value. Developing on the success of this project, Lee and Evans developed the Spinal Mobiliser [*Lee and Evans,* 1992] to investigate the effect of the PA loading characteristics and relative intervertebral mobility. The Spinal Mobiliser applied loads to the surface of the skin overlying the selected lumbar vertebra and measured displacements of the indenter over the adjacent vertebra providing an ICC of 0.95 for maximal displacements. Using this device, Lee and Evans were able to detect a significant increase in mobility from L3 to L5. Although both the SPS and the Spinal Mobiliser provided highly reliable measurements of PA stiffness others have commented that the technology is bulky [*Latimer et al.,* 1996] and difficult to operate [*Kawchuk et al.,* 2006].

Latimer et al. improved upon these initial devices by developing a smaller, portable device that could be used in clinics to assess symptomatic LBP subjects [*Latimer et al.,* 1996]. This device provided highly reliable measurements (ICC of 0.96) with a 90% confidence interval of 1.8N/mm (Newton/ millimeter) for the slope of the linear region of the FD curve. With this portable device, Latimer et al. were able to detect a significant decrease in PA stiffness when LBP subjects experienced an 80% improvement in their pain levels [*Latimer et al.,* 1996]. Edmondston and Allison's group used the Spinal Postero-Anterior Mobilizer (SPAM), to determine the effect of patient position [*Edmondston et al.,* 1998], load orientation [*Allison et al.,* 1998], and mobilizations [*Allison et al.,* 2001] on lumbar PA stiffness. However, Allison et al. were unable to detect changes in stiffness following 2 minutes of manual mobilizations [*Allison et al.,* 2001]. The SPAM consisted of an electronically driven load cell and a linear potentiometer attached to a rigid frame which, similar to that of Latimer et al., mounted onto a padded plinth. The SPAM provided an ICC of 0.98 and a 95% confidence interval of 1.0N/mm for the stiffness coefficients calculated from a section of the slope of

the FD curve. These two devices improved on the SPS and the Spinal Mobiliser with their size and portability [*Latimer et al.,* 1996; *Edmondston et al.,* 1998].

To better simulate clinical assessments of PA stiffness, investigators have created devices combining manual loading and mechanical measurements. Owens' portable PAS system required human examiners to apply manual PA forces with the device while electronic sensors recorded the force and the displacement [*Owens et al.,* 2007]. The PAS system consisted of an electromagnetic tracking device and a force transducer connecting to a block mounted plastic rod held by the examiner. For this system, an ICC of 0.79 was reported for a section of the slope of the FD curve in patients with LBP.

The Passive Movement Assessment Device (PMAD), developed by Tuttle et al. [*Tuttle et al.,* 2008], also required forces to be applied by an examiner. The PMAD was similar to previous devices in that it consisted of a load cell and a linear potentiometer [*Edmondston et al.,* 1998], however, loading of the cervical spine was performed by the examiner's thumb pressing through the indenter. The reliability of the PMAD was assessed using coefficients of multiple determinations which yielded values over 0.96 when comparing curve shapes; stiffness coefficients were not calculated. Using this equipment on a cervical segment, Tuttle noted significant differences between tender and non-tender sides [*Tuttle et al.,* 2009], and, in another study, observed significant decreases in PA stiffness for hypomobile cervical levels treated with mobilizations [*Tuttle et al.,* 2008]. These two latest devices, the PAS and the PMAD, better replicate PA stiffness assessments in the clinical setting; however, they sacrifice control over the loading rate.

Each of these devices offers highly reliable measurements, significantly improving on manual assessment techniques. Unfortunately, these devices were

tested on a wide variety of subjects and used different definitions of stiffness, making the reliability coefficients difficult to compare. Inanimate object testing was not performed in most of these studies to confirm the absence of a systematic measurement error. All of these devices are inappropriate for the small feline model investigation planned in this thesis because of their size and inability to control a range of loading rates.

2.5 Factors affecting stiffness measurements

The devices presented above offer reliable stiffness measurements, yet some sources of measurement variation have been identified. Factors such as patient activity, loading protocol, device characteristics and soft tissue properties are discussed in the following section.

2.5.1 Protocol and patient related factors

2.5.1.1 Patient activity

Protocol and patient related factors can cause variations during in-vivo PA stiffness testing. Kawchuk and Fauvel identified factors including intra-abdominal pressure changes due to breathing, muscular response, patient position, and device repositioning error between trials [*Kawchuk and Fauvel,* 2001]. When investigating breathing and muscle response, they did not find significant differences in stiffness at full inhale or exhale. However, they did find an increase in spinal stiffness from voluntary trunk extensor contraction and from increasing intra-abdominal pressure using the Valsalva maneuver [*Kawchuk and Fauvel,* 2001]. In another study, Shirley et al. noted that EMG of the erector spinae and intra-abdominal pressure measurements were positively correlated with changes in lumbar stiffness, which increased when lung volume was held above or below normal tidal volume [*Shirley et al.,* 2003]. In another study, Shirley et al. found

that increased activity of the lumbar extensors as low as 10% on EMG resulted in significantly higher PA stiffness [*Shirley et al.,* 1999].

2.5.1.2 Positioning and angle of loading

Patient position and direction of PA loading was also shown to impact measurements. Edmondston et al. compared passively supported patient positions. Flexion and extension positions both generated increased stiffness values by 12.4% and 31.9% respectively compared to the neutral spine position [*Edmondston et al.,* 1998]. Caling and Lee applied PA forces at the same angle used by clinicians and at 10 degrees cranial and caudal from this base angle. They found that stiffness values taken at L3 were significantly different for each angle [*Caling and Lee,* 2001]. This could be due to the joints being more mobile in certain directions because of their shape. Forces applied away from normal may also be ineffectively transmitted, requiring greater forces to be applied for vertebral displacement to occur [*Kawchuk and Perle,* 2009; *Bereznick et al.,* 2002]. To reduce the effect of position and angle changes that could result from subject movement, Kawchuk and Fauvel devised a restraint system. This system effectively reduced undesirable movements, although the direct impact on spinal stiffness measurements was not reported [*Kawchuk and Fauvel,* 2001]. Kawchuk and Fauvel also reported another positioning issue with the indenter; they observed an average error of 4.53mm when examiners attempted to relocate the target vertebra through visualization and palpation [*Kawchuk and Fauvel,* 2001]. In studies where therapies are applied between stiffness tests [*Allison et al.,* 2001; *Tuttle et al.,* 2008], inaccurate relocation of the indenter or repositioning of the patient may lead to measurement errors between the first and second test. Treatments must therefore be applied without disrupting the original indenter position, or more reliable techniques must be employed to locate the target vertebra.

2.5.1.3 Equipment

The specific equipment used in various indentation studies also affects stiffness coefficients. Maher et al. found that tests performed with subjects lying on a padded plinth yielded lower stiffness values than when performed on a rigid plinth [*Maher et al.,* 1999]. Squires et al. performed PA stiffness testing on 36 asymptomatic subjects using three different indenter head sizes (300mm^2, 720mm^2, 1564mm^2); they obtained lower stiffness coefficient values with the largest indenter head [*Squires et al.,* 2001]. Not only is the size of the contact area relevant, but the shape of the tip may also affect the effectiveness of the contact between the tip and the vertebra. The tip of the indenter can directly influence the stiffness measurements because of the area of contact or indirectly by affecting the effectiveness of the contact and preventing slipping or discomfort [*Squires et al.,* 2001; *Latimer et al.,* 1996; *Edmondston et al.,* 1998; *Lee and Svensson,* 1990]. To optimize the accuracy of PA stiffness testing, patient activity, indentation protocol and equipment must be closely controlled. Basic science models allow for precise control to be imposed on variables which may not be easily performed in humans.

2.5.2 Viscoelastic tissue properties and stiffness measurements

Another source of variation in spinal stiffness measurements is the complex and dynamic nature of *in vivo* tissues [*Lee and Evans,* 1992; *Nicholson et al.,* 2001; *Nordin and Frankel,* 2001; *Little and Khalsa,* 2005]. Spinal tissues are viscoelastic materials; they exhibit the fluid properties of viscous resistance to flow, and the solid properties of elasticity and plasticity [*Nordin and Frankel,* 2001]. Viscoelastic materials such as ligaments, exhibit three basic characteristics not displayed in non-biological materials: creep, hysterisis and rate-dependency. Given the viscoelastic properties of soft tissues, indentation parameters and protocols must be controlled to produce reliable measurements.

2.5.2.1 Creep

Creep is observed when a sustained load is applied. The intervertebral displacement will continue to increase over time given a constant load, although the rate of creep gradually declines over time. Lee and Evans investigated the effect of the viscoelastic properties of the spine during PA indentations. They performed sustained indentation at L4 and measured the relative displacement achieved at 30sec, 1min and 2min of sustained 100N loading. The mean displacement achieved increased at each time point, although the difference was greater between the first and second time point [*Lee and Evans,* 1992]. Figure 2.7 shows the creep response of the supraspinous ligament.

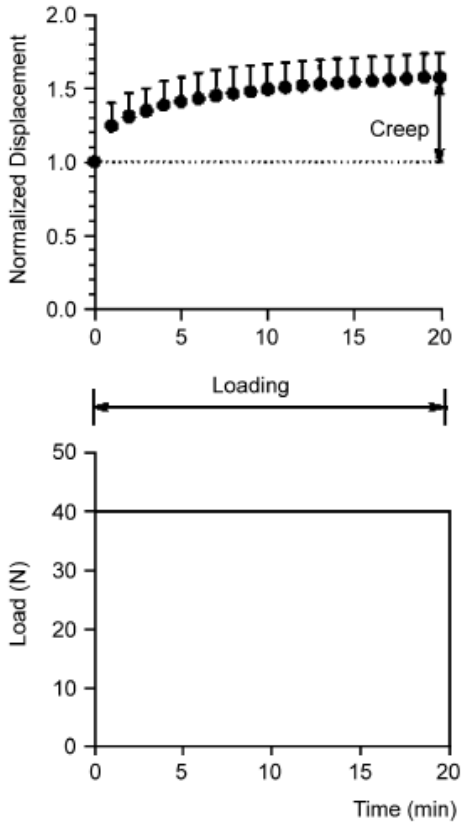

Figure 2.7 Creep response (top) of the supraspinous ligament to a constant load (bottom) applied for a 20 min period. Creep is observed when a sustained load is applied. The intervertebral displacement will increase given a constant load, although the rate of creep gradually declines over time (and eventually stops)[*Solomonow,* 2009]**.**

2.5.2.2 Hysterisis/ Repeated indentations

Hysterisis, the loss of energy within tissues, is observed when the same segment is repeatedly loaded to fixed amplitude (Fig 2.8). The tension developed in viscoelastic tissues will gradually decrease with each repeated load applied [*Solomonow,* 2009]. Lee and Evans performed three consecutive 150N loading cycles at L4 in their previously discussed study on viscoelastic properties of the spine during PA indentations. The mean maximal intervertebral displacement increased with each cycle, although the increase between the second and third cycle was lesser than that of the first and second [*Lee and Evans,* 1992].

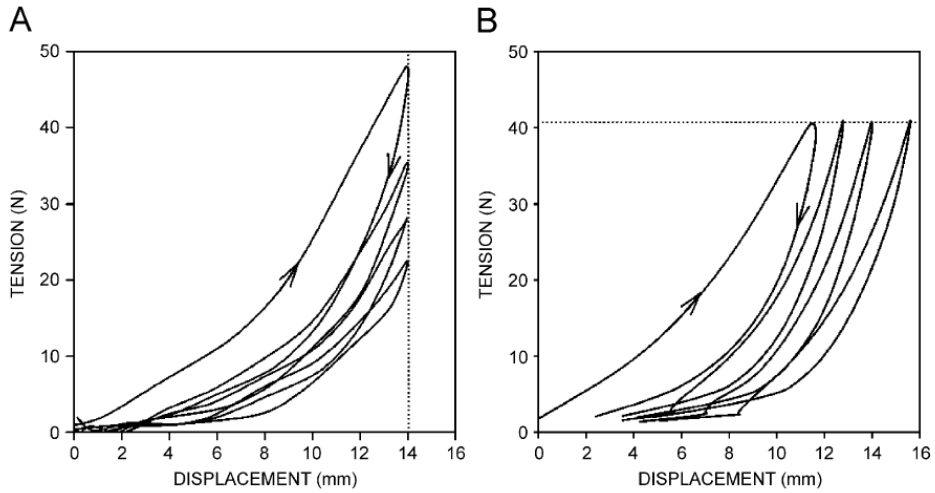

Figure 2.8 Hysterisis developed in a ligament loaded to a constant displacement (A) or force (B) peak amplitude. Hysterisis, the loss of energy within tissues, is observed when the same segment is repeatedly loaded to fixed amplitude [*Solomonow,* 2009]**.**

Each of these viscoelastic properties must be considered when performing repeated stiffness measurements. Shirley et al. reported lower stiffness coefficients for the first of five cycles of loading at L4, although they reported no significant difference between the four subsequent cycles. Five minutes later, they performed a second test consisting of the same five indentation cycles and obtained the same values as for the first test [*Shirley et al.,* 2002]. Indicating that 5 minutes is sufficient time for tissues to recover following five cycles of indentations, as shown in Figure 2.9. When PA stiffness testing is performed, sufficient time must be allowed for soft tissues to recover between repeated

indentation [*Lee and Evans,* 1992; *Little and Khalsa,* 2005]. Tissues can also be preconditioned by performing a sufficient number of indentations at the same rate until equilibrium is achieved [*Latimer et al.,* 1996; *Lee and Evans,* 1992; *Shirley et al.,* 2002].

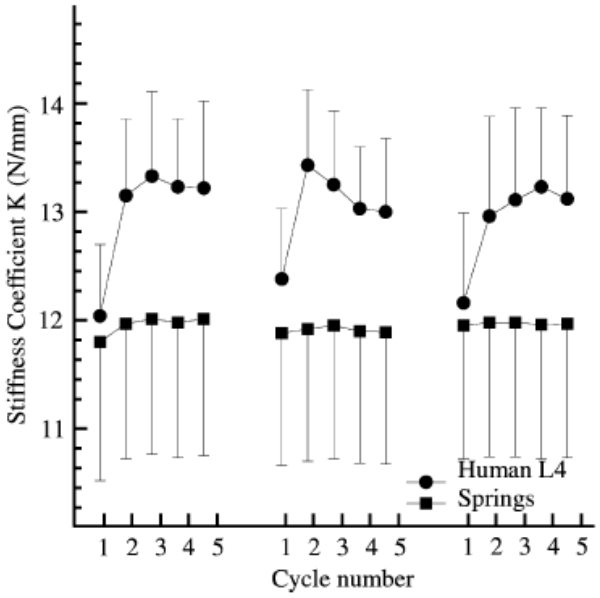

Figure 2.9 Means±SE for L4 loading and springs for stiffness coefficients during five repeated loading cycles on each of three test occasions. Lower stiffness coefficients can be observed for the first of five cycles of loading at L4, although no significant difference are observed between the four subsequent cycles. Five minutes later, a second test consisting of the same five indentation cycles provides the same values as for the first test [*Shirley et al.,* 2002]**.**

2.5.2.3 Loading rate

Third, the rate of indentation will determine the ability of the fluids to seep out of the tissues. Maximal displacements will, therefore, be reached at slower loading rates [*Nigg and Herzog,* 2007; *Lee and Evans,* 1992]. Loading rate will significantly affect the result of stiffness testing. Lee and Evans applied two loading rates; they obtained greater displacements for the 150N indentation performed in 30 seconds than for the one performed in 0.5 seconds [*Lee and Evans,* 1992]. Similarly, Keller and Colloca reported that stiffness increased by 3.7 fold when frequencies of PA indentation were increased from 0.5 to 19.7Hertz (Hz) [*Keller and Colloca,* 2007].

Studies do not report the rates of indentation in the same way. Some report rates of indentations, in mm per second (mm/s), while others report loading frequencies, in Hz to a maximal load. For those studies reporting loading rates in mm/s, rates ranged from 0.58mm/s [*Edmondston et al.,* 1998] to 10mm/s [*Kawchuk et al.,* 2006]. Inconsistent rates of indentation limit comparisons between study findings. Initially, the indentation rates were set to replicate rates consistent with those applied by clinicians [*Lee and Svensson,* 1990; *Lee and Evans,* 1992; *Snodgrass et al.,* 2006]. However, it is not known if certain rates may be more sensitive to changes in force-displacement characteristics, or if rates of PA stiffness measurements must significantly differ from rates of mobilization/manipulation (0.15-1Hz) [*Snodgrass et al.,* 2006] so that measurements do not confound treatment effects. Regardless, rate of indentation must be controlled to ensure consistent results [*Lee and Evans,* 1992; *Little and Khalsa,* 2005].

2.5.2.4 Soft tissue compression

Compression of overlaying soft tissue can also influence the stiffness measurements by delaying intervertebral movement. McGregor et al. produced magnetic resonance images (MRI) of static indentations in humans, which suggested that static indentations generated little vertebral movement, but caused approximately 9.7mm of soft tissue compression in the cervical spine [*McGregor et al.,* 2001]. Kawchuk et al. validated an ultrasound-based technique capable of quantifying true osseous displacement resulting from indentation [*Kawchuk et al.,* 2000]. Although the addition of osseous displacement quantification would improve the validity of stiffness measurements, the small size of the feline model under investigation in the current study could not accommodate the additional space required for an ultrasound transducer. To address this issue, a contact load that is sufficiently high to fully compress the overlying soft tissues will be applied prior to indentation. Each property of

tissues undergoing testing must be considered in the planning of the measurement protocol to ensure reliable values are produced.

2.6 Analysis techniques of stiffness measurements

Stiffness, the main outcome measure of this study, represents how strongly the local soft tissue complex resists deformation or displacement. It is typically measured as the force in N divided by the displacement in mm, stiffness being therefore measured in N/mm. Stiffness measurements provide a curve of continuous data (Fig 2.10), rather than a single scalar value. Measures must therefore be calculated to quantify the characteristics of the force-displacement (FD) curve and allow comparisons.

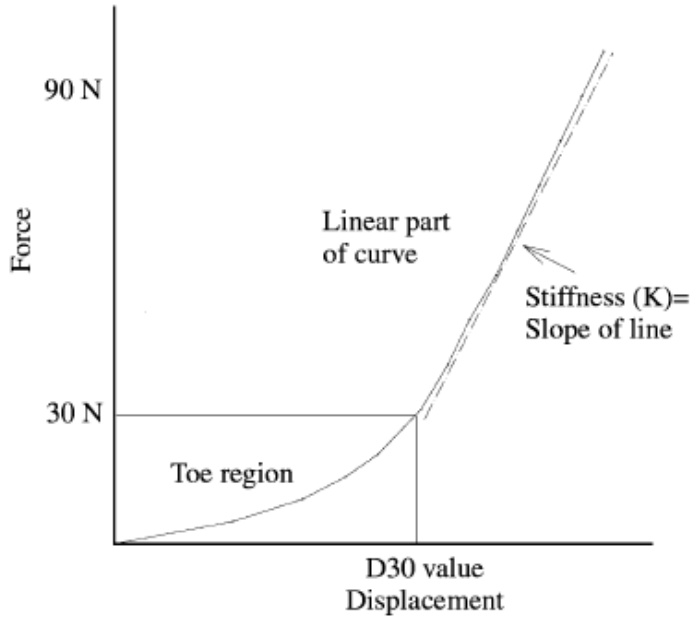

Figure 2.10 Force-displacement (FD) curve showing K: the stiffness coefficient calculated from the slope or the linear portion of the curve and D30: the displacement at 30N of loading, indicating the end of the toe region [*Shirley et al.,* 2002]**.**

2.6.1 Soft tissue stiffness

When PA stiffness is tested mechanically, continuous force and displacement data is collected and can be plotted. This FD graph (Fig 2.10) can be divided into two sections where the initial non-linear toe region is attributed to the uncrimping of ligamentous tissue and compression of overlaying skin and soft tissues [*Snodgrass et al.,* 2008]. The initially relaxed collagen fibers offer little resistance, yet progressively change their organization with loading. When the collagen fibers are straightened and the soft tissues are compressed, the applied force needs to increase at a greater rate in order to increase the displacement continuously. This later portion of the force displacement curve is steeper and relatively linear; its slope represents the stiffness coefficient (K) (Fig 2.10) [*Nordin and Frankel,* 2001].

2.6.2 FD curve analysis using K

Prior investigations have not adopted a standard variable to compare FD responses in all studies. Although most calculated the K of selected force intervals, these intervals varied greatly across studies [*Latimer et al.,* 1996; *Owens et al.,* 2007; *Allison et al.,* 2001; *Shirley et al.,* 1999]. In the human lumbar spine, lower bound force values selected ranged from 15N [*Lee and Svensson,* 1990] to 55N [*Owens et al.,* 2007] and upper bound force values ranged from 75N [*Owens et al.,* 2007] to 100N [*Shirley et al.,* 1999]. Latimer et al. compared different force interval widths and sections of the FD curve [*Latimer et al.,* 1998]. They found that wider sections provided more reliable stiffness coefficients, but that higher force intervals provided poor reliability in asymptomatic subjects. These variations may be present because non-linear curve sections are being fitted with linear regression lines.

2.6.3 Alternative FD curve analysis for PA stiffness testing

As a result, previous studies have considered other approaches to FD curve analysis. For instance, Nicholson et al. proposed the use of a non-linear equation and damping to analyze in-vivo FD curves and provide a more complete description of the whole FD response. This equation included contributions of linear and non-linear elasticity and viscosity to account for over 99% of the variance in FD curves obtained from asymptomatic subjects [*Nicholson et al.,* 2001]. Tuttle et al. advocated analyzing FD curves as a whole by comparing confidence bands from pairs of symptomatic and asymptomatic sides in patients with cervical pain. Using this technique, he observed greater variation in stiffness and displacement, and greater stiffness above 12N on the affected side [*Tuttle et al.,* 2008]. This approach analyzing patterns of stiffness may better characterize whole FD responses, although Latimer et al. were able to obtain similar variability findings using K. Variability of K was greater in symptomatic than in asymptomatic lumbar spine testing [*Latimer et al.,* 1996]. In an attempt to better characterize the FD response, the displacement reached at 30N has also been used to quantify the length of the low-stiffness or "toe" region of the FD curve [*Latimer et al.,* 1996; *Shirley et al.,* 2002]. Gay et al. and Zhao et al. reported that this region may be related to the stability of the spine following disc degeneration [*Gay et al.,* 2006; *Zhao et al.,* 2005]. The region of the FD curve more affected by SMT or by LBP is unknown. The toe region will not be assessed in the current study because it is uncertain which amount will be taken up by the initial contact load. In addition, whole curve analysis will not be possible because the considerable amount of curves to be compared in this study requires scalar values for statistical analysis purposes. Calculating both the terminal instantaneous stiffness (TIS: stiffness at end displacement) and the K values for each curve may offer insights into the FD response of the material under investigation and provide quantifiable scalar values.

2.7 Alternative techniques of stiffness measurements and analysis

As described in section 2.4.1, PA stiffness tests are used to assess passive accessory intervertebral movement (joint play). However, they also cause passive extension, a physiological movement, of the adjacent joints [*Powers et al.,* 2003]. Lee (2005) created a biomechanical model relating PA loading of the spine to a three point bending system where the spine is represented as a beam suspended between the anterior superior iliac spine and T8-T9. In this model, the distance between the supports and the load applied as well as the magnitude of the load can be used to determine the moment produced. FD curves from PA stiffness measurements can therefore be referenced to the torque-angle curves generated when physiological movements are tested [*Lee et al.,* 2005]. Physiological movement techniques used to assess peripheral joint stiffness in neurology research and spinal biomechanics in *in vitro* spines are described and compared against PA stiffness testing.

2.7.1 Peripheral joint stiffness measurements in neurology research

The stiffness or rigidity of physiological movements has been used as an outcome in studies investigating neurological conditions (e.g. spinal cord injury or Parkinson's disease) [*Prochazka et al.,* 1997; *Mushahwar et al.,* 2005]. In these studies, peripheral joints (e.g. elbow, ankle) are typically moved sinusoidally through flexion and extension at set angles of displacement and at a set frequency, while measuring the forces generated.

Lissajous graphs (torque-angle curves) are then used to display the torque generated (Nm) against the angular displacement (deg) imposed (Fig 2.11), similarly to the stiffness graphs that display the force generated (N) against the displacement imposed. The torque angle curve can be divided into 2 limbs: the ascending limb representing loading into flexion (or dorsiflexion in the fig below)

and the descending limb representing loading into extension (or plantarflexion in the fig below). The right half of the descending limb also represents the unloading of the flexion movement. Using this graph, several outcomes can be calculated to characterize the biomechanical properties of the tested joint: the passive resistance torque at controlled positions (ROMs), quasistatic stiffness or elastic stiffness (slope of the limbs), energy loss or viscous stiffness (width of the loop). Mechanical impedance can be calculated by adding the vectorial sum of the viscous and elastic stiffness. However, the components of impedance can be more accurately estimated by fitting a second-order model to the torque and displacement data. For sinusoidal inputs of frequency ω:

Equation 1

$$T = (K + j\,B\omega)x + C$$

Where T is the torque, K is the elastic force $B\omega$, is the viscous stiffness and x is the displacement [*Prochazka et al.,* 1997]. Therefore, this type of curve analysis requires data from loading and unloading of the joint unit and cyclical (repeated) loading of a single condition.

