# MANUAL THERAPY AND THE OSTEOPOROTIC SPINE

by

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## ABSTRACT

Among older adults, osteoporosis and back pain are common alone, and also in combination. These conditions can cause enormous personal suffering and societal burden. A mainstay of physiotherapy treatment of back pain is the category of hands-on treatments known as 'manual therapy'. These are routinely used to assess and treat back pain in various clinical settings but their safety, efficacy, and mechanism of action has not previously been studied in individuals with back pain and osteoporosis.

The objectives of this thesis were to investigate, (1) the evidence for the effectiveness of manual therapy for spinal pain, (2) physiotherapists' perceptions and practice behaviors with respect to the use of manual therapy on individuals with osteoporosis, (2) the safety of posteroanterior (PA) spinal mobilization in the osteoporotic spine, (3) detection and determinants of spinal fracture under a PA load, and (4) whether PA stiffness can predict intervertebral range of motion (ROM) and flexibility in the cadaveric midthoracic spine of older adults.

To achieve these objectives I used a variety of research methods that included; a systematic review, a survey (171 physiotherapists), biomechanical testing, plain radiography, computed tomography (CT), dual energy X-ray absorptiometry, ash weight, and micro-computed tomography (12 cadaveric spine segments, one intact cadaver, 2 physiotherapists, 7 participants).

The systematic review indicated that: (i) physiotherapy that included manual therapy at a dose of 30-45 minutes per session, for 4-8 weeks was effective in adult populations with back or neck pain, and (ii) clinically relevant differences between the manual therapy interventions used in clinical trials may influence the outcomes. My survey of physiotherapists found that 91% of respondents were concerned about fracture as a complication of treatment when using manual therapy in patients with osteoporosis.

Among the key findings in my study of vertebral biomechanics using cadaveric midthoracic spine segments was that vertebral body injury is an unlikely complication of PA mobilization in the midthoracic spine. Simulated PA mobilization using a mechanical testing machine produced spinous process fractures in every case and no vertebral body fractures. There was a reasonable margin between the failure load, in vitro, and the applied mobilization load, in vivo, for most specimens, however the lowest fracture thresholds (200N) approached the same force as the upper range of the applied loads (223N). Bone mineral density (BMD) of the whole vertebra was not a good predictor of PA failure load ($r=0.18$, $p=0.68$) but micro-CT measures of regional bone volume fraction of the spinous process base and middle regions, the sites of fracture, were strongly correlated with PA failure load (base: $r=0.74$, $p=0.01$; mid: $r=0.73$, $p=0.01$). Plain radiography and CT had poor sensitivity for these spinous process fractures (detected 3/12 and 6/12 fractures, respectively).

DXA scanning was an appropriate surrogate measure for thoracic spine segment bone mineral measurement. Volumetric BMD can be accurately estimated using the elliptical

cylinder method. Trabecular thickness differs significantly between the spinous process and lamina regions, and may have influenced the site of fracture ($p=0.003$).

Cadaveric studies of spine kinematics during PA mobilization showed that the mobilized thoracic vertebra moves into extension as a result of the mobilization. Further, in cadaveric midthoracic spine segments from older adults, PA stiffness is inversely correlated with ROM and flexibility at the level at which the PA mobilization is applied ($r= -0.78 - -0.90$).

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## PREFACE

***Publications Arising from this Thesis***

Sections of this thesis have been published or submitted as sole or multi-authored papers in refereed journals. Details of the authors' contribution are provided, where relevant.

We agree with the stated contributions of the thesis author, as indicated below.

____ _____ Dr. Karim M. Khan (thesis co-supervisor)

_____ Dr. Thomas R. Oxland (thesis co-supervisor)

**Published Papers**

**Sran MM.** To Treat or Not to Treat—New Evidence for the Effectiveness of Manual Therapy. *British Journal of Sports Medicine* 2004 38(5):521-525.
(presented here as Chapter Two)

**Sran MM**, Khan KM. Physiotherapy and Osteoporosis: Practice Behaviors and Clinicians' Perceptions—a survey. *Manual Therapy* 2005 10(1):21-27.
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*Authors' contributions:* Meena Sran was responsible for the original ideas behind the paper, data collection, analysis, presentation of findings, writing and editing the paper. Karim M. Khan provided editorial assistance and was the key editor on this paper.

**Sran MM,** Khan KM, Zhu Q, McKay HA, Oxland TR. Failure Characteristics of the Thoracic Spine with a Posteroanterior Load: Investigating the Safety of Spinal Mobilization. *Spine* 2004 29(21):2382-2388.
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*Authors' contributions:* Meena Sran was responsible for the original ideas behind the paper, data collection, analysis, presentation of findings, writing and editing the paper. Karim M. Khan and Thomas R. Oxland provided editorial assistance, stimulated discussion, and were the key editors on this paper. Qingan Zhu provided technical assistance and advice on interpretation of the kinematic data. Heather A. McKay provided editorial assistance and stimulated discussion.

**Sran MM,** Khan KM, Keiver K, Chew JB, McKay HA, Oxland TR. Accuracy of DXA scanning of the thoracic spine: Cadaveric studies comparing BMC, areal BMD, and geometric estimates of volumetric BMD against ash weight and CT measures of bone volume. *European Spine Journal* 2004 Dec.23 (Epub ahead of print).
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*Authors' contributions:* Meena Sran was responsible for the original ideas behind the paper, data collection, analysis, presentation of findings, writing and editing the paper.

Thomas R. Oxland and Heather A. McKay provided editorial assistance and stimulated discussion of the results. Karim M. Khan and Thomas R. Oxland were the key editors on this paper. Kathy Keiver provided technical advice and editorial assistance. Jason B. Chew provided technical advice in the interpretation of CT data.

## Submitted Papers

**Sran MM**, Khan KM, Zhu Q, Oxland TR. Posteroanterior Stiffness Predicts Sagittal Plane Midthoracic Range of Motion and Three-dimensional Flexibility in Cadaveric Spine Segments. *Clinical Biomechanics*
(presented here as Chapter Seven)
*Authors' contributions:* Meena Sran was responsible for the original ideas behind the paper, data collection, analysis, presentation of findings, writing and editing the paper. Karim M. Khan and Thomas R. Oxland provided editorial assistance, stimulated discussion, and were the key editors on this paper. Qingan Zhu provided technical assistance and advice on interpretation of the kinematic data.

**Sran MM**, Boyd SK, Cooper DML, Khan KM, Zernicke RF, Oxland TR. Regional Trabecular Morphology is Correlated with Failure of Thoracic Vertebrae under a Posteroanterior Load—a Micro-CT Investigation. *Spine*
(presented here as Chapter Six)
*Authors' contributions:* Meena Sran was responsible for the original ideas behind the paper, data collection, analysis, presentation of findings, writing and editing the paper. Karim M. Khan and Thomas R. Oxland provided editorial assistance, stimulated discussion, and were the key editors on this paper. Steven K. Boyd and David M.L. Cooper provided advice on interpretation of the data, technical advice and helped edit the paper. Ron F. Zernicke provided editorial assistance, stimulated discussion of the results and helped edit the paper.

## Abstracts

I presented these abstracts orally or as a poster at the conference indicated.

**Sran MM**, Boyd SK, Cooper DML, Khan KM, Zernicke RF, Oxland TR. Regional Trabecular Morphology by Micro-CT is correlated with Failure of Thoracic Vertebrae under a Posteroanterior Load. *NIAMS-ASBMR Scientific Meeting on Bone Quality*, Bethesda, 2005.

**Sran MM**, Khan, KM, Zhu Q, Oxland TR. Can a passive accessory movement predict segmental spine motion? – a cadaveric study of posteroanterior mobilization. *Canadian Physiotherapy Association, National Congress*, Victoria, 2005.

**Sran MM**, Khan KM, Cooper DML, Boyd SK, Zernicke RF, Oxland TR. Regional Trabecular Bone Volume Ratio Predicts Failure of Thoracic Vertebrae under a Posteroanterior Load. *26th Annual Meeting of the American Society for Bone and Mineral Research,* Seattle, 2004.

**Sran MM**, Khan KM, Zhu Q, Oxland TR. Posteroanterior Stiffness Predicts Sagittal Plane Mid Thoracic Range of Motion in Cadaveric Spine Segments. *5th Combined meeting of the Orthopaedic Research Societies of the USA, Canada, Japan and Europe*, Banff, 2004.

**Sran MM**, Khan KM, Zhu Q, McKay HA, Oxland TR. Posteroanterior Mobilization of Thoracic Vertebrae with Low Bone Density: Safety and Intervertebral Movements. *Canadian Physiotherapy Association Congress*, Quebec City, 2004.

**Sran MM** and Khan KM. Physiotherapy and Osteoporosis: Practice Behaviors and Clinicians' Perceptions. *Canadian Physiotherapy Association Congress*, Quebec City, 2004.

**Sran MM**, Khan KM, Zhu Q, McKay HA, Oxland TR. Spine Biomechanics in Osteoporotic Thoracic Vertebrae: Investigating the Safety and Intervertebral Movements during Posteroanterior Mobilization. *Proceedings of the International Federation of Orthopaedic Manipulative Therapists 8th International* Congress, Capetown, 2004.

**Sran MM**, Khan KM, Zhu Q, Oxland TR, McKay HA. Failure Characteristics of the Thoracic Spine with a Posteroanterior Load. *Journal of Bone and Mineral Research*, 18, Suppl 2, Sept 2003, S375.

**Sran MM**, Khan KM, Zhu Q, McKay HA, Oxland TR. Failure of thoracic vertebrae under a posteroanterior load. *1st Annual Meeting of the Alberta CIHR Bone and Joint Health Training Program*, Banff, 2003.

**Sran MM**, Khan KM, Zhu Q, McKay H, Oxland T. Failure of thoracic vertebrae with a posteroanterior load. *International Society for Study of the Lumbar Spine,* Vancouver, 2003.

**Sran, M.** The role of physical therapy in the prevention and management of osteoporosis. *14th International Congress of the World Confederation for Physical Therapy*, Barcelona, 2003.

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*'Education is the one thing no one can take away from you'*, something my dad told me frequently when I was a young girl. Wise words from a man whose family lost everything, including his father, in the partition of India.

This thesis is dedicated to my mom, Jagjit Kaur Sran, and my dad, Surinder Singh Sran, who worked incredibly hard and gave up so much to give my siblings and I the opportunity for formal education.

I've come to associate a number of words beginning with 'p' with 'PhD', in particular persistence, pain, and privilege. The first two are basically self explanatory, so I'll focus on the 'privilege' of being a doctoral student.

When I wasn't enjoying being a doctoral student (which was more than once) I had to remind myself that I chose to take this on, and being able to choose is a privilege that many people in this world don't have.

I had the privilege of working with a number of outstanding individuals who, in one way or another, have enriched my life. In particular my co-supervisors, Karim M. Khan and Thomas R. Oxland, and my committee member, Heather A. McKay. It is important to believe in yourself, but it definitely helps to have others believe in you. I want to thank Karim for believing in me. His continued encouragement, confidence in my abilities, and humor were invaluable in surviving the program. Karim is a true clinician-scientist who possesses an incredible combination of enthusiasm, energy, wit and intelligence. I, like many, find juggling clinical practice and research, while creating a bridge between them, is challenging—Karim is an excellent role model. Tom is one of the most ethical, thorough and successful researchers I have come across. As Phil would say, he has 'a brain the size of a planet' which is a tremendous asset in a supervisor and something for which I am grateful. Tom's willingness to collaborate made this thesis possible. I want to thank Tom for many things but in particular his 1:1 teaching, rigorous research, welcoming demeanor and the opportunity to join his lab. Heather has been a source of guidance, support and insight over the past four years, and I want to thank her for her many contributions to my work.

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## DEFINITIONS

Activities of daily living: everyday activities such as eating, bathing, dressing, toileting, transferring (for example, getting into or out of a chair) and continence; the activities an individual needs to be able to perform in order to live independently

Accessory movements: movements of joints that patients cannot perform actively, but which can be performed on them by another person [1]

Active movement: movement of a mobile segment produced by the muscles that produce movement of the segment

Anisotropic: having different mechanical properties when loaded along different axes

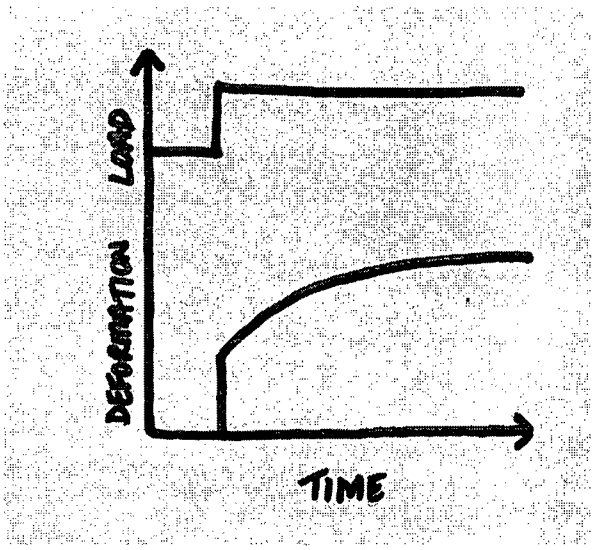
Bone mineral content: total grams of bone mineral as hydroxyapatite within a measured bone region

Bone mineral density (BMD, areal BMD): grams of bone mineral per unit of bone area scanned; cannot make volume determinations

Bone volume: the amount of three-dimensional space occupied by a bone

Cortical bone: the dense outer layer of bone

Creep: when a viscoelastic material is subjected to a constant load it deforms with time; the deformation-time curve approaches a steady-state value [2]




*This figure is a deformation and load vs. time plot which illustrates deformation over time under a constant load (until the deformation-time curve reaches a steady-state). This phenomenon is termed 'creep'.*

Degrees of freedom: the motion of a rigid body in space has six degrees of freedom—three translations and three rotations; when bodies are interconnected certain constraints are placed on their motion, and the number of degrees of freedom decreases [2]

Desiccator: an enclosure containing drying agents (desiccants) in which a substance can be kept in a controlled dry atmosphere

Elastic zone (EZ): That part of the physiological intervertebral motion which is measured from the end of the neutral zone up to the physiological limit. Within the EZ, spinal

motion is produced against a significant internal resistance. It is the zone of high stiffness. [3]

Finite Element Modeling (FEM): mathematical modeling of an object that involves dividing it up for analysis, i.e. dividing an object into an array of discrete elements for structural analysis

Functional spinal unit (FSU): two adjacent vertebrae and their intervening soft tissues. [2]

Fragility fracture: "a fracture caused by injury that would be insufficient to fracture normal bone: the result of reduced compressive and/or torsional strength of bone". [4] In the clinic, it is often defined as a fracture that occurs from a fall from standing height or lower, or as the result of minimal or no identifiable trauma. [5]

Hypomobility: a clinical term used to describe reduced mobility; normally assessed based on end-feel and comparison with adjacent segments.

Hysteresis: energy loss exhibited by viscoelastic materials when they are subjected to loading and unloading cycles [2]

Isotropic: having uniform properties in all directions independent of the direction of load application

Kinematics: the study of the relationships between positions, velocities, and accelerations of rigid bodies, without concern for how the motions are caused (ignoring forces and moments acting on the body) [2]

Linear Variable Differential Transformer (LVDT): a circuit that produces an electrical output proportional to the displacement of a separate movable core; used to measure position

Manipulation: a small amplitude thrust technique performed with speed [1]

Manual therapy: manually performed assessment and treatment techniques; can include joint, neural tissue, and/or muscle techniques

Material properties (of bone): describe the behavior of a specimen of bone tissue without regard to its size (i.e. a size-independent parameter); depends on organic and inorganic components of bone; small uniform specimens are loaded under well-defined conditions [6]

Micrometer (μm): unit of length equal to one millionth of a meter, or one micron

Midsagittal plane: the median plane of the body which divides it into two equal halves

Mobilization: a passive movement performed such that it is at all times within the ability of the patient to prevent the movement if he or she so chooses. [1] Mobilization is typically

performed for the purpose of relieving pain and restoring full-range, pain-free, functional movements or to maintain a functional range of movement in patients who are unconscious or who have an active joint disease such as rheumatoid arthritis. [1]

Moment: a quantity equal to the product of a force and the perpendicular distance from that force to the point of interest; unit of measure is the newton meter (Nm) [2]

Morphology: the form and structure of an organism

Neutral zone: a region of intervertebral motion around the neutral posture where little resistance is offered by the passive spinal column [3]; the zone of high flexibility or laxity[2]; typically expressed in meters and degrees (translation and rotation respectively)

Newton (N): the basic metric unit of force giving a mass of one kilogram (2.205 pounds) at an acceleration of one meter (1 yard) per second per second

Nominal: an approximate measurement; the actual measurement may vary slightly

Opto-electronic: the combination of optical and electronics phenomena in a single device; lasers, light-emitting diodes (LEDs), and light detectors of various sorts fall under this definition

Osteoporosis: a skeletal disease characterized by compromised bone strength predisposing an individual to an increased risk of fracture [7]

Passive movement: movement of a mobile segment produced by any means other than by the muscles that produce movement of the segment [1]

Passive Accessory Intervertebral Movements (PAIVMs): movements are applied which the individual cannot perform actively, but which can be performed on them by another person

Passive Physiological Intervertebral Movements (PPIVMs): a manual assessment technique for the spine in which the physiological movements of flexion, extension, lateral flexion and rotation are repeated passively in the non-weight bearing position [1]

Physiological movements: movements that patients can perform actively by themselves [1]

Posteroanterior (PA) spinal mobilization: a mobilization technique where load is applied in the posterior to anterior direction; often performed with the patient lying prone

Radiography: the making of film records (radiographs) of internal structures of the body by exposure of film specially sensitized to x-rays [8]

Range of Motion: the entire range of the physiological motion (includes both the neutral and elastic zones) [2]

Resolution: the number of pixels per square inch on a computer-generated display; the greater the resolution, the better the picture

Rigid Body: an idealization of a real object; assumes that the body is absolutely rigid so that it does not stretch, compress, or otherwise deform no matter how large the forces and moments acting on it. [2]

Rotation: spinning or angular displacement of a body about some axis[2]

Safe: administered without causing harm or injury

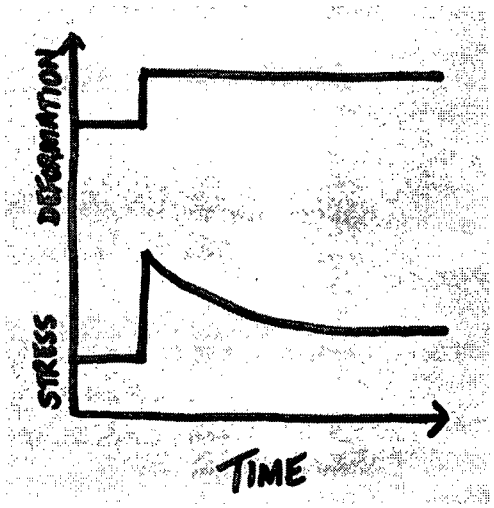
Sagittal plane: any vertical plane parallel to the midsagittal line that divides the body into left and right portions

Servohydraulic: motion is controlled by a servo-controlled valve and high pressure liquids actuate pistons

Stereology: the study of estimating geometrical quantities

Stiffness: a term used to describe the force needed to achieve a certain deformation of a structure; a steeper curve represents a stiffer structure

Stress relaxation: decrease in stress in a material subjected to prolonged constant strain at a constant temperature. Stress relaxation behavior is determined in a relaxation test and data is often presented in the form of a stress vs. time plot. The stress relaxation rate is the slope of the curve at any point.




*This figure is a stress and deformation vs. time plot to illustrate 'stress relaxation'—the decrease in stress in a material subjected to prolonged constant strain at a constant temperature*

Structure: the manner of construction and arrangement of parts; a thing constructed

Structural Properties: describe the behavior of whole bone, which can include reference to bone size, shape, cortical thickness, cross-sectional area, and trabecular architecture

Three-dimensional motion: most human body joints can move in any of six possible degrees of freedom

Torque: synonymous with 'moment'

Trabecular bone: bone tissue with a spongy honeycomb structure, typically found at the ends of long bones and the middle of vertebrae

Translation: at a given time, all particles in the body have the same direction of motion relative to a fixed point [2]

Vertebroplasty: a medical grade cement is injected through a needle into a painful fractured vertebral body with the aim of stabilizing the fracture

Viscoelastic: time dependent property where the deformation of the material is related to the rate of loading, hysteresis, creep, stress relaxation

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8. O'Toole M ed. Encyclopedia & Dictionary of Medicine, Nursing, & Allied Health. 5th ed. Toronto: W.B. Saunders Company, 1992.

## LIST OF ABBREVIATIONS
*(commonly used abbreviations)*

| | |
|---|---|
| aBMD | areal bone mineral density |
| AP | anteroposterior |
| BC | British Columbia |
| BMC | bone mineral content |
| BMD | bone mineral density |
| BV/TV | bone volume/total volume; bone volume fraction |
| CT | computed tomography |
| Deg | degrees |
| DXA | dual energy X-ray absorptiometry |
| g | grams |
| μCT | microcomputed tomography |
| PA | posteroanterior |
| ROM | range of motion |
| SD | standard deviation |
| SMI | structure model index |
| Tb.Th | trabecular thickness |
| Tb.N | trabecular number |
| Tb.Sp | trabecular separation |
| UBC | University of British Columbia |

# Chapter One

## *Literature Review and Introduction to the Thesis*

## 1.1 OSTEOPOROSIS

At a consensus development conference on osteoporosis in 2000, osteoporosis was defined as "...a skeletal disorder characterized by compromised bone strength predisposing to increased risk of fracture. Bone strength reflects the integration of two main features: bone density and bone quality." [1]

### 1.1.1 Prevalence

Osteoporosis affects approximately one in four women and one in eight men in Canada and the United States (US). [2,3] Recent data suggest that 16% of Canadian women and 7% of Canadian men over the age of 50 have osteoporosis [4] and at least 1.3 million fractures in the US each year are attributed to osteoporosis. [5] Regions with high trabecular bone content are the most affected by osteoporosis, with spinal compression fractures, proximal femur, distal radius and rib fractures being the most common osteoporotic fractures. [6-12]

### 1.1.2 Pathophysiology

Bone loss is part of normal aging. However in osteoporosis bone mass drops so that fracture risk is elevated (see '1.1.4 Diagnosis of Osteoporosis'). Normal bone physiology requires a balance between resorption and formation, carried out by bone cells under the influence of both the endocrine system and mechanical loading. [13,14] Factors that can cause an individual to lose bone at a faster than normal rate include hormonal and genetic factors, lifestyle factors including physical inactivity, nutrition and smoking, and the use of medications which affect bone remodeling. [15-18]

### 1.1.3 Economic and Social Cost of Osteoporosis

The estimated Canadian acute care costs for osteoporosis in 1993, which includes admission to hospital, outpatient care and drug therapy, was over 1.3 billion Canadian (CDN) dollars. [19] Data from the United States suggest the economic burden of osteoporosis has increased tremendously over the past decade, rising to $17-20 billion CDN dollars annually. [20] The costs will likely increase even further as the prevalence of osteoporosis in Canada is expected to rise with the aging population—25% of the Canadian population is expected to be over 65 years of age by 2041. [21]

In addition to the obvious economic impact of osteoporotic fractures, there are serious social costs including reduced quality of life, [6,22-24] back pain, [25-29] decreased functional ability, [30-32] physical impairments, [33-36] and mortality [37]. This is discussed further in section 1.2.1 'Consequences of Vertebral Fractures'.

### 1.1.4 Diagnosis of Osteoporosis

Clinical diagnosis of osteoporosis is currently based on two factors, (1) bone mineral density (BMD) by dual energy X-ray absorptiometry (DXA) and (2) evidence of fragility fracture*. A decrease in BMD is associated with an increased risk of fracture.[38]

In Canada we use the World Health Organization's (WHO) definitions of osteoporosis. [20]

*(* refers the reader to terms which are defined in the 'Definitions', pages xviii to xxvii)*

The WHO definitions are based on comparison of the individual's BMD to the mean for a normal young adult population of the same sex and race. An individual's results are described as a "T-score" that reflects the number of standard deviations above or below the mean BMD for young normal adults. Specifically, normal BMD is defined as a T-score above -1.0. Osteopenia, in which BMD is lower than normal but not low enough to be categorized as osteoporosis, is associated with a T-score between -1.0 and -2.5. Osteoporosis is defined as a T-score below -2.5, or evidence of a fragility fracture. [39] Not all fractures are associated with an event or incident, but many are. Diagnosis of fragility fracture is determined by a combination of the history of the incident, which is typically fall-related [40,41] and the results of radiography.

### 1.1.5 Physiotherapy and Osteoporosis

Physiotherapy management in the presence of osteoporosis has received little attention to date. Further, much of the currently available evidence relates to exercise prescription for bone health, [14,42-44] which is only one part of physiotherapy management. Physiotherapists are health care professionals with specialist skills in musculoskeletal rehabilitation. Physiotherapists use many methods of conservative management in clinical practice, including manual therapy*. Numerous physiotherapeutic treatment methods are effective for reducing pain, improving function and quality of life in a variety of musculoskeletal conditions, [43,45-51] but few have been studied in a population with osteoporosis. To illustrate this point consider a recent review of musculoskeletal rehabilitation in osteoporosis in which the authors discuss only three methods of rehabilitation after vertebral fracture—exercise, spinal orthoses, and vertebroplasty*.[52]

Since other treatment methods have been shown to be effective in populations without osteoporosis, it is possible that they may also be appropriate in osteoporosis. Thus the safety and effectiveness of rehabilitation strategies, besides exercise and bracing, should be tested in the osteoporotic spine.

## 1.2 VERTEBRAL FRACTURES

Vertebral fractures are the most common type of osteoporotic fracture and they typically manifest as compression fractures of the vertebral body. [53-56] In the US, 5% of 50-year-old white women and 25% of 80 year-old women have had at least one vertebral fracture.[56] After one vertebral fracture, the risk of a second vertebral fracture increases four-fold. [57,58 59]

Vertebral fractures most commonly occur at the thoracolumbar junction and midthoracic region [7,28,60-63] and prevalence is similar in men and women. [64,65] At least 57% of vertebral fractures are fall-related. [66] Most vertebral fractures are related to moderate trauma, defined as less than or equal to a fall from standing height. [66] Minimal trauma vertebral fractures can include those that occur during lifting and bending activities. It is known that static or dynamic forward bending of the spine, as occurs with an excessive thoracic kyphosis or active flexion of the spine, results in a larger proportion of compressive load on the anterior aspect of the vertebral bodies. This concentration of force, combined with decreased BMD, can lead to vertebral body failure. [67]

Vertebral body fracture is typically diagnosed by a radiologist and is based on vertebral morphometry, measured on lateral spine radiographs. Vertebral *deformity* and vertebral *fracture* are often used interchangeably, but not all vertebral deformities result in height loss sufficient to be diagnosed as fractures (Figure 1.1).

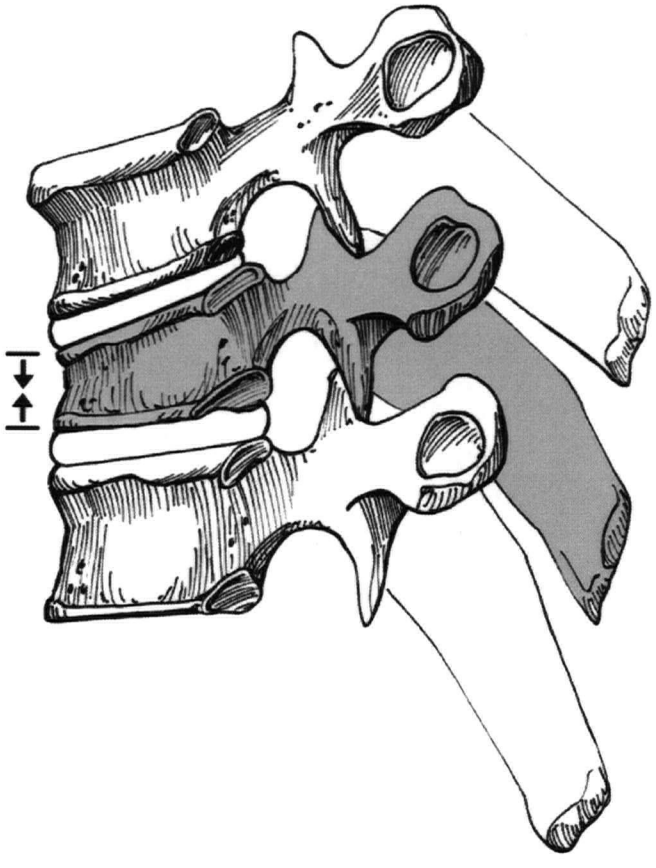

**Figure 1.1.** *Typical vertebral body compression fracture in the midthoracic spine.*

### 1.2.1 Consequences of Vertebral Fractures –Economic and Social Impact

In 1997 vertebral fracture accounted for over 400,000 total hospital days and generated charges of more than 500 million USD in the United States. [68] Hospital charges for individuals admitted for vertebral fracture were between 8000 to 10,000 US dollars (USD) per admission, mean length of stay was just under 6 days, and more than 50% of discharged patients required some form of continuing care. [68]

In addition to the high economic cost, vertebral fractures also have enormous social impact. [11,56,69,70] Back pain, physical and functional impairment, reduced quality of life and increased mortality are common consequences of vertebral fractures. [30-32,37,56,70,71] Surprising to many, vertebral fractures are associated with a 16% reduction in expected five-year survival. [72] Not all vertebral fractures are symptomatic, but both symptomatic and asymptomatic vertebral fractures are associated with increased morbidity [73] and mortality. [56,74,75]

Back pain resulting from vertebral fracture can be acute or chronic, and is associated with an increased number of physician visits and days missed from work. [71] Most clinically diagnosed fractures are detected when the patient seeks medical attention for back pain produced by the fracture. [70]

Individuals have been shown to have significant physical impairments post vertebral fracture. These include reduced back muscle strength, impaired thoracic posture and balance, decreased pulmonary function and height loss. [34,36,74,76,77] Studies suggest that

individuals also suffer from significant functional impairment post vertebral fracture. [30-32] Functional consequences can include limited ability to perform activities of daily living*, restricted function in employment in addition to social and recreational settings. [31] Functional impairment has been documented in the acute period post fracture, as well as several years post fracture. [30] A prospective study of men and women found overall function declined at similar rates among individuals with vertebral or hip fractures[78] and several studies suggest that both back pain and function worsen to a greater extent with the increasing number and severity of fractures. [71,73,79]

Vertebral fractures also have an important effect on quality of life. [6,22-24] Several studies found a negative relationship between vertebral fracture and quality of life, [6,22,23] in both men and women. [22]

## 1.3 BACK PAIN

Studies suggest that 60 to 80 percent of individuals in the Western world will experience acute back pain in their lifetime. [80-82] Back pain is a global problem affecting both men and women [82-87] but some studies suggest it is more prevalent in more affluent countries.[82] Although some studies suggest higher prevalence of back pain in individuals with manual or hard labour jobs, [87] individuals working in office jobs or as homemakers also commonly report back pain.[33] Back pain is also common in older adults. [88,89] Results from the Canadian National Population Health Survey (1994-1995) found 20.9

percent of persons aged 65 or older, in the province of Ontario, reported having back pain. [90]

### 1.3.1 Economic and Social Cost of Back Pain

Back pain is associated with high utilization and costs of family physician services, and is one of the top three chronic conditions for which Canadians consult a family physician. [90] Back pain is also one of the ten most costly physical health conditions in the US. [91] Absence, disability and reduced productivity result in enormous cost for employers. [91]

Back pain also has enormous social costs. [92] Back pain is associated with reduced quality of life, sleeping problems, fatigue, physical limitations and risk of major depression. [93-97]

### 1.3.2 Back Pain and Osteoporosis

For many years, back pain has been discussed as an important clinical sequel of osteoporosis. [25-29] Both back pain and osteoporosis are prevalent conditions, so it is not surprising that many individuals have both. [43,98,99] However, with the high prevalence of back pain in individuals with osteoporosis, many researchers have investigated whether factors such as low BMD, increased kyphosis, or vertebral deformity are associated with an increase in back pain.

Studies have generally found that back pain in a population with osteoporosis is only significantly related to severe vertebral deformity. For example, Ettinger et al. [73] found vertebral deformity was only associated with substantial pain in women with vertebral

height ratios four standard deviations below the population mean and studies suggest that low BMD is not associated with back pain. [29,100] One study found that women with kyphosis reported only slightly more back pain and back disability, which was not statistically significant, [101] while another study found the degree of kyphosis was associated with severity of thoracic but not lumbar back pain. [102]

With respect to gender, one study found similar prevalence of back pain in men and women over the age of 50, up to the age of 70-79. [103] After age 79 the prevalence was higher in women and those with a greater number of previous vertebral fractures. [103] In a study of the clinical characteristics of osteoporosis in men, back pain was found to be the chief complaint of 69 of 81 (85%) of participants. [104] Further, in another recent study the prevalence of back pain was 75% in a population of older women with osteoporosis, and back pain was a determinant of both balance and functional mobility. [105]

### 1.3.3 Back Pain Management—Physiotherapy

Back pain is the most common reason for visiting a physiotherapist *(Physiotherapy Association of British Columbia (PABC), October 2001)*, and many physiotherapists use manual therapy techniques such as spinal mobilization to assess and treat back pain.[106-108] One study investigated therapy use and costs for patients with back pain for longer than 7 weeks and found physiotherapy was better than exercise at improving quality of life, and use of health care services and absenteeism tended to decrease after a course of physiotherapy. [96]

## 1.4 MANUAL THERAPY

Manual therapy is the umbrella term for manually performed joint, muscle and neural tissue assessment and treatment techniques (Figure 1.2). This thesis focuses on joint techniques. Joint techniques can be divided into assessment and treatment techniques. Assessment techniques aim to measure joint motion and stability. These include passive physiological intervertebral movements* (PPIVMs), [108] passive accessory intervertebral movements* (PAIVMs), [108-110] and stability tests. [111,112] Treatment techniques aim to restore full-range, pain free, functional movements and relieve pain. [108] These include mobilization and manipulation.

In 2002 approximately 40 percent of Canadian registered physiotherapists, with direct patient care as their primary responsibility, identified 'orthopaedics' as their area of clinical practice. [113] Another seven percent selected sports injuries, which are also predominantly orthopaedic cases. Further, approximately 25% of physiotherapists registered to practice in British Columbia between the years of 2001 and 2004 participated in postgraduate specialization courses in orthopaedics *(based on information from the College of Physical Therapists of British Columbia and the BC Section of the Orthopaedic Division, Canadian Physiotherapy Association)*. These courses focus on advanced manual assessment and treatment skills. In summary, more Canadian physiotherapists practice in orthopaedics and specialize in orthopaedic manual therapy than any other area of clinical practice or specialization.

### 1.4.1 Spinal Mobilization

Spinal mobilization* refers to passive movement (typically oscillatory but can be sustained) which can be performed in various parts of the range of motion, as either small or large amplitude movements. [108,114] Mobilizations are typically graded I through IV. [108] Each grade is defined as follows and is diagrammatically represented in Figure 1.3, according to the commonly used method of Maitland. [108] Clinicians routinely use spinal joint mobilization for clinical assessment of individuals with back pain. Interpretation of findings is based on the degree of stiffness and the motion relative to segments above and below, [108] as well as the 'end feel', the sensation the examiner feels in the joint at the end of the range of motion. [115] Spinal mobilization is also used in treatment, to relieve pain and restore full-range, pain free, functional movements. [108] Spinal mobilization is different from manipulation*. Manipulation can be defined as a small amplitude high velocity thrust performed at the limit of a range of movement.

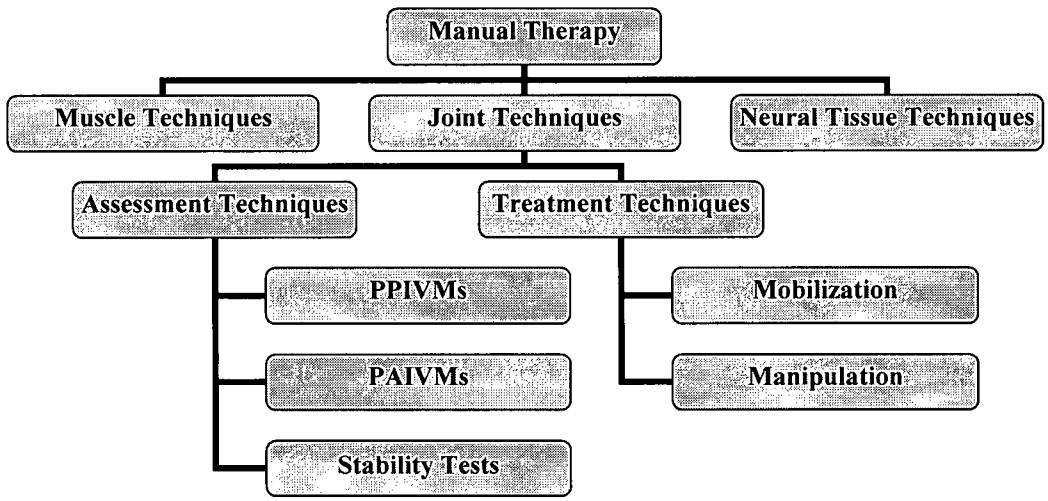


**Figure 1.2.** *Overview of manual therapy techniques. This thesis focuses on joint techniques. PPIVMs= passive physiological intervertebral movements; PAIVMs= passive accessory intervertebral movements*

*Grade I:* a small amplitude-movement at the beginning of the range

*Grade II:* a large amplitude movement in that part of the range that is free of stiffness or muscle spasm (i.e. beginning to middle of range)

*Grade III:* a large amplitude movement that moves into stiffness or muscle spasm (i.e. middle to the end of range)

*Grade IV:* a small amplitude movement that stretches into stiffness or muscle spasm, applied at the end of range

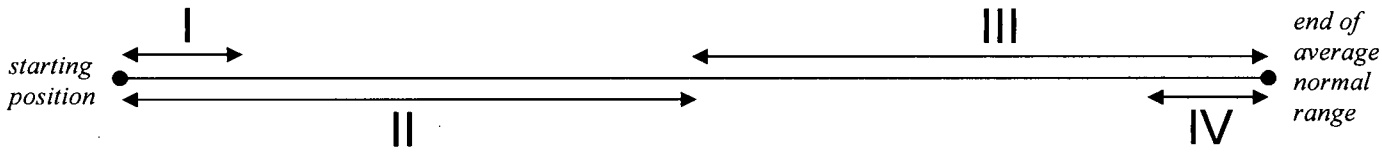


**Figure 1.3.** *Grades of mobilization in a normal range with a hard end-feel.* [108]

A number of studies have investigated therapist inter and intrarater reliability in applying grades of mobilization and measuring PA stiffness. Results are conflicting in that some studies found good reliability [116,117] and others found poor reliability. [118-120] Of interest, one group found therapists had much better ability to judge spring stiffness than the PA stiffness of human spines. [121] The authors suggested that mechanical stiffness may not be equivalent to the clinical concept of PA stiffness in that PA stiffness of the human spine may be multidimensional. [121] Another study showed that therapists can accurately judge spinal stiffness using a matching task. [122]

### 1.4.2 Effectiveness of Manual Therapy Including Spinal Mobilization

In the *assessment* of spine pain, two studies found that manual examination by a physiotherapist is highly accurate in detecting the segmental level responsible for a patient's complaint when compared against a spinal block. [123,124] A third study found good reliability for pain ratings, [120] and another study found that results of manual segmental mobility assessment correlated with disability. [125]

In *treatment*, recent randomized clinical trials found manual therapy to be more effective than other methods of conservative management of back and neck pain. [50,51,126-128] Specifically, manual therapy including spinal mobilization reduces spinal pain, [127,129-131] and it is more effective [127] than other physiotherapy modalities that do not include spinal mobilization (in the treatment of chronic neck pain). Also, a recent RCT found physiotherapy including spinal mobilization was more cost-effective than physiotherapy without spinal mobilization or routine treatment by a general practitioner. [132] However some older randomized clinical trials [133-140] systematic reviews [141] and meta-analyses [142] concluded that there was no evidence that spinal manipulative therapy is superior to other standard treatments for patients with spinal pain. Reviews typically focus on methodological differences, such as the randomization procedure, blinding of patients and outcome assessments, adequate follow-up period, and dropouts, [143,144] when trying to explain the discordant outcomes in clinical trials of manual therapy for back and neck pain. Yet there may be differences between the interventions that constitute

'manual therapy'. No review has focused on whether such differences exist yet they could have an important effect on the outcome of clinical trials.

### 1.4.3 Mechanism of Action of Spinal Mobilization

The biological mechanisms underpinning the effectiveness of spinal mobilization may be related to it stimulating sympathetic nervous system activity [131,145,146] and promoting motor activity. [131] For example, emerging evidence suggests that spinal joint mobilization techniques applied to the cervical spine elicit concurrent effects on pain perception, autonomic function, and motor function in patterns that are similar to the patterns of change elicited by stimulation of the periaqueductal gray region of the midbrain. [131,146,147]

Spinal mobilization is also used with the aim of restoring normal joint motion. It is thought that spinal mobilization may act by stretching the joint capsule or reducing muscle tone, thereby reducing stiffness. One study assessed the effect of T4-5 spinal manipulation (high velocity thrust technique) on stiffness in asymptomatic individuals, and found stiffness was not altered after spinal manipulation. [148] Whether spinal mobilization or manipulation can change stiffness in individuals *with back pain* is not known.

### 1.4.4 Safety of Spinal Mobilization in Osteoporosis

There appears to be agreement amongst leading clinicians that spinal *manipulation* is contraindicated in individuals with osteoporosis, [108,149-151] yet clinical experience [152] and

published cases [153] suggest that these techniques are still being used by some chiropractors. Clinical experience indicates that while some physiotherapists have expressed concern about the safety of manual therapy (including spinal *mobilization*) other clinicians routinely use manual therapy in older people, a proportion of whom will have osteoporosis. There are no data on the safety of manual therapy in individuals with osteoporosis to guide clinical practice.

### 1.4.5 Posteroanterior (PA) Spinal Mobilization

One spinal mobilization technique used very commonly in clinical practice is posteroanterior (PA) mobilization. [154-156] It can be applied at an individual spinous process [108,111] to assess stiffness, quality and range of motion [108] at that specific level. In manual assessment, PA mobilization is a passive accessory intervertebral movement (PAIVM) that is typically used in combination with other tests. In treatment, PA mobilization is typically the first technique used in the thoracic spine, [108] most commonly to improve sagittal plane* motion. It can be used alone or in combination with other spinal mobilization techniques. Figure 1.4 shows a physiotherapist applying PA mobilization to T6. Figure 1.5 shows the hand contact during PA mobilization in the midthoracic spine.

It is routine to assess the thoracic spine in patients presenting with lumbar, thoracic, cervical or shoulder symptoms. Thoracic vertebral motion contributes to end range cervical motion and shoulder elevation through flexion, and greater stiffness in the

thoracic spine may lead to compensatory changes in the more mobile lumbar and cervical regions. [157,158]

Structural changes in the vertebral bodies due to osteoporosis and disc degeneration will tend to bring the thorax into flexion. The ensuing decrease in intervertebral and rib cage mobility will limit the potential for thoracic extension. [157] Application of the PA mobilization technique, in the straight PA or caudad direction, is thought to produce intervertebral extension in the thoracic spine. Further, Maitland recommends that the central PA mobilization technique should be used first in all cases where symptoms arise from the thoracic vertebrae. [108] For these reasons the central PA mobilization technique is relevant to the care of older individuals with back pain and osteoporosis.

Some researchers have studied applied load during spinal mobilization[35,130,159,160,161] or manipulation[162-164] in vivo or in cadavers. However, no previous study has compared the load required to fracture a vertebra, in vitro, and the load applied during PA mobilization, in vivo.

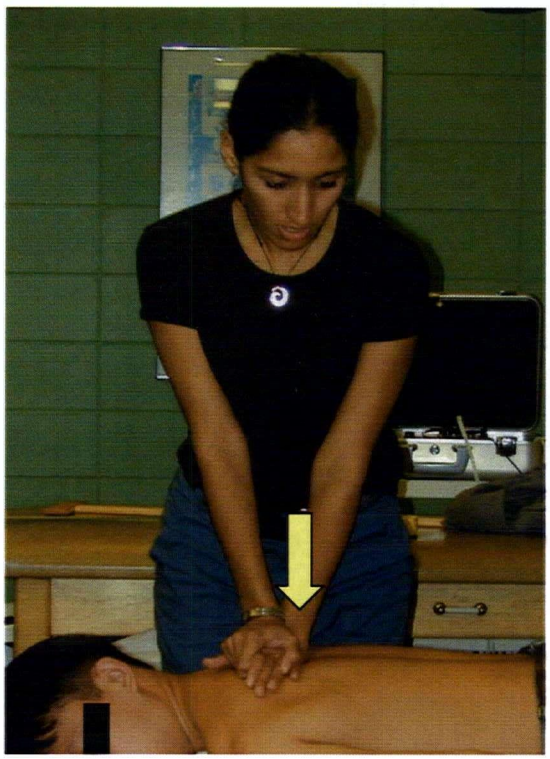

**Figure 1.4.** *Photograph of a physiotherapist applying PA mobilization to T6. The arrow depicts the direction of the applied load.*

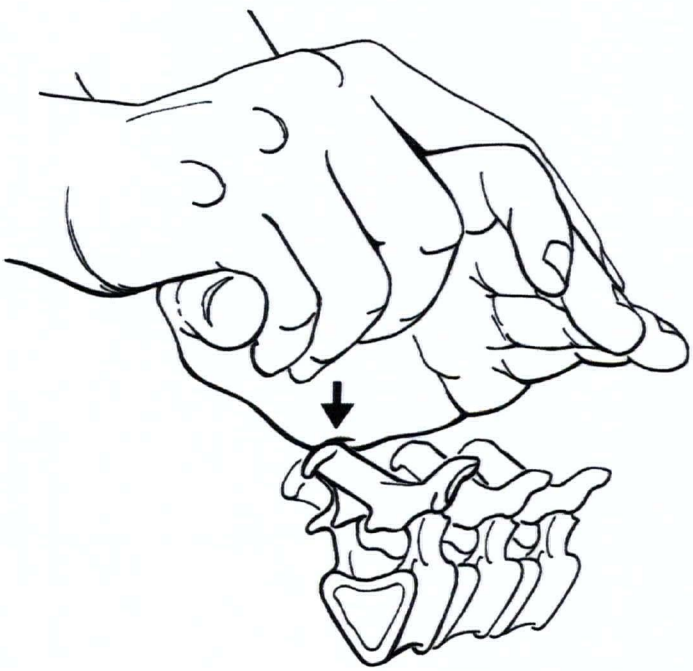

**Figure 1.5.** *Diagram of hand contact during PA mobilization in the midthoracic spine.*

## 1.5 SPINAL FRACTURES: DETECTION AND DETERMINANTS

Plain radiography is the traditional means of detecting vertebral fractures, clinically. Other methods, such as computed tomography, are also used for fracture detection in some clinical situations. Sensitive methods of vertebral fracture detection are necessary because the presence of fracture is related to future risk of fracture. [57-59]

The load at which fracture occurs in any structure is influenced by both material properties* and geometry. Further, external factors such as the loading direction and rate significantly influence the failure load. Bone mineral content (BMC*), areal bone mineral density (aBMD*), volumetric bone mineral density (vBMD), cortical* and trabecular* bone morphology* are parameters that reflect both material properties and geometry of any bone structure* and therefore, influence bone strength. A number of imaging technologies are used to measure these parameters, such as DXA and microcomputed tomography.

### 1.5.1 Plain Radiography

This is a method of X-ray examination in which an X-ray beam is passed through the patient onto a photographic plate. The main role of plain radiography in osteoporosis is in the diagnosis of vertebral compression fractures. Vertebral morphometry is typically measured on lateral spine radiographs. Some approaches have focused on describing the type of vertebral deformity, such as wedge, biconcave or compression, but the semiquantitative grading scale of Genant [165,166] measures severity of the vertebral fracture solely on the extent of vertebral height reduction and morphologic change. The degree of

severity is typically graded from 0-4 where 0 corresponds to normal, 1= mild fracture, 2= moderate fracture and 3= severe fracture. [165,166]

### 1.5.2 Dual energy X-ray Absorptiometry (DXA)

Bone density is a determinant of bone strength. DXA represents this as an areal bone mineral density. DXA uses X-ray beams of two distinct energy levels and measurements are based on the decrease in energy of the photon beam as it passes through bone and nonmineralized soft tissue. Traditionally, bone mineral data are reported as areal BMD (aBMD) (grams per $cm^2$), calculated by dividing the quantity of bone mineral within the scan area (BMC) by the projected area within the region of interest. Previous studies have shown that lumbar spine BMC measured by DXA correlates closely with the gold standard— ash weight, the weight of the inorganic component of bone. [167-169] Areal BMD explains up to 90% of the breaking strength of excised bone, [170] and a 7% increase in BMC is equivalent to a three fold increase in bone stiffness and twice the breaking strength.[171] Since DXA is the best predictor of fracture risk among individuals who have not yet suffered a fragility fracture, it may also accurately predict failure load of the vertebral body in those undergoing manual therapy.

Areal BMD values have clinical utility but can be confounded by changes in bone thickness (or depth). Bones of larger width and height also tend to be thicker yet bone thickness is not factored into estimates of aBMD due to the two-dimensional nature of the measurement. [172,173] Converting aBMD to 'volumetric bone mineral density' (vBMD) reduces its dependence on vertebral size. [174] This concept of vBMD aims to overcome

the limitation of 2-dimensional planar DXA scanning. [174-176] However, this mathematical derivation has never been compared with an ash-weight gold standard at the thoracic spine. Previous models for estimating vBMD assume vertebral geometry resembles a cylinder or a cube, yet human thoracic and lumbar vertebral endplate geometry is best estimated as an ellipse. [177,178]

Although aBMD explains a large percentage of the breaking strength of bone, [170] bone quantity is not sufficient to fully evaluate fracture risk. [172] Bone strength also relies on bone quality.[179,180] Bone quality can be defined as the characteristics of bone that are needed in order to perform its function. Quality is influenced by morphologic features such as a bone's cross-sectional geometry, trabecular architecture, and the composition of the matrix. [172] Thus another limitation of DXA, relevant to this thesis, is its inability to provide a measure of bone microarchitecture (i.e. trabecular number, trabecular thickness). Osteoporosis involves changes in bone architecture in addition to loss of aBMD. [179,181]

### 1.5.3 Computed Tomography

Tomography is a variation of simple radiography which permits cross-sectional images to be obtained. [182] Computed tomography (CT) is considered a very good technology for imaging bone [183-188] yet it is not typically used in the care of older adults with suspected osteoporotic vertebral fractures. To my knowledge, there have been no reports evaluating the sensitivity of radiography and CT scan for the detection of vertebral fractures produced during simulated spinal mobilization.

Further, current software allows for measures of bone volume from CT scans. This measure, used with BMC measured by DXA, could provide a more accurate measure of volumetric bone mineral density than previous methods combining vertebral body geometry and DXA measures. [174,176,189]

### 1.5.4 Microcomputed Tomography

Bone mineral density is only one factor associated with bone strength. [179,190] Other aspects of bone morphology, such as trabecular microarchitecture, also contribute to bone strength and fracture risk. [179,181] Research suggests a predisposition to loss of the horizontal trabeculae in osteoporosis, [191] leading to decreased interconnectivity of the internal scaffolding of the vertebral body and reduced ability to support loads. [67]

Microcomputed tomography (μCT) is a fast, nondestructive, highly accurate measure of microscopic bone structure. [192] In the spine, μCT has most commonly been used to measure three-dimensional trabecular bone morphology in small bone specimens. [193] In the past, most quantitative information on three-dimensional trabecular bone structure was based on applying stereology* to two-dimensional sections. However stereology provides a biased estimate of trabecular bone morphology because it is two-dimensional. The clinical measurement technique, DXA, does not provide any indication of the number, thickness, or orientation of individual trabeculae in a given region, nor does it differentiate between cortical and trabecular bone. [194] Three-dimensional μCT image analysis allows for direct measurement of trabecular thickness (Tb.Th), trabecular number (Tb.N) and trabecular separation (Tb.Sp) which is model-independent (it does

not assume a fixed structure model, i.e. plate or rod model). [195] Thus μCT may highlight determinants of fracture that cannot be measured using DXA. [196]

## 1.6 THORACIC SPINE BIOMECHANICS

### 1.6.1 Failure Modes— Compression vs. Other Directions

Failure load of a structure, the point at which there is a loss in the load-bearing capacity,[197] can be measured using a mechanical testing device. A load-deformation curve, including the failure load, is shown in Figure 1.6. The load-deformation relationship represents mechanical behavior of a structure.