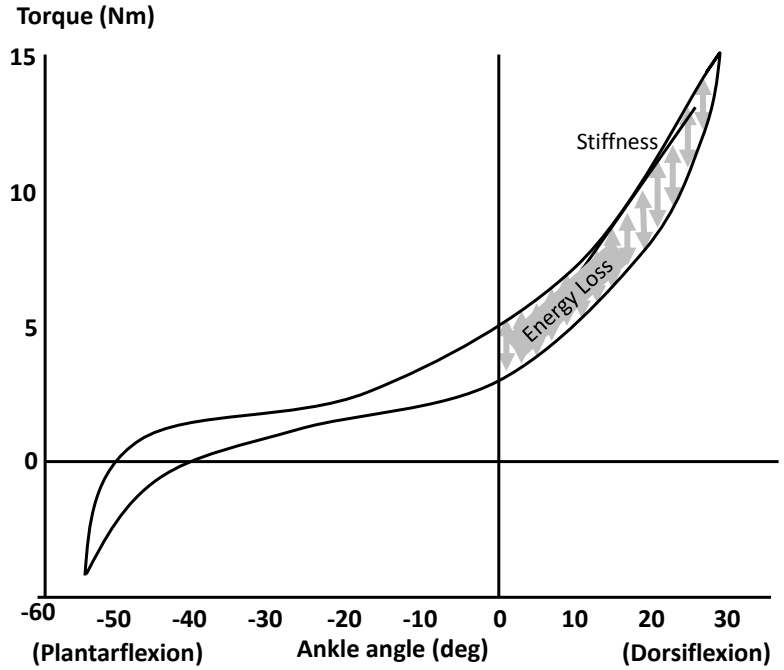

Fig 2.11 Torque-angle or Lissajous graph displays the torque generated (Nm) against the angular displacement (deg). This graph shows an example of the ankle joint being taken from dorsiflexion (ascending limb) to plantarflexion (descending limb).

2.7.2 *In vitro* spinal stiffness measurement and analysis

Physiological movements are difficult to assess directly in the *in vivo* spine due to the inability to isolate and stabilize one joint at a time. Functional spinal units, consisting of the upper and lower vertebra and the joint and ligaments that join them, have been used to investigate the biomechanical properties of the spine. The two vertebrae are fixed and moved alternately through pure movements such as flexion and extension. Similarly to the neurological peripheral joint studies, the data collected by moving the functional spinal unit can be plotted as torque-angle graphs (Fig 2.12).

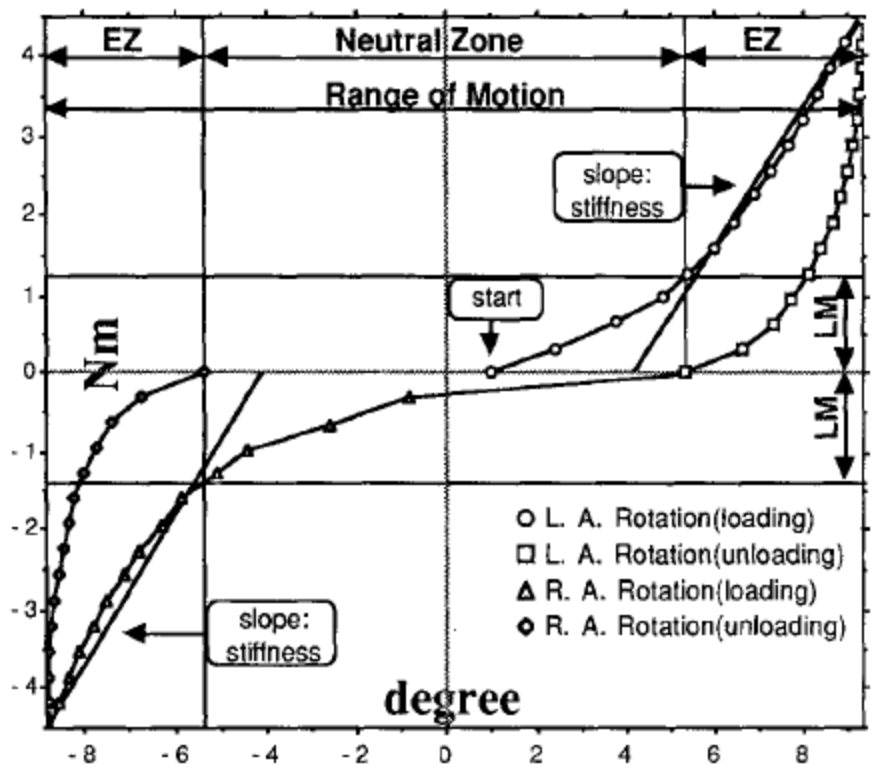

Fig 2.12 Torque angle graph in Nm/deg indicating the different parameters that can be calculated. EZ: elastic zone, LM: limit moment, neutral zone, range of motion and slope stiffness [*Wen et al.,* 1993].

These graphs, although similar to the one in Fig 2.11, are analyzed using some different parameters. The neutral zone is the range of motion through which the spine can be displaced against little resistance. The loading part of the curve can be used similarly to the force displacement curve to calculate the stiffness using a linear regression of the elastic region, which spans from the inflection point showing increasing stiffness and indicating the end of the neutral zone to the end of the curve. The ROM (deg) reached at the peak torque can also be quantified.

Using this type of technique, Wen (1993) investigated the influence of ligaments on cervical spine stability. The subsequent sectioning of ligaments lead to an increase in ROM, an increase in neutral zone and a decrease in stiffness *[Wen et*

al., 1993], indicating that all three of these outcomes, including stiffness, were sensitive to the loss of these different structures. Busscher (2009) was also able to detect significant differences between the thoracic and lumbar spine stiffness calculated from a torque interval (3.5-4Nm) [*Busscher et al.,* 2009]. In recent studies, Hasegewa (2009-2010) used an *in vivo* intraoperative technique and generated moments in a functional spinal unit by clamping on to the spinous process with minimal soft tissue damage. Levels affected by degenerative lumbar spondilolysthesis were compared to normal levels in human subjects undergoing decompression surgery. Significant changes were observed in the neutral zone and in the stiffness, but not in the absorption energy (viscous stiffness) [*Hasegewa et al.,* 2009; *Hasegawa et al.,* 2010]. Although physiological movement techniques provide additional outcomes, stiffness is calculated similarly to that of FD curves and provides comparable observations.

2.7.3 Comparison of alternative techniques to PA stiffness technique

The data obtained from PA testing is limited compared to the two physiological movement techniques. PA stiffness measures only capture the loading of the vertebra because the tip of the indenter is not attached to the spinous process of the vertebra tested. Therefore the loss of energy or viscous component of stiffness cannot be calculated from this technique. In contrast with the sinusoidal loading applied for peripheral joint techniques, the spine is only tested once through PA loading and does not provide multiple windows of data to fit equation 1. In contrast with the ROMs obtained from physiological movements which corresponds to limb position and have normative values, PA accessory movements have not been fully characterized. The order in which the soft tissues and bony restrictions are each engaged to contribute to the force displacement response is unknown. The interpretation of individual sections of the FD is therefore limited. However, the portion of a PA movement or of a

physiological movement or the component of stiffness (viscous vs. elastic) which is more responsive to SMTs has not been identified.

In spite of the limitations in interpreting PA measurement, previous studies have detected differences in various variables by calculating the stiffness coefficients (K). For example, Latimer et al. (1996) found lower PA stiffness in patients experiencing LBP compared to when their pain had resolved by more than 80% [*Latimer et al.,* 1996]. Kawchuk et al. (2001) detected increased stiffness with induced disc degeneration [*Kawchuk et al.,* 2001]. Changes in level of muscle contraction have also caused detectable changes in PA stiffness [*Shirley et al.,* 1999; *Hu et al.,* 2009].

The advantage of PA stiffness testing technique is that it allows the reliable and non-invasive quantification of spinal stiffness *in vivo*. The procedures required to test physiological stiffness, such as death, freezing and tissue removal, can alter some of the tissue properties, but most importantly change the response to repetitive loading [*Adams MA et al.,* 2002] and the response to a treatment intervention. *In vivo* spinal physiological movement testing has only recently been developed it is invasive, alters the spines position between tests and has never been used in small animal models. In contrast with PA testing, the device used to test physiological movements cannot perform simulated SMTs.

2.8 Theories of mechanisms behind effects of SMT

SMT is performed by applying a rapid force to a specific point of the spine. This high velocity, low amplitude (HVLA) thrust passively takes a joint beyond its physiological limit of motion, but within its anatomical limit, with the intent to restore optimal motion, function and/or reduce pain [*Isaacs et al.,* 2002;

Maitland GD, 2001]. Research and theory suggest that a combination of neurophysiological and biomechanical mechanisms initiated by SMT lead to beneficial clinical outcomes [*Triano,* 2001; *Pickar,* 2002]. These two underlying mechanisms will be discussed in regard to how they may impact spinal stiffness.

2.8.1 Biomechanical mechanism

One assumption underlying the effect of SMT is the presence of a joint dysfunction (lesion). Chiropractic literature suggests that mechanical overloads lead to spinal buckling, a deformation which alters spinal alignment and disrupts the instantaneous center of rotation. SMT is intended to restore normal biomechanics to the site of dysfunction and to the spinal system by redistributing joint stresses and improving joint play [*Haldeman,* 2004].

Mechanically, HVLA-SMT distracts the facet joints and stretches the joint capsule and surrounding spinal tissues through a high rate of loading [*Brodeur,* 1995]. The high velocity at which SMT is performed has critical effects on spinal tissue response because of their viscoelastic properties (described in section 2.5). At slow mobilization rates fluids are forced out and loads can be transmitted to adjacent segments and dissipated throughout the spine. Using MRI, Powers observed significant displacement three vertebrae away from the mobilization site [*Powers et al.,* 2003; *Cramer et al.,* 2002] Alternatively, tissues behave like stiffer non-viscous solids when responding to the high loading rates of SMT. A study by Gal et al. shows greater displacements at the targeted joint than at more remote segments [*Gal et al.,* 1997], suggesting that SMT causes a greater, targeted strain. A study by Khalsa and Ianuzzi revealed that facet joint strain magnitudes caused by SMT were within those experienced during maximal physiological motion [*Ianuzzi and Khalsa,* 2005]. However, in a later study, the same group detected significantly smaller vertebral displacements and different

patterns of facet joint strain when comparing SMT to physiological rotation [*Ianuzzi and Khalsa,* 2005].

2.8.1.1 Cavitation

Cavitation (cracking sound), sometimes associated with SMT, has been proposed as a critical component of SMT mechanisms. Originally, the theory behind cavitation is that the facet joint gets distracted or gapped, causing the joint capsule to be pulled in towards the joint line [*Brodeur,* 1995]. When the capsule snaps back to its original position, it gets stretched, the intra-articular pressure suddenly drops, and dissolved synovial fluid gases are released causing a cracking sound (Fig 2.13). Brodeur amended this original model, and proposed that the capsule snapping back was actually the cause of the cracking sound [*Brodeur,* 1995].

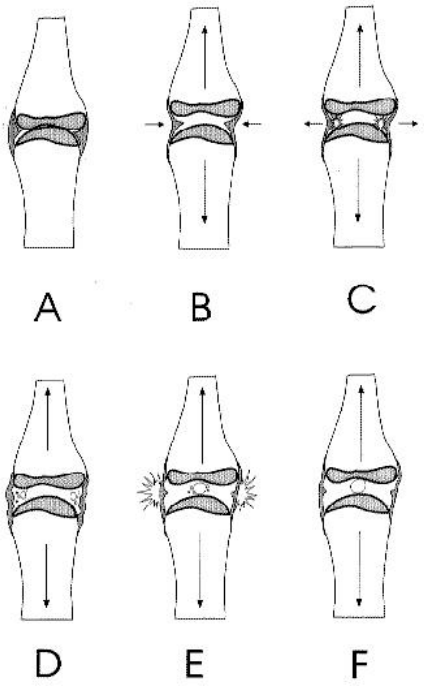

Figure 2.13 Joint cavitation model. A. joint at rest. B. Small tension applied to joint but the gap between the two joint surfaced is filled with synovial fluid. The joint volume remains constant because the capsule invaginates. This causes stress on the capsular ligaments. C. Tension continues to increase and the capsule cannot invaginate further. Excessive stress causes an elastic recoil of the capsule, which then snaps away from the synovial fluid causing cavitation. D. The volume of the joint increases, decreasing internal joint pressure, and resulting in release of dissolved gasses. E/F. The gasses form a single bubble within the capsule [*Brodeur,* 1995]**.**

A study by Herzog et al. also suggests that cavitation corresponds to novel events at the vertebral segment which can be perceived. While performing PA SMT on T4 transverse processes of symptomatic patients, Herzog et al. recorded accelerations at T3. A specific frequency of the acceleration signal corresponded to the occurrence of a perceived cavitation compared to the signal in absence of cavitation [*Herzog et al.,* 1993]. A recent study by Cramer et al. supports that distraction occurs during a SMT. Side lying MRI scans of healthy subjects before and after receiving an SMT showed a temporary increase facet joint separation [*Cramer et al.,* 2002]. Conversely, Flynn et al. found no relationship between the occurrence of an audible cavitation and improvement of outcomes when a sacroiliac technique was performed on patients with LBP [*Flynn et al.,* 2003]. Regardless of the role of cavitation and its origin, the chiropractic treatment model has long proposed that SMT gaps the facet joints breaking adhesions and restoring mobility [*Isaacs et al.,* 2002].

2.8.2 Neurophysiological

The fast impulsive tension on the capsule caused by SMT is believed to trigger reflex stimulation of the neurophysiological system [*Ianuzzi and Khalsa,* 2005]. However, conflicting reports on the specific systems and pathways stimulated have been published. Of interest to this study is the hypothesized ability of these neurophysiological stimuli to modulate resting motor system activation levels because they have been related to alterations in stiffness levels and to LBP (see Section 2.2). Given that the current understanding of the underlying neurophysiological mechanisms of SMT is still in development, evidence of varying strength is presented without concluding to one mechanism. The following sections have been subdivided into theoretical categories explaining how various nervous system components, such as the somotosensory system,

the pain processing system, and the motor system, mediate responses to SMT (Fig 2.14) [*Pickar,* 2002].

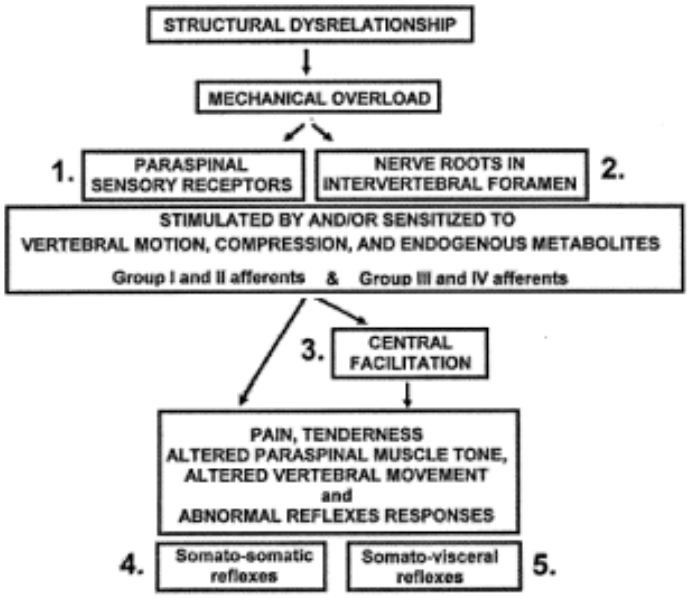

Figure 2.14 Theoretical model showing the relationship between physiological, biomechanical and neurophysiological components which could respond to SMT. The neurophysiological effects could be mediated at any of the boxes [*Pickar,* 2002]**.**

2.8.2.1 Peripheral somatosensory receptors

Biomechanical effects of SMT are speculated to stimulate somatosensory receptors contained within muscles and ligaments (Fig 2.14, 1) [*Lundy-Ekman,* 2002]. Pickar and Wheeler performed simulated SMT on the L6 spinous process of a feline model. Single unit Golgi tendon organ and muscle spindle afferents recordings showed more increased discharge frequencies with the manipulation than with the preload. At the end of the manipulation, receptors resumed their resting state of silence [*Pickar and Wheeler,* 2001; *Pickar and Kang,* 2006]. Using human patients undergoing lumbar decompression, Colloca et al. measured S1 mixed spinal nerve root discharge. They observed compound action potentials that corresponded to movement experienced by the manipulated segment [*Colloca et al.,* 2004]. The exact source of this neurophysiological response

cannot be determined, but it is thought that it would be attributed in part to mechanoreceptor afferents as measured by Pickar et al. Figure 2.15 shows the sensory pathways believed to be influenced by SMT. Consequently, evidence strongly supports a stimulating effect of SMT on the proprioceptive system.

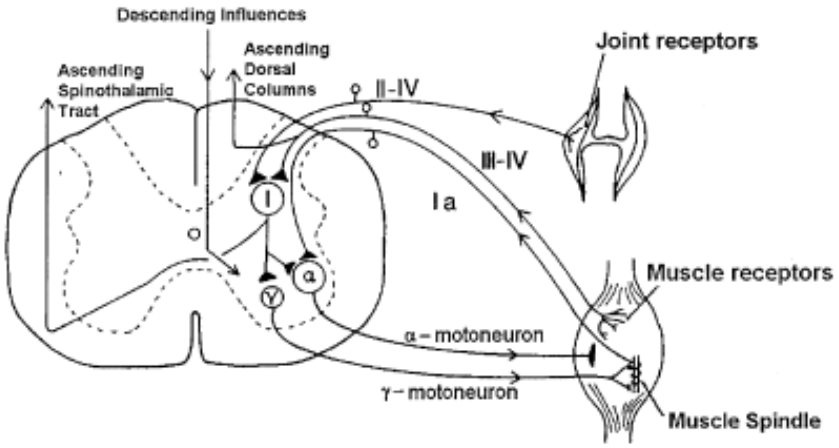

Figure 2.15 Schematic of sensory pathways believed to be influenced by SMT, which could modulate γ motorneuron activity. Discharge from joint and muscle receptors may affect descending input to the γ motorneuron [*Pickar,* 2002]**. This input may affect resting muscle activation levels which could alter spinal stiffness.**

Theory also suggests that free nerve endings (Aδ and C), joint receptors responsible for pain, tissue damage and temperature perception, could also be affected by SMT [*Lundy-Ekman,* 2002]. Pickar and McLain recorded graded response activity from group III and IV afferents (free nerve endings) to a SMT of the L5-L6 facet joints in felines, supporting the role of these afferents in SMT mechanisms of effect [*Pickar and McLain,* 1995]. Further basic science research is needed to confirm the interactions between peripheral neural stimulation and resulting clinical improvements.

2.8.2.2 Pain modulation/ Analgesic effect

Melzack and Wall formulated the first scientific theory behind the ability of external stimuli, such as SMT, to modulate pain transmission. In brief, Melzack and Wall's gate control theory proposed that the stimulation of the low-

threshold, large fibre mechanoreceptors could inhibit the transmission of information from small nociceptive fibres [*Melzack and Wall,* 1965]. Melzack later updated this theory to incorporate influences from sensory, cognitive, affective, hormonal, and intrinsic neural modulation components [*Melzack,* 1999]. Given the above, SMT could stimulate the peripheral nervous system and somehow modulate pain at the perception, transmission or processing level [*Lundy-Ekman,* 2002]. The impact of SMT on pain modulation may also operate on the premise that the CNS can become sensitized to afferent input. Sensitization refers to the ability of the CNS to increase the responsiveness to sensory input (Fig 2.14, 3). Through modulating effects SMT could reset or desensitize CNS pain perception. The effects of SMT on nociceptive processing have been assessed using methods like area of sensitivity to pinprick, maximal pain tolerance levels to current, pressure pain threshold, and β-endorphin levels [*Boyling JD and Jull GA,* 2004; *Pickar,* 2002]. Evidence supports modulating effects of SMT on analgesia through decreased area of pain perception and increased mechanical pain threshold [*Boyling JD and Jull GA,* 2004]. Although divergent findings have resulted from these various methods, Pickar suggested that pain modulation following SMT might only be detected in symptomatic or sensitized sites [*Pickar,* 2002].

2.8.2.3 Motor system

Given the above, altered peripheral somatosensory stimulation and modulation of pain perception could influence somatosensory reflexes (Fig 2.14, 4). Altered neuromuscular stimulation may then restore mobility indirectly by altering a pain/spasm/pain cycle, or SMT induced reflex motor inhibition may directly restore normal muscle activation levels [*Wright,* 1995]. Detectable effects of SMT on the motor system are transient increased EMG activity, decreased H-reflex (Hoffman), decreased muscle inhibition, and increased motor evoked potentials. Both increased and decreased EMG responses to SMT have been

reported, but discrepancies in methodological approaches such as the use of asymptomatic or symptomatic subjects, and the selection of sites and types of neural measurements taken may explain these divergent results [*Herzog et al.,* 1999; *Colloca and Keller,* 2001; *Lehman and McGill,* 2001; *Boyling JD and Jull GA,* 2004]. Attenuation of the tibial nerve H-reflex amplitude, a muscular reaction in response to electrical stimulation of Ia muscle spindle afferent fibers, has also been demonstrated in symptomatic and asymptomatic subjects within 60s following SMT [*Dishman and Bulbulian,* 2000; *Murphy et al.,* 1995; *Dishman and Bulbulian,* 2001]. These studies support the theory that motor neuron excitability could be reduced by afferent input from the joint structures being manipulated. These somewhat discordant findings may indicate multilevel neural responses dependent upon the preexisting status of the spine. These various changes in neural response following SMT could contribute to reduction of muscle spasms and ROM limitations.

2.8.3 Summary

To summarize, SMT is a mechanical intervention that causes novel strains on the spinal tissues. Biomechanical mechanisms lead to stimulation of surrounding structures triggering complex neurophysiological responses. Biomechanical strain and modulation of neural activity could contribute to restoring normal spinal stiffness [*Triano,* 2001; *Pickar,* 2002].

2.9 Effect of parameters on SMT outcome

It is assumed that the mechanical characteristics or parameters of SMT application techniques modulate both neurophysiological and biomechanical mechanisms, which may lead to changes in spinal stiffness. Maitland emphasized the importance of deciding the appropriate manner and duration of the

technique applied [*Maitland GD,* 2001]. Previous research has outlined various SMT characteristics including preload, force, displacement, duration, position, direction and area of contact. Figure 2.16 shows the load-time profile of a SMT. When performing a SMT, the clinician positions the patient to target a segment or pretension tissues and position their hand to contact the desired area on the vertebra in the desired direction. The spine is then preloaded by applying a force to compress overlaying tissues and place initial tension on spinal structures. Subsequently, a greater force is applied at a high velocity to reach the peak force in a short time duration [*Haldeman,* 2004]. Although these SMT characteristics have been defined, no studies have quantified optimal SMT parameters or their specific contribution to these mechanisms of effect. Parameters thought to affect SMT mechanisms of effect are discussed in this section and values from the literature are summarized in Table 2.1.

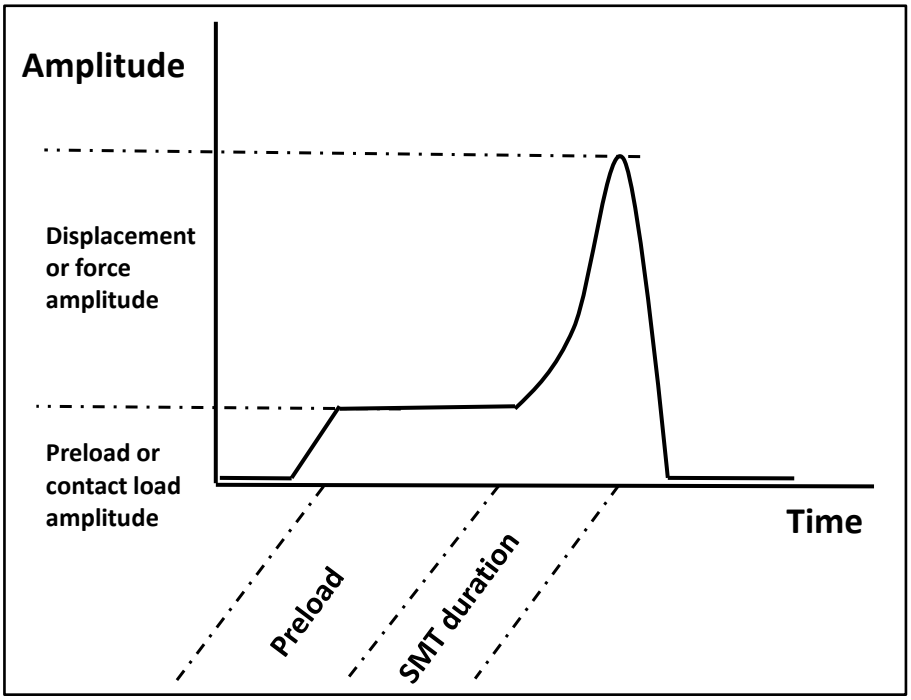

Figure 2.16 SMT load time profile. A preload is a force typically applied 0.5 to 5 seconds prior to the start of the SMT [*Herzog,* 2000]. Its purpose is to compress the overlaying soft tissues, to place tension on the relaxed collagen fibers, and to take the joint to end range. The duration of the SMT is the time elapsed between an increase in load from the preload the moment when the peak displacement or force amplitude is reached. The SMT load is then quickly removed.