Bone can be viewed as a material (i.e. a uniform specimen of bone tissue) or a structure (i.e. a vertebra). As a material or a structure, the deformation of bone is dependent on the rate and direction of loading.

Geometry refers to the size and shape of a structure. Vertebral strength is determined not only by the quantity of bone, but also by geometry. [181] Differences in vertebral size may increase the risk for vertebral fracture. For example, it is thought by some that Asians have a higher rate of vertebral compression fractures than Caucasians due to their proportionately smaller vertebrae. [67] Various geometric parameters can be measured to investigate the influence of vertebral geometry on vertebral strength. These include low-tech methods such as calipers and two-dimensional measures from plain radiographs, to

more complex geometric parameters measured using a variety of current imaging technologies.

Spinal failure or fracture has most commonly been studied with axial compressive loading and a number of studies have investigated the relationship between vertebral failure load in axial compression and bone mineral measurements using DXA. [62,198-200] Based on a search of Medline (1966 to present) and Cinahl (1982 to present) databases, there are no published studies of vertebral failure using modes simulating spinal mobilization or manipulation. Thus, there are no data to guide clinicians on the use of this potentially important therapeutic modality (spinal mobilization). Specifically, is spinal mobilization safe for use with individuals who have osteoporosis?

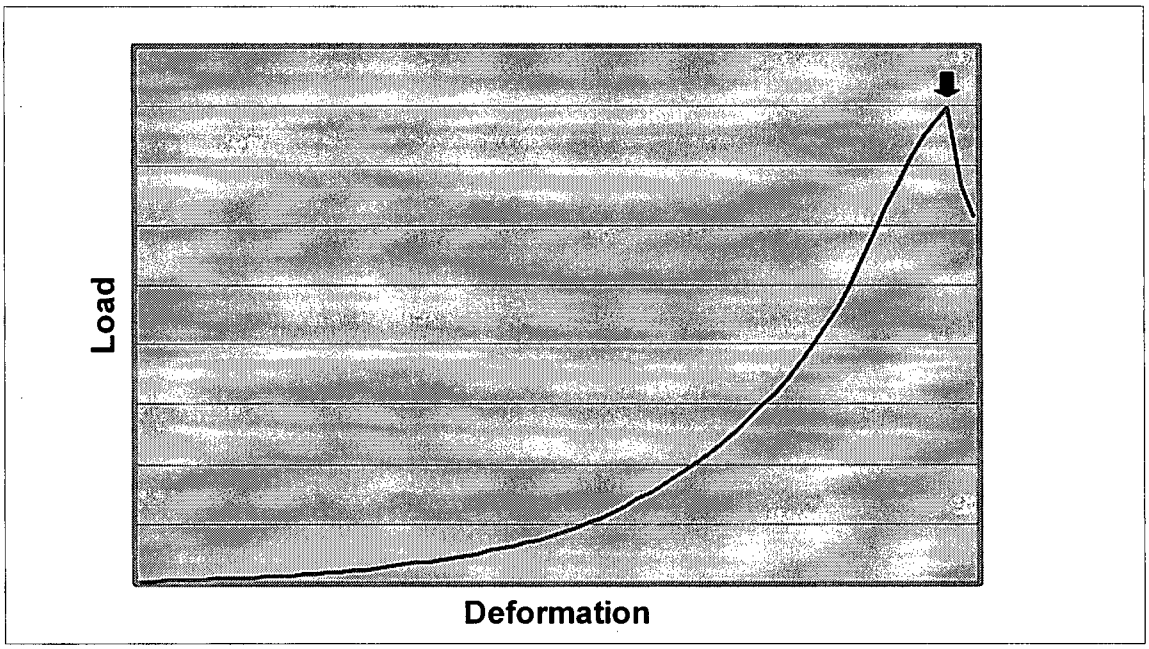


**Figure 1.6.** *Load-deformation relationship. The first decrease in load-bearing capacity is termed the failure load (⬇).*

### 1.6.2 Spine Kinematics

Kinematics, the study of motion, [201] is used to describe motion of one bone with respect to another without reference to the forces that cause the motion. Three-dimensional motion of a rigid body* is typically defined by motion in six directions, three translational* motions and three rotational* motions. [201] The right-handed orthogonal (90° angle) coordinate system is typically used for orientation (Figure 1.7).

Skilled clinicians have combined biomechanical theory, knowledge of anatomy and clinical experience to develop numerous manual therapy techniques, [108,112,150] but the theory underpinning many of these techniques has not been formally investigated. For example, central PA spinal mobilization is often used to restore thoracic spine motion in the sagittal plane*, yet the magnitude and direction of motion of thoracic vertebrae during this technique have not been measured.

To date, investigations of movements resulting from PA spinal mobilization in the cervical and lumbar spine, in vivo, have been conducted by inferring vertebral translations from the motion of an indenter at the skin surface or by measuring translations and rotations by digitizing radiographs. [35,156,202,203] These studies report sagittal translations of less than 2 mm (150 N load; in vivo) [156] up to 3.8 mm (variable loads; spinal model). [35] Mean anterior displacement of the spinous process was found to range between 8.8 and 13.0 mm.[156,203] Mean sagittal rotation ranged from 1.2–2.4°, and all lumbar motion segments tended to extend except L5-S1 which tended to flex. [156] One group studied cervical spine motion during PA mobilization using interventional

magnetic resonance imaging (iMR), but the analysis of the images was still based on radiographic techniques.[204] They reported little or no rotation and less than 0.5 mm translation (load not quantified). [205]

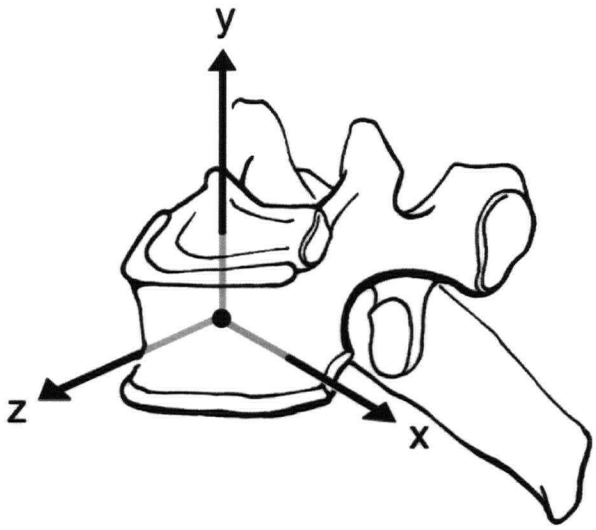


**Figure 1.7.** *Right-handed orthogonal (90° angle) coordinate system. Human motion is typically a combination of translation along any direction and rotation about any axis in space.* [206,207]

### 1.6.3 Spine Stiffness

Stiffness is a term used to describe the force needed to achieve a certain deformation of a structure. It is calculated as the slope of the load-deformation curve.

When clinicians use passive accessory intervertebral movements (PAIVMs) they note the stiffness, [122] quantity [108,125] and quality [108,123] of motion at one intervertebral joint relative to joints above and below. [108] Three previous studies have measured PA spinal stiffness in the thoracic spine using measures of displacement at the skin-surface [148,208,209] and

reported T7 mean PA stiffness measures of 10.7 N/mm, [208] 12.5 N/mm, [209] and T4 PA stiffness of 13.6 N/mm. [148] Yet, whether or not PA spinal stiffness can predict segmental spine motion has not been formally investigated.

Of note, some previous in vivo studies of PA stiffness during PA mobilization in the lumbar spine were performed with participants holding their breath during the application of the mobilization to avoid vertebral displacement caused by breathing. [155,210] This is problematic in that spinal stiffness has been shown to change throughout the respiratory cycle. [211]

### 1.6.4 Spine Flexibility

In the spine, flexibility refers to the ratio of the amount of rotation produced to the load applied. [206] Flexibility can be calculated as the slope of a moment-rotation curve (Deg/Nm). Range of motion* and neutral zone motion* can also be measured. [212-214] Panjabi and colleagues [215] measured flexibility in 11 motion segments, one for each thoracic level from five thoracic spines using a 2-vertebra construct. Applying a 5 Nm torque*, they found mean flexibility values (Deg/Nm) of: flexion 0.45, extension 0.35, right lateral bending 0.4, left lateral bending 0.38, right axial rotation 0.39 and left axial rotation 0.33. [215] Although techniques such as PA mobilization are routinely used in clinical assessment, [108,216] whether range of motion, three-dimensional flexibility, or neutral zone motion can be predicted by a passive accessory movement such as PA mobilization has not been tested.

## 1.7 SUMMARY

Back pain and osteoporosis are common in older adults and each is associated with enormous economic and social costs. In addition, there is a high prevalence of back pain among those who have osteoporosis. [25-29] Back pain is the most common reason for visiting a physiotherapist *(Physiotherapy Association of British Columbia (PABC), October 2001)*, and many physiotherapists use manual therapy techniques such as spinal mobilization to assess and treat back pain in conventional populations.

My literature review, which included searching Medline and Cinahl databases, highlighted five substantial gaps in knowledge.

Previous systematic reviews focused only on methodologic factors such as the randomization procedure, blinding of patients and outcome assessments, adequate follow-up period, and dropouts, [143,144] but failed to undertake critical analysis of the manual therapy intervention itself. Further, previous reviews and meta-analyses, including one published in 2003, [142] only included studies published in 2000 or earlier. Since the late 1990s physiotherapy practice has changed considerably based on the results of research. [217-228] **No systematic review has assessed the results of more recent studies, which are more likely to accurately represent current clinical practice, nor has any review critically analysed the content of the manual therapy intervention used.**

Second, recent randomized clinical trials suggest that manual therapy is effective for the treatment of spinal pain [50,51,126-128,229] so it seems reasonable that clinicians would consider using such techniques in individuals with osteoporosis who present with back pain. On the other hand, the literature cautions against the use of manual therapy in individuals with osteoporosis. [108,149,216] **There are no studies of physiotherapists' perceptions and current practice patterns with respect to the management of individuals with osteoporosis or the use of manual therapy.** Specifically, how many physiotherapists use manual therapy in this population and how many of them have concerns about fracture as a complication of treatment?

Third, although manual therapy is effective for back and neck pain in other populations,[50,51,126-128] there are no data on the safety of manual therapy in the osteoporotic spine. If patients are not offered manual therapy due to the clinician's fear of fracture then back pain management in this population may be suboptimal. If, however, some patients' skeletons are at risk of fracture because of the forces associated with manual therapy this would be important to know. **No studies have been conducted to assess the likelihood of fracture with manual therapy in the osteoporotic spine.**

Fourth, PAIVMs are used in spine assessment and clinical dogma suggests these movements provide information about intervertebral motion, but this theory has never been tested. **Specifically, there are no data reporting whether PA stiffness predicts intervertebral motion in older spines.**

Finally, the breaking strength of a bone depends on a number of factors including BMD and bone geometry. [179,181,190] Knowing whether BMD, geometry, and/or microscopic bone structure can predict the load at which a vertebra will fracture from a manual therapy technique will further our understanding of the determinants of spinal fracture. **There are no published data on the relationship of BMD, vertebral geometry or morphology with vertebral failure load during common manual therapy techniques.**

## 1.8 AIMS, OBJECTIVES & SCOPE OF THE THESIS

### Global Aim of the Thesis

My overall aim is to improve the understanding of manual therapy related spine biomechanics and determinants of fracture among older adults with back pain and osteoporosis. This research has the potential to be readily translated to treatment of back pain in this population.

### Objectives

My thesis focuses on clinically-relevant questions related to manual therapy in the osteoporotic spine. Specifically, I seek new knowledge regarding:

(1) **the effectiveness of manual therapy including spinal mobilization for spinal pain**

What might explain the apparent inconsistencies in clinical trials?

(2) **clinicians' perceptions and practice behaviors with respect to manual therapy in patients with osteoporosis**

Are clinicians using manual therapy in patients with osteoporosis and if so, do they have concerns about its use?

(3) **the safety of spinal mobilization in the osteoporotic spine**

Is a commonly used spinal mobilization technique, posteroanterior (PA) mobilization, likely to be safe in individuals with osteoporosis? How likely is it that a clinician could cause a vertebral fracture using this technique?

(4) **predicting spinal failure during manual therapy**

Can traditional measures of bone parameters such as BMC, BMD, and/or vertebral geometry predict failure load of thoracic vertebrae under a PA load? If not, can novel measures of vertebral morphology, obtained using μCT, better predict failure load and location under a PA load?

(5) **vertebral kinematics during manual therapy and the ability to predict intervertebral motion with a commonly used manual therapy technique**

Can segmental spine stiffness, during simulated PA spinal mobilization, predict segmental spine motion?

**Scope of the Thesis**

This thesis includes six studies (4 published, 2 submitted) presented in the following six chapters. First, in Chapter Two, I undertook a systematic review of the effectiveness of manual therapy including spinal mobilization for spinal pain. I critically analysed the literature to provide possible explanations for inconsistent outcomes in recent clinical trials of manual therapy. In Chapter Three, I used survey methodology to investigate perceptions about and use of manual therapy by physiotherapists in British Columbia when treating individuals with osteoporosis. Specifically, I investigated what treatment modes are being used, whether or not manual therapy is being used and if there is concern about fracture as a complication of manual therapy. Then, in Chapter Four, I report on an in vitro biomechanical study to measure whether a commonly used spinal mobilization technique (PA mobilization) is safe for use in older midthoracic cadaveric spines with low bone mineral density. This study also investigated vertebral kinematics during simulated PA mobilization and the sensitivity of plain radiography and CT scan to detect fractures produced by simulated PA mobilization. In Chapter Five, I report my investigation of the accuracy of AP and lateral DXA scans in cadaveric midthoracic spine segments and calculations of volumetric bone mineral density against the gold standard of bone content by ashing. Following on from those findings, Chapter Six, reports a study that aimed to measure regional vertebral trabecular morphology, using μCT, as a possible predictor of vertebral failure under a PA load. Finally, Chapter Seven reports a study testing whether PA stiffness can predict intervertebral motion in cadaveric spine segments of older adults.

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# Chapter Two

## *Evidence for the Effectiveness of Manual Therapy for Spinal Pain— a systematic review.*

## ABSTRACT

**Background.** In recent randomized clinical trials (RCTs) manual therapy was more effective than other methods of conservative management of spinal pain, yet earlier randomized controlled trials, systematic reviews and meta-analyses concluded manual therapy was not superior to other standard treatments for patients with back or neck pain.

**Objectives.** To systematically review randomized clinical trials comparing manual therapy including either spinal joint mobilization (with or without manipulation) or manipulation alone, with other conservative treatments for back or neck pain. A secondary goal was to explore possible explanations for apparently inconsistent findings.

**Methods.** I searched Medline, Cinahl, and Embase databases for randomized clinical trials comparing manual therapy including either spinal joint mobilization (with or without manipulation) or manipulation alone with other conservative treatments for back or neck pain. Only studies published as full papers, in English, between January 1, 1998 and December 31, 2003 were included.

**Results.** Thirteen studies met the inclusion criteria and five reported positive results. Four of the five studies with positive results used manual therapy in combination with another physiotherapy treatment mode. Assessment and treatment protocols used in RCTs did not always mirror clinical practice guidelines and the dose of manual therapy used varies greatly among studies. Physiotherapy including manual therapy at a dose of 30-45 minutes per session, for 4-8 weeks was found to be effective in adult populations with back or neck pain.

**Discussion.** There are clinically relevant differences between studies reporting positive results of manual therapy and those reporting no significant difference over other conservative treatments.

**Conclusions.** Interventions based on 'best practice' guidelines or textbooks written by experts appear to be more successful, and physiotherapy that includes manual therapy at a dose of 30-45 minutes per session, for 4-8 weeks is effective in adult populations with back or neck pain.

## 2.1 INTRODUCTION

In recent randomized clinical trials (RCTs), manual therapy was more effective than other methods of conservative management for low back and neck pain. [1-5] On the other hand, some older randomized clinical trials [6-13] systematic reviews [14] and meta-analyses[15] found no evidence that spinal manual therapy was superior to other standard treatments for patients with low back or neck pain.

An updated systematic review on this topic is necessary for two reasons. First, previous reviews and meta-analyses, including one published in 2003, [15] only included studies published in 2000 or earlier. Clinical practice evolves in response to new scientific evidence and since the late 1990s physiotherapy practice has changed considerably. For example, spinal segmental motor control and stabilization research has particularly influenced the physiotherapy management of low back pain through the addition of specific low load exercise therapy. [16-25] Another example is the improved understanding of pain physiology and the influence of neurophysiology education. [26] These clinical advances were not incorporated into clinical trials undertaken before the late 1990s. Thus, there is a need for a systematic review of more recent trials of spinal manual therapy that are more likely to accurately represent current clinical practice.

With good reason, previous systematic reviews critically evaluated methodologic factors such as the randomization procedure, appropriate blinding of patients and outcome assessments, adequate follow-up period, and dropouts. [27,28] Although these factors are undoubtedly important, the quality of the intervention itself must also receive close

scrutiny. Yet analysis of the intervention is a significant omission among previous systematic reviews.

Therefore, the primary objective of this review was to systematically identify, select and critically appraise randomized clinical trials, published between 1998 and 2003, that compared spinal manual therapy including spinal joint mobilization (with or without manipulation) or manipulation alone, with other conservative treatments for back or neck pain. The secondary objective was to explore possible reasons for the apparently inconsistent findings among various manual therapy trials.

## 2.2 METHODS

### Definitions

The term 'manual therapy' is used in a wide range of ways with a wide range of meanings, but for this review it includes manually performed assessment and treatment methods (which can include joint, neural tissue, and/or muscle techniques). [29-33]

### Inclusion criteria

The systematic review was restricted to randomized clinical trials comparing manual therapy including either spinal joint mobilization (with or without manipulation) or manipulation alone with other conservative treatments for acute or chronic back or neck pain. Only studies published as full papers, in English, between January 1, 1998 and December 31, 2003 were included. Pilot studies were not included.

### Search strategy

I searched Medline, Cinahl, and Embase databases for randomized clinical trials comparing manual therapy including either spinal joint mobilization (with or without manipulation) or manipulation alone with other conservative treatments for back or neck pain. Search strategies for each database are outlined in Table 2.1.

**Table 2.1.** *Search strategy.*

| Database | MeSH Headings | Limits |
|---|---|---|
| Medline | Manipulation, Orthopedic | Human |
| | Manipulation, Chiropractic | English |
| | Manipulation, Osteopathic | 1998-2003 |
| | Physical Therapy Techniques | |
| | Musculoskeletal Manipulations | |
| | Comparative Study | |
| | (back or neck) and pain | |
| Cinahl | manual therapy | English |
| | chiropractic | Clinical Trial |
| | chiropractic manipulation | 1998-2003 |
| | Manipulation, Orthopedic | |
| | osteopathy | |
| | (back or neck) and pain | |
| Embase | manipulative medicine | Human |
| | (back or neck) and pain | English |
| | | 1998-2003 |

**Search results**

Thirteen studies met the inclusion criteria (Table 2.2). One study of bone-setting by Finnish folk healers who lacked formal education [34] was excluded as all other studies involved formally educated professionals.

**Table 2.2.** *Summary of studies reviewed. MT= manual therapy, LBP= low back pain, PT=physiotherapy, GP= general practitioner*

| Author, yr | Population (n) | MT limited to Manipulation Only | Manual Treatment Delivered By: | Clinically Relevant/Guideline Based Manual Treatment | Interventions/Groups | Control Group | Dose (Manual Therapy or Manipulation) | Results | Effect Size for Positive Studies |
|---|---|---|---|---|---|---|---|---|---|
| Aure OF, Nilsen JH, Vasseljen O. Spine 2003;28:525-31. | 20-60 yrs; chronic LBP>8 wks, less than 6 mos (49) | No | Physical Therapists | Yes | 1. Manual Therapy plus Exercise Therapy<br>2. Exercise Therapy alone | No control group | 45 min. (15 min MT); 2 sessions/wk, 8 wks | Significantly larger improvements in MT group (maintained at 1 year follow-up) | .78 |
| Hoving JL, Koes BW, de Vet HC, et al. Ann Intern Med 2002;136:713-22 | 18-70 yrs; pain or stiffness in the neck for at least 2 wks (183) | No | Physical Therapists | Yes | 1. Manual therapy plus specific exercise training<br>2. Active exercise focused physical therapy<br>3. Continued care by GP | Continued care by a GP | 45 min.; 1 session/wk for up to 6 wks | Physical Therapy including MT more effective than Physical Therapy without MT or continued care by a GP | Not given |
| Jull G, Trott P, Potter H, et al. Spine 2002;27:1835-43. | 18-60 years; cervicogenic headache at least 1X/wk for a period of 2mos-10yrs (200) | No | Physical Therapists | Yes | 1. Manual Therapy<br>2. Exercise Therapy (low load endurance training)<br>3. Combined Manual Therapy and Exercise Therapy<br>4. Control | No treatment control group | 30 min, 8-12 sessions,6 wks | MT as effective as ET and both significantly better than control | .80 |
| Moseley L. Aust J Physiother 2002;48:297-302 | Chronic low back pain> 2 mos. (57) | No | Physical Therapists | Yes with respect to clinical relevance (individualized and variety of techniques allowed) but no references cited for manual therapy techniques. | 1. Manual therapy, specific exercise training, and neurophysiology education<br>2. Medical management by GP | Management by a GP | 2x/wk, 4 wks | Combined physiotherapy treatment including MT, specific exercise training, and neurophysiology education resulted in improved function and pain at 1 and 12 mos. | Not given |
| Giles LG, Muller R. Spine 2003;28:1490-502 | 17 years or older; mechanical back or neck pain for a minimum of 13 wks (115) | Yes | Chiropractors | Yes (for low back pain).<br>No (for neck pain). | 1. Spinal manipulation<br>2. Sports physician follow up (limited) and medication<br>3. Acupuncture (needle) | No control group | 20 min, 2x/wk, maximum 9 wks | Greater short term benefit for back pain with manipulation, but not for neck pain. Acupuncture more effective for neck pain. | Not given |
| Andersson GB, Lucente T, Davis AM, et al. N Engl J Med 1999;341:1426-31. | 20-59 years; LBP lasting at least 3 weeks but less than 6 mos (178) | No | Osteopaths | Yes | 1. osteopathic treatment<br>2. 'standard care' by physicians | 'standard care' by physicians which could include active PT | 1x/wk for 4 wks then 1x/2 wks for 8 wks | No significant difference between groups. Both groups improved. | |

| Author, yr | Population (n) | MT Limited to Manipulation Only | Manual Treatment Delivered By: | Clinically Relevant/Guideline Based Manual Treatment | Interventions/Groups | Control Group | Dose (Manual Therapy or Manipulation) | Results |
|---|---|---|---|---|---|---|---|---|
| Bronfort G, Evans R, Nelson B, et al. Spine 2001;26:788-97 | 20-65 years; mechanical neck pain for at least 12 weeks (191) | Yes (but this group also received 45 min of sham microcurrent therapy) | Chiropractors | No. A reference for the use of spinal manipulation for low back pain is cited, but only cervical and thoracic spine techniques were used. | 1. Spinal manipulation plus upper body and neck strengthening exercise<br>2. Aerobic exercise plus MedX cervical extension and rotation machine<br>3. Spinal manipulation | No control group | 20 1 hour sessions over 11 wks | No significant difference between groups with respect to pain, neck disability, medication use. |
| Cherkin DC, Deyo RA, Battie M, et al. N Engl J Med 1998;339:1021-9. | 20-64 years; LBP minimum 7 days after seeing physician, (321) | Yes | Chiropractors | No, side lying only | 1. Chiropractic manipulation<br>2. Education Booklet<br>3. McKenzie exercises | No control group | Up to 9x over 1 month | No significant difference between groups. |
| Curtis P, Carey TS, Evans P, et al. Spine 2000;25:2954-60 | 21-65 yrs; acute LBP of less than 2 mos (295) | No (Manipulation plus muscle energy techniques) | Physicians with limited training (18 hrs) in manual therapy | No | 1. Manipulation and Muscle Energy Techniques plus Enhanced Care<br>2. Enhanced care alone | No control group | Initial plus 4 follow-ups; 2x/wk for 2 wks | Only 43% of patients in the MT group actually received the planned treatment; no significant difference between groups |
| Hsieh CY, Adams AH, Tobis J, et al. Spine 2002;27:1142-8. | 18 yrs or older; LBP>3 wks and less than 6 mos (200) | Yes | Chiropractors | No, limited techniques | 1. Back School<br>2. Myofascial Therapy<br>3. Joint Manipulation<br>4. Combined Joint Manipulation & Myofascial Therapy | No control group | 3x/wk for 3 wks | All groups improved; no significant between-group differences at 3 or 6 months |
| Hurwitz EL, Morgenstern H, Harber P, et al. Spine 2002;27:2193-204 | 18 years or older; LBP (681) | Yes | Chiropractors | Yes | 1. Medical care only<br>2. Chiropractic care only<br>3. Medical care with limited physical therapy<br>4. Chiropractic care with modalities | No control group | Treatment dose not prescribed | Chiropractic no better than other groups; Physical therapy plus medical care group had less pain at 6 wks and 6 mos than medical care only |
| Jordan A, Bendix T, Nielsen H, et al. Spine 1998;23:311-8 | 20-60 yrs; chronic neck pain at least 3 mos (167) | No | Mobilization by Physical Therapists; Manipulation by Chiropractors | Yes with respect to clinical relevance (individualized) but no references cited for mobilization or manipulation techniques. | 1. Manipulation<br>2. Physiotherapy without manipulation<br>3. Strength training (with a focus on neck muscle training) | No control group | Physiotherapy: 30 min, 2x/wk, 6 wks<br><br>Chiropractic: 15-20 min, 2x/wk, 6 wks | No significant difference between groups. |
| David J, Modi S, Aluko AA, et al. Br J Rheumatol 1998;37:1118-22. | 18-75 yrs; neck pain> 6 wks duration (70) | No | Physical Therapists | Not Clear | 1. Physiotherapy<br>2. Acupuncture | No control group | 1x/wk, 6 wks (maximum) | No significant difference between acupuncture and physiotherapy groups. Both groups improved. |

## 2.3 RESULTS

Table 2.2 summarises descriptive information on the studies. Examining the trials for homogeneity revealed that the mean age of participants was similar amongst the studies and most participants were of Caucasian origin (with the exception of two studies [1,2]). One study [3] had a 'no treatment' control group. Two studies had a 'standard care' control group, consisting of treatment by a general practitioner.[4,5] The other ten studies did not have a 'no treatment' or 'standard care' control group (Table 2.2).

Less than one third of the studies reviewed reported prospective power calculations. [3,6-8] One study reported what appears to be retrospective power. [9]

### Primary Analysis: Effectiveness of Manual Therapy

In seven of the thirteen studies analysed, there was no difference between the manual therapy group and other treatment groups (Table 2.2). Four of these seven studies used manipulation only, one compared physiotherapy with acupuncture, and in one, the practitioners administering the intervention were physicians with 18 hours training in manual therapy.

Five of the thirteen studies in the past six years (1998-2003), however, reported that manual therapy was superior to exercise therapy alone, continued care by a general practitioner, sports physician follow-up plus medication, acupuncture and no treatment. [3-6,10]

**Secondary Analysis: Differences Between Effective and Ineffective Interventions**

Manual therapy vs. manipulation only

Four of the thirteen studies reported better results in the manual therapy group as compared with the other group(s). [3-6] Five of the remaining nine studies used *manipulation only* and all but one[10] reported no significant difference or a poorer response as compared with the other group(s). [2,7,9,11]

Time per session

Only six studies reported the time per session. Time varied from 20-60 minutes per treatment. Three of the five studies with positive results allowed between 30 and 45 minutes per treatment. One (of the studies with positive results) did not report treatment time [5] and the other had mixed results (positive for back pain but not for neck pain) and allowed 20 minutes per treatment. [10]

Total number of sessions

The total number of sessions varied from five to twenty, with a frequency of between once per week and three times per week. Some studies did not prescribe a maximum or minimum number of sessions per week (Table 2.2).

Number of weeks of treatment

The number of weeks of treatment varied from three to twelve. The five studies with positive results used between four and nine weeks of treatment. [3-6,10]

Combining manual therapy with other physiotherapy treatment modes

Four of the five studies with positive results used manual therapy in combination with another aspect of physiotherapy treatment (exercise therapy, [4,6] specific exercise training,[3,5] and neurophysiology education [5]).

## 2.4. DISCUSSION

This systematic review confirmed that a number of recent studies found that manual therapy, in particular physiotherapy that included spinal mobilization, was superior to a range of comparison therapies. Physiotherapy including spinal mobilization was found to reduce pain, improve function, improve spinal range of motion, improve general health, and achieve earlier return to work. [3-6] While this supports many clinicians' impression that manual therapy is effective in certain patients, there are sufficient data to permit critical analysis of at least five differences between effective and ineffective interventions, and to speculate as to how these differences may underpin the reported results.

### Trial Intervention: Manual Therapy or Manipulation Alone

This systematic review revealed that interventions that consisted of a variety of manual therapy techniques, rather than joint manipulation alone, appeared to yield better results. For example, Jull et al [3] compared the effectiveness of (i) manual therapy delivered by physiotherapists, (ii) specific exercise therapy delivered by physiotherapists, (iii) combined manual and specific exercise therapy, and a (iv) no treatment control group, for treatment of cervicogenic headache. At 12-month follow up both manual therapy groups and also the specific exercise group had significantly reduced headache frequency and intensity, neck pain, and disability. In this study, [3] manual therapy included both low-velocity cervical joint mobilization techniques and high-velocity manipulation techniques. These results are relevant to physiotherapists with postgraduate certification in manual therapy as they receive extensive training in both of these techniques.

Similarly, Hoving et al [4] compared physiotherapy including manual therapy with physiotherapy without manual therapy for individuals with chronic neck pain. Of note, these authors allowed the use of low-velocity joint *mobilizations* but no high-velocity low amplitude thrust techniques (manipulation).

**Trial Intervention: Guideline Based or Apparently Empirical?**

Assessment and treatment protocols used in RCTs do not always mirror clinical practice guidelines, which are typically set out in textbooks or published as guidelines written by experts in the field and based on current available evidence. Some studies tested protocols that differed substantially from clinical practice. For example, Andersson et al.[1] compared osteopathic treatment (including manual therapy) with 'standard care' by physicians. However the reported 'standard care' included medication, active physiotherapy, ultrasonography, diathermy, hot or cold packs (or both), use of a corset, or transcutaneous electrical nerve stimulation (TENS)! Clearly health maintenance organization (HMO) physicians have neither the time (45 minutes), equipment, or skills (i.e. active physiotherapy) to provide this treatment. Further, two studies of manipulation by chiropractors included participants with back or neck pain, yet the intervention protocol they employed appeared to be directed exclusively toward low back pain management. [10,11] Three studies used very restricted manual assessment and/or treatment techniques [7-9] which do not reflect 'best practice'. Three of the five studies with positive results used manual treatment (by physiotherapists) based on published guidelines or clinical textbooks written by experts in the field. [3,4,6]

**Association Between the Dose of Manual Therapy or Manipulation (minutes, sessions, weeks) and Outcome**

As with pharmacological therapy, the dose-response of therapy warrants examination. Time devoted to therapy per treatment session, the number of treatment sessions, and the number of weeks of treatment, are all important factors for therapists, patients and payers.

Treatment duration would influence not only cost-effectiveness, but may also impact the effectiveness of manual therapy treatment. Despite the potential clinical importance of dose of therapy, doses varied substantially between protocols. One study compared chiropractic care only, medical care only, medical care with limited physiotherapy, and chiropractic care with modalities but did not prescribe a treatment dose. [2] The authors monitored utilization of the various treatment modes and time per session and found that 1/3 of patients randomly assigned to medical care with physiotherapy had no physiotherapy visits, and 20% of patients in the chiropractic groups received concurrent medical care, whereas only 7% of patients in the medical care groups received concurrent chiropractic care. They also reported that chiropractors and medical providers in their study spent an average of 15 minutes with patients at each visit, and physiotherapists averaged 31 minutes per patient visit.

**Single or Combined Therapy and Outcome**

A number of the studies I reviewed investigated a combination of therapies such as care provided by two health care professionals or a combination of manual therapy or manipulation with another mode of treatment. Of note, four of the five studies with

positive results used manual therapy in combination with another aspect of physiotherapy treatment (exercise therapy [4,6], specific exercise training [3,5], and neurophysiology education [5]). Similar positive results were not seen in chiropractic studies of spinal manipulation combined with exercise[9,11] or modalities.[2]

**Methodological Factors**

This critical appraisal also examined two key methodological factors that can influence RCT findings. First, the presence or absence of a control group is an important factor. Of the five studies with positive results, one [3] had a 'no treatment' control and two used 'standard care' by a general practitioner as the control group (Table 2.2). In one of these studies the 'continued care by a GP' group received more than routine GP care, including ergonomic advice, advice on psychosocial issues and home exercises. [4] In the second study, 6/28 participants in the control group received weekly manipulations from their general practitioner. [5]

One study reported using a 'standard care by physicians' control group but close scrutiny revealed that this group also received active physiotherapy, ultrasonography, diathermy, hot or cold packs (or both), use of a corset, and/or transcutaneous electrical nerve stimulation (TENS). [1]

Lack of a robust control group is a common problem among clinical trials in manual therapy, resulting in many sources of bias. Many factors that are unrelated to the treatment, such as the therapist's enthusiasm, patient-provider rapport and patient and

health care provider expectations are all thought to contribute to the therapeutic effect. [12-15]

Second, an important issue when examining discordant outcomes of RCTs is power [16] as underpowered studies can lead to Type II error. Fewer than one third of the studies reported prospective power calculations [3,6-8] and one study reported what appears to be retrospective power [9]. Experts suggest that it is illogical to calculate retrospective power, and recommend that researchers report effect sizes for both significant and non-significant findings to evaluate whether the sample size might have been too small to detect a real effect. [17]

**Conclusions**

My primary objective was to systematically identify, select and critically appraise randomized clinical trials comparing spinal manual therapy including spinal joint mobilization (with or without manipulation) or manipulation alone, with other conservative treatments for back or neck pain. I found clinically relevant differences between studies reporting positive results of manual therapy and those reporting no significant difference over other conservative treatments. Specifically, those interventions in which the treatment protocol reflected what therapists do in clinical practice (i.e. using more than one manual therapy technique or combining manual therapy with other modes of treatment such as specific exercise training) appeared to be consistently more effective than those using manipulation or exercise therapy alone. Interventions based on 'best practice' guidelines were effective, and physiotherapy

including manual therapy at a dose of 30-45 minutes per session, for 4-8 weeks was effective in reducing pain and improving function. [3-6]

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# Chapter Three

## *Physiotherapy and Osteoporosis: Practice Behaviors and Clinicians' Perceptions—a survey.*

## ABSTRACT

**Background.** Physiotherapists typically use a variety of modes to treat their clients, including manual therapy. The literature cautions against the use of manual therapy in individuals with osteoporosis, yet clinical experience and published cases suggest that these techniques are used by at least some, if not many, clinicians.

**Objectives.** To measure the most common treatment modes used by a random sample of physiotherapists practicing in the province of British Columbia (BC) in the treatment of individuals with osteoporosis. To assess whether physiotherapists in BC have concerns about the use of manual therapy in individuals with osteoporosis, particularly whether physiotherapists have concerns about fracture as a complication of treatment.

**Methods**. I developed a questionnaire and sent it to 171 randomly selected physiotherapists working in the province of BC.

**Results**. The response rate was 39% (67/171). Ninety-seven percent of respondents reported using strength exercises and postural reeducation, while 45% reported using manual therapy in this population. Ninety-one percent of respondents reported having concerns about the use of manual therapy. Vertebral fracture and rib fracture were the most commonly reported concerns.

**Conclusions**. Most physiotherapists practicing in BC, Canada use evidence based methods (i.e. strength training) when treating individuals with osteoporosis, a large number use manual therapy, and most have concerns about its use. Physiotherapists are most concerned about fractures, in particular vertebral fracture, but injury to other musculoskeletal tissues is also of concern. Studies of safety and effectiveness of manual therapy in this population are needed to guide clinical practice.

## 3.1 INTRODUCTION

Osteoporosis, characterized by low bone mass and increased fracture risk, affects 1 in 5 postmenopausal women. [1,2] Given the population prevalence, and also the various secondary causes of osteoporosis, it is likely that physiotherapists in all areas of practice see patients with compromised bone health. [3] Further, an individual may present to physiotherapy for any number of problems, related or unrelated to osteoporosis. For example, back pain is also common in older adults [4,5] and is associated with reduced mobility, independence, and health related quality of life. [6,7] Back pain is also the most common reason for visiting a physiotherapist *(Physiotherapy Association of British Columbia (PABC), October 2001)* and there are many individuals with both osteoporosis and back pain. [7-9]

Physiotherapists can use a variety of modes to treat clients with osteoporosis. Pain relief, increased strength, improved posture and improved range of motion are a few common goals of therapy for such individuals. [10,11] Given the effectiveness of manual therapy in various populations, [12-17] it seems reasonable that clinicians would consider using such techniques in individuals with osteoporosis. The biological mechanisms underpinning this effectiveness may be related to spinal mobilization stimulating sympathetic nervous system activity [15,17,18] and promoting motor activity.[19] For example, emerging evidence suggests than spinal joint mobilization techniques applied to the cervical spine elicit concurrent effects on pain perception, autonomic function, and motor function in patterns that are similar to the patterns of change elicited by stimulation of the periaqueductal gray

region of the midbrain. [15,17,20] However, the literature cautions against the use of manual therapy in individuals with osteoporosis. [21-23]

There appears to be agreement amongst leading clinicians that spinal *manipulation* (high velocity thrust) techniques are contraindicated in individuals with osteoporosis, [21-24] yet clinical experience [25] and published cases [26] suggest that these techniques are still being used by chiropractors. Clinical experience indicates that while some colleagues have expressed concern about the safety of manual therapy (including *spinal mobilization*) other clinicians routinely use manual therapy in older people, a proportion of whom will have osteoporosis.

There are no previous studies of clinicians' practice behaviors and perceptions with respect to the management of individuals with osteoporosis. Although there is vast literature on the effects of mechanical loading on bone (which physiotherapists can use to prescribe appropriate exercises) there are no data on the safety of manual therapy in this population. [24,25] For these reasons the aims of this study were 1) to measure the most common treatment modes used by a random sample of physiotherapists practicing in the province of British Columbia (BC) for treating individuals with osteoporosis and 2) to assess whether physiotherapists in BC have concerns about the use of manual therapy in individuals with osteoporosis, such as fear of fracture as a complication of treatment.

## 3.2 METHODS

### Design

This cross-sectional study was approved by the University of British Columbia Clinical Research Ethics Board and the Research Review Committee at Children's & Women's Health Centre of British Columbia (BC Women's Health Centre).

### Materials

I developed a brief questionnaire (Appendix I) to (1) measure the most common treatment modes used by a random sample of physiotherapists practicing in the province of BC in the treatment of individuals with osteoporosis, and (2) to assess whether physiotherapists in BC have concerns about the use of manual therapy in individuals with osteoporosis, particularly whether physiotherapists have concerns about fracture as a complication of treatment.

### Subjects and procedures

The questionnaire and accompanying cover letter (Appendix I) was faxed to a random sample of physiotherapists in the province of BC. The fax was sent to every fifth member with a fax number, from a list of members of the provincial association. The survey was sent to physiotherapists working in all areas of practice. A total of 208 questionnaires were sent but 37 were not transmitted. Thus a total of 171 questionnaires were both sent and transmitted. Sixty-seven individuals responded by completing the questionnaire and returning it to the BC Women's Health Centre by fax or mail within three weeks.

**Data analysis**

The response rate was calculated by dividing the number of respondents by the number of questionnaires that were both sent and transmitted. The number of respondents who

1) used each treatment mode (Appendix I, Question 1)
2) had concerns about the use of manual therapy
3) had concerns about injury to each of the tissues/regions listed (i.e. vertebral fracture, other fracture, disc injury, muscle injury) (Appendix I, Question 3)

was expressed as a percentage of the total respondents.

## 3.3 RESULTS

The response rate (67/171) was 39%. The percentage of all respondents who selected each treatment mode is presented in Figure 3.1. Two respondents (3%) reported that they do not treat individuals with osteoporosis. Thirty-nine percent of respondents reported using treatment modes 'other' than those listed. A wide variety of responses were received in the 'other' category, including dietary calcium, weight bearing activity, fall prevention education, pain and time management, energy conservation, endurance training, referral to physician for medications, hydrotherapy, support/bracing and education of personal trainers.

Forty-five percent of respondents reported using manual therapy in this population (Figure 3.1). In Question 2, 91% of respondents reported having concerns about the use of manual therapy techniques on individuals with osteoporosis, 6% did not have concerns and 3% stated that they do not treat individuals with osteoporosis. With the exception of one individual, respondents who reported using manual therapy (in Question 1, Appendix I) also reported concern about its use (in Question 2, Appendix I).

The percentage of respondents concerned about each of the tissues/structures listed is presented in Figure 3.2. Vertebral fracture and other fracture were the most commonly reported concerns. Of the respondents who were concerned about 'other fractures' (Figure 3.2), 13% reported concern about rib fracture. Hip, wrist, and humerus fracture were of concern for a small number of respondents (3%, 1% and 2% respectively).

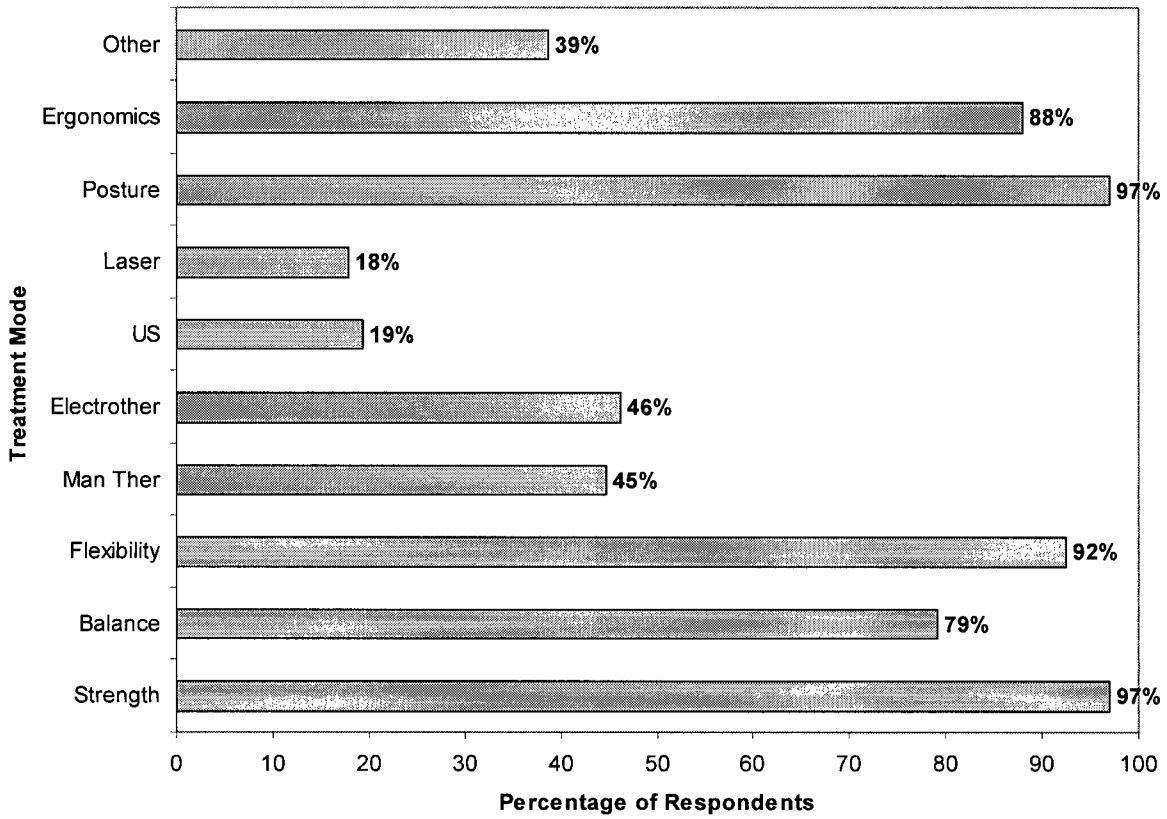


**Figure 3.1.** *Percentage of respondents who chose each of the treatment modes listed in Question 1: "Which of the following treatment modes would you likely use with an individual with osteoporosis?" Strength= strength exercises; Balance= balance exercises; Flexibility= flexibility exercises; Man Ther= manual therapy; Electrother= electrotherapy; US= ultrasound; Laser= laser; Posture= posture reeducation; Ergonomics= ergonomic advice*

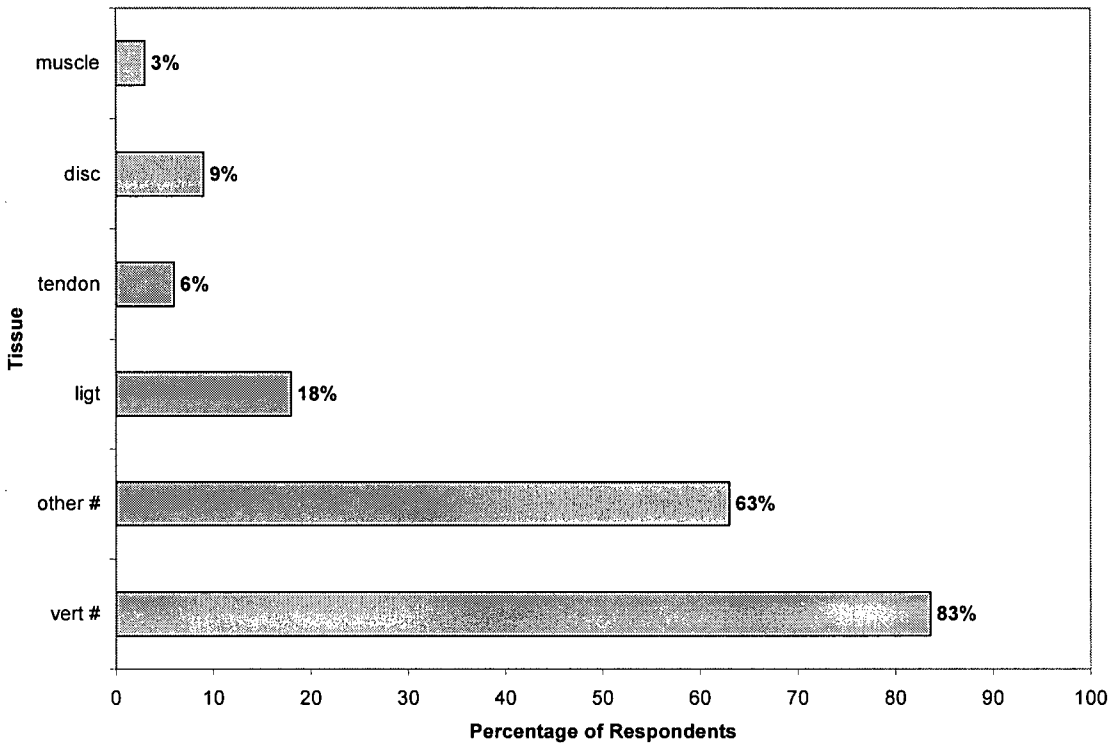


**Figure 3.2.** *Percentage of respondents reporting concerns related to each of the tissues/structures listed in Question 3. vert # = vertebral fracture; other # = other fracture; ligt= ligament injury; tendon= tendon injury; disc = disc injury; muscle= muscle injury*

## 3.4 DISCUSSION

This study presents novel data about current practice behaviors and perceptions of physiotherapists with respect to the management of individuals with osteoporosis in BC. Most respondents reported concern about the use of manual therapy in this population. Despite this concern, the results suggest that many clinicians (45% of the sample) use manual therapy in individuals with osteoporosis. Studies suggest that manual therapy can relieve pain [12-17] and improve motor control [15,27] so it seems reasonable that physiotherapists would consider the potential benefits of manual therapy for individuals even if they have osteoporosis.

The questionnaire did not specifically state whether the individual was being treated for osteoporosis or an unrelated condition. However, two respondents reported that they do not treat osteoporosis. One stated that 'we are a hand-only clinic'. This response is of interest as one would speculate that a hand clinic would treat some individuals during recovery from wrist fracture. Colles' fracture is a common sentinel osteoporotic fracture and a strong predictor of future fracture. [28,29]

### Treatment modes

As expected, most respondents marked a number of treatment modes. Strength exercises, postural reeducation, flexibility exercises, and ergonomic advice were utilized by a vast majority of respondents (Figure 3.1), while balance training was less commonly used yet is also thought to be an important factor in preventing falls and subsequent fractures. [7,30-

[32] Manual therapy was used by almost half the respondents (Figure 3.1) yet few data exist with respect to its safety or efficacy in this population.

**Concern Regarding Fracture or Other Tissue Injury**

The results suggest that physiotherapists are concerned about fracture as a complication of manual therapy treatment, in particular vertebral fracture and rib fracture. Surprisingly, ligament, tendon and disc injury were also of concern, albeit for a much smaller number of respondents (Figure 3.3). This may reflect a lack of data about secondary tissue changes associated with osteoporosis, or lack of knowledge on the part of physiotherapists with respect to whether or not they should be concerned about these tissues.

**Response Rate**

The response rate in this study is among the upper range found in surveys among other health care professionals. [33,34] While some previous studies of physiotherapists report response rates as high as 53% [35] and 65%, [36] I feel the 39% response rate in my study is acceptable for numerous reasons. First, the study included a random sample of all physiotherapists who were members of their professional association in a specific jurisdiction. Research topic has been shown to affect response rates [37] yet few clinicians treat primarily individuals with osteoporosis. Clinicians may be more motivated to respond to a study about direct-access [36] (which more obviously affects their caseload and earning potential) or a questionnaire specific to their area of special interest. [38,39]

Some previous studies with higher response rates only involved clinicians in a specific area of practice [39] or education. [40]

Second, while incentives have been shown to affect response rates [41] I did not offer any in this study. A study evaluating the use of prepaid incentives suggested that some incentives increase response rate yet introduce further bias because some incentives will appeal more to certain individuals. [42] Finally, using data from the Community Tracking Study's physician survey, researchers examined how survey estimates and data quality changed as additional respondents completed the survey. They found that differences in response rates are unlikely to significantly impact the quality of data collected unless one achieves a response rate significantly above 65%. [43]

A reason to consider the response rate is to avoid drawing biased conclusions. My response rate indicates that a substantial proportion of clinicians have concerns about the use of manual therapy in patients with osteoporosis. Even in the unlikely event that all clinicians who did not reply had no concern about the use of manual therapy in this population, my results would still suggest that 36% of clinicians have concerns. This would still warrant further research.

**Clinical Implications**

These findings suggest that a large percentage of physiotherapists practicing in BC use evidence based methods (specifically strength training [32,44,45]) when treating individuals with osteoporosis. Many also use manual therapy in this population and most have

concerns about its use. Given the similarities in physiotherapy training across the various provinces in Canada, [46,47] it is likely that these BC data would generalize nationwide. Further, manual therapy is an internationally practiced and researched treatment [12,13,15-17,21,22,48] so these data may even have international relevance. This suggests a need for appropriately designed studies to provide data to address the safety concerns reported in this study.

Physiotherapists are most concerned about fractures, in particular vertebral fracture, but injury to other musculoskeletal tissues is also of concern. Clinical leaders agree that *manipulation* is contraindicated in this population, [21-24] but consensus on other manual therapy techniques has not been reached. The results of this study suggest that a significant number of physiotherapists use manual therapy in this population. Evidence suggests manual therapy is effective for some conditions, so it seems appropriate that physiotherapists would consider using it in this population. However, there are no data with respect to the safety of manual therapy for individuals with osteoporosis. As clients with osteoporosis could potentially benefit from manual therapy, trials are needed to examine its safety and effectiveness in this population.