Study	Subject / Location	Measurement / SMT application	Preload	Force	Displacement	Duration or rate	Outcome / Relevant findings
Herzog 1993	Human / T4 transverse process sacroiliac joint	pressure mat / manual	139N (SD: 46N) 88N (SD: 78N)	399N (SD: 119N) 328N (SD: 78N)		150ms (SD: 77ms)	
Herzog 2001	Human / T3-T10 transverse process	pressure mat / manual	23.8N (SD: 24.5N)	total peak forces of 238.2N; local average peak pressure of 5N/25mm^2		160ms (SD: 21ms)	
Sung 2005	Feline model / L6 vertebra	Mechanical application		33%, 66% and 100% of body weight		25ms to 800ms	1. Responses to the magnitude of the load applied did not systematically affect afferent activity when performed at a range of durations 2. Abrupt increase in mechanoreceptor neural discharges as the duration decreased and approached that used clinically (200 to 100ms)
Pickar 2006	Feline model / L6 vertebra	Mechanical application		33%, 66% and 100% of body weight	3	25 to 800ms	Greater discharge frequencies from individual multifidus and longissimus muscle spindles with SMT durations below a threshold of about 200ms
Pickar 2007	Feline model / L6 vertebra	Mechanical application	0N		1mm and 2mm	12.5ms to 400ms	1. Increases in lumbar paraspinal muscle spindle discharge with an inflexion around the 100ms duration 2. The smaller displacement yielded greater discharge
Colloca 2004	Human / Lumbar facet joints and spinous process	Activator Adjusting Instrument / accelerometer	~20N	30N (sham) to 150N	0.10 to 1.28mm	100-150ms	Compound action potentials significantly greater (though inconsistent across patients) at higher load amplitudes

Colloca 2006	Ovine model / L3 spinous process	Mechanical / accelerometer	10N	80N 20N to 60N	4.35mm to 17.84mm	10, 100 and 200ms 100ms	1. Greater load resulted in graded increases in segmental and in adjacent segments displacement, and in EMG responses 2. 10ms resulted in smaller displacements (5x) and greater accelerations than 100 and 200ms SMTs
Keller 2006	Ovine model / T12 spinous process	3 mechanical chiropractic adjusting instruments / accelerometers	20N	114N to 380N	mean: 1.76; SD: 1.55mm		Increased force settings increased PA displacements and accelerations

Table 2.1 Quantified SMT parameters

2.9.1 Preload

A preload is a force typically applied 0.5 to 5 seconds prior to the start of the SMT [*Herzog,* 2000]. Its purpose is to compress the overlaying soft tissues, to place tension on the relaxed collagen fibers, and to take the joint to end range. Herzog et al. reported clinically applied mean preload forces of 139N (SD: 46N) in the thoracic spine and of 88N (SD: 78N) in the sacroiliac joint [*Herzog et al.,* 1993]. When a preload is applied, this force gets added to the force of the SMT. As a result, greater forces can be effectively transmitted placing greater stress onto the tissues. In addition to affecting mechanical tissue stress, preload may also affect neural responses. Pickar and Wheeler noted that preload caused some increase in discharge frequencies from mechanoreceptors even in the absence of a thrust [*Pickar and Wheeler,* 2001].

2.9.2 Force and displacement

The total applied force amplitude influences biomechanical and neurophysiological responses. A range of forces applied clinically to the lumbar spine have been reported in the literature (Table 2.1). Discrepancies can be explained by the variable SMT application techniques of individual clinicians [*Harms and Bader,* 1997], as well as the different experimental measurement techniques and the challenges they pose [*Triano,* 2001]. In a study performed on human subjects undergoing lumbar decompression surgery, Colloca et al. observed increases in vertebral accelerations and displacements when load amplitudes increased from 30N (sham) to 150N, although average PA displacements only ranged from 0.10 to 1.28mm. Compound action potentials (unspecified sources of neurophysiological responses measured in the nerve root) were significantly greater at higher load amplitudes, but these findings were not consistent for all 9 patients [*Colloca et al.,* 2004]. Keller et al. tested 3 mechanical SMT instruments, with peak force amplitudes ranging from 114N to 380N, on the T12 spinous process of ovine spines. Increased force settings

tended to increase PA displacements (mean: 1.76; SD: 1.55mm) and accelerations [*Keller et al.,* 2006]. SMT studies involving animals require certain scaled adjustments in order to simulate the application of SMT in humans. When using a feline model, Sung, Kang and Pickar applied loads according to body weight percentages. Loads of 33%, 66% and 100% of body weight were applied to the L6 vertebra and single unit afferent activity was recorded, although responses to the magnitude of the load applied did not appear to systematically affect afferent activity when performed at a range of durations, as shown in Figure 2.15 [*Sung et al.,* 2005].

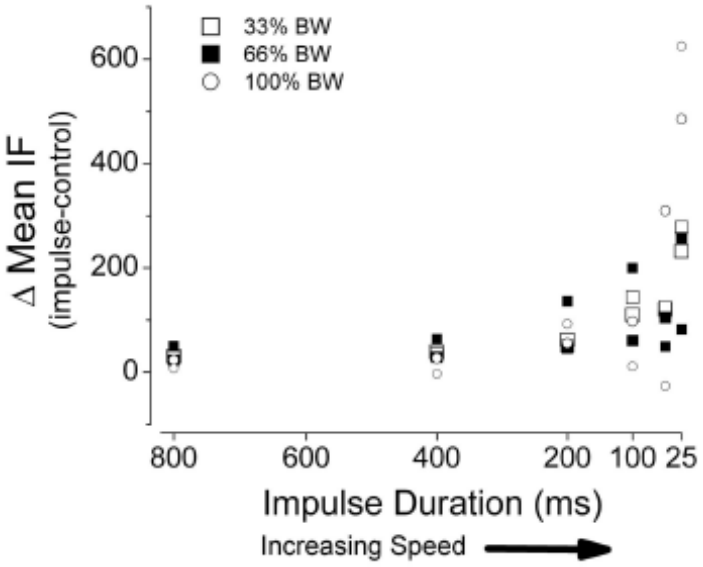

Figure 2.17 Effect of loading amplitude on neural response as the duration of SMT shortens. ΔMean IF represents the mean difference between the mean instantaneous frequency (IF) during mechanical loading and the mean IF during the 10 seconds prior to the SMT [*Sung et al.,* 2005]**.**

Colloca et al. performed SMT loads of 20 to 80N at a fixed duration of 100ms to an ovine lumbar model, following a 10N preload, although they did not state how the loads were scaled. In this study, greater load amplitudes resulted in graded increases of 4.35mm to 17.84mm in segmental displacement and in greater PA accelerations of adjacent segments. EMG responses also increased with higher load amplitudes [*Colloca et al.,* 2006]. Therefore, SMT applied at higher force and displacement amplitudes appear to increase biomechanical and

neurophysiological effects, although the specific effect of SMT amplitude on spinal stiffness has not been quantified.

2.9.3 Duration

The duration of a SMT is the time elapsed between the baseline preload and the moment the peak load is reached. As described in section 2.7, the brief duration or high velocity of a SMT (100 to 200ms clinically [*Herzog,* 2000]) is thought to be a critical characteristic which leads to the novel effects of this intervention. Because of the viscoelastic properties of spinal soft tissues, faster SMT will cause tissues to become stiffer (Fig 2.16) [*Nordin and Frankel,* 2001; *Triano,* 2001]. Mechanically, the brief duration distracts the two joint surfaces at a rate assumed to causes a sudden change in intra-articular pressure leading to a selective stretch of the periarticular tissues [*Brodeur,* 1995]. It has also been shown that less force is required to produce a cavitation at higher rates of loading [*Herzog,* 2000].

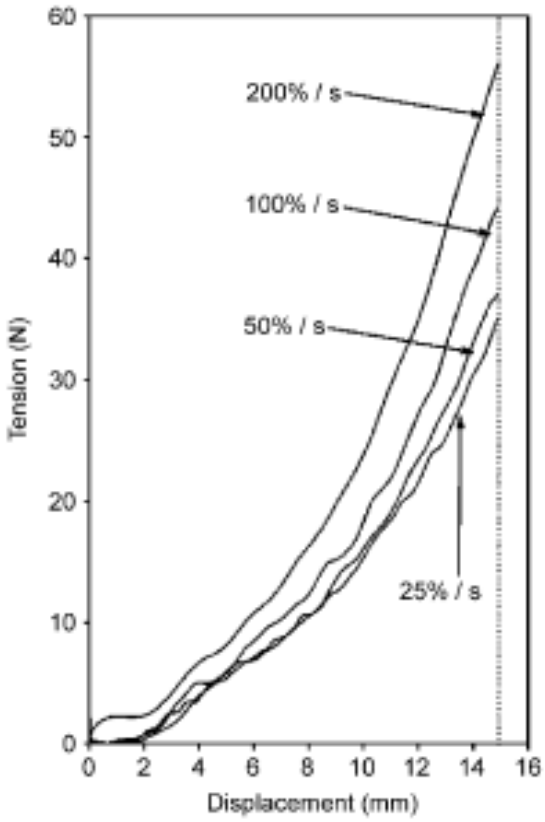

Figure 2.18 The length-tension relationship of a ligament stretched at different rates. Increasing the rate of stretch from 25% to 200% develops nearly 50% more tension in the supraspinous ligament [*Solomonow,* 2009]**.**

A number of studies have shown that the duration of a SMT affected neural responses. Pickar developed a feline model to investigate the effect of mechanically controlled SMT parameters on single unit afferent discharge. The feline model was chosen because access to the nerve root of the manipulated L6 vertebra could be maximized while most supporting musculoskeletal structures could remain intact [*Pickar,* 1999]. Using this model, Pickar's group performed simulated SMT durations from 12.5ms to 800ms in three consecutive studies. They consistently reported significantly greater discharge frequencies of mechanoreceptor as the duration decreased and approached that used clinically (200 to 100ms), as shown in Figure 2.15 [*Sung et al.,* 2005; *Pickar and Kang,* 2006; *Pickar et al.,* 2007] . In the latest study, Pickar et al. performed the various SMT durations at two displacements, the smaller, 1mm, displacement yielded

greater discharge than the 2mm displacement, shown in Figure 2.17 [*Pickar et al.,* 2007].

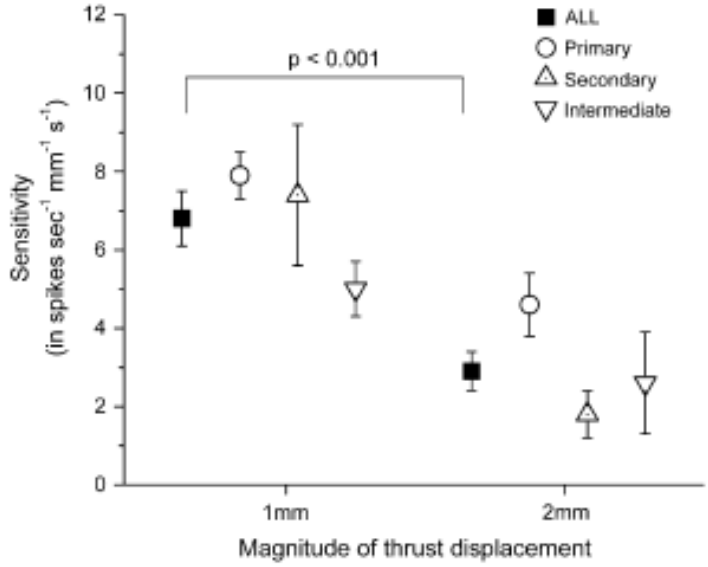

Figure 2.19 Effect of the magnitude of SMT displacement on the sensitivity of paraspinal muscle spindles. The smaller, 1mm, displacement yielded greater discharge than the 2mm displacement [Pickar et al., 2007].

These three studies consistently demonstrate that short SMT durations approaching those used clinically produce novel mechanoreceptor afferent discharge, although the direct relation between SMT duration-amplitude parameters and stiffness outcomes has not been fully quantified.

2.9.4 Patient Position, location and direction

Patient positioning [*Cramer et al.,* 2002], location and direction [*Caling and Lee,* 2001; *Kawchuk and Perle,* 2009] of loading are parameters also believed to affect the outcome of SMT. In a study by Cramer et al. MRI scans showed that side lying posture increased facet joint separation prior to SMT application [*Cramer et al.,* 2002]. In addition, Ge et al. observed that spinal positioning and duration of position hold affected muscle spindle discharge [*Ge et al.,* 2005]. Patient positioning may affect the outcome of SMT by altering the joint position, the preexisting proprioceptive discharge, and the overall stresses placed on the

spinal soft tissues [*Edmondston et al.,* 1998]. Location and direction of SMT may also affect the resulting intervertebral motion. Using bone pins, Colloca et al. found that SMTs applied to the spinous process resulted in greater PA accelerations and SMTs applied to the facet joint resulted in greater mediolateral and axial accelerations [*Colloca et al.,* 2004]. Kawchuk and Perle also used bone pins to assess vertebral acceleration responses to spinous process thrusts. All non-normal angles of force application resulted in decreased forces being effectively transmitted to the target vertebra [*Kawchuk and Perle,* 2009]. However, impact of location and directions parameters may not be limited to spinal biomechanics. Pickar and Wheeler found that distractive SMT caused greater increases in muscle spindle discharges than compressive SMT, suggesting that individual Golgi tendon organs responded preferentially to specific directions of loading [*Pickar and Wheeler,* 2001]. Colloca and Keller noted that SMTs applied to the transverse processes elicited 5% more positive EMG responses than those performed over the spinous process [*Colloca and Keller,* 2001]. SMT effects are therefore modulated by these parameters of application.

2.10 Summary

Based on this review of the literature, it is clear that the biomechanical effects of SMT parameters have not been defined. For SMT effectiveness to be optimized the parameters of application and the mechanisms through which they operate must be understood and quantified. Stiffness has been highlighted as a spinal property relevant to LBP which can be reliably and accurately measured by mechanical indentation. This thesis will determine if different SMT parameters will affect spinal stiffness.

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CHAPTER THREE

EXPERIMENT 1

Performance and reliability of a variable rate force/displacement application system

Note: A version of this chapter has been accepted (May 2010) for publication in the Journal of Manipulative and Physiological Therapeutics, by Vaillant M; Pickar J; Kawchuk G.

Abstract

Purpose: Spinal manipulation therapy (SMT), an intervention used to treat low back pain, has been demonstrated to affect the stiffness of the spine. To adequately quantify the effects of SMT on stiffness, a device capable of applying specific parameters of manipulation in addition to measuring force-displacement values has been developed previously. The reliability of stiffness measurements performed by the newly adapted device was assessed in this study.

Methods: Seven springs of varying stiffness were each indented 10 times by a Variable Rate Force/Displacement (VRFD) device. Indentations were performed at a rate of 0.5mm/s to a maximal displacement of 4 mm. The stiffness coefficients for a middle portion (2-2.5mm) of the resulting force-displacement graph and the terminal instantaneous stiffness (stiffness at end displacement) were calculated. The intra class correlation coefficients and confidence intervals were calculated for these stiffness measurements to assess device reliability.

Results: Repeated spring stiffness measures yielded an ICC (3, 1) value of 1.0. The mean stiffness values had narrow 95% confidence intervals ranging from 0.01 N/mm to 0.06 N/mm and small coefficients of variation of <0.03%.

Conclusion: This VRFD device provides highly reliable stiffness measurements in controlled conditions. Although in vivo reliability remains to be established, the

results of this study support the use of the VRFD device in future trials investigating the impact of various SMT parameters on spinal stiffness.

3.1 Introduction/Background

Low back pain [*Latimer et al.,* 1996] and spinal degeneration [*Kawchuk et al.,* 2001] are often associated with changes in spinal stiffness. To assess these changes, clinicians most often employ a manual technique where postero-anterior forces are applied to the spine and the resulting tissue response is appreciated. Unfortunately, manual spinal stiffness assessment has been shown to have poor performance. Specifically, prior investigations have demonstrated that clinicians are unable to apply consistent forces [*Simmonds et al.,* 1995], perceive changes in the force displacement relationship [*Bjornsdottir and Kumar,* 2003] or judge spinal stiffness [*Maher and Adams,* 1994]. As a result, many investigators have designed mechanical devices to increase measurement precision and accuracy when assessing spinal stiffness [*Latimer et al.,* 1996; *Kawchuk et al.,* 2006; *Tuttle et al.,* 2008; *Owens et al.,* 2007; *Allison et al.,* 2001].
The mechanical device described in this study has been used previously by Pickar et al. [*Pickar,* 1999; *Pickar and Wheeler,* 2001; *Pickar and Kang,* 2006] to apply rapid forces that simulate spinal manipulation therapy (SMT) in a feline model. Because this device can change the rate at which forces are applied, it may be possible to use the same device to apply lower force rates used in stiffness testing as well as the higher rates used in SMT application. Before using the Variable Rate, Force/Displacement (VRFD) device in an experimental setting to assess spinal stiffness, the device's reliability should be established with respect to stiffness assessment. Therefore, the objective of this study was to determine the reliability of the VRFD device in a bench-top setting. Given prior technology assessments [*Latimer et al.,* 1996; *Edmondston et al.,* 1998], device reliability could be considered to be excellent with intraclass correlation coefficients (ICC) values of 0.8 or higher [*Portney and Watkins,* 2008] during replicate tests to determine the stiffness of inanimate objects.

3.2 Methods

3.2.1 Variable Rate Force/Displacement Device

3.2.1.1 VRFD Overview

The VRFD device is capable of performing vertebral postero-anterior indentations at high rates of loading to simulate SMT or at low rates to quantify stiffness. The VRFD device is comprised of 5 major components (four are shown in Fig 3.1): 1) a graphical computer interface, 2) a data acquisition board (USB-6212, National Instruments, Austin Texas) 3) an electronic feedback, motor control system (Aurora Scientific, Dual Mode Lever System, Model 310C, Aurora, ON, Canada) 4) a custom-made indenter connected to the motor via a rotary to linear converter and 5) a custom-made 3D positioning frame. In brief, the computer interface sends a voltage signal whose magnitude represents the desired output of the motor which in turn is controlled by the electronic feedback system. Transducer outputs from the control system provide both feedback control to the motor and output voltage to the computer. These signals represent the amount of displacement and force applied by the indenter respectively. Paired values for applied displacement and force can then be plotted and stiffness derived from the resulting plot.

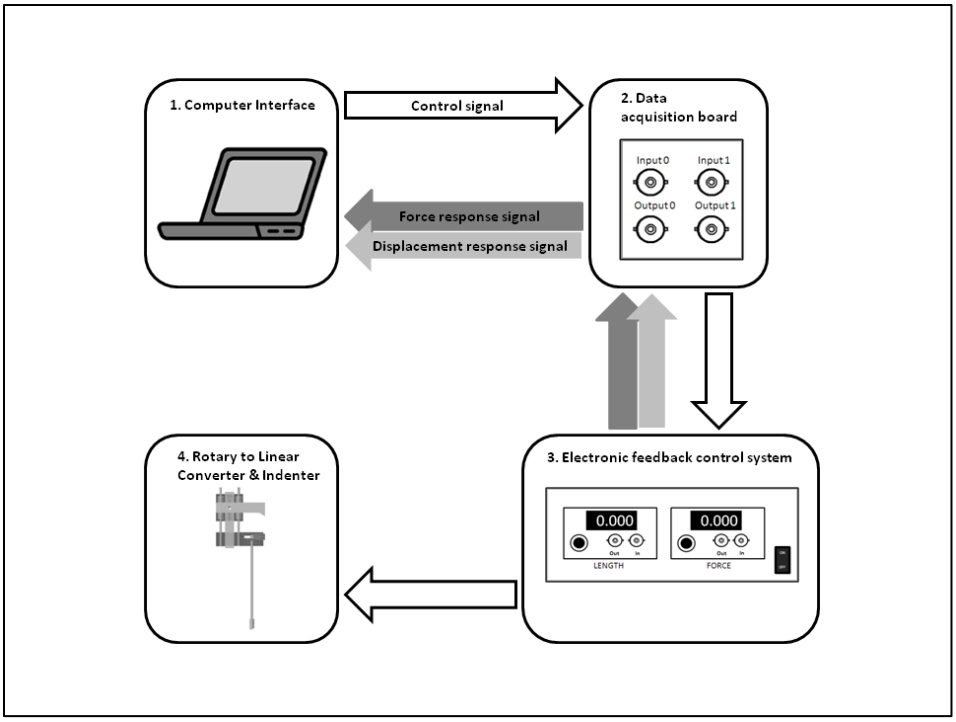

Figure 3.1 Diagram representation of the VRFD device. The voltage control signal is sent through the device and the force and displacement response signals are returned in a continuous loop. A graphical computer interface (3.1.1) enables the operator to program the specific voltage signal according to desired duration, rate of voltage increase and maximum voltage target. This voltage signal is sent through a data acquisition board (3.1.2) then to an electronic feedback interface (3.1.3) and a rotary moving coil motor. A rotary-to-linear conversion device (3.1.4) translates the rotational output of the motor's lever arm to a linear indenter.

3.2.1.2 Components

A custom graphical interface (LabView 8.6 , National Instruments, Austin Texas) enables the operator of the VRFD to program the input voltage signal that will control the magnitude and rate of indenter movement. The waveform constituting the signal is created using customized software (LabView 8.6, National Instruments, Austin Texas) which generates an analog file containing an array of values corresponding to the desired input voltage. The rate at which the data acquisition board will ultimately send the voltage (the rate at which voltage should increase), and the maximum desired voltage, are parameters that determine the number of voltage increments contained in the file and the value of each increment. Files containing unique displacement (voltage) rates and maximum displacement (voltage) magnitudes can be created in advance for

conducting indentations of differing parameters. In the current study, a single rate of 0.5 mm/s was used to assess stiffness.

The data acquisition board (Fig 3.1.2) is powered by, and connects to, a computer through a USB cable. The board sends the input signal for indentation to the electronic feedback control system at a rate of 1 kHz using 16 bit resolution.

The electronic feedback motor control system (Fig 3.1.3) consists of an electronic feedback interface and a rotary moving coil motor (Fig 3.2, item A). The electronic feedback interface connects to the data acquisition board and receives the input voltage signal from the computer. This connection can be modified so that the input voltage controls either the displacement or force generated by the motor. In this study, the motor was used in displacement control exclusively. Motor movement is inherently rotational (Fig 3.2, item B).
Because the lever motion is rotary, a component was fabricated to convert rotational motion to linear motion. A portion of this converter (Fig 3.1. 4 & Fig 3.2, item Cf) was mounted onto a stationary, rigid positioning frame attached to the motor. The movable portion (Fig 3.2, item Cm) had an oblong horizontal opening into which a short shaft from the motor's 8cm lever arm was inserted. The converter's moveable portion was guided by two rods traveling through linear bearings pressed into the converter's fixed portion. Actual indentation was performed by a 6 cm long titanium rod fixed in place at the bottom of C_f (Fig 3.2, item D). The rod was terminated with a 0.5cm thick plastic cap. Consequently, rotary motion of the lever arm created linear motion of the indenter's tip. Step changes in forces or displacement occur with response times of approximately 8 ms.

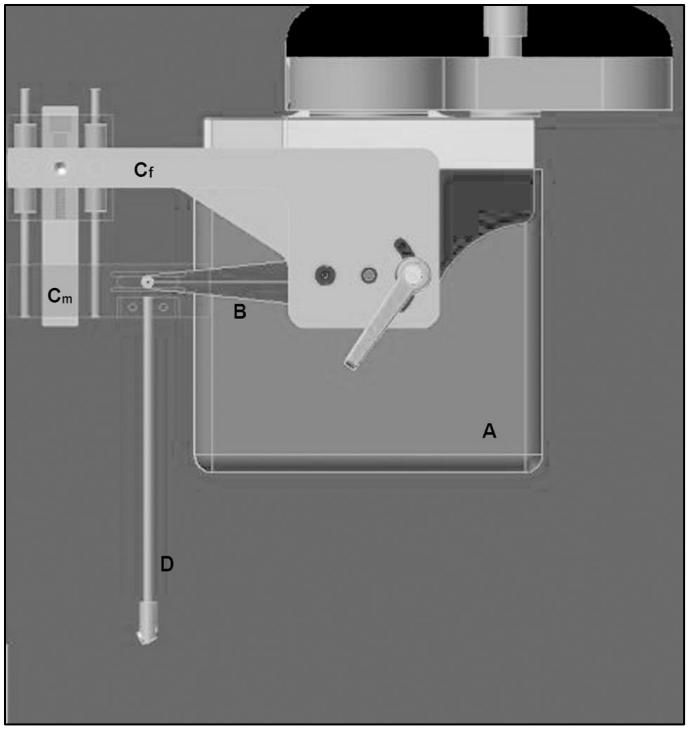

Figure 3.2 Schematic representation of the motor (A) and motor arm (B) connected to the rotary to linear converter which is made of a fixed (Cf) and a movable (Cm) component applying displacements through the rod (D). Motor movement is inherently rotational. Because the lever motion is rotary, a component was fabricated to convert rotational motion to linear motion.

Positioning the motor with the attached lever arm, linear converter, and indentation rod (Fig 3.2) was performed by a custom built 3D frame railing system onto which the motor was mounted. This frame enabled the motor to be positioned along 3 orthogonal axes with a precision of 0.5mm along each axis and 200mm maximum travel.

3.2.2 Calibration

With the rotary to linear converter in place, the maximum force and displacement attainable by the motor was 50.0N and 28.5mm respectively (as determined by the manufacturer). The manufacturer's calibration values (4.9N/V and 2.85mm/V) were confirmed experimentally by tracing the vertical position of the motor arm at 1V increments then using a digital calliper to measure the distance between tracings. In addition, a linear variable differential transducer

(0.1% error, MLT, Honeywell, Intertechnology, Don Mills, Ontario, Canada) was placed on Cm (Fig 3.2) to confirm that the manufacturer's conversion factors attained the desired displacement magnitude.

3.2.3 Spring Piston System

To assess the reliability of the VRFD device, seven compression springs of varying stiffness were used as test media. Springs (A-H) were obtained from Century Spring, Los Angeles California (manufacturer stiffness: 1.19 to 6.68 N/mm; free length: 10.2cm; outer diameter: 2.5cm; wire diameter: 0.3cm). The range of spring stiffness was selected to cover the range of possible stiffness coefficients expected in future experiments (expected mean K: 4.63 N/mm from preliminary *in vivo* testing for experiment 2, Chapter 4) [*Ianuzzi et al.,* 2009]. Each spring was placed around a piston (Fig 3.3) and a 1cm thick rubber pad was placed between the indenter and the piston. The pad provided a compliant interface to prevent uncontrolled motor oscillations.

3.2.4 Repeated Stiffness Testing

The rod (Fig 3.2. item D) was positioned in line with the center of the spring piston system (Fig 3) and perpendicular to its compressive surface. The piston was initially preloaded by lowering the motor using the positioning frame. A 0.61N preload was determined to be sufficiently high to compensate for the system's noise (+/- 0.025N of force output) and yet sufficiently low to prevent overloading the motor statically. The preload was also consistent with contact loads expected to be applied during future investigations [*Ianuzzi et al.,* 2009; *Pickar et al.,* 2007] (and from preliminary *in vivo* testing for experiment 2, Chapter 4).