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# Chapter Four

## *Failure Characteristics of the Thoracic Spine with a Posteroanterior Load: Investigating the Safety of Spinal Mobilization*

## ABSTRACT

**Background.** Osteoporosis and back pain are common alone and in combination among older adults. Spinal mobilization techniques have been shown to relieve back pain and improve function in various clinical settings. However, whether controlled spinal mobilization can cause vertebral fracture in individuals with osteoporosis is not known.

**Objectives.** To quantify failure load and pattern of midthoracic vertebrae under a posteroanterior (PA) load and to compare failure load, in vitro, with applied load, in vivo.

**Methods.** Twelve T5-8 cadaveric specimens (mean age 77 yrs) were scanned using DXA, radiographed, and measured for bone size. I measured failure load, failure site, and intervertebral motion (using a precision opto-electronic camera system) when a PA load was applied at the spinous process of T6 using a servohydraulic material testing machine. Post test radiography and CT scan were used to verify failure site. These tests were repeated in an intact cadaver, using a Tekscan I-Scan sensor to measure applied loads. I also quantified in vivo applied loads during PA mobilization during seven trials by two experienced physiotherapists.

**Results.** Mean (SD) in vitro failure load of 479 N (162 N) was significantly higher than the mean (SD) in vivo applied load of 145N (38 N) ($p=.0004$). Macroscopic observation revealed a fracture at the T6 spinous process in eleven specimens, and one at the T7 spinous process. These fractures were detected by plain radiography in three of twelve cases and by CT scan in six of twelve cases. The mobilized vertebra (T6) extended with respect to the inferior vertebra and the vertebra above typically flexed during PA mobilization.

**Conclusions.** The results of this study suggest a reasonable margin between failure load, in vitro, and applied mobilization load, in vivo.

## 4.1 INTRODUCTION

Back pain is common in older adults [1,2] and is associated with reduced mobility, independence, and health related quality of life. [3,4] Spinal mobilization is a widely used manual therapy technique among physiotherapists and osteopaths to treat back pain. There is evidence that manual therapy including spinal mobilization may be therapeutic in that it can reduce spinal pain, [5-8] stimulate sympathetic nervous system activity, [6,7,9] and promote motor activity. [6]

However, there is concern that manual therapy could cause fracture in individuals with osteoporosis (Chapter Three), a condition characterized by low bone mass and increased fracture risk that affects 1 in 5 postmenopausal women. [10,11] Osteoporosis is generally painless until complicated by a fracture, [12-16] so it can be present without the patient's knowledge. Thus, unless a clinician treating back pain recognizes the major clinical risk factors for osteoporosis (such as age, sex, family history), he or she may unwittingly use spinal mobilization in a patient with osteoporosis. My clinical experience suggests that many practitioners treat older people without considering osteoporosis, while others eschew the potential therapeutic effect of spinal mobilization in patients with osteoporosis for fear of causing fracture.

PA mobilization is a commonly used spinal mobilization technique [17-19] yet previous studies do not provide data on PA spinal fracture thresholds. While some investigators reported applied load with this technique, [5,20,21] or spinal stiffness, [18,22-24] they did not also measure spinal failure or fracture. Spinal failure has most commonly been studied with

axial compressive loading [25-28] (mimicking the compressive and bending loads associated with trauma), but not the force generated by therapeutic spinal mobilization. To my knowledge, spinal failure with a PA load, and the relationship of bone quality and geometry to PA failure load, has not been previously investigated. Investigation of the intervertebral movements resulting from PA spinal mobilization in the lumbar spine, in vivo, have been conducted using indirect measures, specifically radiography [19] as well as a load cell, two linear variable differential transformers (LVDTs) and a motor driven force applicator to measure displacement of the skin over the spinous process. [29]

My primary objective was to quantify failure load and pattern of midthoracic vertebrae, in vitro, when a PA load was applied to T6 in T5-8 cadaveric spine segments of older spines and compare this in vitro failure load with the load applied in vivo. My secondary goal was to measure the amount and direction of motion produced during cyclic PA loading of T6 in vitro, and to validate these in vitro measures by comparison with kinematics during PA mobilization in an intact cadaver. My final aim was to examine the relationship of bone density and geometry with PA failure load.

## 4.2 METHODS

### Study Design

I performed (1) failure load measurements and kinematic analyses on cadaveric thoracic spine segments, (2) kinematic analysis and applied load measurement in an intact cadaver, and (3) applied load measurements in human volunteers.

### Sample Size Calculation

Sample size for this study is based on previous studies of applied load during PA mobilization and porcine pilot tests of PA failure load and assumes beta equal to 0.2 (power equal to 0.80) and alpha equal to 0.05. Assuming 2-samples of unequal variance, with a mean (SD) in group 1 (in vivo applied load) of 200 N (60 N) and, in group 2 (in vitro failure load) of 800 N (200 N), I require 2 samples in group 1 and 7 samples in group 2. As there are no available data on PA failure load in cadaveric vertebrae, I estimated the mean (SD) failure load based on my porcine pilot experiments and previous studies of axial compressive failure load in cadaveric spine segments. Due to the uncertainty in the estimate for the mean and standard deviation I included 7 samples in group 1 and 12 samples in group 2.

### In Vitro Failure Load

Specimen preparation

Fresh-frozen (unembalmed) human cadaveric spines were obtained from the UBC Department of Anatomy. Donors included 6 females, 5 males and 1 unknown. Age at death ranged from 62-93 years, mean 77 years. Each specimen was assigned an

identification number to maintain anonymity. This study was approved by the UBC Clinical Ethics Review Board.

Each specimen was dissected to isolate a segment consisting of T5-T8. The fifth through ninth ribs were removed. An axial cut was made to separate T4-T5 and T8-T9 at the intervertebral disc. Incisions were made between the facet joints and spinous processes at the same levels. The ligaments and discs between T5 and T8 were left intact. The isolated segments were stored frozen at −20 degrees C until testing.

Pretest measurements

Bone area (BA, $cm^2$), bone mineral content (BMC, grams) and areal bone mineral density (aBMD, grams/$cm^2$) were assessed in the AP and lateral orientation for each T5-T8 segment using a Hologic QDR 4500W bone densitometer (DXA). A qualified technician analyzed all scans using standardized procedures as outlined in the Hologic User's Guide.[30] AP acquisition parameters were used for both AP and lateral scans. For lateral scans, the posterior elements were excluded from the region of interest. Members of my research group had conducted a short-term precision study, in vivo, with 17 subjects measured twice, using this instrument. The coefficient of variation for BMC and aBMD at the lumbar spine (LS) (L1-L4) was less than 0.7%. A spine anthropomorphic phantom was scanned daily for quality assurance of the QDR 4500. As in other studies, [31-33] bags of rice were used to simulate soft tissue surrounding the spine segment. Lateral and AP radiographs were taken of each specimen prior to testing.

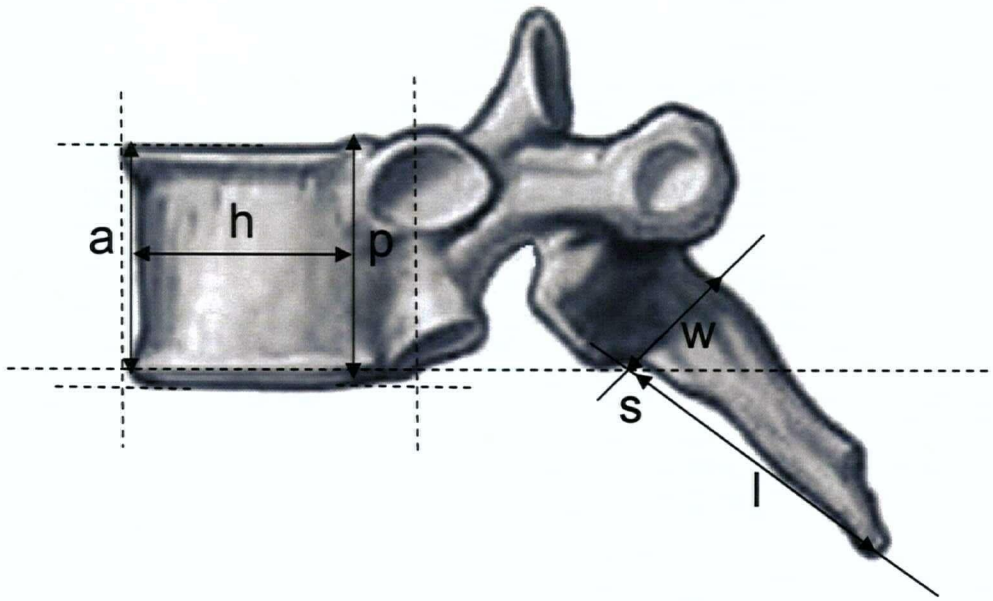


**Figure 4.1.** *Lateral view of a thoracic vertebra with typical measures of vertebral body area, spinous process length and spinous process width. (s= intersection of line from anterior inferior vertebral body along the inferior endplate with the anterior border of the spinous process; w= spinous process width; l= spinous process length; a= anterior height; p= posterior height; h= length of the perpendicular line between the two parallel lines, a and p)*

Measures of vertebral body area, spinous process length, and spinous process width were obtained from the lateral radiographs. In the sagittal plane, T6 spinous process dimensions were measured by first drawing a line from the most anterior inferior point of the vertebral body along the inferior endplate. The intersection of this line with the anterior border of the spinous process was labeled (s). Spinous process length was measured as the distance from (s) to the inferior tip of the T6 spinous process. Spinous process width was measured as the distance from (s) across the spinous process. Vertebral body dimensions included anterior height, posterior height, superior endplate depth and inferior endplate depth. Assuming the

anterior and posterior borders were parallel, the area of the T6 vertebral body was calculated for each specimen using the following equation: $A = [(a+p)/2]\ h$ where a= anterior height, p=posterior height, and h= the length of the perpendicular line drawn between the two parallel lines, a and p (Figure 4.1).

Mechanical testing

Steel (24 gauge) wire was secured to the pedicles of T5 and T8 of each spine segment. Each specimen was embedded in dental cement such that half of the vertebral bodies of T5 and T8 and the attached steel wire were fixed in cement. Thus, the T5 transverse processes were fully embedded and half of the T8 transverse processes were embedded. The T5-6 and T7-8 facet joints remained free, as did all parts of T6 and T7. Marker carriers with four infrared light emitting diodes (LEDS) were secured to the vertebral body of T5 (middle) and the transverse processes of T6-8 with a 3.5 mm cancellous bone screw. In cases where the transverse process was too weak to sufficiently secure the marker carrier, the middle of the vertebral body was used. Each marker carrier was positioned to be in clear view of the cameras while avoiding contact with dental cement or another marker carrier during the test (Figures 4.2A and 4.2B).

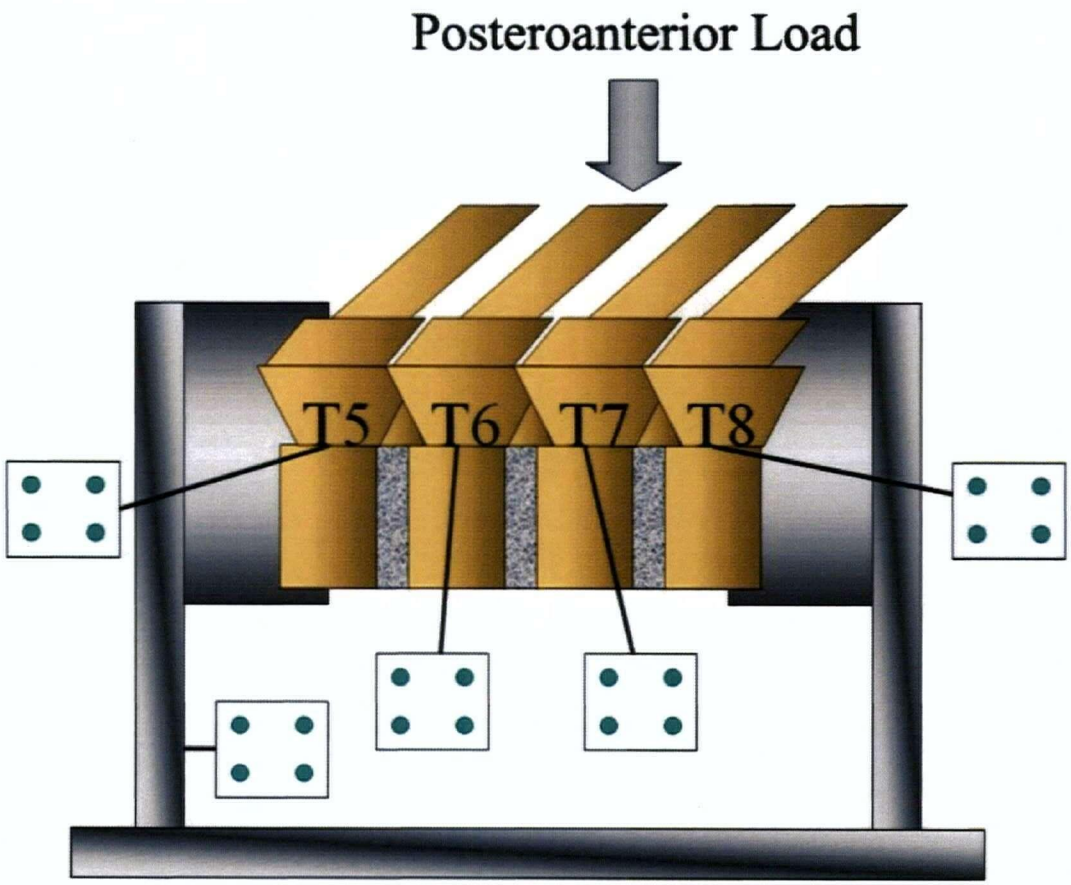


**Figure 4.2A.** *Schematic of posteroanterior (PA) loading at the T6 spinous process in T5-T8 cadaveric spine segments. The opto-electronic marker carriers are shown attached to each vertebra.*

The specimen was oriented horizontally in the testing machine (Instron 8874, Instron Corp. Canton, MA) to facilitate the PA load application (Figure 3.2A and 3.2B). The T5 and T8 specimen mounts were clamped rigidly, such that the T6 spinous process was aligned with the linear actuator of the machine. Load was applied through a circular delrin indenter (20 mm diameter, Young's Modulus 3.1 GPa), mounted on the end of the actuator. This indenter had a 7 mm diameter groove for the spinous process and 3 mm foam (PPT, Langer Biomechanics Group Inc, NY) was attached to the bottom of the indenter to enable a distributed load transmission and to prevent slipping of the spinous process. A very low

load (5 N) functional test was used to verify that the intended PA load did not produce noticeable coupled axial rotation.

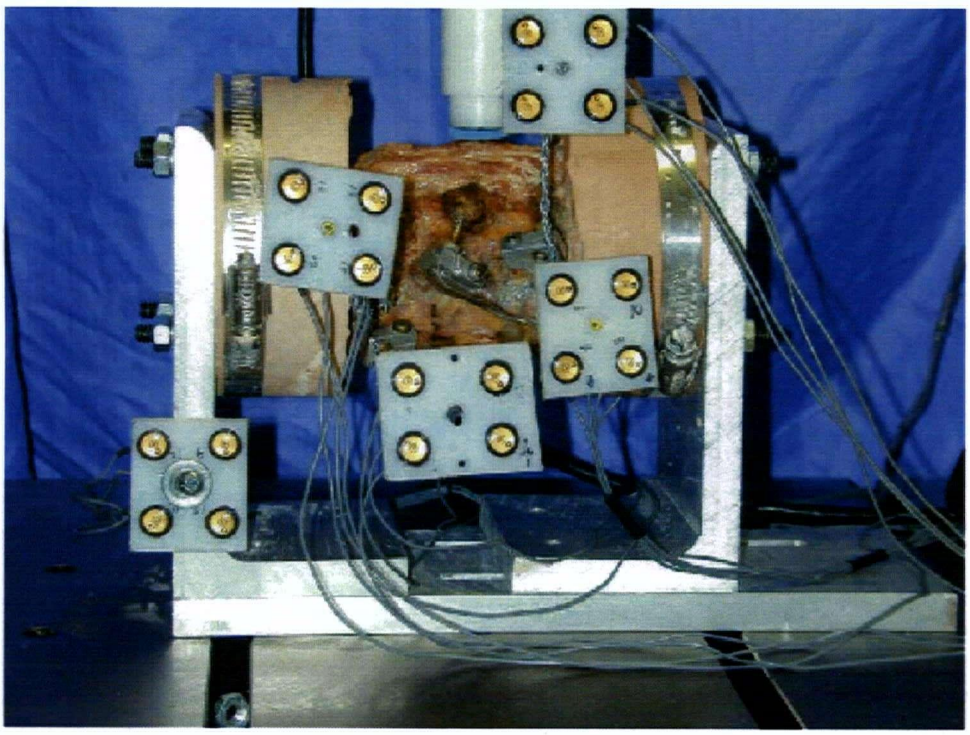

**Figure 4.2B.** *A typical T5-T8 cadaveric specimen secured in the custom testing jig. The opto-electronic marker carriers, base marker fixed to the testing machine (lower left), and the delrin indenter with foam padding (above the specimen) are also shown.*

A cyclic PA load of 50-200 N was applied to the most posterior point of the T6 spinous process at 0.5 Hz for 30 seconds. Kinematic data were recorded during the test at 10 Hz using a precision opto-electronic camera system (Optotrak 3020, Northern Digital, Waterloo, Ontario). The accuracy of this system exceeds 0.1°. [34] After the cyclic test, the specimen was loaded to failure at a displacement rate of 2 mm/sec.

Post-test measurements

Immediately after failure, we used macroscopic observation, gentle dissection, and digital

photography to identify and document the fracture. I repeated lateral and AP radiography using identical settings as in the pre-test films. The radiographs were reported by the same musculoskeletal radiologist for evidence of fracture. Each specimen was scanned with CT using 1.3 mm helical scans at an image interval of 0.6 mm on bone algorithm (display field of view: 16 cm). Together with the radiologist, I generated sagittal and coronal reconstructions on the scanner to simulate the plain radiographs. All CT scans were reported by one radiologist.

**Intact Cadaver**

A fresh whole cadaver (male, age 74 years) without significant scoliosis (on examination) was tested at the UBC Department of Anatomy. K-wires (2.4 mm diameter) were secured to the T5, T6, T7 transverse processes and the T8 spinous process by a spine surgeon. I attached opto-electronic marker carriers to the wires (Figure 4.3). I performed PA mobilization to T6 (Figure 4.4) and the applied load was measured using a Tekscan I-Scan sensor (Tekscan 5051, Boston, MA, Appendix II) (Figure 4.3). I followed a metronome to ensure mobilization was applied at a rate of 0.5 Hz for 15 cycles. Kinematics were recorded simultaneously at 10 Hz using a precision opto-electronic camera system (Optotrak 3020, Northern Digital, Waterloo, Ontario). This cyclic mobilization was followed by three attempts to fracture the spine with a maximal manual PA load.

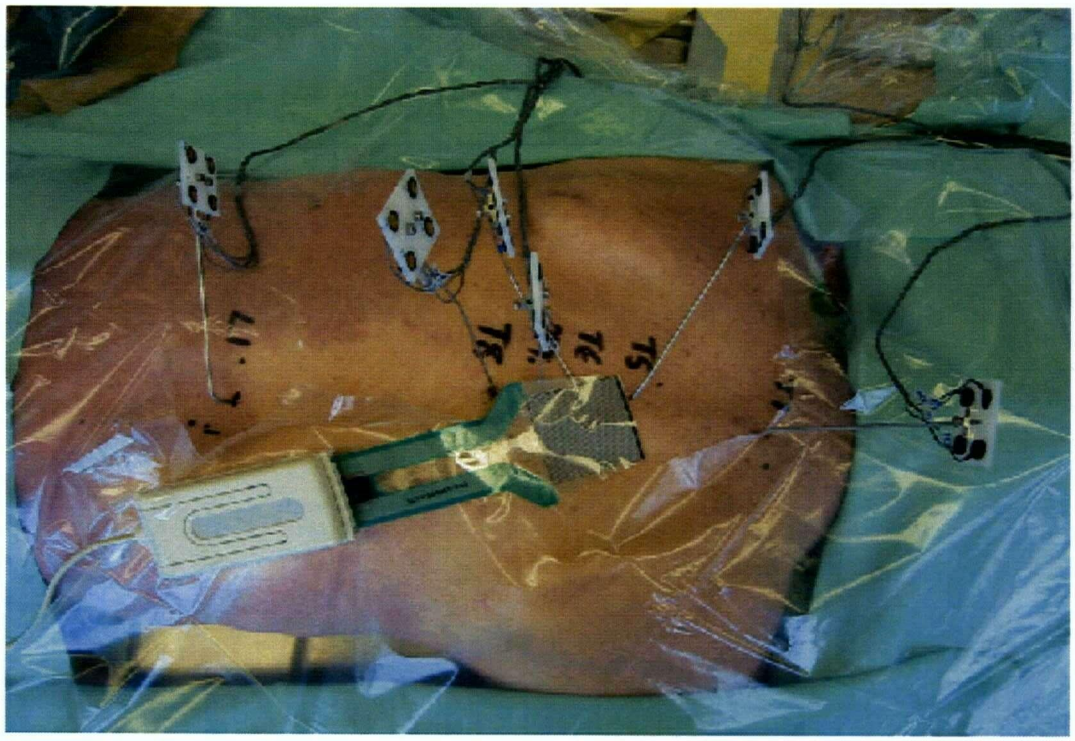


**Figure 4.3.** *Marker set up for the intact cadaver test and the Tekscan I-Scan sensor for measuring applied load.*

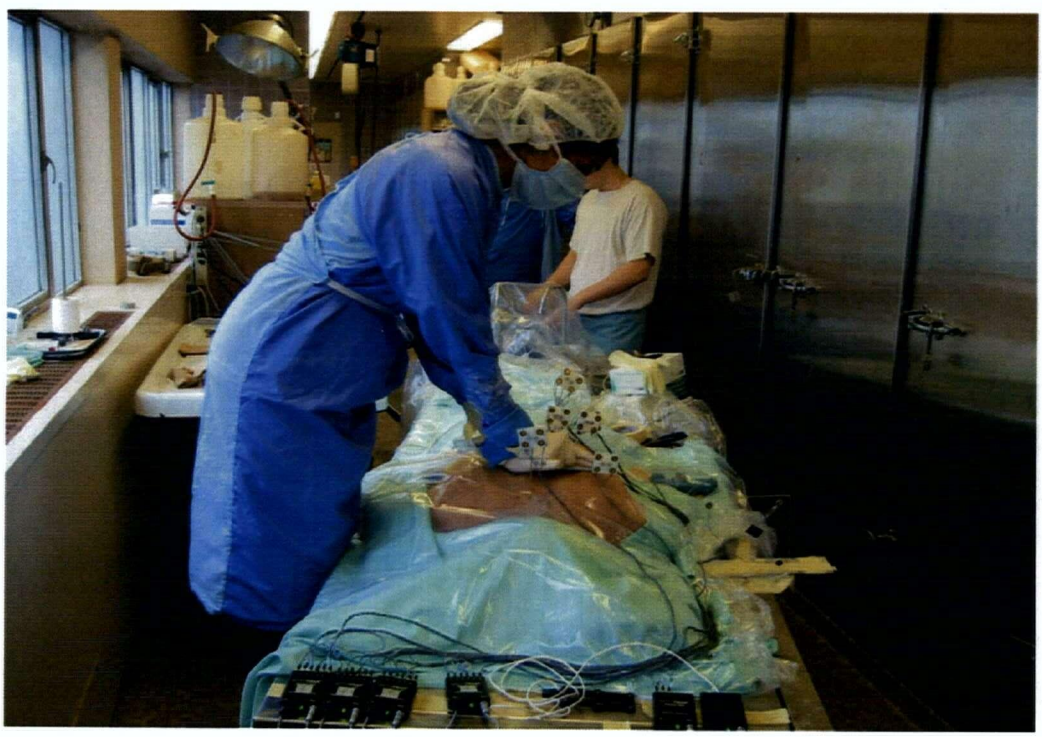

**Figure 4.4.** *The physiotherapist applying PA mobilization to T6 of an intact cadaver.*

**In Vivo Applied Load**

For comparison with clinical mobilization, I measured applied load during grade IV PA mobilization (see sections 1.4.1 and 1.4.5) of T6 in human volunteers during seven trials by two experienced physiotherapists (including the author). Applied vertical load to the spine was estimated indirectly by the decrease in force on a floor mounted force platform while the therapists performed PA mobilization at the T6 spinous process.

**Data Analysis**

In the spine segment tests and in the intact cadaver, I determined vertebral kinematics for each spinal level via the opto-electronic marker carriers. The anterior inferior vertebral body was the origin in the T5-T8 spine segments and the spinous process was the origin in the intact cadaver. A global coordinate system was used for all tests. For the spine segment tests a base marker was fixed to the jig. The x axis was medial-lateral and the y axis cephalad-caudad. For the intact cadaver test axes were identified by digitizing the left and right scapulae (directly opposite the T6 spinous process), and the T1 and L1 spinous processes (x and y axes respectively). I assumed each vertebra to be a rigid body for measurement, and used custom software (KIN 2000, written in LabVIEW 6.0, National Instruments, USA).

For each in vitro failure test, there was a deviation from the real-time load-displacement curve and an audible 'crack'. Failure was defined as the first decrease in load (Figure 4.5).

I used Pearson correlation coefficients to assess the relationship between failure load, BMD

and bone geometry measures, and Student's t-test to compare failure load, in vitro, and applied load, in vivo. Statistical significance was set at $p < 0.05$.