Following preload application, a 4 mm indentation was performed at 0.5mm/s. In a previous study [*Kawchuk et al.,* 2006], a relatively fast indentation rate of

2.5mm/s was shown to have diagnostic accuracy but a slower rate of 0.5mm/s was selected to differentiate stiffness testing from the rate at which simulated SMT is to be performed in future experiments (1-3mm/s). Each spring was compressed in this manner 10 times to provide repeated measures for reliability analysis [*Kawchuk G and Herzog W,* 1996]. Between each of the 10 compressions, 5-10 seconds were allowed to pass to confirm or re-establish the preload magnitude using the 3D frame.

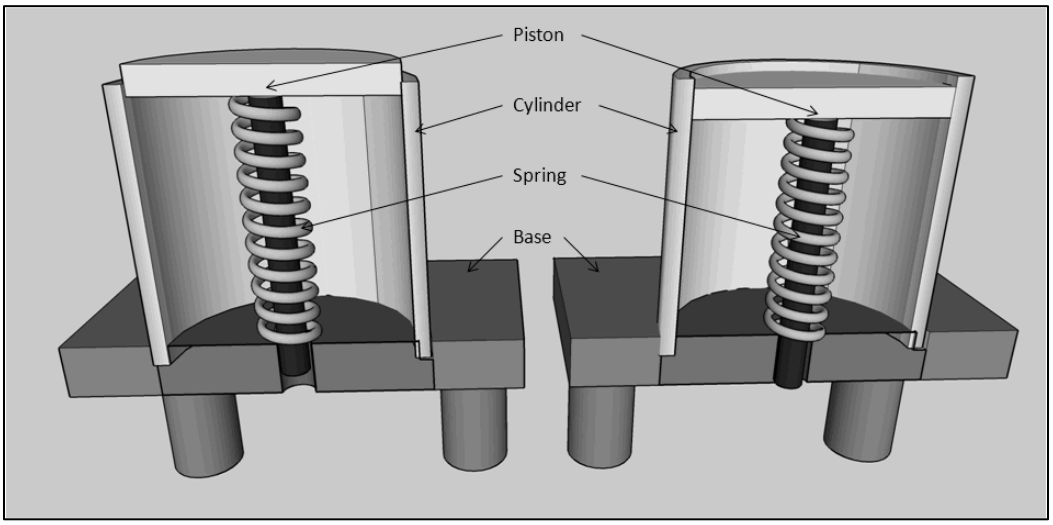

Figure 3.3 Spring and piston system. The piston (left) gets pushed down along the cylinder by the indenter and compresses the spring (right).

3.2.5 Analysis & Statistics

Continuous values for displacement and force during each indentation were recorded at 10 kHz and placed into separate files (Labview 8.6) resulting in 70 files (7 springs x 10 repetitions). For each indentation, the ascending portion of the force-time and displacement-time curves was cropped for the same time interval (Fig 3.4). Voltages were converted to engineering units (N and mm) using the motor's calibrated values. Force-displacement (FD) curves were created by plotting displacement on the x-axis and force on the y-axis. The beginning of each FD curve was established as zero spring displacement by subtracting the first value of the displacement signal from all displacement values. Each force

and each displacement curve was smoothed by fitting the data to a 5th order polynomial [*Kawchuk and Fauvel,* 2001].

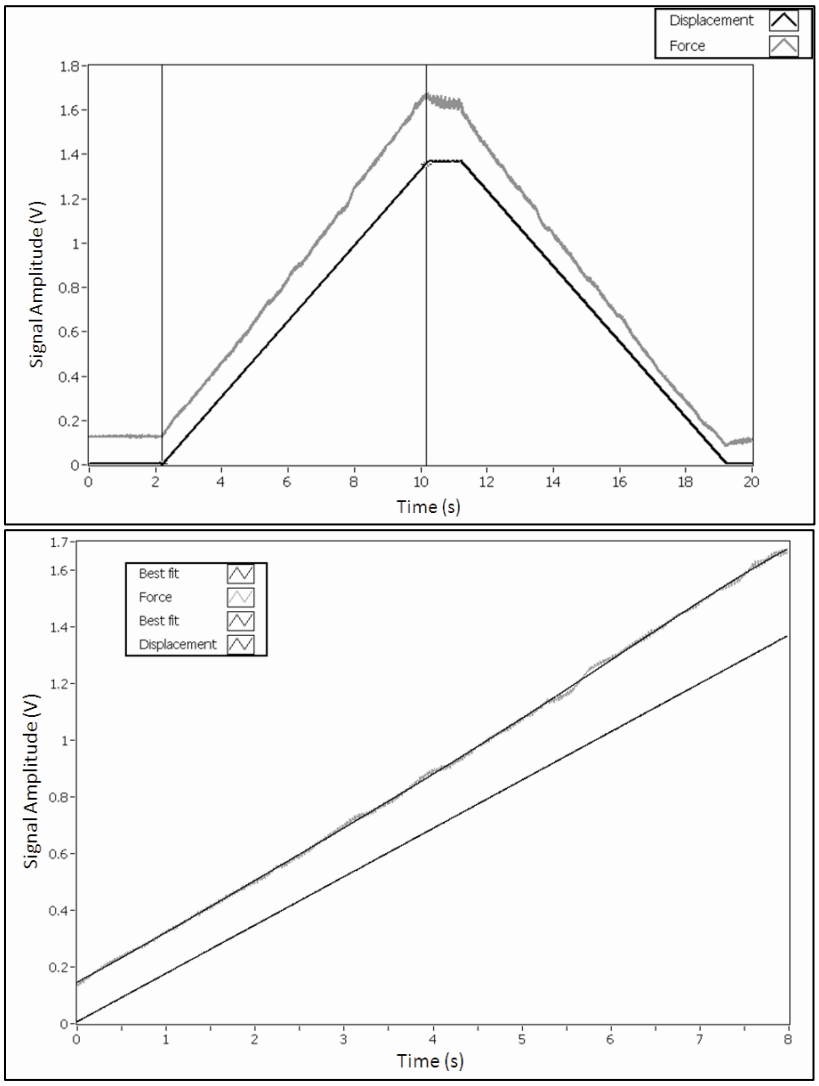

Figure 3.4 A voltage time graph demonstrating displacement and force signals collected by the VRFD device (top). The ascending portion of these plots defined to occur between the point in time where displacement increased from baseline to where displacement reached its first maximal value (bottom).

From each smoothed FD curve, a midpoint experimental stiffness coefficient (K_e) was calculated for a 0.5mm interval beginning at the midpoint (2mm total displacement) from the maximum displacement of 4.0mm [*Kawchuk and Fauvel,* 2001; *Petty et al.,* 2002]. The coefficient K_e was calculated by dividing the change in force by the change in displacement between 2 and 2.5mm. In addition, a terminal instantaneous stiffness coefficient (TIS) was calculated based upon the

force developed at 3.8mm displacement (Fig 3.5). The maximal programmed displacement of 4mm was not selected as the terminal displacement point in order to prevent calculation artefacts (+/- <0.01V) caused when the motor reversed direction and decompressed the spring.

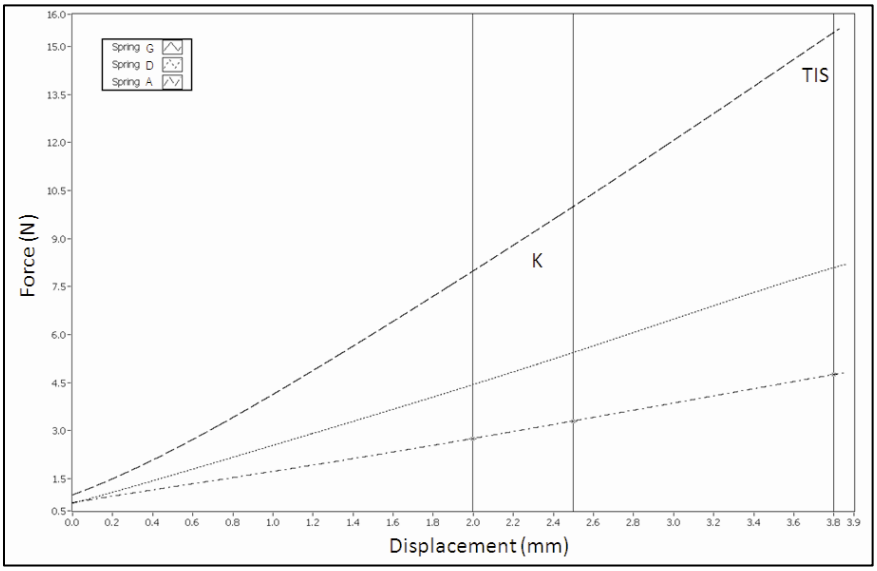

Figure 3.5 FD curve analysis. A midpoint interval stiffness coefficient (K) was calculated by dividing the change in force by the change in displacement between 2 and 2.5mm. The terminal instantaneous stiffness (TIS) was also calculated in the same manner at 3.8mm – a common displacement to all trials collected.

The Intraclass Correlation Coefficient (ICC(3,1)) was calculated for K_e and TIS values using a two-way mixed model analysis of variance for the reliability of a single measurement (PASW Statistics 17.0, SPSS, IBM, Chicago, Illinois). The 95% confidence interval and the coefficient of variation for spring stiffness were calculated for each spring to provide an estimate of precision [*Latimer et al.,* 1996; *Portney and Watkins,* 2008; *Kawchuk et al.,* 2001] .

3.3 Results

Summary statistics for the K_e and TIS values of each spring are displayed in Table 3.1.

Spring	Midpoint interval (2.0 to 2.5mm) Mean stiffness	Terminal Instantaneous Stiffness (3.8mm) Mean stiffness
A	1.08 (1.06-1.10)	1.28 (1.25-1.31)
	0.01%	0.02%
B	1.47 (1.44-1.50)	1.65 (1.62-1.68)
	0.02%	0.01%
C	1.61 (1.59-1.63)	1.78 (1.77-1.79)
	0.01%	0.00%
D	1.99 (1.96-2.02)	2.13 (2.11-2.15)
	0.01%	0.00%
E	2.47 (2.41-2.53)	2.59 (2.57-2.61)
	0.04%	0.00%
F	3.65 (3.62-3.68)	3.60 (3.54-3.66)
	0.01%	0.03%
G	4.03 (3.97-4.09)	4.07 (4.01-4.13)
	0.02%	0.02%

*coefficient of variation is given in % = (σ^2/mean stiffness) *100

Table 3.1 Summary statistics: mean stiffness and coefficient of variation from the midpoint interval and the TIS. Values are shown in Newtons per milimeter (95% Confidence Interval).

3.3.1 Reliability

The average ICC(3,1) for both K_e and TIS coefficients was 1.00. These ICC ratings can be considered to be "excellent" [*Portney and Watkins,* 2008]. K_e and TIS values from 10 repeated indentations for each of seven springs are shown in Figures 3.6 and 3.7 respectively. Least squared regression lines were fitted to the repeated stiffness measurements for each spring. All regression line slopes ranged between 0.01N/mm and -0.01N/mm (Fig 3.6, 3.7), suggesting there was no change in the stiffness of the springs with repetitive loading.

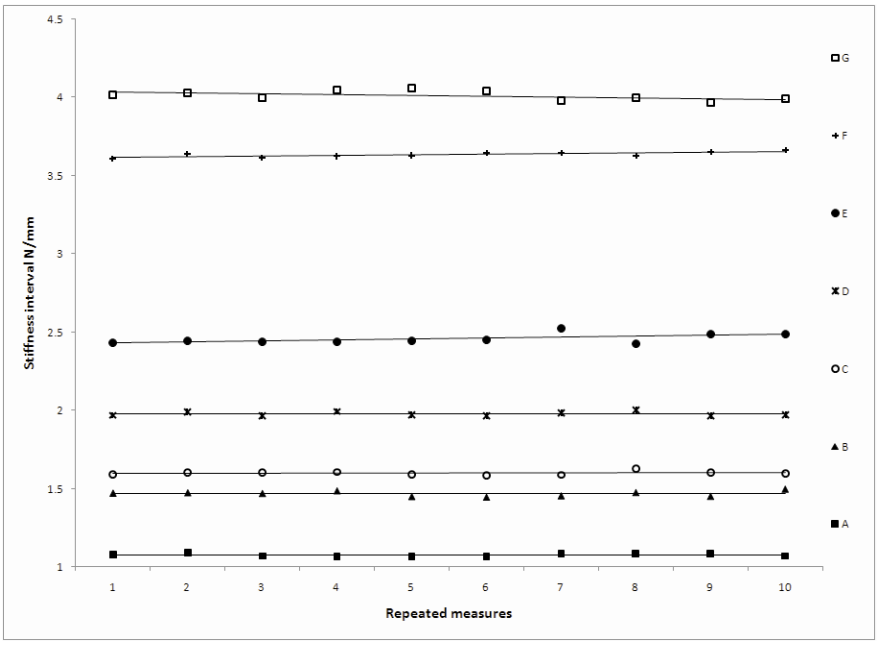

Figure3.6 Mid-point interval (2.0 to 2.5mm of displacement) stiffness coefficients taken from each force displacement curve in order of repeated trial (each letter designates a spring) and linear trend line.

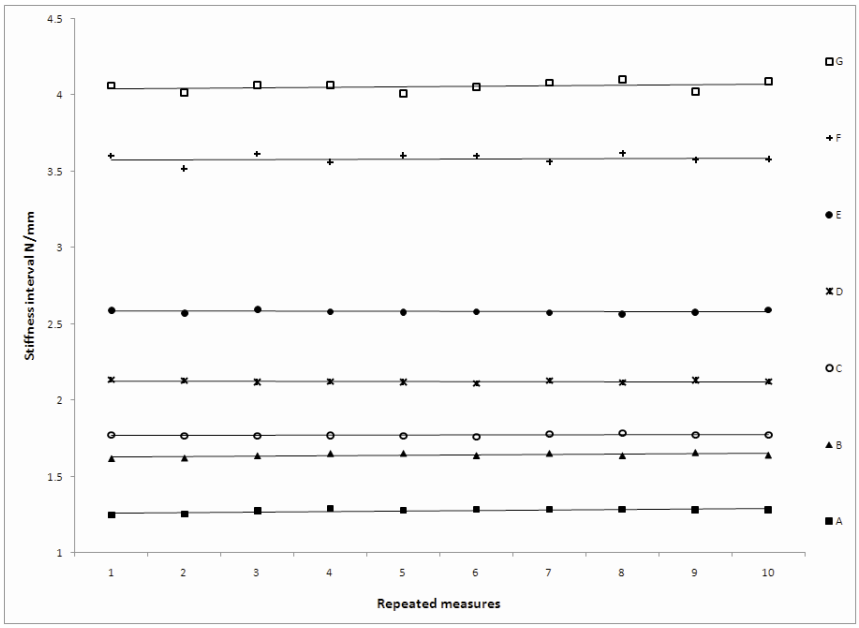

Figure 3.7 Terminal Instantaneous Stiffness (at 3.8mm) stiffness coefficients taken from each force displacement curve in order of repeated trial (each letter designates a spring) and linear trend line.

3.4 Discussion

In this paper, stiffness data acquired by the VRFD device were assessed for their reliability. Our results show the VRFD device had high ICC values.

3.4.1 Previous Postero-anterior stiffness testing

Postero-anterior (PA) stiffness is most commonly assessed by clinicians using manual techniques. Maher and Adams reported that judgements of stiffness made in this way had poor reliability with ICC values for PA stiffness estimates of the lumbar spine ranging from 0.03 to 0.37 [*Maher and Adams,* 1994]. Simmonds et al. reported that clinicians are also unable to perceive applied force and resultant displacements accurately [*Simmonds et al.,* 1995].

As a response to the poor performance of manual stiffness testing, various mechanical PA stiffness testing devices have been developed. Their performance has been established by measuring the stiffness of beams, cadaveric spines, and live subjects (Table 3.2). Specifically, Lee and Svensson developed the Spinal Physiotherapy Simulator [*Lee and Svensson,* 1990] (SPS) which they reported as having an ICC of 0.88 for stiffness coefficients calculated from the linear portion of the FD curve obtained in asymptomatic subjects. In addition, Lee and Evans developed the Spinal Mobiliser [*Lee and Evans,* 1992] to investigate the effect of tissue mobilisation and relative intervertebral mobility. The Spinal Mobiliser applied loads to the surface of the skin overlying the selected lumbar vertebra and measured displacements of the indenter over the adjacent vertebra. This device was shown to have an ICC of 0.95 for maximal displacements.

Although both the SPS and the Spinal Mobiliser provided highly reliable measurements of PA stiffness, others have commented that the technology is bulky [*Latimer et al.,* 1996] and may be difficult to operate [*Kawchuk et al.,*

2006]. In addition, these devices are not able to perform higher rate indentations [*Lee and Svensson,* 1990; *Lee and Evans,* 1992; *Lee et al.,* 1998] for dual use in SMT application .

Latimer et al. [*Latimer et al.,* 1996] improved upon these initial devices by developing a smaller, portable device that could be used in clinics to assess symptomatic LBP subjects. This device provided highly reliable measurements (ICC of 0.96) with a 90% confidence interval of 1.8N/mm for the slope of the linear region of the FD curve between 30N and 90N. Similarly, Edmondston and Allison's group used the Spinal Postero-Anterior Mobilizer (SPAM) to determine the effect of patient position [*Edmondston et al.,* 1998], load orientation [*Allison et al.,* 1998], and mobilizations [*Allison et al.,* 2001] on lumbar PA stiffness. The SPAM provided an ICC of 0.98 and a 95% confidence interval of 1.0N/mm for the stiffness coefficients calculated from the 35N to 80N section of the slope of the FD curve. These two devices improved on the SPS and the Spinal Mobiliser with their size and portability, but still lacked the ability to perform higher rate indentations [*Latimer et al.,* 1996; *Edmondston et al.,* 1998].

Study	Device	Subjects	FD curve analysis	Reliability	Accuracy
Lee and Svensson 1990	SPS	Aluminum alloy beams		N/A	Within 1% of true value
		L3 segment of symptomatic human subjects		ICC 0.88	
Lee and Evans 1992	Spinal Mobiliser	Lumbar segments of asymptomatic human subjects		ICC 0.95	Maximum error range ± 0.8mm
Latimer et al. 1996	Portable stiffness device	Beams		N/A	Maximal error 2.5%
		Lumbar segments of symptomatic human subjects	Stiffness coefficient	ICC 0.96	± 1.8 N/mm 90% confidence interval
Edmontston 1998	SPAM	Lumbar segments of asymptomatic human subjects	Stiffness coefficient from 35-80N interval	ICC 0.98	± 1.0N/mm 95% confidence interval
Owens 2007	PAS system	Lumbar segments of symptomatic human subjects	Stiffness coefficient from 55-75N interval	ICC 0.79	Standard error of measurement 1.62 N/mm
Tuttle 2008	PMAD	Cervical segments of asymptomatic human subjects	Curve shapes	CMD 0.96	N/A

Table 3.2 Previous devices: force-displacement (FD) curve analysis, reliability and accuracy.

Each of these devices offers highly reliable measurements which is a significant improvement over manual assessment techniques. Unfortunately, these devices have been tested on different types of subjects and spinal locations, which make the reliability coefficients difficult to compare.

3.4.2 Analysis techniques

In addition to difficulties in comparing ICCs derived from different devices and experimental conditions, a standard measure of stiffness has not been adopted to enable comparisons across studies although most have calculated stiffness coefficients from a pre-selected force interval [*Latimer et al.,* 1996; *Owens et al.,* 2007; *Allison et al.,* 2001; *Shirley et al.,* 1999]. To address this issue, Latimer et al. [*Latimer et al.,* 1998] compared different force interval widths and sections of

the FD curve and found that wider sections provided more reliable stiffness coefficients but that higher force intervals provided poor reliability in asymptomatic subjects. In the present study, a displacement interval was deemed preferable because a standard force interval would not have covered the same region of the FD curve due to the range of stiffness coefficients of our springs [*Shirley et al.,* 1999]. The testing in this study was performed in displacement-control mode, which further supports the selection of a displacement interval. Disparities in the confidence interval widths occurred between the stiffness coefficient K_e and TIS for each spring, however, there was no trend indicating which of these two stiffness measures was over all more reliable. It should be noted that the plotted FD data from each spring is in most instances linear. Although this data can be modelled with a single stiffness coefficient, complementary techniques to calculate stiffness from plotted data were employed as these techniques (K_e and TIS) have been used previously to evaluate force displacement data in clinical trials [*Stanton and Kawchuk,* 2008].

3.4.3 Limitations

This study design did not rule out the possibility of a systematic measurement error present in our collected data. Our use of stiffness measures used previously in clinical studies (K_e and TIS) ruled out the possibility of comparing our spring stiffness values with the manufacturer's values (K_m) which were derived and calculated with unknown methods. Therefore, comparisons between K_e, TIS and K_m were not considered valid.

The VRFD device was designed for animal studies, it is small and has limited force (50N) and displacement (28mm) capabilities compared to the devices reviewed above. As a result, the VRFD is ideal for the small animal model to be used in future investigations although it would not be capable of generating sufficient load or displacement to test humans at parameters used previously (>100N)

[*Latimer et al.,* 1996; *Lee and Evans,* 1992]. In its present form, the VRFD device would be inadequate for human experimentation unless the motor was replaced with a more powerful model and the ability to provide a greater linear displacement during the indentation possible.

The stiffness coefficient measured on the springs ranged from 1.08 to 4.03N/mm. After performing experiment 2, we observed higher stiffness coefficients in the feline spines (up to 12.87N/mm) than those covered by the springs. The average contact load/preload in Experiment 2 (1.25N) was also higher than what was estimated for this study, (see table 4.2). The benchtop reliability of the device at these higher force ranges remains unknown.

Even with the mechanical reliability of the VRFD device, it is important to consider that the reliability of stiffness measurements obtained may change when used in an *in-vivo* setting. *In-vivo* tissues are known to be more difficult to measure given their rate-dependant properties and may therefore produce less reliable measurements due to their complex and dynamic nature [*Lee and Evans,* 1992; *Nicholson et al.,* 2001; *Nordin and Frankel,* 2001; *Little and Khalsa,* 2005]. Furthermore, Kawchuk and Fauvel identified factors that reduce the reliability during *in-vivo* PA stiffness testing including intra-abdominal pressure changes due to breathing, muscular response, patient position, and indenter repositioning error between trials [*Kawchuk and Fauvel,* 2001].

3.4.5 Significance

Changes in spinal stiffness have been associated with low back pain [*Latimer et al.,* 1996], spinal degeneration [*Kawchuk et al.,* 2001] and range of motion [*Sran et al.,* 2005]. Therefore, stiffness assessments may provide insight into relevant changes in spinal properties attributed to disease or therapy. Latimer & al. [*Latimer et al.,* 1996] found an 8% decrease in stiffness coefficients as LBP

decreased in patients, however, investigations into the effect of manual therapies aimed at normalizing spinal stiffness have been unable to detect significant changes [*Allison et al.,* 2001; Goodsell, 2000; Shirley, 2002]. The reliability of the VRFD device is equivalent if not superior to that of previously reported devices. The high reliability [*Portney and Watkins,* 2008] of this device suggests that the detection of small changes in stiffness following SMT intervention may be possible.

3.5 Conclusion

In a benchtop setting, the VRFD device provides highly reliable stiffness measurements over a range of stiffness coefficients related to future clinical trials. The results of this study support the future use of the VRFD device in trials investigating the impact of SMT and other interventions that may influence spinal stiffness. Protocols to establish the reliability of *in vivo* measurements using the VRFD device are still necessary; the full characterization of the accuracy of stiffness measurements using this device is unknown.

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CHAPTER FOUR

EXPERIMENT 2

The effect of duration and amplitude of spinal manipulative therapy on the spinal stiffness of a feline model.

Abstract

Purpose: To determine the effect of spinal manipulation therapy (SMT) duration and amplitude on spinal stiffness of a feline preparation. We hypothesize that threshold duration and amplitude will result in a maximal change in spinal stiffness.

Methods: A mechanical device performed simulated SMTs at the L6 spinous process in 22 anesthetized felines. Subjects were divided into four groups. Groups 1 and 2 (no preload, preload) received SMT having maximal displacements of 1.0mm, 2.0mm and 3.0mm of total displacement (displacement control). Groups 3 and 4 (preload, no preload), SMTs were applied with maximal loads of 25%, 55% and 85% body weight (force control). Each of the SMTs were applied in order of increasing displacement or force amplitudes, at increasing durations ranging from 25 to 250 ms. The local stiffness of the region was quantified by applying an indentation load to the vertebra.

Results: A linear regression analysis showed that repeated SMTs caused minimal increases in stiffness ($p<0.01$) detected in the slope of the FD curve and minimal decreases in stiffness detected in the terminal stiffness ($p<0.01$) in Group 2. A mixed model repeated measures analysis detected a significant interaction effect of duration X displacement in Groups 1 and 2 ($p\leq0.05$), and an effect of duration in Group 2 and 3 ($p<0.05$).

Conclusion: In this anesthetized, uninjured, suspended, *in vivo* feline spine model, repeated SMTs cause minimal changes in stiffness thought to be due to a viscoelastic response and to the interaction effect between SMT duration and SMT amplitude. This study provides guidance for future investigations into the biomechanical effects of individual SMT parameters.

4.1 Introduction

The high prevalence of low back pain (LBP) [*Deyo et al.,* 2006] remains a burden on health care resources [*Wynne-Jones et al.,* 2008] despite growing efforts to improve treatment methods and diagnostic guidelines. Spinal manipulation therapy (SMT) is one of many common approaches that clinicians use in the treatment of LBP; however, evidence regarding the efficacy of SMT are mixed [*Assendelft et al.,* 2003; *Bronfort et al.,* 2004]. For example, a previously validated clinical prediction rule has identified a subgroup of patients who demonstrate significant improvements in pain and function following SMT [*Child et al.*, 2004]. In a subgroup of patients identified by this CPR, Cleland et al. noted greater pain and disability improvements following either of two thrust techniques (SMT) compared to a non-thrust technique [*Cleland et al.,* 2007; *Cleland et al.,* 2009]. This study highlights the importance of SMT parameters of application. Discrepancies in the results of SMT studies may be explained in part by varied SMT provision. Therefore, in order to better understand the effects imparted by SMT, further knowledge is needed regarding the different biomechanical parameters used in SMT provision.