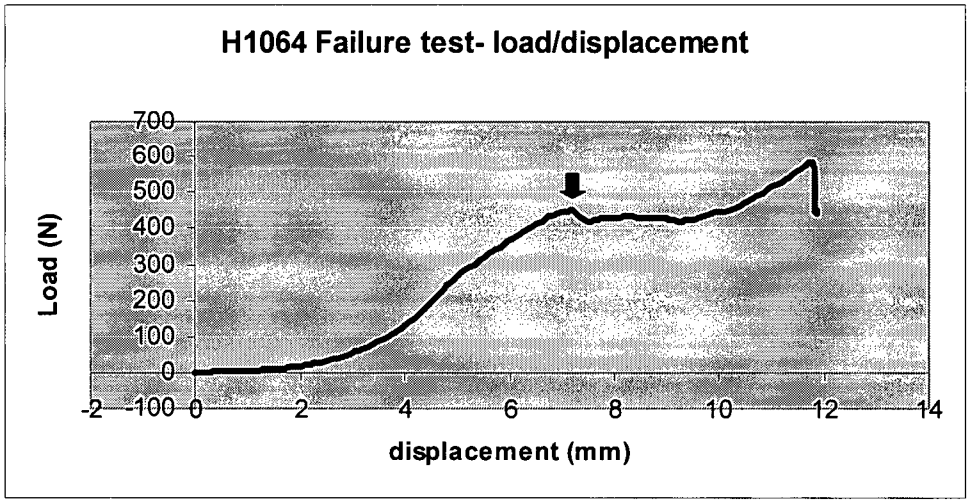


**Figure 4.5.** *Load (N) and displacement (mm) for a typical specimen during the failure test. (in vitro cadaveric spine segment) Failure point was defined as the first decrease in load.* ⬇

## 4.3 RESULTS

### Pretest Bone Measures

Bone mineral density ($g/cm^2$) ranged from 0.463-1.020 (mean=0.686, SD=0.165) with the anteroposterior scan, and 0.270-0.636 $g/cm^2$ with the lateral scan (mean 0.386, SD=0.098). Vertebral body area ranged from 460-988 $mm^2$ (mean= 642 $mm^2$, SD=145 $mm^2$). Spinous process width was, on average 1.1 cm (SD=0.2, range= 0.8 to 1.7 cm) while spinous process length ranged from 2.6 to 4.5 cm (mean= 3.5, SD=0.5). No specimen showed any sign of malignancy. One specimen had a 20% wedge compression fracture of T8.

### Failure Load and Failure Site, In Vitro, and Applied Load, In Vivo

In vitro failure load ranged from 200-728 N with a mean of 479 N+/-162 N(SD). Macroscopic observation revealed a fracture at the T6 spinous process in eleven specimens, and one at the T7 spinous process. The fractures identified post testing were evident on plain radiographs in only three of twelve specimens despite very close scrutiny (Figure 4.6A). CT scans detected the fracture in two of the three detected on plain radiographs, and four other specimens (Figure 4.6B). Thus, five fractures identified macroscopically remained undiagnosed by either imaging method. There was no evidence of damage to the vertebral body in any specimen.

Applied loads, in vivo, ranged from 106-223 N, with a mean of 145+/-38 N(SD) (Figure 4.7). There was a significant difference between failure load, in vitro, and applied load, in vivo (p=.0004).

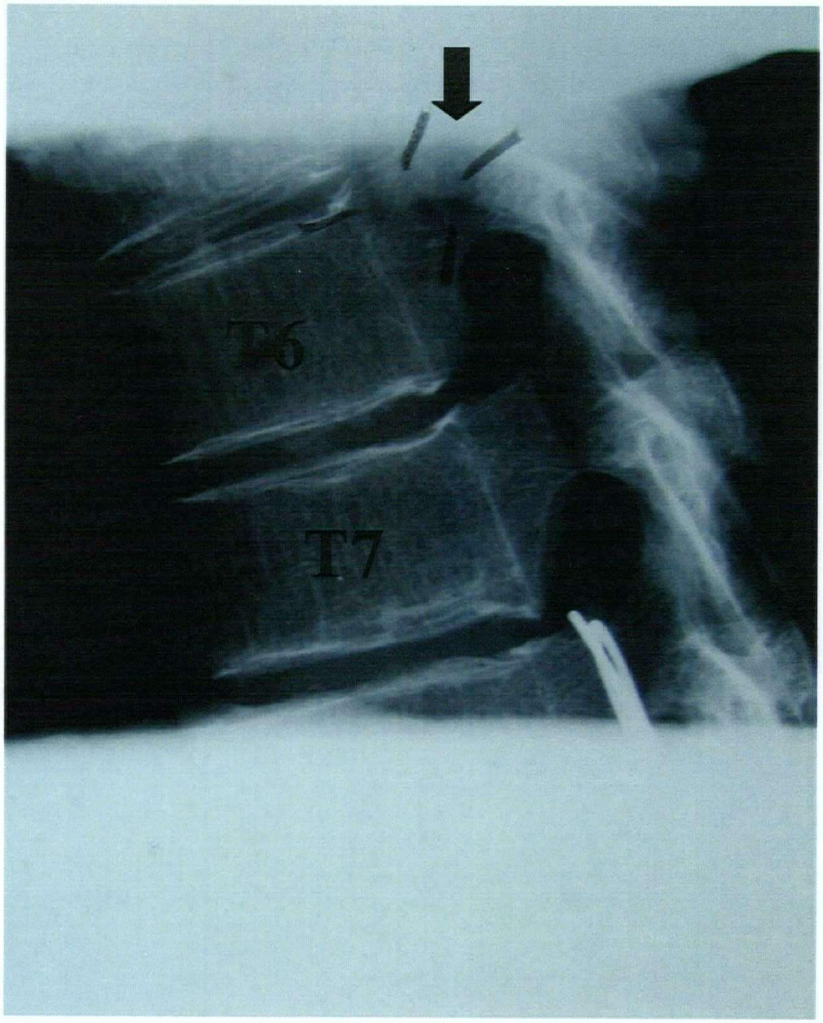


**Figure 4.6A.** *Post test radiography detected the site of fracture in only 3 of 12 cases. This radiograph shows a fracture at the base of the T6 spinous process (see arrow).*

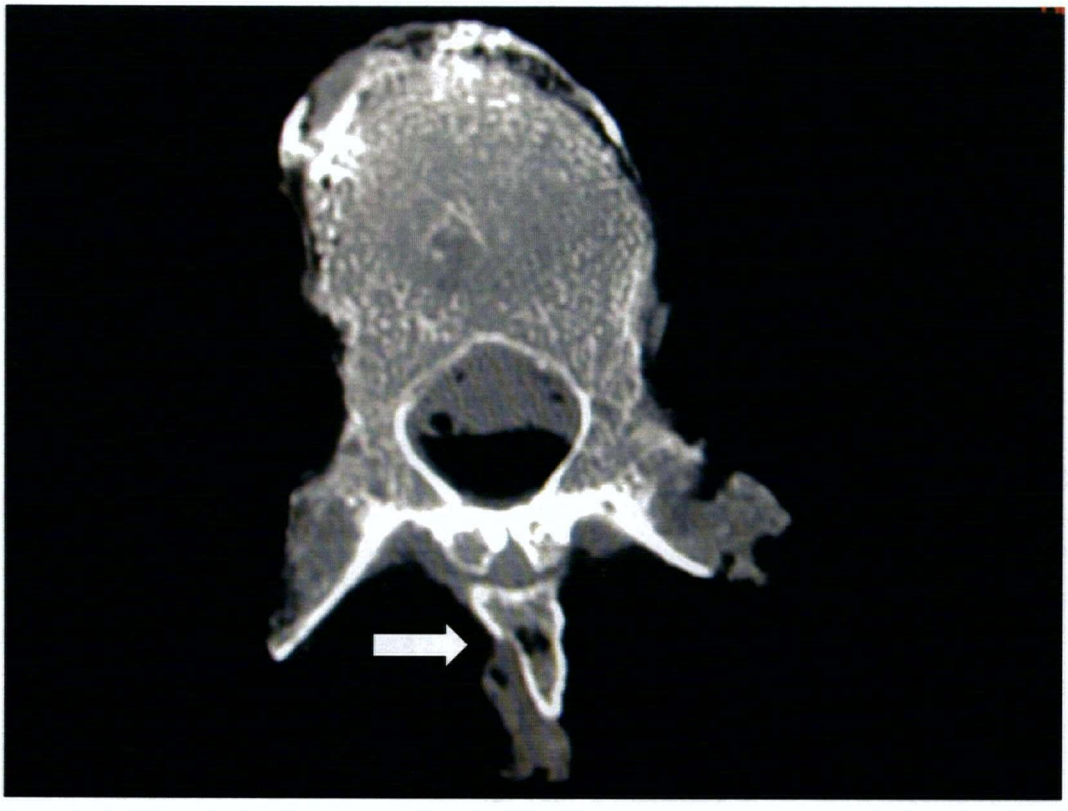

**Figure 4.6B.** *Post test CT scan detected 6 of the 12 fractures. The neuroradiologist interpreted the step in the cortical bone (see arrow) as a fracture.*

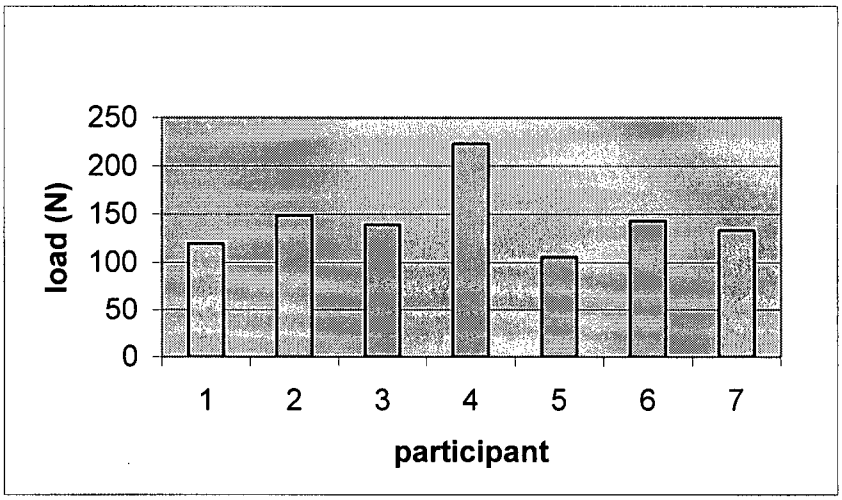


**Figure 4.7.** *Graphical representation of the in vivo applied load data. Participants are listed on the horizontal axis and load in N on the vertical axis. Load ranged from 106-223 N, with a mean of 145 N. Similar loads were applied in young and old participants.*

The physiotherapist was unable to produce a fracture in the intact cadaver. Figure 4.8 shows a sample of the force data collected in the intact cadaver tests. The maximum load applied was 135 N. Calibration of the Tekscan sensor with a six axis load cell showed that Tekscan consistently underestimated applied loads by 15-20% (see Appendix II).

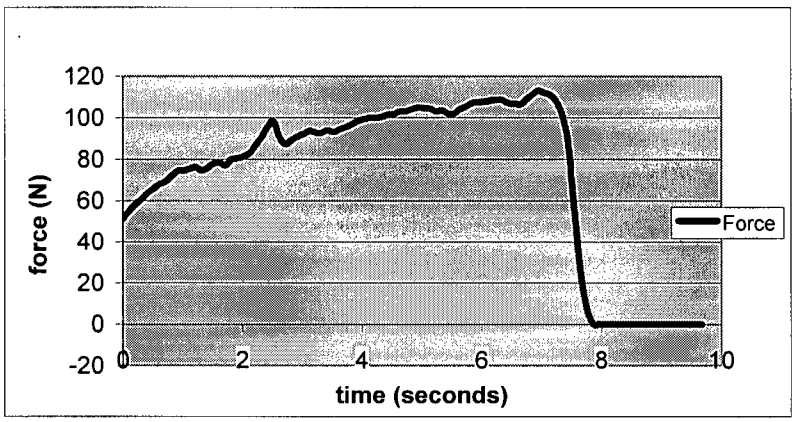


**Figure 4.8.** *A sample of the force data collected with Tekscan during the intact cadaver test. In this example the peak load is approximately 115 N and it was reached after almost 8 seconds.*

**Failure Load and Bone Measures**

There was a weak, non-significant, relationship between failure load at the spinous process and vertebral areal BMD by DXA (Pearson r=0.18 with AP DXA, p=0.57 (Figure 4.9); r=0.13 with lateral DXA, p=0.68). Non-significant correlations were found between bone size and failure load (r= −0.14 spinous process length; r= −0.34 spinous process width; r= −0.27 vertebral body bone area).

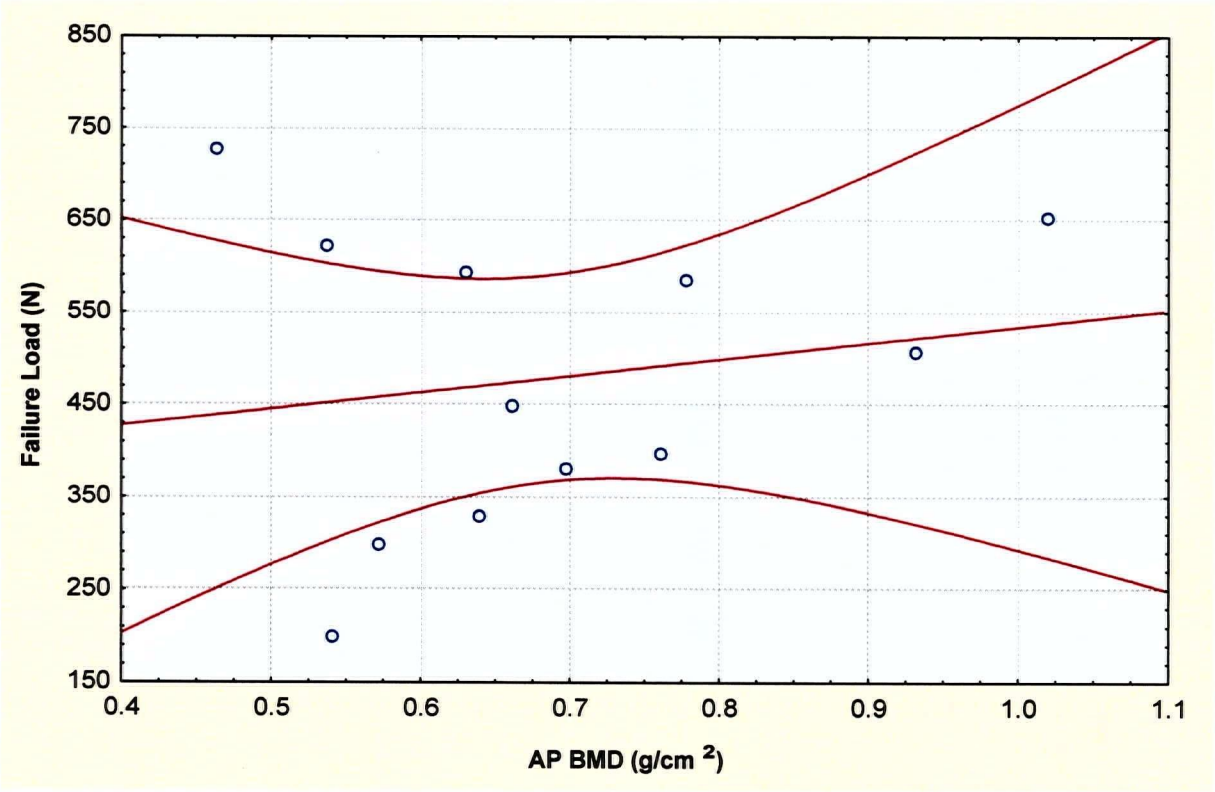


**Figure 4.9.** *Pearson correlation coefficient for PA failure load (N) and AP bone mineral density (g/cm$^2$): r=0.18.*

**Intervertebral Movements During PA Mobilization**

When a 50-200 N cyclic PA load was applied to the most posterior part of the T6 spinous process, 10 of 12 segments flexed at T5-6 and 11 extended at T6-7. At T7-8 the T7 vertebra flexed in nine specimens and extended in two (one excluded because T8 marker carrier not secured). In the intact cadaver there was flexion at T5-6, extension at T6-7 and flexion at T7-8. The magnitudes of rotation at T5-6, T6-7, and T7-8 (cadaveric segments and intact cadaver) are presented in Table 4.1.

**Table 4.1.** *Magnitude (°) of rotation [flexion (+) and extension (−)] at T5-6, T6-7, and T7-8 in T5-8 cadaveric spine segments and an intact cadaver during PA mobilization.*

| **Spine Segments** | **T5-6** | **T6-7** | **T7-8** |
|---|---|---|---|
| Mean (Range) | 0.11 (−0.18 - 0.39) | −0.38 (−1.04 - 0.03) | 0.14 (−0.26 - 0.43) |
| Standard Deviation | 0.14 | 0.30 | 0.20 |
| **Intact Cadaver** | 0.20 | −0.20 | 0.22 |

## 4.4 DISCUSSION

In this chapter, I report novel data of failure load and failure site with spinal mobilization using a cadaveric spine segment model. This provides insight into whether spinal mobilization may have a margin of safety when performed in older people. However, before discussing the clinical relevance of my findings I outline biomedical engineering issues of the measurement technique, my findings of the determinants of failure load, the kinematic data as well as factors that determine the likely generalizability of my cadaver model to a patient population.

### Failure Load, Site and Detection in the Cadaveric Thoracic Spine Model

To my knowledge, the failure load of vertebrae under a posteroanterior load has not previously been reported, despite the long-term and widespread use of this technique in clinical practice to treat back pain. [35,36] It appears that thoracic posteroanterior failure load ranges from 200-727 N in cadaveric specimens. This failure load is much lower than that reported for the midthoracic spine with axial loading. [25,27,28] This is likely due to the cantilever loading of the spinous process during PA mobilization. My data suggest that aBMD of the whole vertebra is not a good predictor of PA failure load, despite its strong correlation with axial compressive failure load in previous studies. [27,28] This may be due to the fact that aBMD is an integrated measure of the entire vertebra, whereas the fractures occurred in the posterior elements.

Although macroscopic observation and load-displacement data clearly indicated structural failure in every test, plain radiography had poor sensitivity for revealing any evidence of

fracture. CT scan was superior to plain radiography in this study, but it nevertheless failed to detect 50% of spinous process fractures. These data, while novel in the setting of spinal mobilization and fracture detection, are consistent with imperfect sensitivity of plain radiography in detecting pars intra-articularis stress fractures. [37] I note that small fractures can also elude CT scan. [38]

**Kinematic Analysis in Spine Segments and Intact Cadaver**

It appears that real-time intervertebral motion at the thoracic spine may be different from that reported for the lumbar spine. Using a cyclic load, I found less motion than reported in lumbar spine studies that used a static load. A strength of my study was the direct measurement of vertebral motion using bone pins, compared with indirect measurement (e.g., radiographs [19]) in other studies. [19,29] In both of my in vitro studies I found that the mobilized vertebra (T6) extended with respect to the inferior vertebra and the vertebra above typically flexed (relative to the mobilized vertebra) during PA mobilization. This behavior is due mainly to the length of the thoracic spinous process which results in the load application point being more inferior than would occur in the lumbar spine. This may explain differing results in the lumbar spine where all lumbar motion segments tended to extend except L5-S1 which tended to flex. [19] I note that previous studies of intervertebral motion, in vivo, during PA mobilization were performed with participants holding their breath during the application of the mobilization to avoid vertebral displacement caused by breathing. [18,24] This is problematic in that spinal stiffness has been shown to change throughout the respiratory cycle. [39]

**Clinical Implications**

Before drawing conclusions about my study, I discuss the clinical relevance, and limitations, of the thoracic spine segment model. I used fresh-frozen cadaveric specimens that retain their biomechanical properties despite freezing [40] and thus, are preferable to formalin-fixed specimens. [41] My specimens were of the appropriate age and I studied T6 as it appears to be the most vulnerable of the thoracic vertebrae to osteoporotic compression fractures. [27,42-45] The spine segment kinematics were similar to those seen in the intact cadaver, which supports the contention that the segment mirrors whole-body behavior. Furthermore, I applied cyclic PA mobilization with loads similar to those applied, in vivo,[5,19,21] and at a frequency of 0.5 Hz, consistent with clinical guidelines. [36] The loads I measured, in vivo, were similar to loads measured by other research groups using a custom instrumented treatment couch [5] (60-230 N) and a load cell [21] (58-178 N). My applied load tests measured only the vertical force vector of the PA mobilization technique with the patient lying prone, but vertical forces contribute between 90 and 99.8% of the total force during PA mobilization. [20,46]

My primary research question was to determine PA failure load in a spine segment model. I found that while the mean in vitro failure load was greater than the load a physiotherapist applied to a whole cadaver and to volunteers, one specimen failed at a level that was lower than the maximum in vivo load applied. While my novel data provide a baseline for comparing in vitro failure loads with applied in vivo loads, I must be cautious when comparing data obtained from a spine segment with data obtained in vivo. Nevertheless, my in vivo data are corroborated by other studies [5,19,21] and my spine segment model has

strengths as outlined above. While muscle contraction, the rib cage, intraabdominal organs and intraabdominal pressure are likely to increase spinal stiffness in vivo,[47-50] there is no evidence to suggest they would increase strength of the spinous process. Thus, if pressed to give an opinion, I would speculate that failure load of the spinous process in a patient, in vivo, would be similar to the failure loads we measured in spine segments.

My results suggest that vertebral body injury is an unlikely complication of PA mobilization in the midthoracic spine. My finding that fractures occurred at the spinous process is novel and suggests that clinicians may wish to remain alert to the potential for injury to this structure when PA mobilization is used. I could find no case report of a spinous process fracture associated with mobilization. My data, and that of others [51] suggest that if such pathology were to occur, plain radiography would have poor sensitivity to detect it. Also CT scan had only 50% sensitivity for the fracture, raising the question of whether patients complaining of back pain, that may be associated with spinous process fracture, should be investigated with radioisotopic bone scan.

I note one technical point about the terminology of spinal mobilization techniques. Physiotherapists, chiropractors, and osteopaths all learn a variety of manual therapy techniques with which to mobilize spines. [36,52-55] It is crucial to note that my data are limited to posteroanterior mobilizations performed by physiotherapists. My data do not necessarily generalize to other techniques performed by other professionals. Future research should test a variety of mobilization and manipulation techniques to determine failure load using each of them.

In summary, a cadaveric thoracic spine segment can withstand upwards of 200 N but physiotherapists can deliver up to 223 N with thoracic posteroanterior spinal mobilization. Kinematic data suggest that the mobilized thoracic vertebra moves into extension as a result of the mobilization. Although there was a reasonable margin between the failure load, in vitro, and the applied mobilization load, in vivo, for most specimens, the lowest fracture thresholds were around the same force as the upper range of the applied loads.

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# Chapter Five

## *Accuracy of DXA Scanning of the Thoracic spine: Cadaveric Studies Comparing BMC, Areal BMD and Geometric Estimates of Volumetric BMD against Ash Weight and CT Measures of Bone Volume*

## ABSTRACT

**Background.** Biomechanical studies of the thoracic spine often scan cadaveric segments using DXA to obtain measures of bone mass. Only one study reported accuracy of lateral scans of thoracic vertebral bodies. The accuracy of DXA scans of thoracic spine segments and of anteroposterior (AP) thoracic scans has not been investigated.

**Objectives.** To (1) investigate the accuracy of AP and lateral thoracic DXA scans by comparison with ash weight, the gold standard for measuring bone mineral content; (2) to compare three methods of estimating volumetric bone mineral density (vBMD) with a novel standard— ash weight (g)/bone volume ($cm^3$) as measured by computed tomography (CT).

**Methods.** Twelve T5-8 spine segments were scanned with DXA (AP and lateral) and CT. The T6 vertebrae were excised, posterior elements removed, and then the vertebral bodies were ashed in a muffle furnace. I proposed a new method of estimating vBMD and compared it with two previously published methods.

**Results.** BMC values from lateral DXA scans displayed the strongest correlation with ash weight ($r=0.99$) and were on average 12.8% higher ($p<0.001$). As expected, BMC (AP or lateral) was more strongly correlated with ash weight than aBMD [AP ($r=0.54$) or lateral ($r=0.71$)] or estimated vBMD. Estimates of vBMD with any of the three methods were strongly correlated with vBMD calculated by dividing ash weight by CT-derived volume, but the mean difference was lowest when using the novel elliptical cylinder method.

**Conclusions.** These data suggest that readily available DXA scanning is an appropriate surrogate measure for thoracic spine bone mineral and the elliptical cylinder method should be used when calculating vBMD of the vertebral body.

## 5.1 INTRODUCTION

Thoracic spine osteoporosis often results in compression fractures with significant personal and societal cost. [1-3] In spine research, bone mass (aBMD and BMC) is often quantified by DXA. Previous studies have shown that *lumbar* spine BMC measured by DXA correlates closely with the gold standard— ash weight, the weight of the inorganic component of bone. [4-6] In addition, *lumbar* bone mass by DXA predicts failure load in vitro, [7-10] and fracture risk, in vivo. [11] The same relationship has not been established (and therefore cannot be assumed) for the thoracic spine.

Ash weight is the most accurate measure of BMC. This method involves removing water and the organic matrix of bone, leaving only mineral. Bone is composed of water, mineral, proteins and other macromolecules such as lipids and sugars. The mineral or inorganic phase makes up to 60% of bone tissue. Most of the organic matrix, approximately 90%, is collagen while a much smaller 5 to 8% is noncollagenous proteins. Anatomic site, age, dietary history and presence of disease can result in differences in bone composition. [12]

Although numerous researchers have used DXA methodology to assess bone mineral in biomechanical studies of the thoracic spine, [13-18] the accuracy of DXA must be tested specifically at the thoracic spine for several reasons. First, soft tissue mass (i.e. ligament, disc) and composition of nonmineralized connective tissue can limit the accuracy of aBMD results [19] and the thoracic and lumbar regions differ in this respect. Second, some laboratories use bags of rice to simulate soft tissue, [13,20,21] as opposed to the typically

recommended water bath. There are no published data describing how this technical variant may influence the relationship between thoracic BMC measured by DXA scans and ash weight. Third, researchers often examine spine *segments* that include two or more complete vertebrae and accompanying ligaments and intervertebral discs. [14,17,20,22] In the thoracic spine, such specimens have not been scanned with DXA and then compared with a gold standard.

Finally, an accuracy study is needed because more recent equations to estimate vBMD have never been tested against ash weight gold-standard. Traditionally, bone mineral data are reported as aBMD (grams per $cm^2$), calculated by dividing the quantity of bone mineral within the scan area (BMC) by the projected area within the region of interest. Areal BMD values have clinical utility but can be confounded by changes in bone thickness (or depth). Bones of larger width and height also tend to be thicker yet bone thickness is not factored into estimates of aBMD. [23] By converting aBMD to vBMD the dependence on vertebral size is reduced. [24] This concept of vBMD aims to overcome the limitation of 2-dimensional planar DXA scanning. [24-27] However, this mathematical derivation has never been compared with an ash weight gold standard at the thoracic spine. Further, previous methods assume vertebral geometry resembles a cylinder or a cube, yet human thoracic vertebral endplate geometry is best estimated as an ellipse. [28] Thus, I proposed a new method of estimating vBMD, assuming vertebral body geometry resembles an elliptical cylinder.

To provide a solid methodological foundation for the use of DXA scan in thoracic spine research, my primary aim was to test the accuracy of AP and lateral thoracic spine DXA measures when rice provided the surrogate for soft tissues. The objective was to correlate DXA measures of the sixth thoracic vertebra (T6) from twelve fresh-frozen cadaveric spine segments with the ash weight of this vertebral body. My secondary aim was to compare three different methods of estimating vBMD and their relationships with vBMD calculated by dividing ash weight by bone volume measured by CT.

## 5.2 METHODS

I obtained fresh-frozen (unembalmed) human cadaveric spines from the UBC Department of Anatomy. Specimen donors included six females, five males, and one unknown. Age at death ranged from 62-93 years, mean 77 years. This study was approved by the UBC Clinical Ethics Review Board. Specimens were stored at −20° C until dissection.

### Scanning with DXA

Thoracic vertebrae T5-8 were separated as a segment from the rest of the spine (see Chapter Four, 'Specimen preparation'). Bone area (BA, $cm^2$), BMC (g) and aBMD, ($g/cm^2$) were assessed in the AP and lateral orientation for each vertebra in the segment (T5-T8) using a Hologic QDR 4500W bone densitometer (DXA). A qualified technician analyzed all scans using standardized procedures as outlined in the Hologic Users Guide.[29] For lateral scans, the posterior elements were excluded from the region of interest. Members of my research group had conducted a short-term precision study, in vivo, with 17 subjects measured twice, using this instrument. The coefficient of variation for BMC and aBMD at the lumbar spine (L1-L4) was less than 0.7%. A spine anthropomorphic phantom was scanned daily to maintain quality assurance of the QDR 4500. As in other studies, [14,20,21] bags of rice were used to simulate soft tissue surrounding the spine segment.

### Scanning with CT and Measuring Bone Volume

Each specimen was scanned with CT using 1.3 mm axial helical scans at a slice interval of 0.6 mm on bone algorithm (display field of view: 16 cm). Together with a radiologist,

I generated sagittal and coronal reconstructions on the scanner. Bone volume was measured on a GE Advantage Workstation 4.1 using the Fast Volume Rendering application by isolating the T6 vertebral body on a 3D model. Test-retest reliability was conducted with the same radiologist calculating bone volume for each specimen twice, with the second measure being made two weeks after the first. Reliability ranged from 0.2-9.7% (mean 2.7%, SD 2.7%).

**Determining Ash Weight**

I dissected each T6 vertebra from its T5-8 segment and cleaned it of soft tissues after immersion in distilled water (75° C for 12 hours). The vertebral body was then separated from the posterior elements at the junction of the pedicle and body using a 200 μm diamond saw (EXAKT 300, Norderstedt, Germany).

Each specimen was placed in a Coorstek (Fisher Scientific, Nepean, ON) ashing crucible (High Form 250 ml) with a cover (90 mm). The crucibles and covers were washed with distilled water and dried (at 95° C) for 48 hours prior to use. Vertebral bodies were dried (95° C for 48 hours) then ashed at 600° C for 42 hours in a Thermolyne 30400 muffle furnace. The maximum temperature of this muffle furnace is 900° C and the crucibles can be used to a maximum temperature of 1150° C. The furnace was turned up and down in increments of 200° C per hour to avoid rapid heating or cooling of the crucibles or samples (total time equaled 48 hours but time at 600° C was 42 hours). The temperature versus time profile for this furnace near the time of testing is presented in Appendix III.

Following each step the crucibles were transferred to a desiccator* for 24 hours and then weighed using a Sartorius BP 210 S scale (4 decimal places, Figure 5.1). Then they were returned to the desiccator for another 24 hours, after which they were weighed again to ensure a stable weight. The only exception was the ash weight measure, which was conducted three times (24 hours, 48 hours, and 72 hours) after transfer to the desiccator.

The following measurements and calculations were made (all from the desiccator):

a) weight of the crucible and lid

b) weight of the crucible

c) weight of crucible and dried vertebra

d) weight of crucible and vertebra after ashing

e) weight of ash (d-a)

**Volumetric BMD**

Volumetric BMD of the vertebral body was calculated as the ash weight (g)/ bone volume ($cm^3$) from the CT scans. One specimen was excluded from vBMD measurement due to missing CT scan data.


**Figure 5.1.** *Crucible and cover measurement with the Sartorius BP 210 S scale.*

**Estimated vBMD**

Volume was estimated using two previously reported methods. The Kroger et al. method [24,27] assumes vertebral body geometry resembles a cylinder using the equation:

$$\text{vBMD} = \text{aBMD}\left(\frac{4}{\prod \times depth}\right)$$

where depth= vertebral body depth on a lateral radiograph (average of middle and inferior width). The AP/lateral pair method [26] assumes the shape of the vertebral body approximates a cube:

$$\text{vBMD}= \frac{aBMD}{width}$$

Vertebral body width was measured on AP radiographs (average of middle and inferior width). Lateral aBMD values were used in both equations.

A third method was proposed and compared with the two previously described methods. This method assumes vertebral body geometry resembles an elliptical cylinder:

$$\text{vBMD}= \left(\frac{4}{\prod \times a}\right)\text{aBMD}$$

where a= vertebral body width from the AP radiographs, and aBMD was taken from the lateral DXA scans, as in the previous two methods.

**Statistical Analysis**

One specimen was excluded from statistical analysis as severe degenerative changes artificially elevated bone mass values obtained by DXA (i.e. lateral BMC of 5.25 g), and the T6 vertebra could not be dissected from the segment without removal of some osteophytes. A paired t-test was used to measure whether there was a statistical difference between ash weight (g) and BMC (g) by lateral DXA. Pearson correlation coefficients were used to assess the association between the primary outcome variables [ash weight (g), BMC (g) and aBMD ($g/cm^2$) by DXA, vBMD [ash weight (g)/ CT bone volume ($cm^3$)], estimated vBMD ($g/cm^3$)]. I calculated standard error of the estimate (SEE) for the ash weight (g) and lateral DXA BMC (g) regression equation as well as the vBMD and estimated vBMD regression equations. I compared two methods of measuring vertebral body BMC, lateral DXA and ash weight, using the Bland-Altman method to determine the level of agreement and detect any outliers. [30-32] I also used the Bland-Altman method to determine the level of agreement between each of the three methods of estimating vBMD (elliptical cylinder, cube and cylinder) and vBMD by ash weight and CT. Analysis was conducted using standard statistical software (SPSS). Statistical significance was set at $p< 0.05$.

## 5.3 RESULTS

Range, mean, and standard deviation for all primary outcome variables are presented in Table 5.1. Ash weight (g) and BMC by lateral DXA (g) for individual specimens is shown in Figure 5.2.

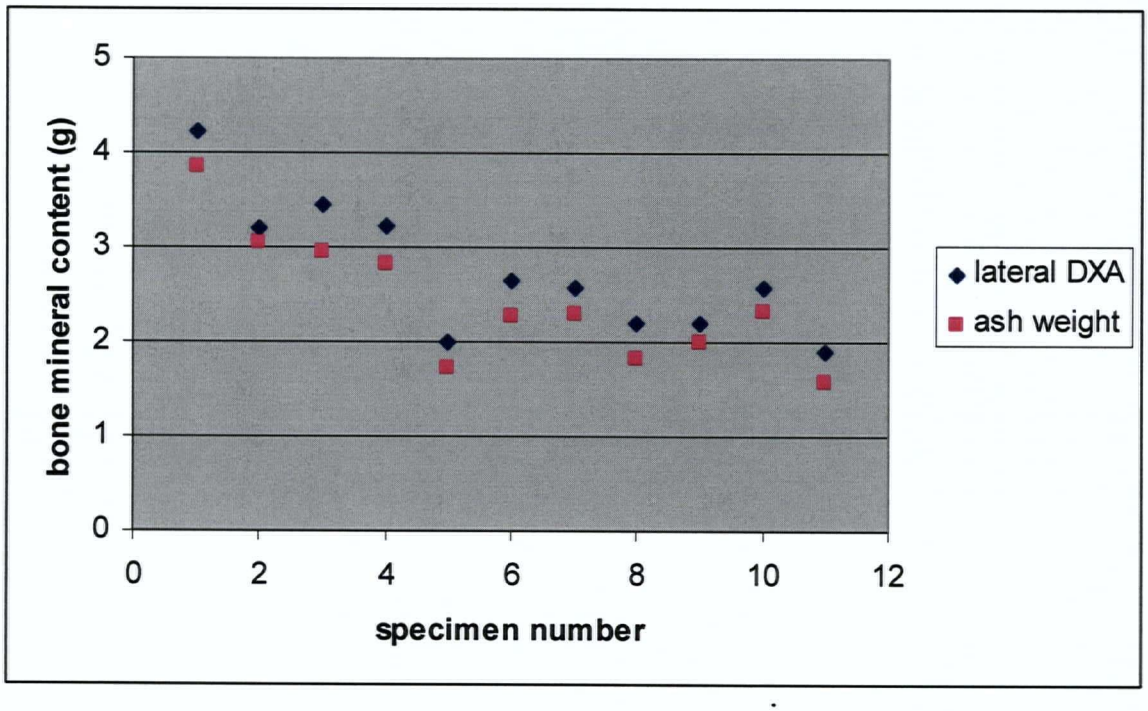


**Figure 5.2.** *Bone mineral content (g) data: lateral DXA and ash weight for all specimens.*

Ash weight (g) and lateral DXA BMC (g) were statistically different ($p<0.001$) yet highly correlated ($r= 0.99$, $p<0.05$). Pearson correlation coefficients for primary outcome variables are presented in Table 5.2. Lateral BMC (g) displayed the strongest correlation with ash weight (g), followed by AP BMC (g), lateral aBMD ($g/cm^2$), AP aBMD ($g/cm^2$), and finally vBMD ($g/cm^3$). The mean difference between ash weight (g) and lateral

DXA BMC (g) was 0.31 g +/- 0.10 (SD) (0.37 - 0.24 = 95% CI of the difference), which was a 12.8% mean difference [mean difference (g)/mean ash weight (g) X 100]. The standard error of the estimate (SEE) for the ash weight and lateral DXA BMC regression equation was 0.09 g. The SEE for the vBMD (ash weight/CT bone volume) and elliptical cylinder, cube, and cylinder regression equations was 0.01 g/cm$^3$. Figure 5.3 shows the level of agreement between two methods of assessing vertebral body BMC (lateral DXA and ash weight). The mean difference between the methods is 0.31 g (SD=0.10 g).

Estimating vBMD as a cube, cylinder, or elliptical cylinder was similarly correlated with volumetric BMD measured by ash weight and CT (r=0.94 for cube, r=0.95 for cylinder, r=0.92 for elliptical cylinder), and statistically significant (Table 5.2). However, Bland-Altman plots of each method of estimating vBMD against vBMD measured using ash weight and CT suggest some differences between the three methods. The mean difference between estimated vBMD using the elliptical cylinder method and ash/CT derived vBMD was −0.001 g/cm$^3$ (SD=0.014), whereas the mean difference was −0.027 g/cm$^3$ (SD=0.014) for the cube method, and 0.013 g/cm$^3$ (SD=0.011) for the cylinder method. Figures 5.4 A, B and C show the three Bland-Altman plots for the vBMD measures.

**Table 5.1.** *Mean, standard deviation (SD), and range for primary outcome variables at the T6 vertebra [AP and lateral BMC (g), AP and lateral aBMD (g/cm$^2$), ash weight (g), vBMD-CT (g/cm$^3$), estimated (est) vBMD using cylinder, cube and elliptical cylinder methods (g/cm$^3$)]*

| | Mean | SD | Range |
|---|---|---|---|
| **AP BMC (g)** | 4.99 | 1.42 | 2.83-6.83 |
| **Lateral BMC (g)** | 2.74 | 0.71 | 1.89-4.22 |
| **AP BMD (g/cm$^2$)** | 0.66 | 0.13 | 0.46-0.93 |
| **Lateral BMD (g/cm$^2$)** | 0.36 | 0.06 | 0.27-0.48 |
| **Ash weight (g)** | 2.43 | 0.68 | 1.58-3.84 |
| **vBMD-CT (g/cm$^3$)** | 0.14 | 0.03 | 0.09-0.23 |
| **est vBMD (g/cm$^3$) (cylinder)** | 0.16 | 0.03 | 0.11-0.24 |
| **est vBMD (g/cm$^3$) (cube)** | 0.12 | 0.03 | 0.08-0.18 |
| **est vBMD (g/cm$^3$) (elliptical cylinder)** | 0.14 | 0.03 | 0.09-0.21 |

**Table 5.2.** *Pearson correlation coefficients for primary outcome variables (ash weight (g) with AP and lateral BMC (g), and AP and lateral aBMD (g/cm$^2$); ash weight (g) and vBMD-CT (g/cm$^3$) with estimated (est) vBMD (g/cm$^3$) as a cube, cylinder, and elliptical cylinder * = significant at p< 0.05*

| | ash weight (g) | vBMD (g/cm$^3$) |
|---|---|---|
| **AP BMC (g)** | *r=0.87, p<0.01 | — |
| **Lateral BMC (g)** | *r=0.99, p<0.01 | — |
| **AP aBMD (g/cm$^2$)** | r=0.54, p=0.09 | — |
| **Lateral aBMD (g/cm$^2$)** | *r=0.71, p=0.01 | — |
| **est vBMD (g/cm$^3$) (cylinder)** | r=0.09, p=0.80 | *r=0.95, p<0.01 |
| **est vBMD (g/cm$^3$) (cube)** | r=0.24, p=0.48 | *r=0.94, p<0.01 |
| **est vBMD (g/cm$^3$) (elliptical cylinder)** | r=0.37, p=0.26 | *r=0.92, p<0.01 |

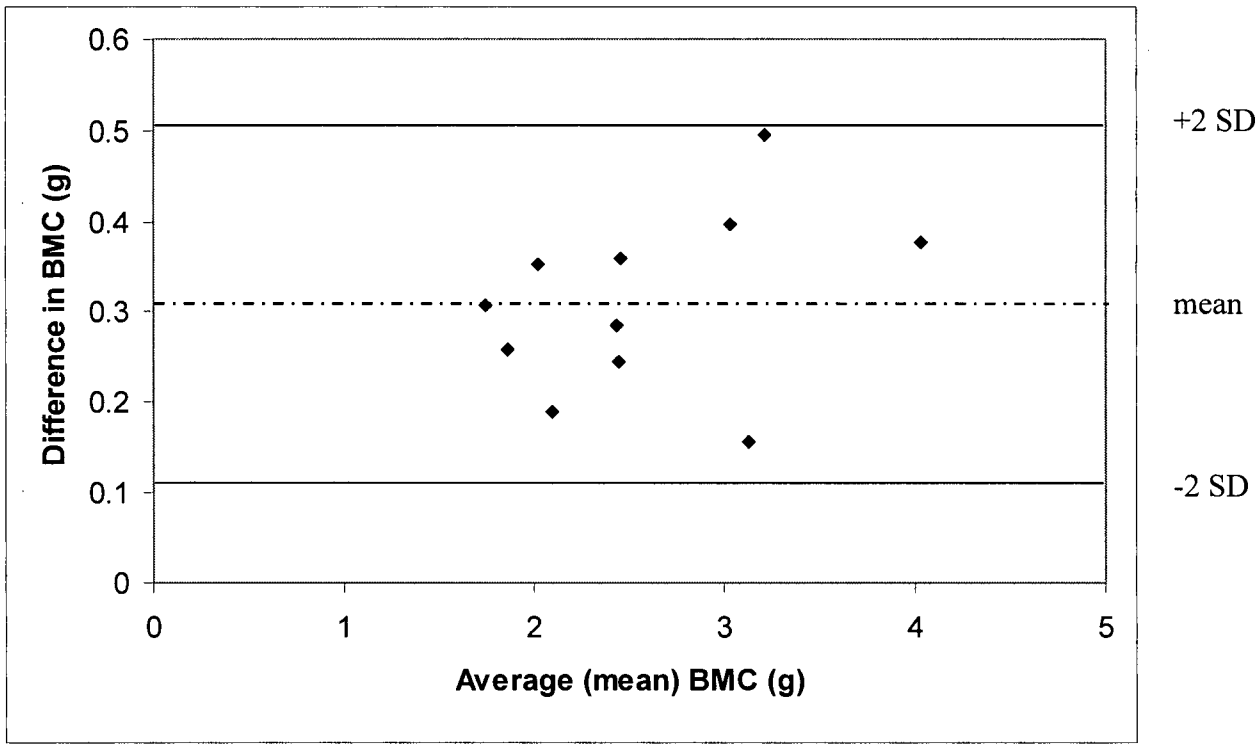


**Figure 5.3.** *Limits of Agreement: difference in BMC (g) (difference of lateral DXA BMC and ash weight) vs. average BMC (g) (sum of lateral DXA and ash weight divided by 2).*

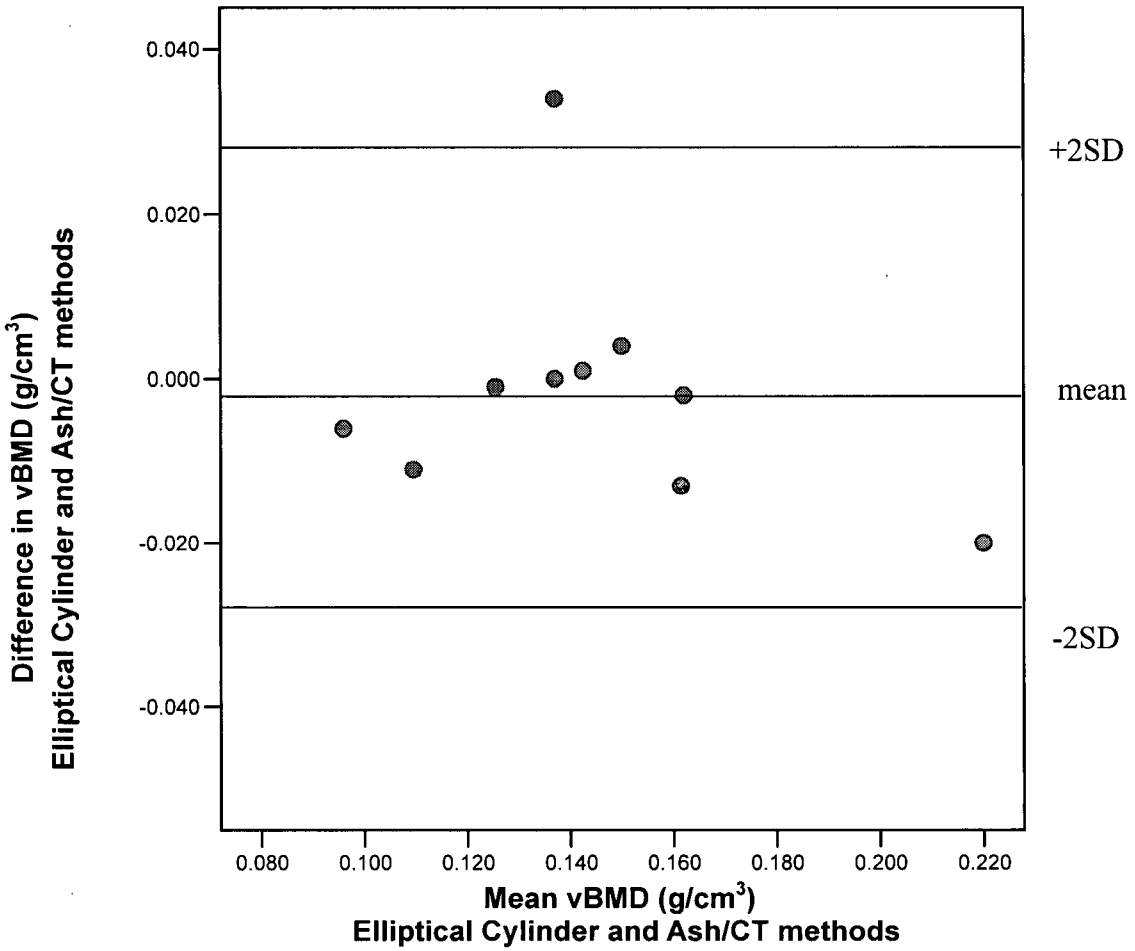


**Figure 5.4A.** *Limits of Agreement: difference in vBMD (g/cm$^3$) (difference of elliptical cylinder estimated vBMD and ash weight/CT vBMD) vs. mean vBMD (g/cm$^3$) (sum of elliptical cylinder and ash/CT vBMD divided by 2).*

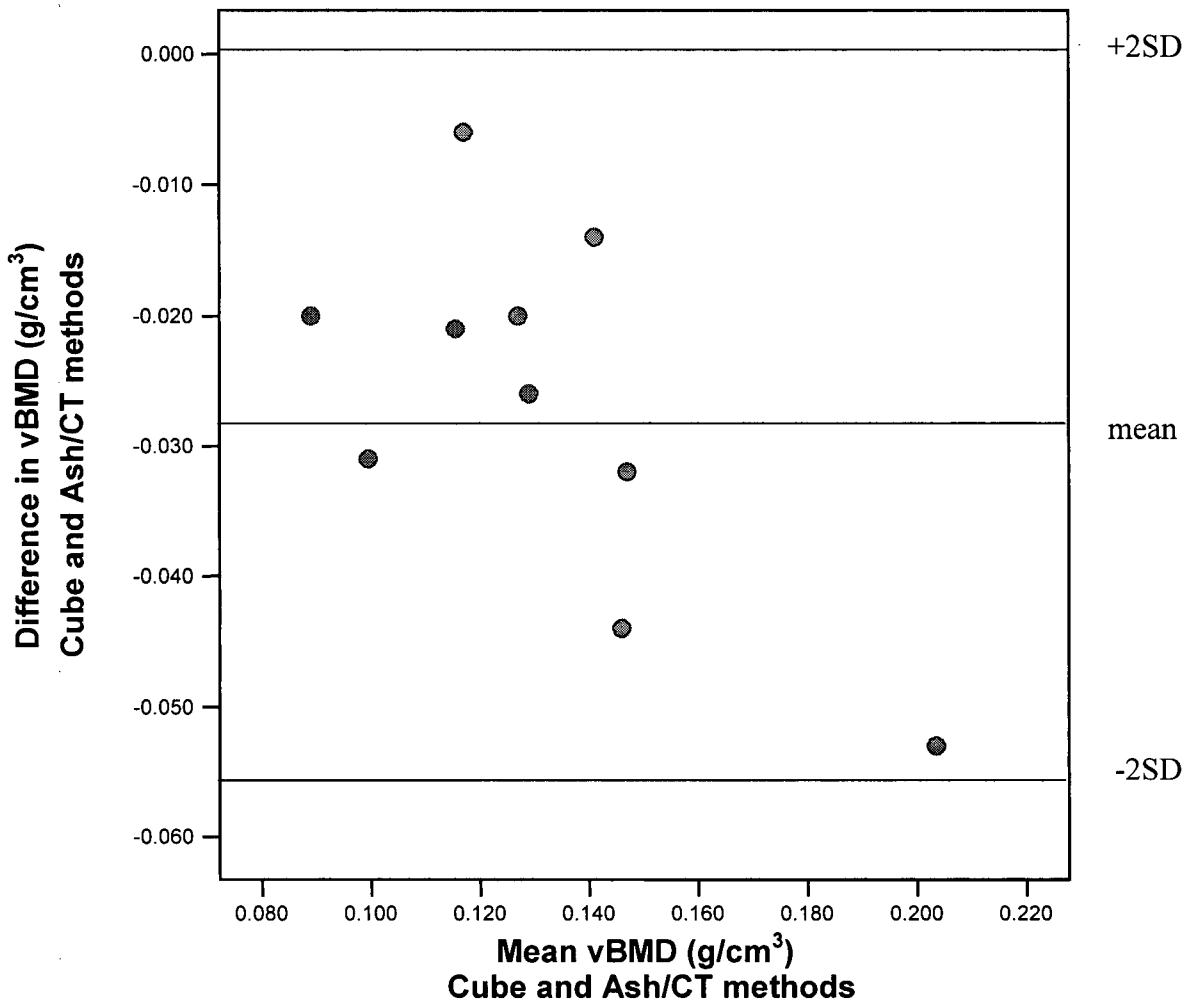


**Figure 5.4B.** *Limits of Agreement: difference in vBMD (g/cm$^3$) (difference of cube estimated vBMD and ash weight/CT vBMD) vs. mean vBMD (g/cm$^3$) (sum of cube and ash/CT vBMD divided by 2).*

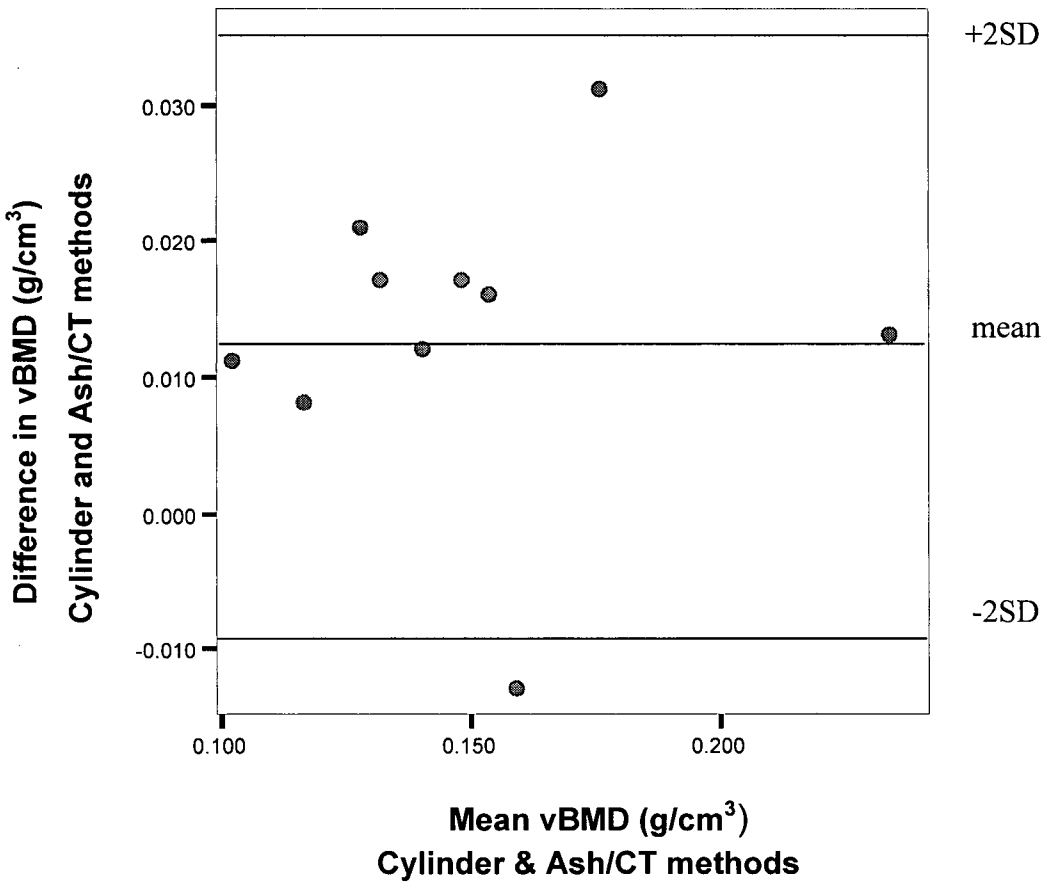


**Figure 5.4C.** *Limits of Agreement: difference in vBMD (g/cm$^3$) (difference of cylinder estimated vBMD and ash/CT vBMD) vs. mean vBMD (g/cm$^3$) (sum of cylinder and ash/CT vBMD divided by 2).*

## 5.4 DISCUSSION

My results suggest that thoracic spine researchers may obtain the most accurate representation of midthoracic vertebral body bone mineral by using the lateral DXA scan BMC analysis. When the AP scan was used, the correlation of BMC and ash weight remained acceptably high (Table 5.2). These data, taken together with the previous study of lateral scanning of thoracic vertebrae, [4] suggest that lateral scanning may be preferable to AP scanning if investigators are aiming to estimate BMC of thoracic vertebrae using DXA. This finding extends those previously limited to the lumbar spine. [6]

DXA measures of aBMD did not correlate as closely with ash weight as did BMC (Table 5.2). This difference between BMC and aBMD in assessing ash weight of mineral is consistent with BMC being a closer biological correlate of mineral than aBMD which includes a measure of bone area, not mineral alone.