Because SMT is a mechanical intervention by nature, it is believed that the mechanical parameters that define SMT application techniques modulate the neurophysiological and biomechanical mechanisms which lead to clinical changes [*Triano,* 2001; *Pickar,* 2002]. Previous research has outlined various SMT parameters including preload, force, displacement and duration that may modulate therapeutic effect [*Colloca et al.,* 2006; *Herzog et al.,* 1993]. Specifically, the high peak forces and short duration of the manipulation are mechanical characteristics of SMT that distinguish it from other types of manual therapies, and are believed to contribute to its unique effects [*Colloca et al.,* 2006; *Pickar et al.,* 2007]. Mechanically, the short duration distracts the two joint

surfaces at a high rate [*Brodeur,* 1995; *Ianuzzi and Khalsa,* 2005; *Ianuzzi and Khalsa,* 2005; *Gal et al.,* 1997]. The rapid impulsive tension believed to be imparted on facet joint capsules is expected to cause a stretch [*Nordin and Frankel,* 2001; *Triano,* 2001] and, therefore, a reflex stimulation of the neurophysiological system [*Pickar et al.,* 2007; *Ianuzzi and Khalsa,* 2005; *Pickar and Kang,* 2006].

To investigate these neurophysiological theories underlying SMT, Pickar and Kang (2006) used a feline model to measure the immediate neurological potentials evoked by mechanically simulated SMTs [*Pickar and Kang,* 2006]. They observed greater discharge frequencies from individual muscle spindles with SMT durations below a threshold of about 200ms. In a later study, Pickar et al. observed increases in lumbar paraspinal muscle spindle discharge occurring around the 100ms duration [*Pickar et al.,* 2007]. Although reports of the neurophysiological effect of SMTs applied at higher force amplitudes are mixed [*Colloca et al.,* 2004; *Sung et al.,* 2005], they were shown to generate greater vertebral displacement [*Colloca et al.,* 2006; *Keller et al.,* 2006] which could place greater strains on surrounding structures.

These neurophysiological and mechanical responses are proposed to cause desirable clinically outcomes. The neural discharge observed in response to SMT [*Pickar et al.,* 2007; *Dishman and Bulbulian,* 2001] could remove abnormal outputs and lead to decreased in abnormal muscle activation levels (spasms), increased pain threshold and improved proprioception [*Pickar,* 2002; *Bronfort et al.,* 2004]. The sudden distraction and stretch of the periarticular structures is aimed at restoring normal biomechanics to the site of dysfunction and to the spinal system by redistributing joint stresses and improving joint play [*Haldeman,* 2004].

While these studies highlight the relevance of SMT parameters, few have assessed biomechanical outcomes relevant to SMT and LBP. Increasing our understanding of the biomechanical effects of SMT will require outcome measures that reliably and accurately quantify biomechanical changes. While many different measures of various mechanical properties are candidates to fulfill this role (i.e. range of motion, flexion-relaxation response), spinal stiffness is a biomechanical property that is thought to be relevant to LBP. In some cases, increased spinal stiffness has been associated with severity of LBP symptoms [*Latimer et al.,* 1996; *Colloca and Keller,* 2001], the presence of vertebral degeneration [*Kawchuk et al.,* 2001], paraspinal muscle activity in the presence of dysfunction [*Shirley et al.,* 1999] and likelihood of improvement following SMT [*Flynn et al.,* 2002]. Given this association, stiffness traditionally has been assessed by clinicians with manual techniques. Prior investigations have shown that manually assessed spinal stiffness has poor accuracy [*Maher CG et al.,* 1998; *Simmonds et al.,* 1995], but can be quantified reliably and accurately by mechanical devices [*Latimer et al.,* 1996; *Edmondston et al.,* 1998; *Lee and Svensson,* 1990]. Similarly, consistency in the application of SMT parameters can be improved by use of a mechanical device. Several devices have been created to apply SMT, clinically and experimentally [*Pickar et al.,* 2007; *Keller et al.,* 2006], however, few provide control over critical SMT parameters (preload, amplitude, duration, position, direction). Even fewer devices are able to simulate SMTs and subsequently assess spinal stiffness.

Although the results of Pickar et al.'s studies indicate that the duration and amplitude of SMT elicit novel neurophysiological responses, the impact of SMT on spinal stiffness has not yet been explored in this established feline model [*Pickar et al.,* 2007; *Pickar,* 1999]. Given the above, the objective of this study was to determine the effect of SMT duration and amplitude on spinal stiffness of

a feline preparation. We hypothesize that threshold duration and amplitude will result in a maximal change in spinal stiffness.

4.2 Methods

A mechanical device performed 24 simulated SMT conditions at the L6 spinous process in 22 anesthetized felines. Subjects were divided into 4 different SMT protocols. Before and after each SMT event, the local stiffness of the region was quantified by applying an indentation load to the vertebra. The details of this protocol are outlined below.

4.2.1 Preparation

Experiments were performed on 22 deeply anesthetized felines obtained from an authorized facility (UC Davis-University, California). This study was conducted in accordance with the Canadian Council on Animal Care Guidelines and Policies with approval from the Animal Care and Use Committee: Health Sciences for the University of Alberta (see Appendix 1). The animals were given a subcutaneous injection of hydromorphone, glycopyrolate and acepromazine. Anaesthesia was induced with isofluorane via inhalation. An endotracheal tube was inserted to allow for controlled mechanical ventilation (ADS 2000 ventilator, Engler, Florida, USA) and maintenance of anesthesia with isofluorane. Arterial oxygen saturation (SPO2), heart rate, respiratory rate, temperature and reflexes (withdrawal, ear flick, and eye position) were monitored continuously by a trained animal technician. Isofluorane levels were adjusted accordingly to maintain a surgical plane of anesthesia. A catheter was introduced into the brachial artery to provide fluids intravenously as needed.

The lumbar area was shaved from L3 to S1. The L4 vertebra was identified through palpation and incisions were made to expose the spinous process for clamping. A stereotaxic system (David Kopf instruments, Tujunga, California) was used to support the spine through the iliac crests and the L4 spinous process (Fig 4.1). An L4 clamp and iliac crest hip pins were raised to suspend L5 to S1 in a horizontal position. This setup was adapted from Pickar's (1999) preparation developed to study neural responses to SMT [*Pickar,* 1999]. Stiffness measurements are non-invasive therefore further animal preparation is not required.

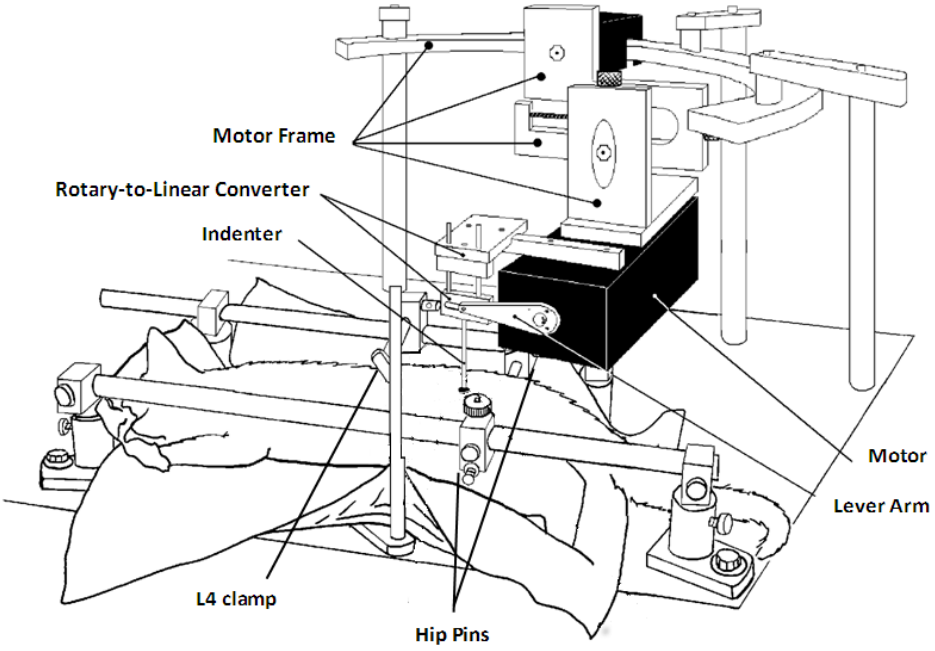


Figure 4.1 Feline setup. The motor, motor arm, rotary to linear converter and indenter can be positioned over the L6 spinous process using the 3D positioning frame. The stereotaxic railing system supports the L4 clamp and the hip pins of a deeply anesthetized feline. Modified from [*Pickar,* 1999]**.**

4.2.2 Indentation / Vertebral Loading

Simulated postero-anterior (PA) SMT and stiffness measurements were performed by a Variable Rate Force/Displacement (VRFD) device placed on the skin overlaying the spinous process of the L6 vertebra. The subject's breath was held at resting exhale for the duration of the measurement and SMTs by setting

the ventilator to 0 breaths per minute. Detailed description of the VRFD device and its reliability are described in Chapter 3. In brief, a graphical interface (LabView 8.6, National Instruments, Austin Texas) enables the operator to program the specific voltage (control) signal according to desired duration, rate of voltage increase (indentation) and maximum voltage target (peak displacement or force). This voltage signal is sent to an electronic feedback interface and a rotary moving coil motor (Aurora Scientific, Dual Mode Lever System, Model 310C, Aurora, ON, Canada). A rotary-to-linear conversion device translates the rotational output of the motor's lever arm to a linear indenter. An inverted U-shaped plastic tip at the end of this indenter rod helps prevent lateral slipping off of the spinous process. The positioning of the motor and the indentation rod can be adjusted precisely (±0.5mm) over the L6 spinous process of the supported feline spine using a 3D frame railing system onto which the motor is mounted. During this indentation process, a second voltage signal (data) is simultaneously returned to a computer providing information that represents the force-displacement (FD) response of the tested segment (stiffness).

4.2.2.1 Contact Load

To ensure adequate contact of the indenter tip with the spinous process (before indentation), an initial contact load was determined for each of the subjects prior to testing, to identify the loading point that corresponded to the point at which the tissues overlaying the spinous process were fully compressed. Loading beyond this contact load would ensure that further displacement of the indenter would produce vertebral displacement. To determine each contact load, a 0.049N load was first applied by the indenter before performing a 4mm indentation at a rate of 1.33mm/s. Force and displacement data were obtained and plotted as a FD curve. A linear regression line was fitted to the linear portion of the FD curve prior to the curve inflection point. The point where this linear fit

diverged away from the FD curve was identified as the contact load (Figure 4.2). This process was validated using invasive bone tracking to confirm that any load beyond the contact load would produce vertebral displacement (performed by J. Pickar's group at the Palmer Chiropractic Institute in Iowa).

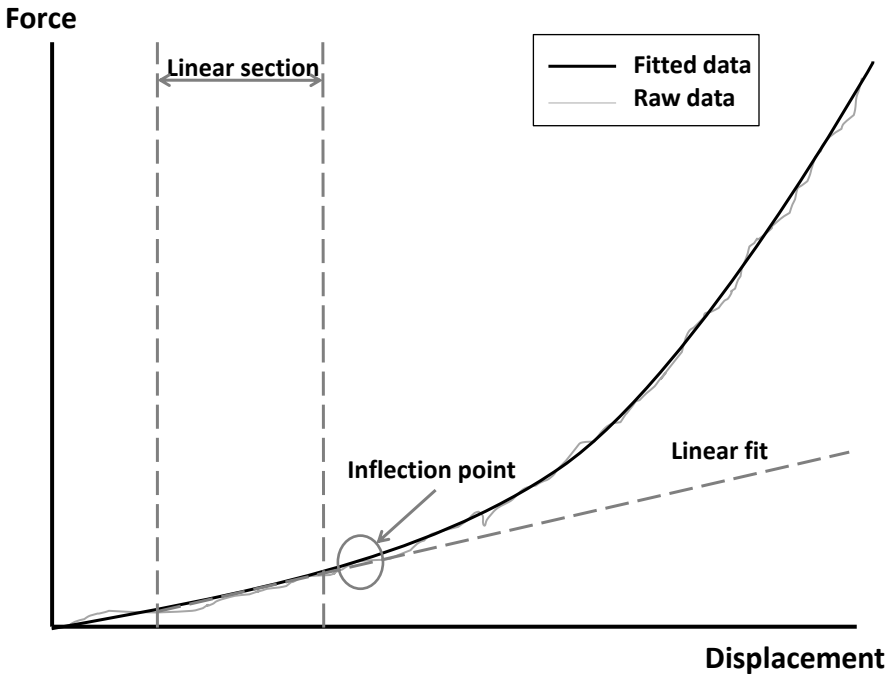
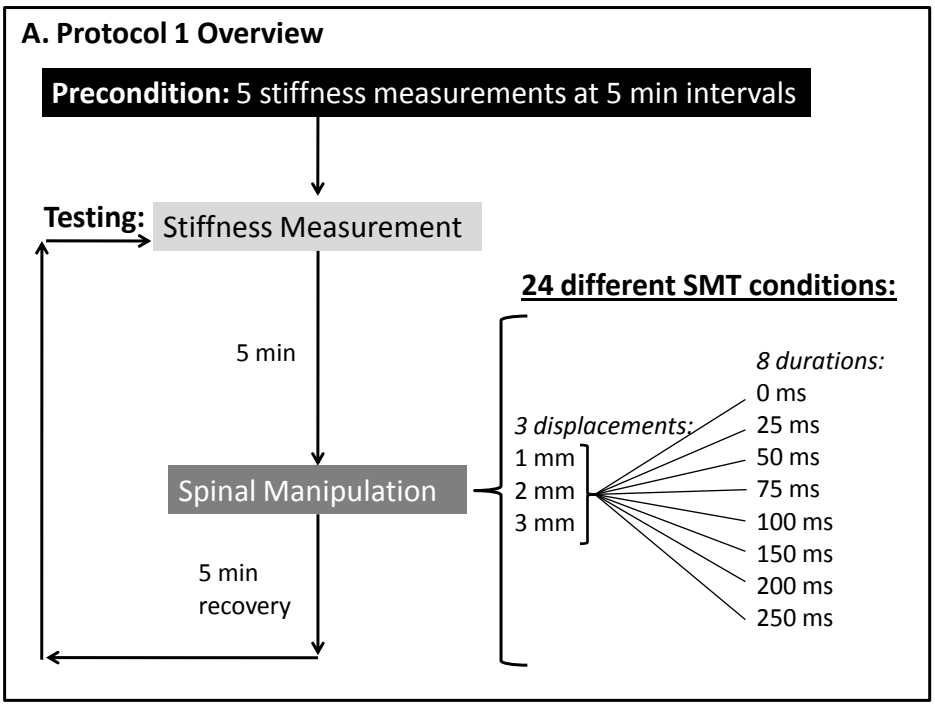


Figure 4.2 Force displacement curve showing the critical locations used to calculate the contact load. A 4mm indentation was performed at a rate of 1.33mm/s. Force and displacement data were obtained and plotted as a FD curve. A linear regression line was fitted to the linear portion of the FD curve prior to the curve inflection point. The point where this linear fit diverged away from the FD curve was identified as the contact load.

4.2.2.2 Stiffness testing

The predetermined contact load was manually applied prior to performing each stiffness test by lowering the indenter using the 3D positioning frame. The stiffness testing was performed by indenting L6 by 4mm at a rate of 0.5mm/sec. For each stiffness test, continuous values of displacement and force were recorded. Prior to the start of the experiments, five stiffness measures were performed at 5 min intervals without any SMT being performed. These 5 measures served to provide repeated measures for repeatability analysis, and to precondition the tissues [*Kawchuk G and Herzog W,* 1996]. The timing of

stiffness measurements between SMT conditions was modified after the first protocol; therefore Protocol 1 will be described separately (Fig 4.3, A and B).



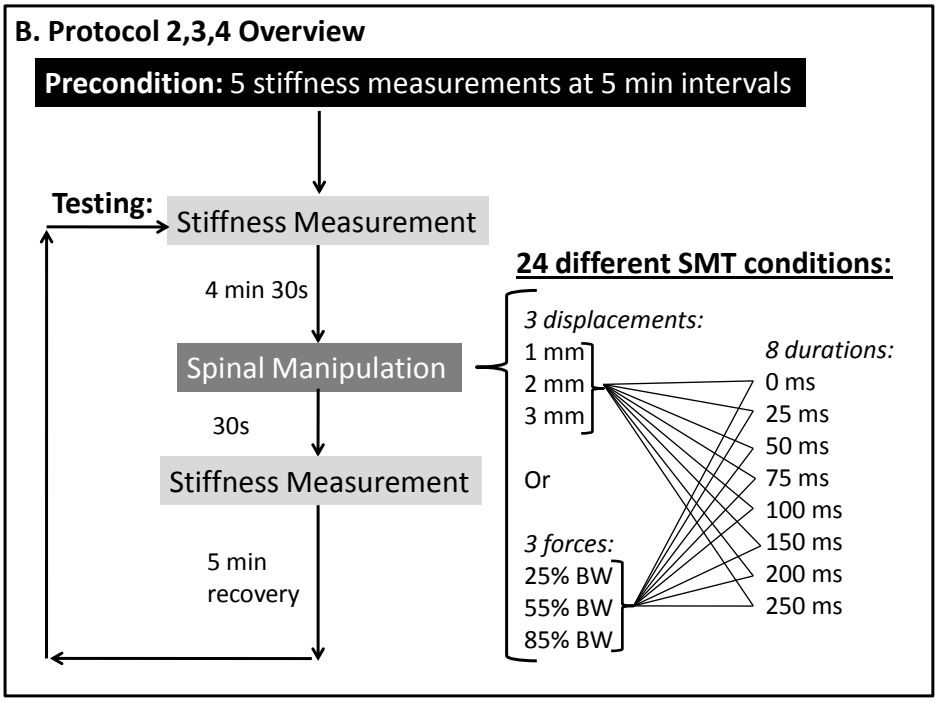


Figure 4.3 Diagram overview of the timing of protocols 1 to 4.

4.2.2.3 Simulated SMT conditions

Spinal manipulation conditions were given at 8 different durations: 0 (control condition, no SMT performed), 25, 50, 75, 100, 150, 200 and 250 ms duration. Each of these durations was performed at three displacement amplitudes or at three force amplitudes. The amplitude and duration values applied were scaled down according to body weight to cover values above and below those documented in human studies (see table 2.1). Over the time of the experiment, these 24 SMT conditions were performed in order of increasing displacement or force amplitude and increasing duration on each subject. Once applied, all SMT loads were removed quickly (20ms) to reproduce clinical load removal [*Herzog et al.,* 1993; *Solinger,* 2000]. The length of time taken to perform the SMT varied, therefore the rate of loading (average 34.4 to 1173N/s) or of displacement changed (4 to 120mm/s). Spinal manipulation conditions were not randomized to enable the detection of a threshold duration-amplitude condition. A contact load (Protocol 1 and 3) or a preload (Protocol 2 and 4) was manually applied prior to each of the 24 SMT conditions and was removed immediately after their completion. Upon review of the experimental data, an average duration of 4.31sec (± 3.16s) between the contact loads or preloads and SMT was identified. Each of the four protocols is described individually below. Figure 4.3, A and B illustrates the timing and order for each protocol and Table 4.1 lists the key variables.

	Protocol 1	**Protocol 2**	**Protocol 3**	**Protocol 4**
Subjects	*n=5*	*n=6*	*n=5*	*n=6*
Variable controlled	*displacement*	*displacement*	*force*	*force*
Amplitude	1, 2, 3mm	1, 2, 3mm	25, 55, 85%BW	25, 55, 85%BW
Pre SMT load	*Contact load*	*10% BW preload*	*Contact load*	*10% BW preload*
Durations	*0, 25, 50, 75, 100, 150, 200, 250ms*	*0, 25, 50, 75, 100, 150, 200, 250ms*	*0, 25, 50, 75, 100, 150, 200, 250ms*	*0, 25, 50, 75, 100, 150, 200, 250ms*

Table 4.1 Key protocol details.

Protocol 1: The first protocol was performed on five subjects. Displacement controlled SMTs were performed at 1.0mm, 2.0mm and 3.0mm of total displacement. Stiffness measures were taken 5 min after each of the SMT conditions followed by a 5 min recovery period before the next SMT condition was performed (Fig 4.3, A). The predetermined contact load was applied prior to each SMT condition.

Timing protocols 2, 3, 4: A pre-SMT stiffness measure was taken 4:30 min prior to each SMT condition and a post-SMT measure was taken 30s after the SMT. A 5 min recovery period separated the next block of pre-SMT, SMT, post-SMT indentations. This provided a pre and post SMT measure for each of the 24 SMT conditions (Fig 4.3, B).

Protocol 2: The second protocol was performed on six subjects. Displacement controlled SMTs were performed at 1.0mm, 2.0mm and 3.0mm of total displacement. Preloads of 10% of BW, calculated for each subject, were applied to better replicate clinical SMT application.

Protocol 3: The third protocol was performed on five subjects. The predetermined contact load was applied prior to each SMT condition. Force controlled SMTs were performed at 25, 55 and 85% of BW, calculated for each subject.

Protocol 4: The fourth protocol was performed on six subjects. Force controlled SMTs were performed at 25, 55 and 85% of BW. Preloads of 10% of BW, calculated for each of subject, were applied to better replicate clinical SMT application.

4.2.3 Curve Analysis

The ascending portion of the force and displacement (FD) curves was cropped at simultaneous points from the start to the end of the increasing voltage values (see Figure 3.4). The raw input values were fitted using a 5th order polynomial (Figure 4.4) and converted to the motor's calibrated values of 4.9N/V and 2.85mm/V for force and displacement signals respectively. From this data, a FD curve was then created by plotting the displacement values on the x axis and the force values and the y axis. The FD curve was normalized by subtracting the first value of the displacement signal to all remaining displacement values (Fig 4.5) [*Kawchuk and Fauvel,* 2001].

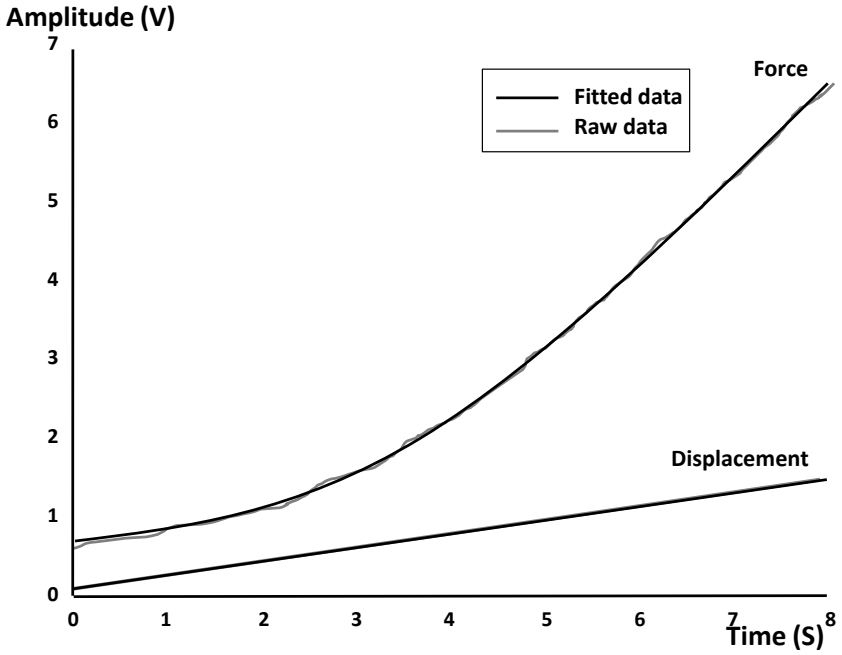


Figure 4.4 Raw force and displacement values in V, fitted with a 5th order polynomial.

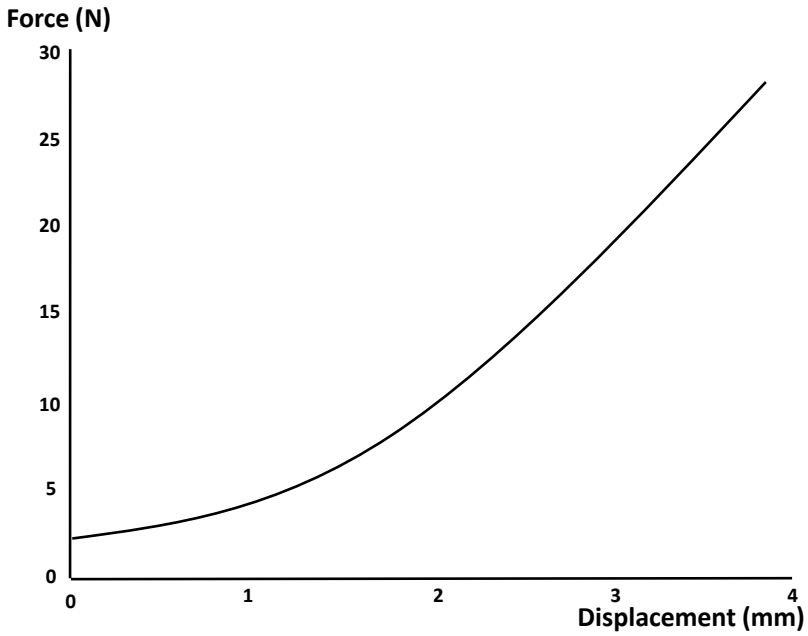


Figure 4.5 Force-displacement (FD) curve with values converted to the motor's calibration 4.9N/V and 2.85mm/V for force and displacement signals respectively and normalized by subtracting the first value of the displacement signal to all remaining displacement values.

The region of the FD curve which was most variable between stiffness measurements was identified for calculation of the stiffness coefficient. First, the variance of the force between post-SMT stiffness tests was plotted against the displacement for each subject (Fig 4.6). This provided one variance curve for each subject. Then, for each subject, the area under the average force variance curve was calculated at each 10% of displacement window. The area under the variance curve was then plotted against the displacement (Fig 4.7). These curves showed inflection points around 60% displacement, indicating that the rate of increase of the variance for most subjects decreased. The most variable section of the FD curve was therefore located after 60% of displacement.

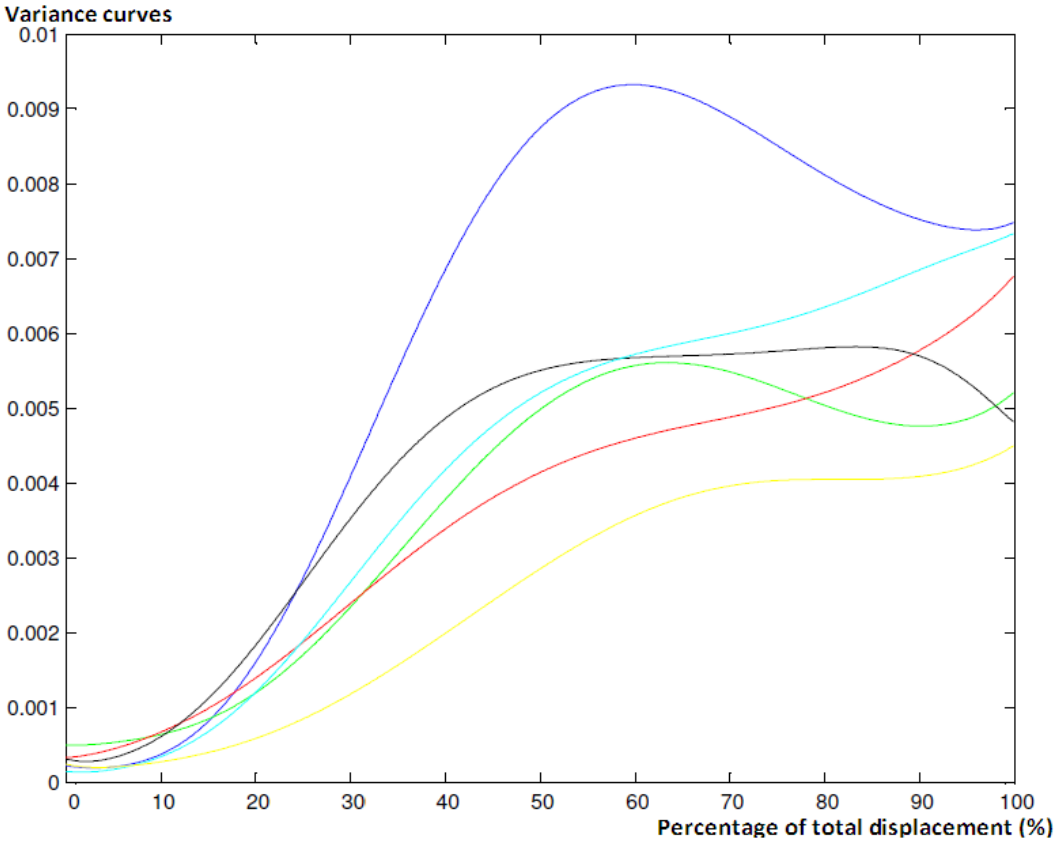


Figure 4.6 Variance curves for Protocol 2 at each 10 percent increment of total displacement.

This 60% inflection point was chosen as the start of the FD curve interval selected to calculate the stiffness coefficient (K). Therefore, the stiffness coefficient (K) was calculated from the slope of the linear regression line fitted to a displacement section (60-90%) of the FD curve for each post-SMT FD curve. The interval spanned from 60 to 90% (2.35 to 3.6mm) of total displacement so that it did not overlap with the second stiffness measurement, the terminal instantaneous stiffness (TIS). The TIS is defined as the stiffness at 3.8mm. The maximal targeted displacement of 4mm was not selected as the terminal displacement to prevent calculation artefacts (+/- <0.01V) caused when the motor reverses the indentation direction.

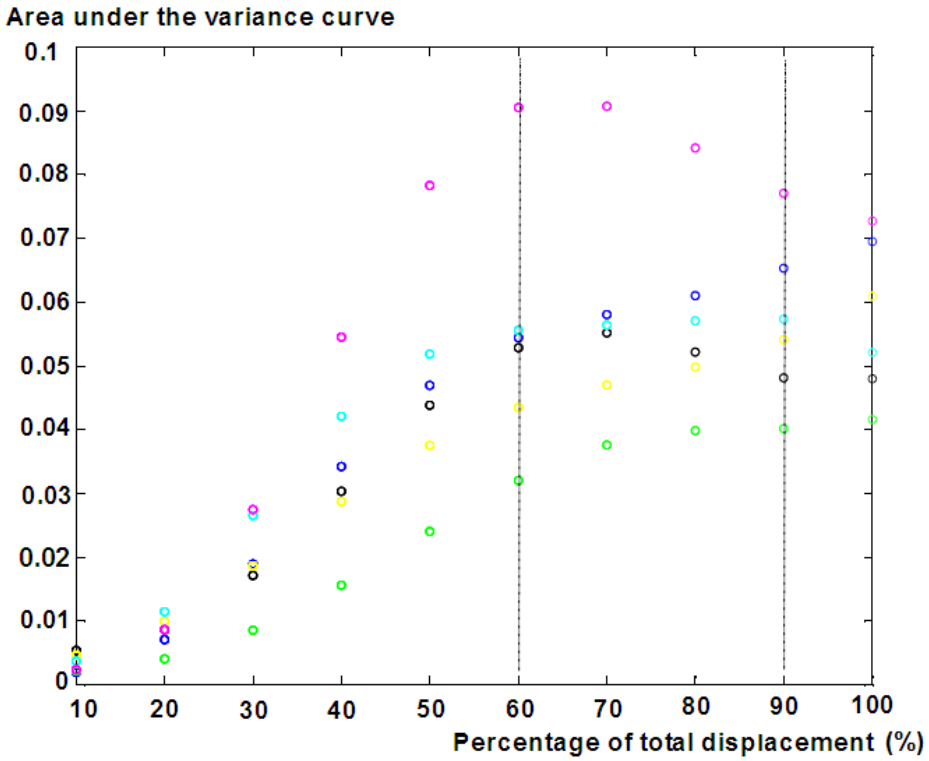


Figure 4.7 Area under the variance curve for Protocol 2 at each 10 percent increment of total displacement. The dotted vertical lines indicate the 60-90% interval selected to calculate K. Using this graph, the region of the FD curve which was most variable between stiffness measurements was identified for calculation of the stiffness coefficient. First, the within-subject variance of the force for each post-SMT stiffness test was plotted against the displacement. Then, for each subject, the area under the average force variance curve was calculated and plotted against the displacement.

4.2.4 Data Analysis

4.2.4.1 Repeatability

An Intraclass Correlation Coefficient (ICC(3,1)) was calculated for the K and for the TIS values of each protocol using a two-way mixed model ANOVA for the reliability of a single measurement (PASW Statistics 17.0, SPSS, IBM, Chicago, Illinois). Five values were used: the last four of the five preconditioning measure and the first pre-SMT stiffness measure. The first preconditioning measure was not included because this value is typically significantly smaller [*Shirley et al.,* 2002].

4.2.4.2 Regression Analysis

A two-stage analysis was performed. First, least squared linear regression lines were fitted to each subject's post-SMT K and post-SMT TIS values at each displacement or force amplitude. The slopes and the y-intercept values of each of these regression lines were then calculated. These values were then used separately for a one-way repeated measures analysis of variance (ANOVA) (PASW Statistics 17.0, SPSS, IBM, Chicago, Illinois) tested at α=0.05. The y-intercept of each regression line, the baseline stiffness value, was used to determine if a significant change occurred between different displacement or force amplitude groupings. The slope of each regression line (the rate of change of the stiffness values across the increasing SMT durations) was used to determine if a change occurred across force or displacement amplitude levels as an indication of a possible effect of SMT duration or number of multiple indentations.

The sphericity assumption, which requires relatively equal variance between set of different scores, was checked using Maulchy's test. The Greenhouse-Geisser correction was used whenever this assumption was violated. This correction adjusts the degrees of freedom for the F-ratio by multiplying them by the correction factor epsilon, therefore making the critical F value larger and correcting for the risk of a type I error. When a significant main effect was noted, post hoc pairwise tests were performed with a Bonferroni correction. This technique adjusts for multiple comparisons and protects against a type I error by dividing α by the number of comparisons [*Portney and Watkins,* 2008].

4.2.4.3 Repeated Measures

For the second stage of the analysis, a mixed effect, repeated measures, analysis (Proc Mixed, SAS) was performed on post-SMT K and post-SMT TIS values to test the main effect of SMT amplitude and SMT duration, and their interaction effect

(α=0.05). The covariance among the repeated measures was modeled using a compound symmetry covariance structure with the first pre-SMT measure added as a covariate to account for the between-subject heterogeneity. The mixed effect approach also accounts for the covariance between repeated measures through the use of a compound symmetry structure which proposes equal correlation between each pair of repeated measure [*Fitzmaurice et al.,* 2004] (this analysis technique is discussed in section 4.4.4.8).

4.3 Results

4.3.1 Descriptive statistics

The mean weight (±standard deviation) of the 22 animals used in the study was 3.51 (±0.71) kg. The mean initial stiffness values (K) (±standard deviation) was 6.13 (±2.80) N/mm. Table 4.2 displays the descriptive statistics for each subject in each protocol.

4.3.2 Repeatability

The repeatability analysis of the K and TIS values yielded similar ICC values of >0.99. The mean change in K and in TIS for the preconditioning measures were 0.05 (±0.10) and 0.03 (±0.07) N/mm respectively.

Protocol	Subject ID	Weight (kg)	Contact load (N)	Initial stiffness (K) (N/mm)	Initial stiffness (TIS) N/mm
1	1A	2.70	1.36	5.97	4.94
	1B	4.58	1.19	4.04	3.07
	1C	3.84	1.02	3.55	3.12
	1D	2.78	1.33	5.21	4.38
	1E	4.60	1.22	4.37	3.89
	Mean (±SD)	3.70 (±0.93)	1.22 (±0.13)	4.63 (±0.96)	3.88 (±0.81)
2	2A	2.77	1.10	4.09	3.53
	2B	3.61	0.77	4.06	3.42
	2C	4.35	1.24	4.64	4.13
	2D	3.67	1.48	3.82	3.59
	2E	3.05	1.67	5.21	4.82
	2F	4.04	1.31	4.54	4.25
	Mean (±SD)	3.58 (±0.59)	1.26 (±0.31)	4.39(±0.51)	3.96 (±0.54)
3	3A	2.77	1.55	4.68	4.49
	3B	2.80	0.72	3.77	3.18
	3C	4.00	0.92	5.87	4.95
	3D	2.90	0.85	5.54	4.13
	3E	2.40	1.38	10.48	9.14
	Mean (±SD)	2.97 (±0.60)	1.08 (±0.36)	6.07 (±2.60)	5.18 (±2.31)
4	4A	2.80	0.95	5.50	4.31
	4B	3.70	1.03	5.62	4.85
	4C	3.48	1.76	12.87	10.46
	4D	4.50	1.60	10.98	7.86
	4E	3.60	2.19	11.22	8.19
	4F	4.30	1.01	8.89	6.38
	Mean (±SD)	3.73 (±0.61)	1.42 (±0.51)	9.18 (±3.08)	7.01 (±2.30)

Table 4.2 Descriptive statistics for each subject and mean (±SD) per protocol. Weight, average contact load applied at the post-SMT measurements and initial stiffness.

4.3.3 Regression analysis

4.3.3.1 Amplitude effect

To determine the effect of SMT amplitude controlled in either displacement or force, each subject's post-SMT K and post-SMT TIS values at each displacement or force amplitude were fitted with least squared linear regression lines (Figures 4.7-4.10).

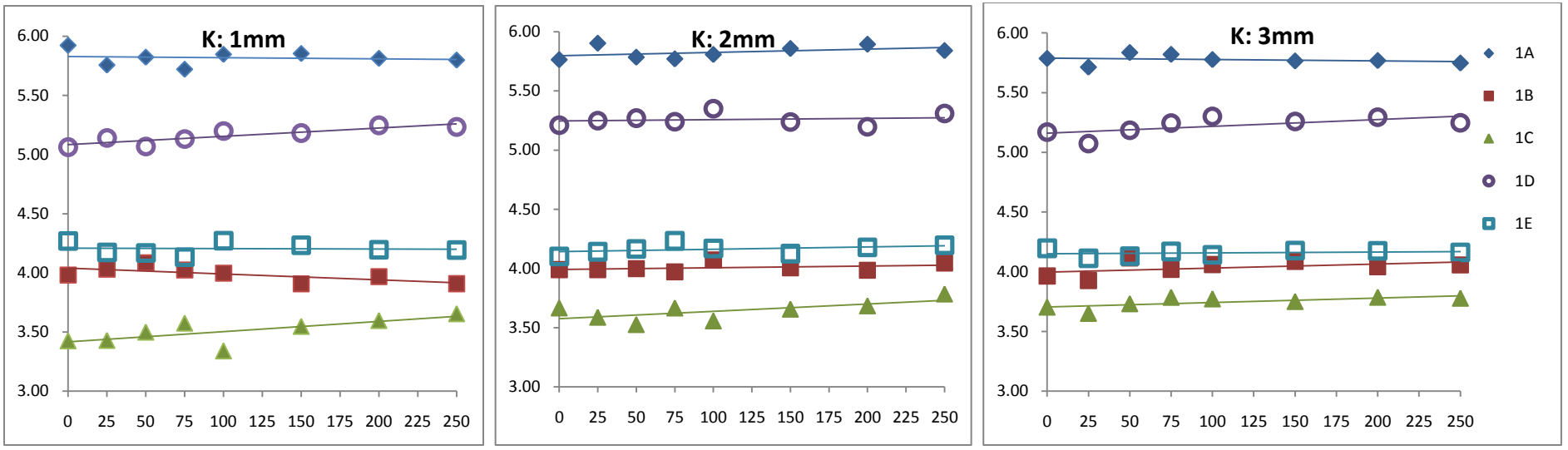
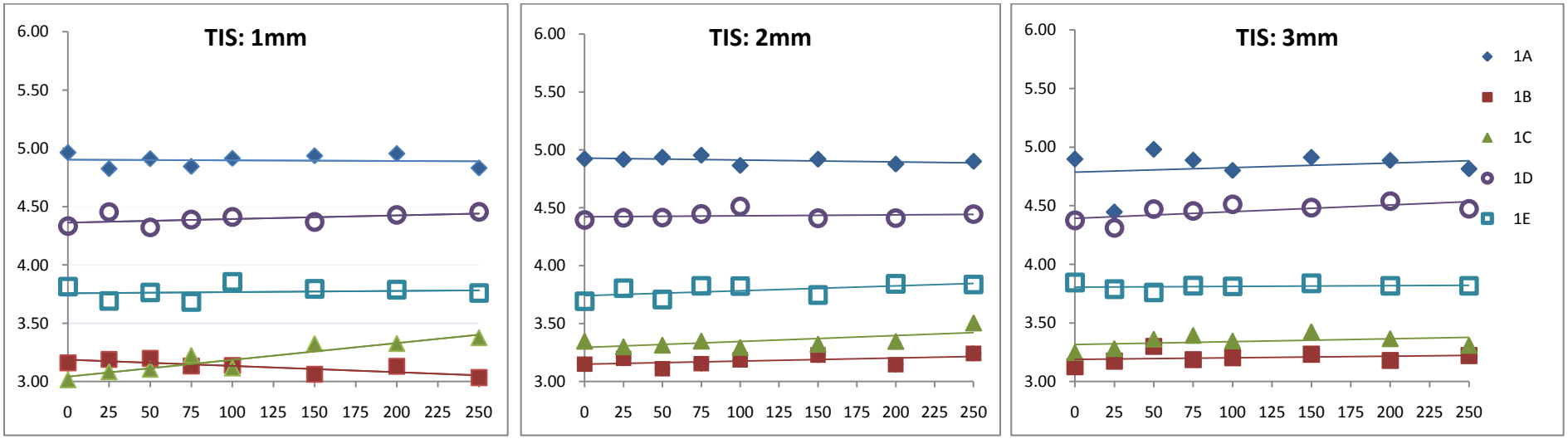


Figure 4.8 Graph of regression analysis for Protocol 1 (displacement controlled, no preload), including least squared linear regression line fitted to K values (above) and TIS values (below). The vertical axis represents the stiffness in N/mm and the horizontal axis represents the SMT duration in ms.



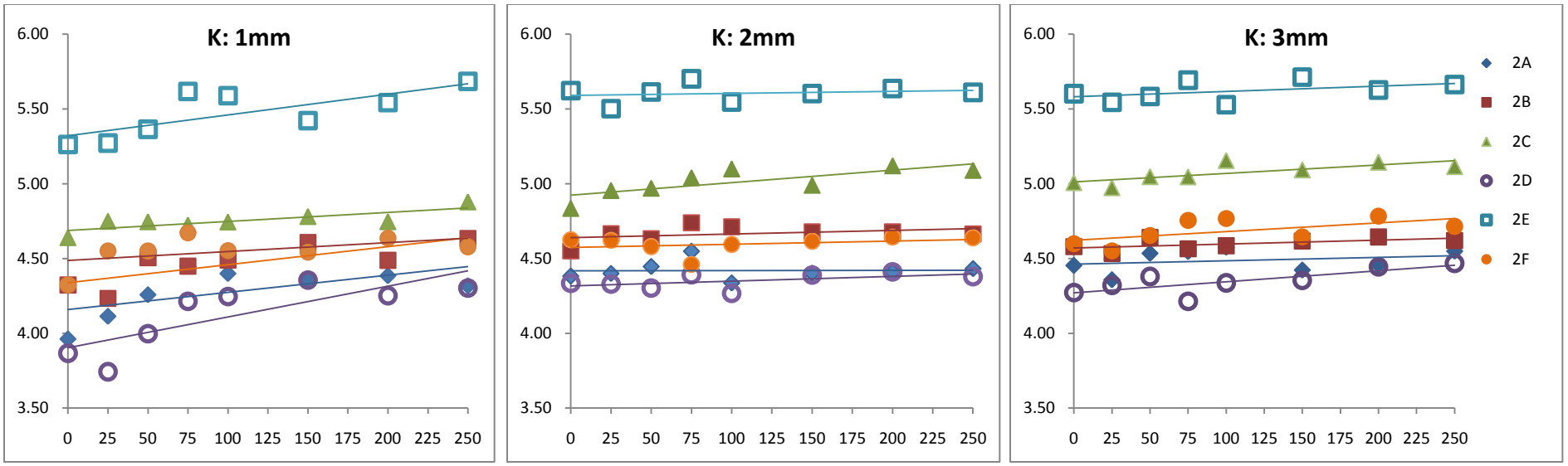
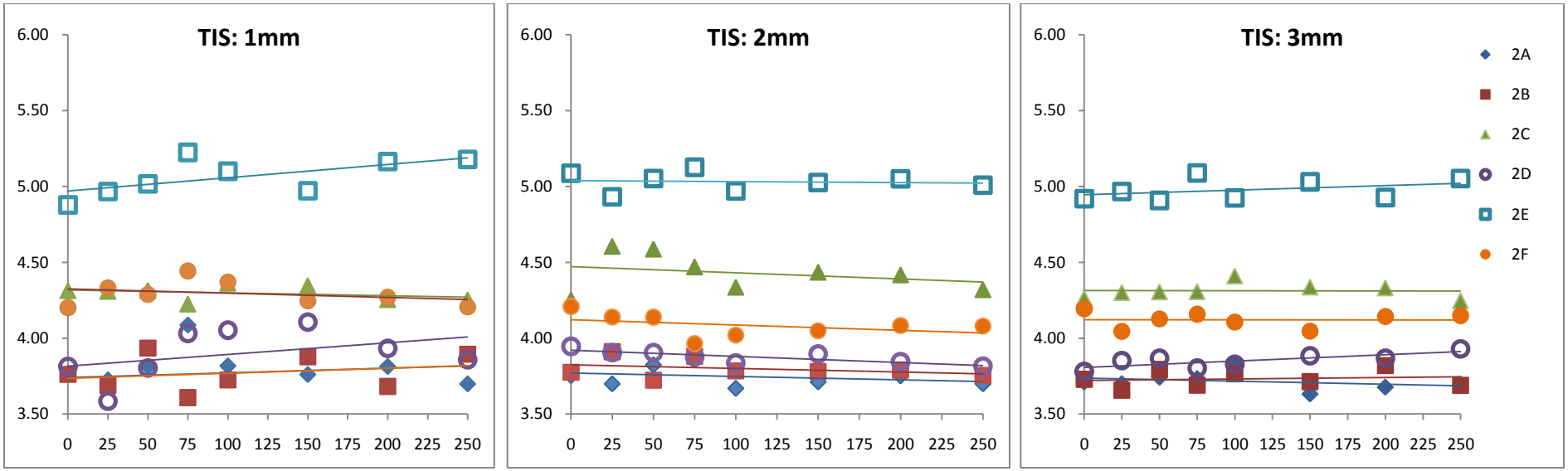


Figure 4.9 Graph of regression analysis for Protocol 2 (displacement controlled, with preload), including least squared linear regression line fitted to K values (above) and TIS values (below). The vertical axis represents the stiffness in N/mm and the horizontal axis represents the SMT duration in ms.



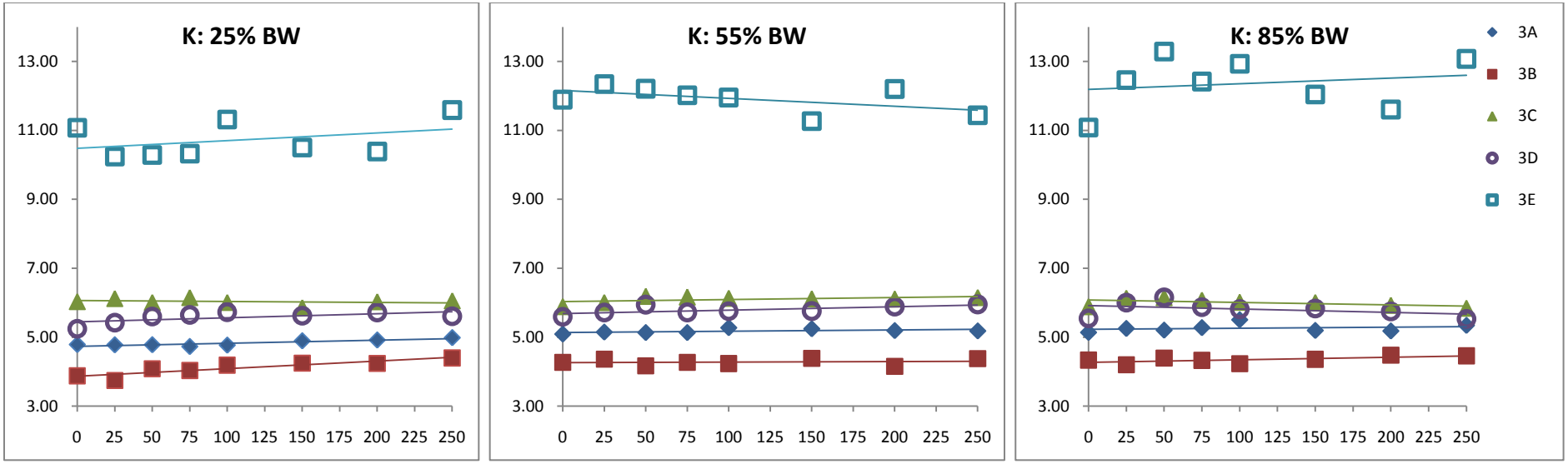
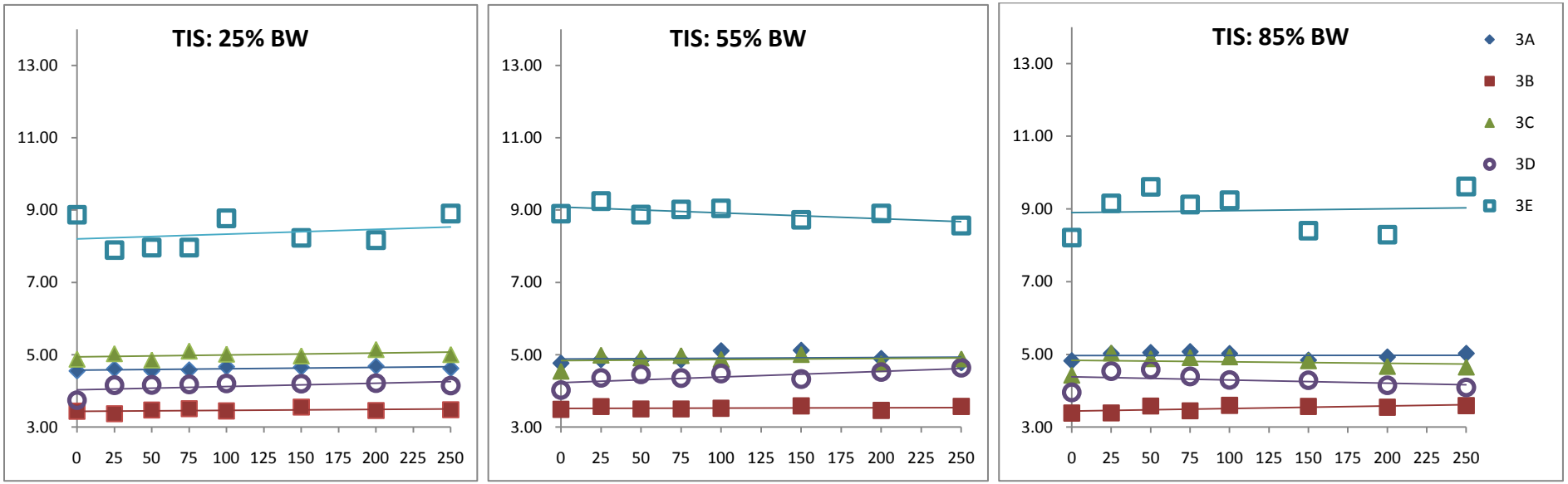


Figure 4.10 Graph of regression analysis for Protocol 3 (force controlled, no preload), including least squared linear regression line fitted to K values (above) and TIS values (below). The vertical axis represents the stiffness in N/mm and the horizontal axis represents the SMT duration in ms.



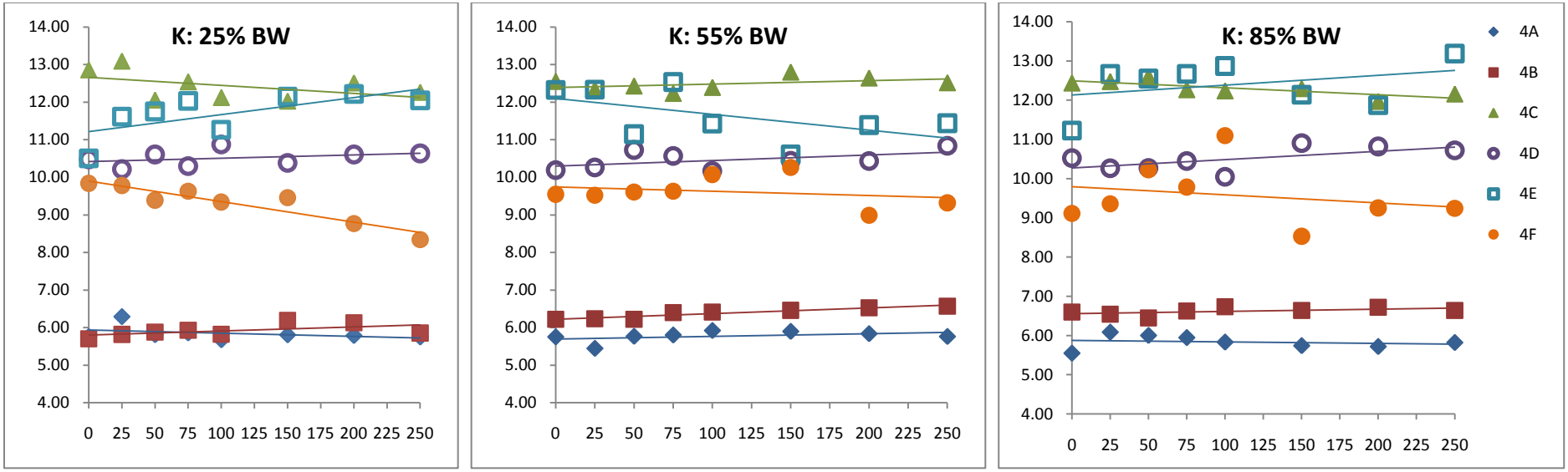
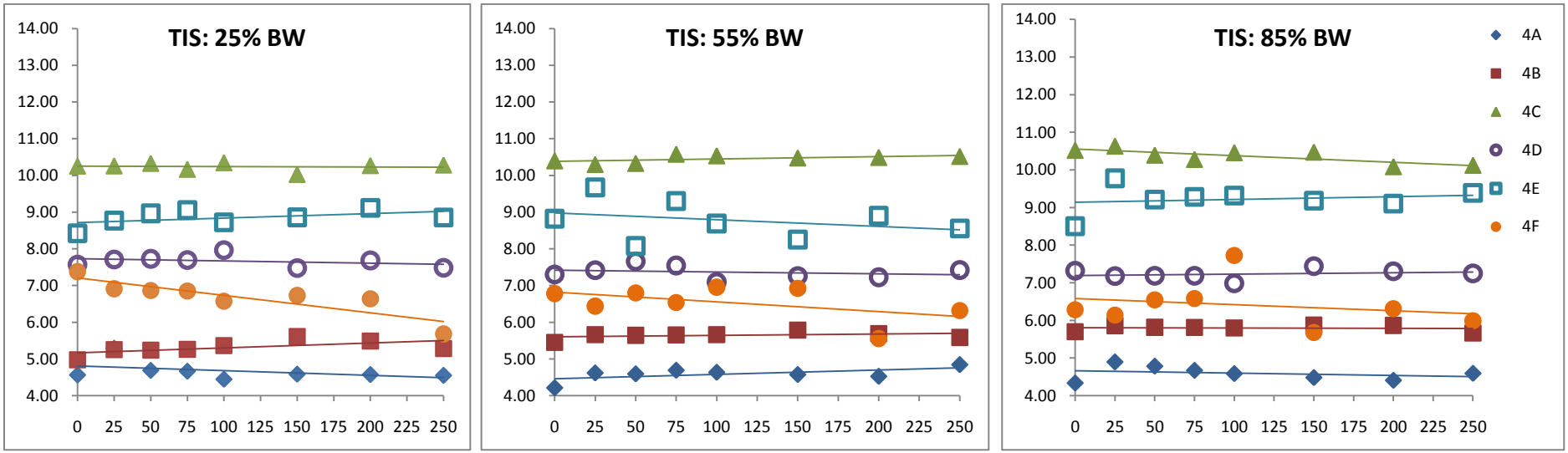


Figure 4.11 Graph of regression analysis for Protocol 4 (force controlled with preload), including least squared linear regression line fitted to K values (above) and TIS values (below). The vertical axis represents the stiffness in N/mm and the horizontal axis represents the SMT duration in ms.



The y-intercept of each regression line represents the baseline stiffness value for that subject for a given series of SMT durations grouped by either displacement or force amplitude. A significant change in the value of the regression line's y-intercept stiffness between different amplitude conditions is an indication of possible change in baseline conditions between displacement or force amplitude groupings (Fig 4.12). The slope of each regression line represents the rate of change of the stiffness values across the increasing SMT durations for that subject at a specific displacement or force amplitude. A change in the grade of the slope across force or displacement amplitude levels is an indication of a possible effect of SMT duration or number of multiple indentations (Fig 4.13). Table 4.3 displays the F test and p-values from the slopes and y-intercepts of the regression lines analyzed using a one-way repeated measures ANOVA.

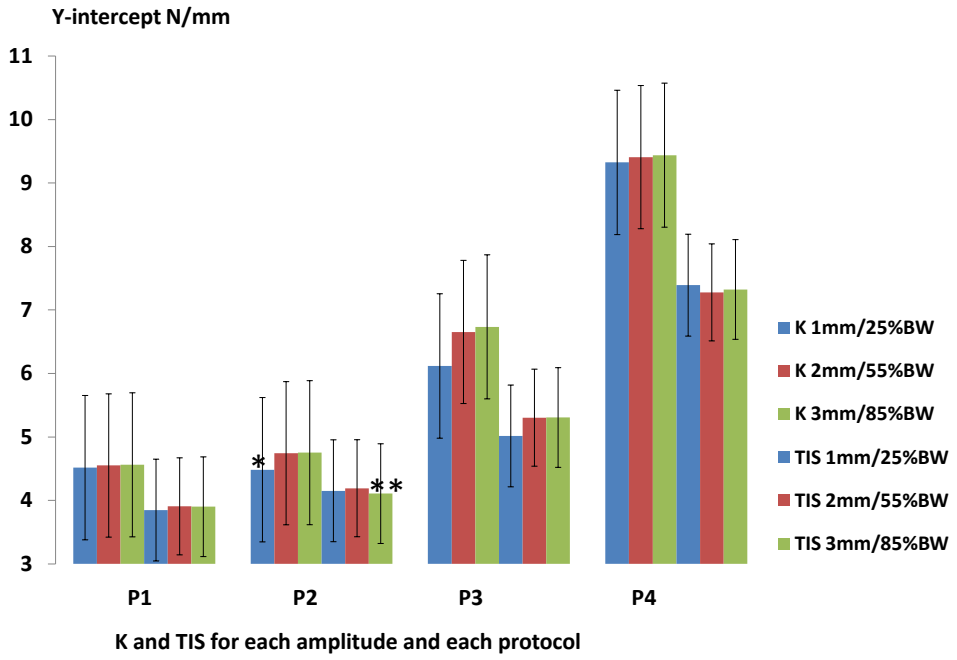


Figure 4.12 Mean y-intercept (in N/mm) of K (first three columns of each grouping) and TIS (last three columns of each grouping) at each SMT amplitude for each Protocol (P1, P2, P3, and P4). P1: displacement controlled SMTs, no preload applied, P2: displacement controlled SMTs, with preload applied, P3: force controlled SMTs, no preload applied, P4: force controlled SMTs, with preload applied. Significantly different y-intercepts, determined by a one-way repeated measures ANOVA are designated by * (K of P2) and ** (TIS of P2).

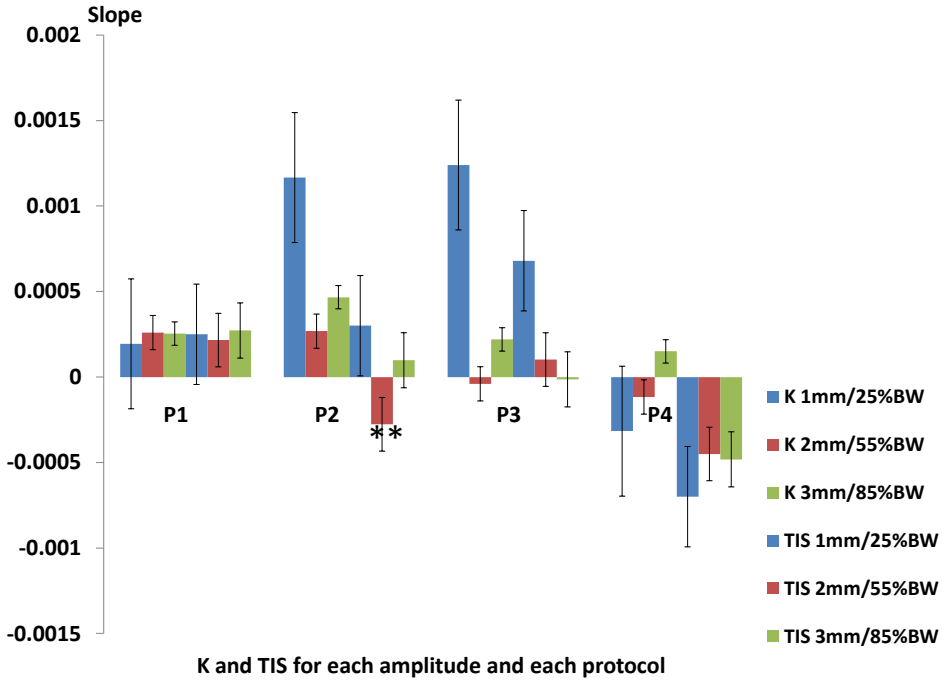


Figure 4.13 Mean slope of K (first three columns of each grouping) and TIS (last three columns of each grouping)at each SMT amplitude for each Protocol (P1, P2, P3, and P4). P1: displacement controlled SMTs, no preload applied, P2: displacement controlled SMTs, with preload applied, P3: force controlled SMTs, no preload applied, P4: force controlled SMTs, with preload applied. Significantly different slopes, determined by a one-way repeated measures ANOVA are designated by ** (TIS of P2).

Protocol 2, K: There was a significant effect of the SMT displacement amplitude on y-intercept but not on slope for the K of Protocol 2. Specifically, SMTs with displacement amplitudes of 2 and 3mm produced higher y-intercepts (mean 4.74 and 4.75 N/mm respectively) than SMTs with displacement amplitudes of 1mm (mean 4.48N/mm, $p<0.01$).

Protocol 2, TIS: The TIS values for Protocol 2 demonstrated a possible effect of SMT duration or number of multiple indentations on the slope and a significant effect of the displacement amplitude on the y-intercept. The slope of the 2mm displacement was significantly lower than the slope of the 3mm ($p<0.05$); the slope of the 1mm was also higher than the slope of the 2mm, but was not

significant. Therefore, the slopes of the 1mm and 3mm displacements were both slightly higher than the 2mm slope, although all three mean slopes were <0.001.

The y-intercept of the 1 and 2mm displacements were both significantly higher ($p<0.01$, $p=0.01$ respectively) than the y-intercept of the 3mm displacement (mean 1mm: 4.15, 2mm 4.19, 3mm: 3.5 N/mm). This indicates that either the repeated indentations or the increase in SMT amplitude from 2mm to 3mm lead to a decrease in the TIS.

Protocol 1, 3 and 4, K and TIS: In the regression analysis of the three other protocols, none of the slopes and y-intercepts were significantly different.

Protocol	Variable	Slope		Y-intercept	
		F(2,8)	P-value	F(2,8)	P-value
1 Displacement, no preload	**K**	0.07	0.94	0.40	0.69
	TIS	0.02	0.98	0.77	0.50
2 Displacement, with preload	**K**	9.16	0.02	36.57	**<0.01**
	TIS	7.97	**0.01**	26.69	**<0.01**
3 Force, no preload	**K**	1.31	0.32	3.93	0.12
	TIS	0.77	0.49	3.69	0.07
4 Force, with preload	**K**	0.06	0.86	0.196	0.83
	TIS	0.06	0.94	0.16	0.72

Table 4.3 F-test and p-values from the regression analysis.

4.3.3.2 Qualitative analysis of regression graphs

A visual analysis of the regression graphs for the K values indicate mostly positive slopes for Protocols 1 to 3 with y-intercepts that increase with the displacement or force amplitude. In contrast, the regression graph for the TIS values indicate no trend in slope values with mostly stable y-intercepts across displacement or force amplitudes. Qualitatively, a minimal increase in stiffness is observed for K

while a minimal change is observed for the TIS with the successive indentations with no consistent trend across protocols.

4.3.4 Repeated measures analysis

4.3.4.1 Amplitude x duration interaction effect

A repeated measures analysis was performed to determine the effect of SMT duration and amplitude. Table 4.4 displays the resulting F test scores and p-values. The interaction effect between amplitude and duration was significant for the TIS in Protocol 1 and for the K and the TIS in Protocol 2. Post-hoc multiple comparisons were not performed due to the small sample size and numerous levels [*Fitzmaurice et al.,* 2004]. However, this interaction suggests that the results of the main effects of amplitude and duration should be interpreted with caution.

4.3.4.2 Amplitude effect

The mixed effect repeated measures analysis was not significant for the main effect of displacement amplitude in Protocols 1 and 2 or for force amplitudes in Protocols 3 and 4.

4.3.4.3 Duration effect

The results of the mixed effect, repeated measures analysis show that there was a significant effect of duration for K values in Protocol 2 and for TIS values in Protocol 3. The K values in Protocol 3 also approach significance.

Protocol	Var	Amplitude	Duration	Interaction Ampl x Dur	Covariate Initial K or TIS
1 Displacement, no preload	**K**	F(2,8)=0.26, p=0.78	F(7,28)=1.68, p=0.15	F(14,56)=1.5, p=0.14	F(1,3)=477.77, p<0.01
	TIS	F(2,8)= 0.61, p=0.57	F(7,28)=1.62, p=0.17	F(14,56)=1.90, **p=0.05**	F(1,3)=597.62, p<0.01
2 Displacement, with preload	**K**	F(2,10)=2.08, p=0.18	F(7,35)=14.06, **p<0.01**	F(14,70)=2.77, **p<0.01**	F(1,4)=125.07, P<0.01
	TIS	F(2,10)=0.45, p=0.65	F(7,35)=1.38, p=0.24	F(14,70)=1.77, **p=0.06**	F(1,4)=149.26, p<0.01
3 Force, no preload	**K**	F(2,8)= 2.20, p=0.17	F(7,28)=2.03, **p=0.09**	F(14,56)=1.25, p=0.27	F(1,3)=1010.29, p<0.01
	TIS	F(2,8)= 1.75, p=0.23	F(7,28)=2.62, **p=0.03**	F(14,56)=1.55, p=0.12	F(1,3)=1465.13, p<0.01
4 Force, with preload	**K**	F(2,10)=0.71, p=0.52	F(7,35)=0.48, p=0.84	F(14,70)=0.79, p=0.67	F(1,4)=480.00, p<0.01
	TIS	F(2,10)=0.03, p=0.97	F(7,35)=0.99, p=0.45	F(14,70)=0.6, p=0.86	F(1,4)=318.49, p<0.01

Table 4.4 F-test and p-values from the repeated measures analysis (Var: Variable)

4.4 Discussion

4.4.1 Overview

This study was designed to investigate the effect of SMT duration and SMT force or displacement on spinal stiffness in a feline model. To our knowledge, this is the first study to have investigated the effects of individualized SMT parameters on the stiffness of the spine. The results do not indicate that the mechanical parameters of SMT studied in this experiment caused specific effects on local stiffness although minimal changes were observed in some of the protocols.

4.4.2 Findings

The different y-intercepts from the regression analysis of Protocol 2, suggest that SMTs of 2mm amplitudes caused an increase in K compared to SMTs of 1mm amplitudes. This increase was, however, not sustained at SMTs of 3mm

amplitudes. Conversely, the lower y-intercept for the TIS of the SMTs of 3mm amplitude suggests a decrease in baseline TIS at this higher displacement amplitude. This finding indicates that the increase in SMT amplitude from 2mm to 3mm may lead to a decrease in the TIS.

However, the smaller, negative slope of the TIS from the 2mm SMTs in Protocol 2 could have contributed to the lower TIS value observed at the 3mm SMTs. Overall the small slope values of the regression lines are not conclusive. A qualitative interpretation of the regression plots remains limited, as the slopes and y-intercepts observed do not appear to follow a trend as did the regression lines observed for the springs in Chapter 3.

On visual analysis of the regression graphs, most of the data points cluster near the regression line, indicating little variation from the individual subject's baseline value. This suggests that none of the SMTs of varying duration at specific amplitude caused the stiffness to deviate from the baseline value.

The mixed effect repeated measures analysis was not significant for the main effect of displacement amplitude in Protocols 1 and 2 or for force amplitudes in Protocols 3 and 4. Therefore, amplitude effects noted in Protocol 2 should be interpreted with caution.

The repeated measures analysis indicates an effect of duration for K values in Protocol 2, for TIS values in Protocol 3 and possibly for the K values in Protocol 3, however, the presence of an interaction effect of duration x amplitude in Protocol 2 and the low sample size limit post-hoc testing [*Portney and Watkins,* 2008; *Fitzmaurice et al.,* 2004]. This interaction indicates that the effect of the SMT duration on spinal stiffness may be modulated by SMT displacement or force amplitude. In other words, certain SMT duration may cause significantly

greater changes when applied at a specific amplitude, which may not occur at another amplitude.

4.4.3 Comparison to prior work

4.4.3.1 Expected stiffness changes

Current literature supports increases in spinal stiffness as part of the clinical presentation in some LBP patients (71% of LBP patients [*Fritz et al.,* 2005]). Manual therapy literature suggests that mobilizations and manipulations are intended to restore lumbar mobility through normalization of spinal stiffness [*Maitland GD,* 2001]. Mechanically, SMT distracts the facet joints and stretches the joint capsule and surrounding spinal tissues [*Brodeur,* 1995] which is believed to cause a decrease in spinal stiffness (see section 2.8).

However, the expected decrease in PA stiffness following SMT, proposed by the manual therapy paradigm, was not consistently detected under these experimental conditions. Conversely, an increase in the K (+0.26N/mm or 4%) and a decrease in the TIS (-0.69N/mm or 11%) were observed with the successive SMTs in only one of the protocols. Previous studies investigating the effect of manual therapy have also provided limited evidence to confirm stiffness changes following intervention [*Shirley et al.,* 2002; *Allison et al.,* 2001; *Goodsell et al.,* 2000; *Petty,* 1995].

Allison et al. (2001) applied mobilizations loads of 146N at a frequency of 1.5Hz which is equivalent to ~20% BW (considering an average human weight of 74kg) and 667ms duration. A mean increase of 0.2 N/mm observed at the mobilized segment was determined to be non-significant [*Allison et al.,* 2001]. Goodsell et al. (2010) performed PA mobilizations on the most symptomatic level of patients with non-specific LBP. The average mobilization force reached 137N or ~18% BW (considering an average subject weight of 76kg). Decreases of 0.3N/mm were

detected from the initial K of 15N/mm, a 2% change which did not reach statistical significance [*Goodsell et al.,* 2000].

The aforementioned studies focused on mobilization, however, Lee et al. also found no significant changes in PA stiffness following the application of a PA SMT [*Lee et al.,* 1993]. Stiffness increased by 0.31N/mm in the intervention group and decreased by 0.27N/mm in the control group (initial stiffness 14.8N/mm). There was no statistically significant difference between both groups. These results are comparable to the current study which indicated similar increases (+0.26N/mm) in the K intercepts of Protocol 2.

Studies performed in the last 5 years have shown that patients presenting with spinal hypomobility are more likely to respond to SMT [*Fritz et al.,* 2005; *Brennan et al.,* 2006] and that a stiffness decrease potentially only occurs at symptomatic locations [*Tuttle et al.,* 2008]. Therefore, the lack of pre-existing injury to the system or lack of abnormal stiffness levels in our model may not have provided the potential for significant decreases in stiffness levels. Although few studies have reported *in vivo* stiffness measurements following SMT in symptomatic patients; unpublished data from ongoing human SMT investigations by Kawchuk and Fritz (2010) shows decreases in stiffness of 0.4N/mm following intervention in a specific subgroup of LBP patients fitting the CPR (see section 2.3.1 and 4.1). Taking baseline human values from the previous literature (K=15N/mm [*Latimer et al.,* 1996; *Goodsell et al.,* 2000]), 0.4N/mm represents a 3% decrease in stiffness. Following a standard mobilization intervention on symptomatic cervical segments, Tuttle et al. also detected a significant decrease (~5%) in PA stiffness in the 4-7N and 14-17N regions of the 25N FD curve (16-28% and 58-68% region respectively).

The regression analysis in our study indicated one instance where a significant decrease in the y-intercept occurred which was of greater magnitude (-0.69N/mm or 11%) than these clinically relevant changes. This change was measureable between the TIS following SMTs of 2mm in amplitude and SMTs of 3mm in amplitudes. Furthermore, 55% of subjects presented with some instances of decrease in stiffness that were greater than the 3% observed in the study described above. Qualitatively these instances of clinically significant decreases did not occur consistently at specific amplitude x duration conditions, although this observation could not be confirmed by post-hoc tests of the repeated measures analysis.

The previously mentioned study by Tuttle et al. showed regions from the FD curve of the asymptomatic side with variable stiffness responses and a significant increase (~10%) in the 18-25N region (72-100%) [*Tuttle et al.,* 2008]. These variable stiffness changes across different regions of the FD curve are consistent with our observation of divergent changes when comparing the K to the TIS results in Protocol 2.

4.4.2.2 SMT parameters

SMT displacement or force amplitude

Stiffness changes observed in the intercepts of the regression analysis of Protocol 2 could be attributed to the increasing displacement; however, the results from the analysis of the K and the TIS are inconsistent. The small slope values observed in all protocols (<±0.001N/mm) are also inconclusive. In addition, the mixed effect repeated measures analysis was not significant for the main effect of displacement amplitudes in Protocols 1 and 2 or of force amplitudes in Protocols 3 and 4, which contrasts with the regression analysis for Protocol 2.

Previous studies suggest that the specific parameters that characterize SMT modulate treatment outcomes. Greater vertebral displacements have been reported when higher forces were applied, although findings of neurophysiological responses to graded force amplitudes are inconsistent (see section 2.9.3)[*Colloca et al.,* 2006; *Sung et al.,* 2005]. Mechanically, greater SMT amplitudes should lead to greater local strains and therefore greater decreases in stiffness due to the passive properties of spinal tissues [*Herzog,* 2000]; this theory could not be confirmed or refuted in the current study. Furthermore, the significant changes attributed to the effect of SMT displacement which was only observed in the regression analysis of Protocol 2 possibly indicates a preferential response to velocity (displacement) controlled than to load (force) controlled rates of application.

In parallel studies by Pickar et al. using similar protocols to perform the SMT conditions (unpublished 2010), greater response variability were observed following SMT amplitudes controlled by force compared to those controlled by displacement. This observation was consistent with our results, Protocols 1 and 2 had a variance of $\sigma^2<0.01$ compared to a variance of $\sigma^2>0.2$ for Protocols 3 and 4. This may reflect a common mechanism affecting both stiffness and neurophysiological responses; however, inconsistencies in the application of Protocols 3 and 4 may explain this higher variability.

SMT duration

The results of Protocol 2 and 3 indicate that there may be an SMT duration which causes a significantly different change in stiffness; however the presence of an interaction effect in Protocol 2 limits interpretation and a small sample size prevents post-hoc tests from being performed. Biomechanically, shorter durations of SMT with same peak amplitudes are expected to generate greater stresses, because of the viscoelastic (rate-dependant) properties of spinal tissues

[*Nordin and Frankel,* 2001; *Triano,* 2001]. At slow mobilization rates fluids are pushed out of tissues and loads can be transmitted to adjacent segments and dissipated throughout the spine non-specifically [*Powers et al.,* 2003; *Lee and Evans,* 1992]. Alternatively, tissues behave like stiffer non-viscous solids when responding to the high loading rates of SMT and cause greater displacements at the targeted joint than at more remote segments [*Gal et al.,* 1997], suggesting that SMT causes a greater, targeted strain. Furthermore, clinical trials have shown that thrust (short duration) techniques yield greater improvements in pain and disability compared to non-thrust techniques [*Cleland et al.,* 2007; *Cleland et al.,* 2009]. However, longer durations and greater amplitudes would cause more fluids to be forced out.

However, a study by Khalsa and Ianuzzi (2005) showed no differences in torque or strain magnitudes following SMTs of 47ms to 467ms duration and 2.33mm displacement performed on 7 dissected human lumbar spine specimens. Their results suggest that the effects of SMT duration may not occur through biomechanical responses [*Ianuzzi and Khalsa,* 2005].

The literature provides limited and inconclusive evidence regarding the existence of a duration and amplitude of SMT which will generate greater biomechanical responses. Therefore, comparisons between previous studies and our findings of a duration effect, and a duration x amplitude interaction effect would be inappropriate.

4.4.3.3 Viscoelastic properties

Given the conditions under which the current experiments were performed, the minimal change in stiffness observed throughout the protocols could likely be attributed to changes in the viscoelastic properties of the tissues. The suspension of the spine, the assumed absence of pre-existing injury, and anesthesia, created

a system where the responses measured reflected isolated biomechanical effects of SMT on the passive *in vivo* properties of the spine.

The tissues in this study were preconditioned and were close to equilibrium prior to the start of the protocol; the loss of viscous content of the spinal tissues may have decreased their ability to respond to SMT, which may explain why overall changes were minimal. Tissues are not typically preconditioned prior to intervention in clinical settings and no previous study has established the effect of conditioning prior to SMT or of repeated SMTs on the passive biomechanical properties of the spine.

As described, SMT imposes localized, high rate, compressive and tensile strains onto the spinal tissue which are thought to affect the time-dependant (viscoelastic) behavior of soft-tissues by altering their viscous flow. Previous studies have shown that tension-relaxation leads to a decrease in stress when a cyclic strain is applied [*Solomonow,* 2009]. The progressive loss of interstitial fluids contained within the collagen fibers is likely the mechanism which induced a minimal increase in K and a decrease in TIS in Protocol 2.

As discussed in Section 2.7 K, the slope of the FD curve obtained from loading the spine represents the elastic stiffness and has been widely used as an outcome in studies investigation the PA stiffness of the spine. Conversely, the TIS has not been commonly used. As the indentation approaches the end of the elastic range, the FD response becomes less linear and should not be fitted using a linear regression [*Kawchuk and Fauvel,* 2001]. A similar technique has been previously used to assess the effect of different types of abdominal muscle recruitment on spinal stiffness [*Stanton and Kawchuk,* 2008], however, similar findings were obtained from the K and the point stiffness at the end of indentation (TIS). In Protocol 2 the TIS may represent a different characteristic of

the FD response. Fig 4.14 shows how the K and TIS of two post-SMT FD curves can differ. The bottom graph displays how a change in TIS may provide some information similar to the width between the loading and unloading limbs of a torque angle graph. Therefore, the TIS may be more sensitive to a change in the viscous stiffness (hysteresis).

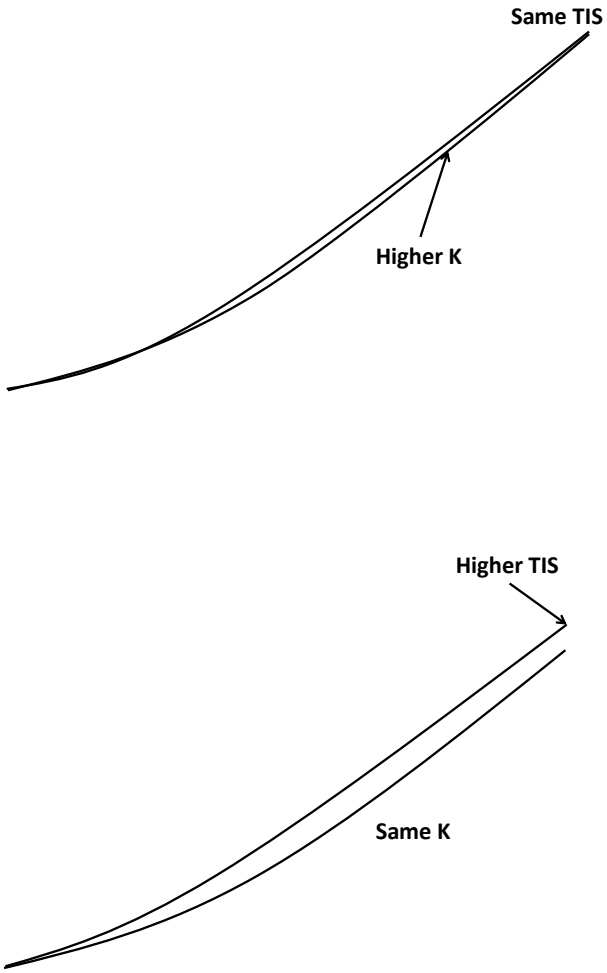


Fig 4.14 FD curves. Above showing two post-SMT FD curves with the same TIS but different K, and below showing two post-SMT FD curves with the same K and different TIS.

In the current study, stiffness changes may not be attributed to specific SMT effects. However, other SMT parameters may not have been optimized and/or

threshold duration and amplitude may not have been reached. Therefore, we can not generalize the absence of effect of SMT of spinal stiffness.

4.4.4 Strengths

This study was the first to investigate the effects of individualized SMT parameters on the stiffness of the spine. The strengths of the methods used to assess this effect are presented in the following section.

4.4.4.1 Device

In this study, SMTs of the spine were performed by a mechanical device, which provided precise control over a range of displacement or force amplitudes and durations, as well as all other SMT application parameters (direction, contact area, preload). Given the excellent ICC values [*Portney and Watkins,* 2008] obtained from previous benchtop testing described in Chapter 3 of this thesis and from the preconditioning measurements, the stiffness measurements obtained can be considered reliable. The device and setup also enabled stiffness measures to be performed without changes to positioning, which previous authors have shown to contribute to measurement errors [*Kawchuk and Fauvel,* 2001]. Measured changes should therefore accurately reflect actual within-subject changes or variations.

4.4.4.2 Model and setup

The feline model used in this study was chosen to remain consistent with the ongoing investigation of the neurophysiological effects of SMT by Pickar et al. The purpose of this model was to increase understanding of the physiological effect of SMT parameters, rather than the impact on specific patient outcomes (pain, function). This model provided a very stable system, as proven by the excellent ICC values [*Portney and Watkins,* 2008], where smaller changes could be detected with less confounding variables. The ICC values obtained in the

current study (>0.99) are comparable or superior to those obtained in humans [*Latimer et al.,* 1996; *Edmondston et al.,* 1998]. Human trials would not have permitted breathing and position to be so precisely controlled, which were identified by Kawchuk and Fauvel as factors influencing stiffness measurements [*Kawchuk and Fauvel,* 2001]. In addition, human subjects presumably would have supplied a more heterogeneous sample of spines.

Different anesthetics are known to cause various effects on the neuro-muscular system [*Ho and Waite,* 2002]. Isofluorane, the anesthetic used in this study, causes analgesia, muscle relaxation and CNS depression [*Muir et al.,* 2007]. This mode of anesthesia is not consistent with that used by Pickar et al. and others investigating neural responses [*Mushahwar et al.,* 2000; *Pickar,* 1999] which can be suppressed by Isofluorane and other inhaled anesthetics [*Ho and Waite,* 2002]. Although neuro-muscular responses may have been altered by the chosen anesthetic, the passive properties of the spinal tissues, targeted by the current study, were likely not affected. It has also been speculated that the decrease in muscle tone caused by anesthetics may enhance therapeutic effects [*Kawchuk et al.,* 2009; *Kohlbeck et al.,* 2005]. In the current study, the anesthetic likely did not alter the stiffness measurements of passive tissue properties.

4.4.4.3 Measurement protocol

After the completion of Protocol 1 experiments, the measurement protocol was modified. The delay of the post-SMT measurement was reduced from 5 min to 30s, and an additional pre-SMT measure was added after 5 min of recovery. The minimal duration of the post-SMT measurement delay provided the operator sufficient time to adjust all necessary experimental parameters, only allowing minimal tissues recovery. This change in timing was implemented to ensure that immediate effects on tissue stiffness were not missed, and therefore maximize

the likelihood of detecting a change. Clinically, PA stiffness is also reassessed immediately after a treatment [*Maitland GD,* 2001].

Previous studies have shown that 5 minutes are sufficient for tissues to recover from an indentation [Shirley et al., 2002]. Furthermore, we performed a single subject experiment, and confirmed that less than 5 minutes was sufficient for the feline spine to recover from the 4mm indentation. Previous studies have also shown that five indentations are sufficient for in vivo spines to reach equilibrium and consistent measurements to be obtained [Shirley et al., 2002]. The measurement protocol allowed sufficient preconditioning and recovery.

4.4.4.4 SMT application

The SMT was performed after a contact load was established, which confirmed that any further loads applied would lead to vertebral displacement. Loads applied were therefore likely efficiently transmitted to the vertebra. Efforts were made to improve the replication of clinical application. In Protocols 2 and 4, a preload of 10% body weight was applied prior to the SMT and the indenter was also programmed to retract quickly (20ms) [*Herzog et al.,* 1993; *Solinger,* 2000]. These details are strengths because they better replicate clinical application.

4.4.4.5 Curve Analysis

Single scalar values were necessary in this study to quantify the characteristics of the FD curve and allow statistical comparisons of the effects of amplitude and duration. The strength in selecting the most variable portion of the curve (60-90% in this case) to calculate K, is that the region most susceptible to change is included, increasing the likelihood of significant findings. Although a single stiffness coefficient has been used in many studies, a complementary technique (TIS) was also employed to calculate stiffness as this technique has been used previously to evaluate FD data in clinical trials [*Stanton and Kawchuk,* 2008] and

may offer further insights into the response of the material under investigation [*Tuttle et al.,* 2008].

4.4.4.6 Stiffness variables

Although the pre and post SMT measures could have been used to obtain delta K and delta TIS values; post-SMT K and TIS values were used instead. When analyzed, the deltas produced results of limited significance and diluted the progressive tissue effect. Alternatively, the post-SMT K and TIS values were analyzed to retain the actual changes in the tissue. The optimal variable was therefore selected to detect changes and accurately reflect tissue behavior.

4.4.4.7 Regression analysis

A linear regression analysis was used to characterize the general tissue behavior across each displacement or force amplitude of repeated measures to compensate for the small sample size and the many levels of variables (3 for amplitude and 8 for duration) that likely underpowered the repeated measures analysis. A one-way repeated measures ANOVA and qualitative analysis of the graph did not provide significant results for each protocol. The strength of this first step of the two step analysis performed is that it contributed to characterizing the general tissue response to the experimental protocol.

4.4.4.8 Repeated measures analysis

Traditionally, a generalized linear model, two-way repeated measures ANOVA have been used to analyze the type of repeated measures data collected in this project. However, this model did not fit the data distribution appropriately. A more advanced, better fitting model was therefore selected. The mixed effect repeated measures model (SAS) uses the assumption that the responses have an approximate multivariate normal distribution to derive estimates and statistical tests, although it does not require normality. It incorporates fixed main effects of

amplitude, duration and their interaction, with random effects. In this model, the first pre-SMT stiffness measure is incorporated as a covariate, to account for differing initial stiffness levels between-subjects. The mixed effect approach also accounts for the covariance between repeated measures through the use of a compound symmetry structure which proposes equal correlation between each pair of repeated measure. Compound symmetry was chosen over other covariance structures (auto-regressive or unstructured). A better covariance structure is the one that maximizes the likelihood by adding parameters while imposing a large penalty for each additional covariance parameter. An unstructured covariance structure, for example, can require a large number of covariance parameters to be estimated (48 in this case) which can be problematic with a small sample size [*Fitzmaurice et al.,* 2004]. Accounting for the covariance between repeated observations provides a more realistic estimate of the sample variability. This choice of analysis technique is a strength because the mixed effect repeated measures analysis is the most rigorous method with the least assumptions which maximized power given our small sample size.

4.4.5 Limitations/Weaknesses

Several limitations to generalizability must be acknowledged, and certain cautions must be given when interpreting the results of this study.

4.4.5.1 Model

A number of differences exist between human and feline spines that may limit transferability of results. The feline spine is more compliant (mean K=6N/mm) than a human spine (K=15N/mm [*Latimer et al.,* 1996]) and may respond differently to SMT [*Ianuzzi et al.,* 2009]. Proponents of the cavitation model would argue that excessive joint mobility in the feline model could prevent the adequate build up of capsular tension believed to cause cavitation [*Brodeur,*

1995]. The occurrence of a cavitation was not monitored during the experiment, and was not qualitatively heard during any of the conditions.

4.4.5.2 Setup

Suspending the spine may also have altered responses to loading. Typically some of the loads of the stiffness test are transmitted and dissipated through adjacent segments [*Powers et al.,* 2003; *Lee and Evans,* 1992], which indicates that stiffness measurements do not precisely reflect the stiffness of one isolated segment. In this case, the L4 clamp prevented any cranial motion beyond L5; however the hip spikes allowed some rotations to occur at the iliac crests. The limited number of spinal segments available for movement could have restricted the total change in stiffness that could be incurred.

The clamp and hip spikes also minimized SMT load transmission. Although clinicians also attempt to "lock" (take up movement) segments above and below the target vertebra, this setup differs from a clinical setting. Furthermore, injury to spinal structures was minimized, although some muscle and fascia damage occurred while exposing the L4 spinous process, and the gluteus muscles were compressed by the hip pins. These tissue injuries could have affected the biomechanics of the spine by increasing compliance.

4.4.5.3 Repeated indentation protocol

The pre-SMT measure 5 min after the post-SMT measure, added in Protocols 2, 3 and 4, was designed as a baseline value from which to compare each post-SMT measure, providing a pre and post SMT pair from which to calculate individual changes in stiffness; however, only the post-SMT measures were used in calculations. The high number of repeated indentations performed for the stiffness measurements (12 additional indentations in Protocol 2 to 4) and the SMTs could have affected the ability of the spinal tissues to respond to an SMT

performed late in the protocol [*Latimer et al.,* 1996; *Shirley et al.,* 2002; *Lee and Evans,* 1992].

Randomization could have redistributed some of the conditioning effect to different SMT conditions performed. However, it would not have enabled the detection of a threshold duration-displacement condition and would have required greater sample sizes. If conditions were randomized, the first sufficient condition performed would have changed the system, invalidating all subsequent measurement conditions. A detectable change which would be sustained throughout the subsequent measurements was expected to occur if one specific SMT condition was effective; however the minimal changes observed were not sustained.

4.4.5.4 Inconsistencies between protocols

Findings of amplitude and duration effects differed between protocols. The differences in results between Protocols 1 and 2 may be explained by the change in timing, as the spinal tissues in Protocol 1 had more time to recover prior to the post-SMT stiffness measure. The type of control imposed on the amplitude parameter (Protocols 1 and 2 under displacement control, Protocols 3 and 4 under force control) may also have altered findings.

In addition, force controlled protocols (3 and 4) required more manual adjustment of the frame to control the contact load; therefore the SMTs were applied with more inconsistent timing compared to the displacement controlled SMTs.

Furthermore, the force amplitude in Protocol 3 and 4 were based on body weight percentage to scale down human force amplitudes as was previously done by Pickar's group [*Sung et al.,* 2005]. The forces applied were therefore not

consistent between individual subjects, for instance, loads ranged from 23N/mm to 37N/mm for the 85% BW conditions (based on weight ranges of 2.80 to 4.50kg). In retrospect, absolute BW % values from the average sample weight may be preferable, so that relative forces applied can be consistent across subjects. In this study we observed a stiffness ratio of 2.5:1 when comparing humans to felines [*Latimer et al.,* 1996; *Goodsell et al.,* 2000] which contrasts with the body weight ratio of 20:1. Scaling of the SMT amplitudes according to body weight may not be appropriate in light of the smaller stiffness ratio.

4.4.5.5 Inconsistencies between experimental conditions

Data points that deviated away from the regression line and subjects that seemed to differ from others in their stiffness levels were investigated further to determine if they could have been caused by experimental errors. For instance, subject 3E, had a higher initial stiffness (3E: 10.48N/mm mean: 6.07N/mm) and data points that showed more variability in K and TIS compared to the other subjects in this protocol (3E σ^2: <1.4; mean: σ^2: 0.2). It was noted that all the bolts of the frame were retightened prior to the start of this protocol. These adjustments could have decreased some of the external play in the system. This note is also applicable for the last 4 subjects (4C, 4D, 4E, 4F) of Protocol 4.

4.4.5.6 SMT application

The PA SMT technique is not the most commonly used in clinical practice or clinical trials. In recent trial supporting the efficacy of SMT, an anterior iliac crest thrust with the patient's spine rotated in side lying has been used [*Flynn et al.,* 2002]. Different positioning and direction of load have been shown to affect the stresses placed on the spinal tissues [*Cramer et al.,* 2002; *Colloca et al.,* 2004]; therefore, PA loading may not have optimally loaded the spine.

4.4.5.7 Stiffness measurement protocol

Viscoelastic properties affect how spinal tissues respond to the rate of loading of the measurement, lower loading rates yielding lower stiffness coefficients [*Lee and Evans,* 1992; *Keller and Colloca,* 2007]. In other studies, a rate of 2.5mm/s has been shown to distinguish between pathological and non-pathological discs in a pig model (see section 2.5.2.3) [*Kawchuk et al.,* 2006]; however, a lower rate of 0.5mm/s was selected in this experiment so that the indentation rate would be different than the rate of simulated SMT (four times slower than the slowest SMT) to prevent the indentation from affecting the tissues similarly to the SMT. To the knowledge of the investigators, no loading rate has been confirmed to be more sensitive to changes due to SMT. Furthermore, data from the unloading of L6 was not obtained because the indenter was not attached to the spinous process. Therefore, the viscous component of stiffness (hysteresis) (see section 2.7) was not assessed in this study [*Mushahwar et al.,* 2005; *Prochazka et al.,* 1997]. However, viscous stiffness has not been shown to provide significantly different outcomes across different conditions [*Hasegewa et al.,* 2010].

The maximal PA displacement available in the suspended spine was not determined. There is also very limited data available for comparison from previous feline studies. Ianuzzi et al. (2009) obtained 80 degrees of global extension from the L2 to S1 segments of an *ex vivo* feline spine (n=1) which was significantly lower than the human range (120 degrees, n=6) [*Ianuzzi et al.,* 2009]. Lee and Evans (1997) obtained intervertebral displacements of <2mm when a 150N PA load was applied to *in vivo*, unsterilized human lumbar spines [*Lee and Evans,* 1997]. Considering these values and the fact that a contact load was applied prior to indentation, the suspended smaller scale feline spine likely underwent sufficient compression to take L6 to end range. However, we cannot confirm that the 4mm indentation took the L6 vertebra to a terminal

displacement or end range. Therefore, tissue responses to SMT occurring in this terminal range and changes in maximal range would have been overlooked.

4.4.5.8 Sample size

Initially, sample size of 11 subjects per protocol (Protocol 1 displacement, Protocol 2 Force) were determined to provide over 99% power for the overall F-test based on a standard deviation of 0.38N/mm estimated from the literature [*Kawchuk et al.,* 2001] and over 80% power to detect mean differences of greater than 0.43 N/mm between adjacent level of SMT durations and amplitudes. However, lack of significant findings from the preliminary interim analysis of the data from the first half of Protocol 1 lead to the decision to divide each protocol so that a preload could be introduced.

The new groups provided sample sizes of 5 or 6 for each of the four protocols. In the current study, the preconditioning measures had a mean SD of 0.10 and 0.07 N/mm for the K and TIS values respectively. Although these values are lower than those used for the sample size calculation; the samples remain underpowered for the many levels of comparisons imposed by the experiment. Sample size and power calculations for repeated measures designs are far more complex than those of univariate responses; however, as a general rule, there should be as many subjects in the sample as there are levels of comparison [*Fitzmaurice et al.,* 2004]. In this case, 5 subjects are insufficient against 24 levels of comparisons. Performing all levels of comparison while applying a correction to prevent a type 2 error would have a high risk of a type 1 error.

The pooling of the data from any of the protocols was not possible because of differences in protocol parameters, such as timing, and mean of amplitude control, and discrepancies in results, such as the inconsistent findings of duration effects. Therefore, our study remains underpowered to perform post hoc

comparisons and determine which duration x amplitude conditions were significant due to our small sample size.

4.4.5.9 Curve Analysis

Stiffness measurements provide a curve of continuous data, rather than a single scalar value. Some have suggested that whole curves [*Tuttle et al.,* 2008] and non-linear equations [*Nicholson et al.,* 2001] should be used to better quantify spinal stiffness response. However, whole curve comparisons were not chosen in the current study, due to the high number of curves generated, and the complex statistical analysis needed to compare main effects and interaction effects of the various conditions. Single scalar values were therefore necessary to quantify the characteristics of the FD curve and allow statistical comparisons. Tuttle (2008) obtained significant stiffness changes in symptomatic cervical spines in a section containing the 16-28% (4-7N) interval of the FD curve [*Tuttle et al.,* 2008]. Changes occurring outside of the intervals analyzed were therefore not captured; whole curve analysis and linear modeling may be more sensitive to differences between intervention changes.

In the current study, the initial portion of the FD curve (<30%) was not considered because the contact load was designed to take up most of the toe region. Therefore, the FD curves could have been shifted to the right by some SMTs without detection because of the consistent “force controlled” contact load applied. This load could have taken the vertebra to a greater pre-indentation displacement without detection and produced a similar FD curve. This hypothesis would suggest that the SMT condition increased the neutral zone or toe region the vertebral segments, while the tissues maintained their K and TIS properties.

However, the curve analysis technique used in this study allowed us to identify the most variable section of the curve. Most changes that occurred in the force displacement response were therefore captured, because the section of the curve that changed the most was analyzed. Other techniques are not likely to have provided different or more significant findings (see section 2.7).

4.4.5 Significance

If PA stiffness is related to patient symptoms, and SMT is aimed at treating this symptom, then the mechanisms by which SMT affects stiffness must be understood. This information will contribute to defining the systems affected by SMT. The findings in this experiment demonstrate that PA stiffness in a feline model was affected by the interaction of the amplitude and duration parameters of SMT. The exact nature of this interaction remains unclear. However, the findings of an interaction effect of duration and amplitude of SMT on spinal stiffness warrant further investigation, because it may reflect the importance of SMT parameters.

Although the results of this study were of limited statistical significance, the current results indicate that in the absence of underlying pathology, and in the presence of restrictive clamping and general anesthesia, SMT causes minimal changes in stiffness that can be attributed to the viscoelastic properties of soft tissues. Other mechanisms such as neuromuscular responses, which are outside the scope of this thesis, are likely to contribute to the observed stiffness decreases in previous studies.

The diverging results in K and TIS within a single protocol potentially reflect variable stiffness responses throughout the FD curve. Our results therefore support the continued use of a combination of stiffness coefficients.

4.4.6 Future studies

Greater sample size and fewer levels of comparison for each variable are needed to indentify levels of SMT duration x amplitude which cause greater effects. Further post hoc comparisons outside the scope of the current thesis should be performed. One approach would be to compare pairs of adjacent conditions within each displacement or force amplitude although this would require 21 comparisons. Comparing all conditions against the control condition in their respective displacement or force amplitude would be another comparison of interest, though it would only reduce the numbers of comparisons to 18.

For similar future protocols, improvements can be made regarding consistency of the application of the protocol parameters and the precision of the timing. These improvements can be achieved by performing both the stiffness measures and the SMT under force control and by pre-programming preload and/or contact load amplitudes and duration to minimize manual adjustments. Calculating percentages of BW loads according to an average sample weight will also improve the consistency of SMT loads and loading rates across subjects.

To provide an additional outcome, the indenter could be attached to the spinous process to provide data regarding the unloading of the spinal tissues. This data could be analyzed to determine the effect of SMT on the viscous stiffness. Each spine could also be indented to failure at the end of each protocol to provide some reference data regarding maximal load and displacement of the spine in the experimental conditions.

A range of values for each SMT parameter has been reported in the literature (see Table 2.1), and each of them is believed to offer a specific contribution to the effects of SMT. Future studies addressing other SMT parameters such as preload magnitude (e.g. 0, 25, 85% BW)and duration (e.g. 1s vs 5s), location of

the load (e.g. spinous process vs transverse process) and position of the subject (e.g. neutral spine vs locking of segments above and below) are therefore needed to establish optimal SMT application.

Recent studies have shown that patients presenting with spinal hypomobility are more likely to respond to SMT [*Fritz et al.,* 2005; *Brennan et al.,* 2006]; and that a stiffness decrease potentially only occurs at symptomatic locations [*Tuttle et al.,* 2008]. Induced injury models are needed to ascertain the biomechanical effects of SMT parameters on the stiffness of injured or painful spines. This could be achieved by injecting inflammatory substrates into the joint capsule or surgically inducing soft tissue injuries 4 months prior to testing [Kawchuk 2001; Cramer 2004].

4.5 Conclusion

In this anesthetized, uninjured, suspended, *in vivo* feline spine model, repeated SMTs cause minimal changes in stiffness thought to be due to a viscoelastic response. Some of the changes observed following select SMT conditions may be the result of an interaction effect between SMT duration and SMT amplitude. However, no specific threshold condition was identified as causing a greater stiffness change. In the majority of the protocols performed, no specific biomechanical effect can be attributed to SMT. However, this study provides guidance for future investigations into the biomechanical effects of individual SMT parameters by providing a reliable model and device to improve upon.

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Appendix I:
Ethics approval for animal use protocol from the University of Alberta Health Sciences Committee

UNIVERSITY OF ALBERTA

ETHICS APPROVAL FOR ANIMAL USE PROTOCOL

RECOMMENDED WORDING TO ACCOMPANY PUBLICATIONS COMPLETED BY PRINCIPAL INVESTIGATORS AT THE UNIVERSITY OF ALBERTA

"All animal studies were conducted in accordance with the Canadian Council on Animal Care Guidelines and Policies with approval from the Animal Care and Use Committee: Health Sciences for the University of Alberta."

ANIMAL CARE AND USE COMMITTEE: HEALTH SCIENCES

Has reviewed and approved the protocol application entitled:

DEVELOPMENTAL CENTER TO STUDY MECHANISMS & EFFECTS OF MANIPULATION
Title

C	527/06/10
Category of Invasiveness	Protocol Number

Submitted by:

Dr. Greg Kawchuk	N/A
Name of Principal Investigator	Co-Investigator(s)

And found the proposed protocol involving animals to meet the standards of the Canadian Council on Animal Care (CCAC), and the proposed facilities in which the animals will be housed and used to comply with the CCAC requirements.

Cat	23
Species	Number of Animals Approved

	July 1, 2009 – June 30, 2010
Signature of ACUC: Health Sciences Chair	Start Date End Date