There was a strong statistically significant ($p<0.01$) correlation between estimated vBMD and vBMD calculated by dividing ash weight by vertebral body volume measured by CT (Table 5.2). Previous estimates of vBMD were performed on lumbar vertebrae and assumed that vertebral body geometry resembled a cylinder or a cube. Yet quantitative three dimensional anatomic studies suggest thoracic [28] and lumbar [33] vertebral body endplate dimensions are best approximated as an ellipse. I proposed a novel method of estimating vBMD that incorporated information gained from these anatomical studies.[28,33] I found the mean difference in vBMD was lowest when using the novel elliptical cylinder method (Figures 5.4 A, B, C). The standard deviation of the difference was similar between the methods.

Laboratory researchers investigating spine biomechanics often scan a whole segment of the spine or functional spinal unit with DXA prior to testing, [13,14,17,22] not only disarticulated vertebrae. The experimental setup for these in vitro tests commonly excludes the ribs and thus, does not mirror the situation in vivo. I scanned each specimen as a segment (T5-8) as did Sabin et al. [6] Other authors have separated the posterior elements from the vertebral body prior to scanning with DXA, with the goal of ashing precisely the bone that was scanned. [4,5] Despite this difference, I report a correlation between lateral BMC and ash weight that is very similar to that found in the only other study of thoracic vertebrae. [4] The consistent results may be related to similar DXA data acquisition and analysis protocols, and/or similar methods for sectioning vertebrae. While soft tissues, such as the ligaments and discs, affect accuracy of bone mineral measurements, my results are similar to Edmondston et al. [4] who scanned only the vertebral body.

There was high agreement between the two methods of measuring BMC (ash weight and lateral DXA; Figure 5.2). I would expect even higher agreement if the specimens were scanned after sectioning.

The relevance of the present study is in providing a methodologic foundation for present and future researchers who study the thoracic spine and use DXA as a method of determining bone mass. This is a field of increasing importance because of the increasing incidence and prevalence of osteoporosis. [34] My data extend the findings of the one other study that addressed this question. [4] Together, these studies allow

researchers to base their interpretation of thoracic DXA scan accuracy on data rather than relying on assumptions based upon lumbar spine experiments.

I conclude that, for testing, *in vitro*, lateral or AP BMC by DXA is highly correlated with ash weight of the vertebral body. This has practical implication in that thoracic spine researchers should use lateral DXA results if the vertebral body is their primary focus. The posterior elements are better represented in the AP scan but failure of the spinous process is predicted by neither AP nor lateral DXA measures (Chapter Four). Calculations of vBMD assuming that vertebral geometry resembles an elliptical cylinder, cube, or cylinder, as may be used in mathematical models, are all highly correlated with vBMD measured by ash weight and CT but the mean difference is lowest when using the novel elliptical cylinder method.

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# Chapter Six

## *Regional Trabecular Bone Morphology is Correlated with Thoracic Vertebral Failure under a Posteroanterior Load*

## ABSTRACT

**Background.** Failure load of thoracic cadaveric vertebrae under a posteroanterior (PA) load (where fracture occurred at the base or middle of the spinous process)—and which may be linked to fracture during spinal mobilization—is not predicted by lateral or AP DXA or geometry of the spinous process or vertebral body. In Chapter Four I hypothesized that this may be due to BMD being an integrated measure of the entire vertebra, whereas these particular fractures occur in the spinous process.

**Objectives.** The primary objective of this study was to measure trabecular bone morphology, including bone volume ratio (BV/TV), trabecular number (Tb.N), thickness (Tb.Th) and separation (Tb.Sp) using microcomputed tomography (μCT) in four regions of thoracic vertebrae and to correlate those measures with PA failure load at the adjacent vertebra. The secondary objectives were to (a) compare trabecular BV/TV, Tb.N, Tb.Th, Tb.Sp and structure model index (SMI) of the spinous process base with that found at the central lamina and middle spinous process regions, as a possible predictor of the fracture site; (b) assess the relationship of trabecular BV/TV at the vertebral body centrum and the spinous process base; and (c) measure cortical thickness in the posterior and anterior compartments of the spinous process base, and to correlate those measures with PA failure load.

**Methods.** The T7 vertebra was dissected from 11 cadaveric midthoracic spine segments and sectioned to produce regional samples of the spinous process, the central lamina, and a central vertebral body core (8 mm diameter). Each sample was scanned with μCT (SkyScan 1072, 15μm nominal isotropic resolution). I segmented and analysed four trabecular regions (spinous process base, spinous process middle, central lamina and

vertebral body centrum). I measured cortical thickness in the posterior (tension) and anterior (compression) compartments of the spinous process base.

**Results.** BV/TV at the base or middle of the T7 spinous process (fracture sites), mean Tb.N and mean Tb.Th at the base were strongly correlated with PA failure load of T6 (BV/TV base: r=0.74, p=0.01; BV/TV middle: r=0.73, p=0.01; mean Tb.N base: r=0.64, p=0.03; mean Tb.Th base: r=0.65, p=0.03). Mean Tb.Th of the central lamina was significantly greater than mean Tb.Th of the spinous process base (p=0.002).

**Conclusions.** These novel data extend the findings of my previous study (Chapter Four) where AP and lateral BMD measures by DXA were not correlated with failure load of the spinous process. BV/TV of the base and middle regions of the spinous process were correlated with failure at those sites, and differences in Tb.Th at the base (compared with the lamina) may have influenced the site of fracture.

## 6.1 INTRODUCTION

In Chapter Four I found that BMD of the whole thoracic vertebra was not a good predictor of PA failure load, despite its strong correlation with axial compressive failure load in previous studies. [1,2] I hypothesized that this may be due to BMD being an integrated measure of the entire vertebra, whereas these particular fractures occur in the posterior elements (Chapter Four, page 118). Also, BMD is only one factor associated with bone strength. [3,4]

Trabecular microarchitecture also contributes to bone strength and fracture risk [4-7] and researchers have improved prediction of bone strength by including certain measures of microarchitecture. [8] In the past, most quantitative information on three-dimensional trabecular bone morphology was based on applying stereology* to two-dimensional sections. Disadvantages of this method are that the serial sectioning technique does not allow for subsequent mechanical testing or other secondary measurements since the samples are destroyed during preparation, both the preparation and analysis is time consuming, and stereology provides a biased estimate of trabecular bone morphology because it is two-dimensional.

Also, another limitation of calculating trabecular morphology from two-dimensional images is that their derivation indirectly assumes a fixed structure model, typically an ideal plate or rod model. With age there is a typical progression of trabecular structure from a more plate-like to a more rod-like structure. [9] If a sample deviates from the assumed model it will result in a bias in the parameters measured. [9] Day et al [10]

investigated the errors created when the parallel plate model was used to calculate morphometric parameters in the human proximal tibia, by comparison with direct thickness measures. They found trabecular thickness was consistently underestimated using the plate model and that use of the plate model resulted in a volume-dependent bias in thickness measures. They attributed this to the more rod-like structure of samples of low volume fraction. [10]

In recent years high-resolution digital imaging techniques, such as microcomputed tomography (μCT), have permitted detailed quantitative nondestructive analysis of three-dimensional microscopic bone structure. [11,12] Three-dimensional μCT image analysis allows for direct measurement of trabecular thickness (Tb.Th), trabecular number (Tb.N) and trabecular separation (Tb.Sp) which is *model-independent.* [13] Three-dimensional data sets represent the complex structure of trabecular bone for visual or biomechanical analysis, as well as for finite element modeling* (FEM) to predict mechanical properties.[12,14] To my knowledge, no studies have used this novel technology to measure regional vertebral trabecular morphology, including regions of the posterior elements.

During PA loading at the most posterior aspect of the spinous process of T6 (as in Chapter Four), the posterior side of the spinous process base is under tension and the anterior side is compressed. The thickness of the cortex in these two compartments (posterior and anterior) may be related to PA failure load.

Thus the primary objective of this study was to measure morphological parameters, including trabecular bone volume ratio (BV/TV), mean Tb.N, mean Tb.Th, and mean Tb.Sp using μCT in four regions of thoracic vertebrae and to correlate those measures with PA failure load at the adjacent vertebra. The secondary objectives were to (a) compare trabecular BV/TV, mean Tb.N, mean Tb.Th, mean Tb.Sp and structure model index (SMI) of the spinous process base with that found at the central lamina and middle spinous process regions, as a possible determinant of the fracture site; (b) assess the relationship between BV/TV of the vertebral body centrum with the spinous process base; and (c) measure cortical thickness in the posterior and anterior compartments of the spinous process base, and to correlate those measures with PA failure load.

## 6.2 METHODS

Eleven fresh-frozen (unembalmed) human cadaveric spines obtained from the UBC Department of Anatomy were used in this study (also used in Chapter Four and Chapter Five). Specimen donors included five females, five males, and one unknown. Age at death ranged from 62-93 years, mean 78 years. This study was approved by the University of British Columbia and the University of Calgary Institutional Clinical Ethics Review Boards. Each specimen was dissected to isolate a segment consisting of T5-T8 with intact disc and ligaments (see Chapter Four, 'Specimen preparation'). The isolated segments were stored frozen at −20° C until testing.

### Posteroanterior (PA) Failure Load

Each T5-8 cadaveric spine segment was loaded to failure at a displacement rate of 2 mm/sec. Load was applied in the PA direction at the most posterior part of the spinous process of T6 using a servohydraulic material testing machine (Instron 8874), simulating the PA spinal mobilization technique. The procedure is detailed in Chapter Four, under the headings 'Mechanical Testing' and 'Post-test Measurements', pages 105-108.

### Specimen Preparation

The T7 vertebra was dissected and sectioned with a rotating diamond blade saw (ISOMET Low Speed Saw, Buehler, Lake Bluff, IL, USA; blade thickness= 0.012 inches) to produce regional samples of the spinous process and the central lamina.

A custom jig, coring bit and a drill were used to extract a central vertebral body core (8 mm diameter), in the posterior to anterior direction from each specimen (Figures 6.1A and 6.1B). Each sample was placed in a custom plastic specimen holder and secured in position using low density foam prior to scanning (Figure 6.2).

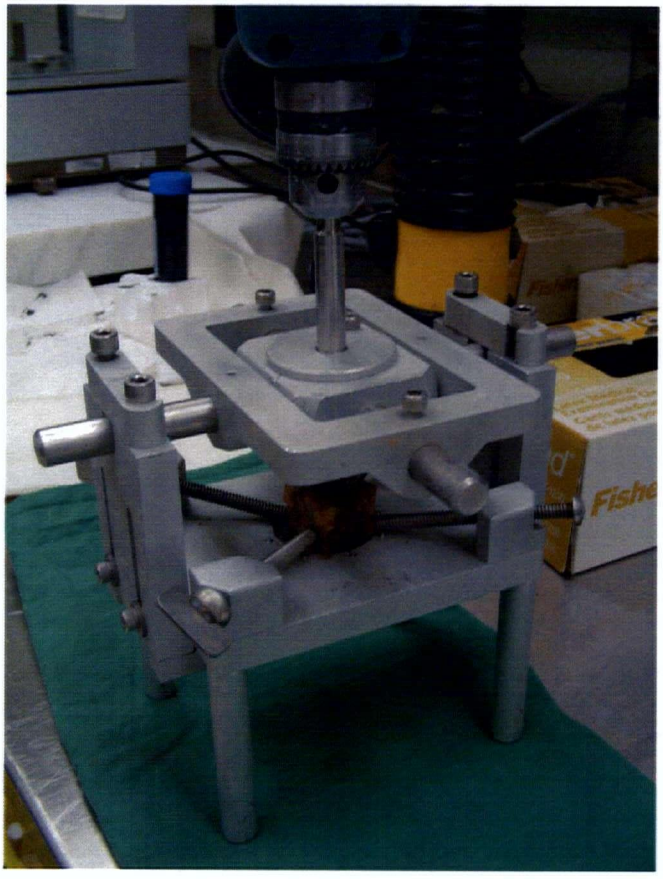

**Figure 6.1A.** *This photograph shows the custom jig, coring bit and drill used to obtain central vertebral body cores from each T7 vertebral body. The vertebral body was held in position by four screws. The platform above the vertebra was adjusted both in tilt and position, to place the drill guide/hole directly over the center of the vertebral body.*

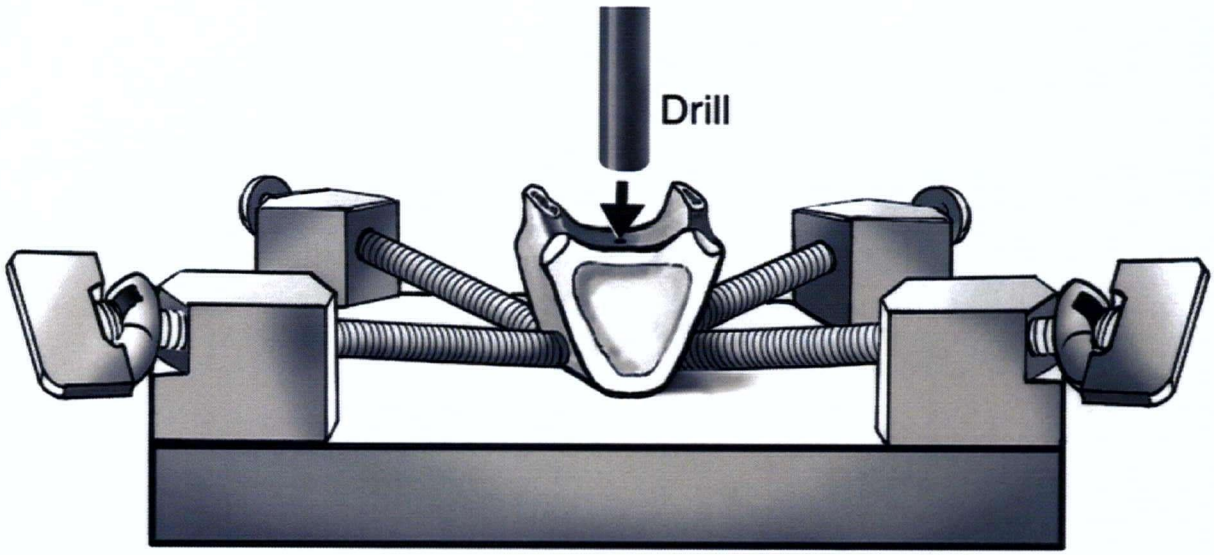


**Figure 6.1B.** *Diagram of method of obtaining a central vertebral body core, with the posterior surface in the superior position.*

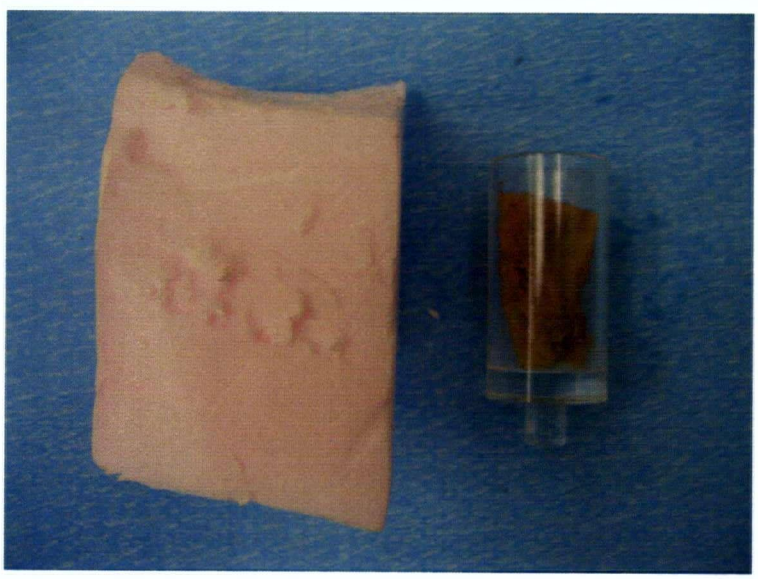

**Figure 6.2.** *Low density foam (left) was used to secure the sample in the custom holder (right) during μCT scanning.*

**Scanning with Microcomputed Tomography (μCT)**

Each sample was scanned with a high-resolution μCT scanner (SkyScan 1072; SkyScan, Aartselaar, Belgium), providing a nominal* isotropic* resolution of 15μm. The samples were rotated through 180 degrees at a rotation step of 0.9 degrees. The X-ray settings were standardized to 100kV and 98μA with an exposure time of 6.0 seconds per frame. Two-frame averaging was used to improve the signal to noise ratio. A 1 mm-thick aluminum filter was employed to minimize beam hardening artifacts. The scan time for each sample was approximately one hour. Given the necessary field of view of 16 mm, the maximum resolution was 15μm. Each scan was reconstructed using a cone-beam two dimensional reconstruction algorithm with superimposed ring-artifact reduction (SkyScan software). Each image series was passed through a median filter (5x5 cubic kernel using Image J v.1.31) to partly suppress the noise in the original data. I segmented four trabecular regions (spinous process base, spinous process middle, central lamina, and vertebral body centrum) using a global threshold value to extract the mineralized bone phase.

**Data Analysis**

Bone volume fraction (BV/TV) was calculated as the proportion of trabecular bone tissue volume with respect to total bone volume. [15] Trabecular thickness (Tb.Th) is determined as an average of the local thickness at each voxel representing bone. [16] A series of spheres is fit inside the bone phase. The largest sphere associated with each bone voxel is found and used to calculate an average thickness. [13] Both a single mean trabecular thickness calculation and a histogram of trabecular thicknesses are produced. [13,15] Trabecular separation (Tb.Sp), a measure of the distance between trabeculae, is measured

directly from the images using the same method used to measure Tb.Th but by applying the analysis to the marrow spaces instead of bone. Trabecular number (Tb.N) is the number of trabeculae per mm. Structure model index (SMI) is a dimensionless index estimating the relative prevalence of rods and plates in trabecular bone where an ideal plate and rod have SMI values of zero and three respectively. [15,17]

BV/TV, mean Tb.Th (mm) mean Tb.N (per mm), mean Tb.Sp (mm) and SMI for each region was measured using standard CT Analyser software (v.1.2.35.3 SkyScan, Aartselaar, Belgium). Studies report high correlations between morphometric analysis performed with μCT and conventional histology. [11,18] Figure 6.3 shows a three-dimensional image of the spinous process base for one specimen. Both the trabecular and cortical compartments are shown.

Cortical thickness of the spinous process base was measured from two-dimensional images extracted from the three-dimensional data volume. I measured cortical thickness of the posterior compartment of the spinous process base (the side under tension during PA loading) and also at the anterior compartment (the side being compressed during PA loading) (Figure 6.4). Twenty-one images, each ten slices apart, were measured and the mean cortical thickness was calculated. Thus this measurement spanned 200 slices, the same 200 slices that were used in the trabecular analysis. Test-retest reliability was conducted by performing three measurements at each of five sites in one specimen. Reliability ranged from 0.004-0.045 mm (mean 0.021 mm, SD 0.014 mm).

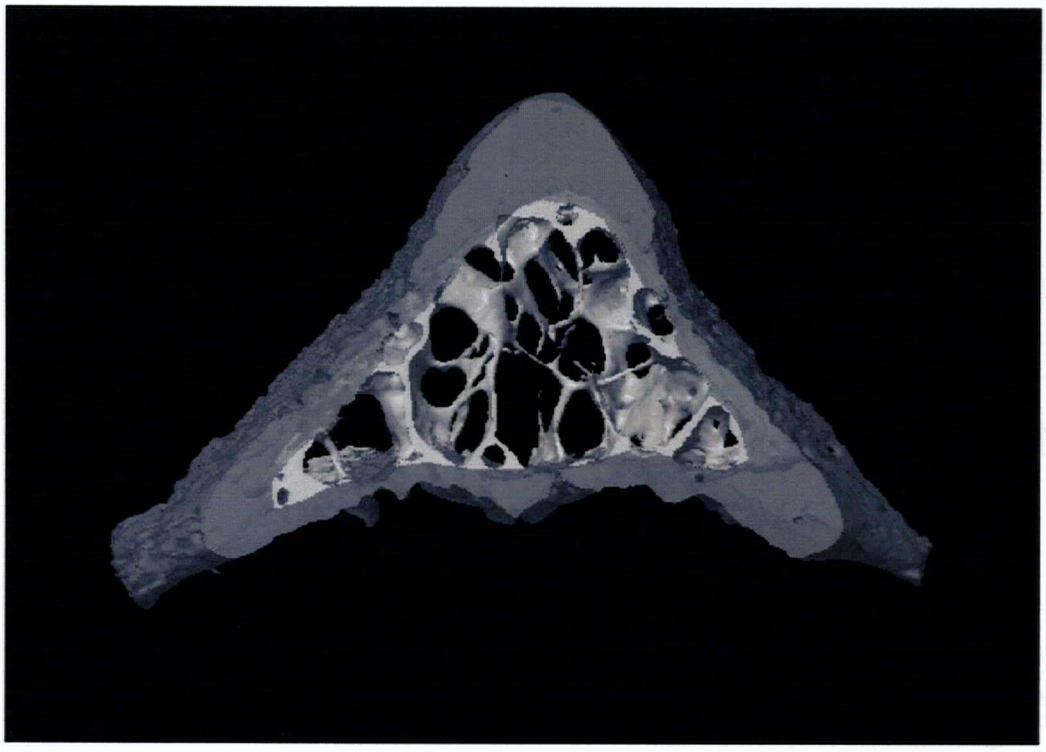

**Figure 6.3.** *Three dimensional image of the spinous process base, of one sample. Both the trabecular and cortical regions are visualized.*


**Figure 6.4.** *Sample of a typical cortical thickness measurement at the posterior compartment of the spinous process, at the midline. Cortical thickness was measured as the length of the red line (2.67 mm).*

**Statistical Analysis**

Statistical analysis was conducted using SPSS 12.0 for Windows. All variables were normally distributed. Pearson correlations were computed to measure the relationship between PA failure load (N) and BV/TV, mean Tb.Th, mean Tb.N and mean Tb.Sp in each of the four regions, as well as PA failure load (N) and cortical thickness at the posterior and anterior spinous process base, at the midline. I used one-way repeated

measures ANOVA to compare trabecular BV/TV, mean Tb.Th, mean Tb.N, mean Tb.Sp and SMI in three regions (spinous process base, spinous process middle, and lamina) with region as the factor. Pearson correlation coefficient was computed to assess the relationship between BV/TV of the vertebral body centrum and the spinous process base. I set the significance level at 0.05 a priori. I used the paired t-test to compare Tb.Th in the spinous process base, middle and lamina, and applied a Bonferroni correction to correct for multiple pairwise comparisons. The Bonferroni correction gave me a new significance level of 0.016.

## 6.3 RESULTS

Range, mean and standard deviation for trabecular BV/TV, mean Tb.N, mean Tb.Th and mean Tb.Sp in each of the four regions (spinous process base, spinous process middle, central lamina, central vertebral body) are presented in Table 6.1. The mean (SD), range for SMI in each of the four regions was: base 1.53 (0.27), 1.23-2.07; middle 1.60 (0.45), 1.21-2.75; lamina 1.40 (0.29), 0.98-1.86; vertebral body 1.65 (0.38), 0.86-2.02. Mean cortical thickness of the anterior and posterior compartments of the spinous process base ranged from 0.18−1.34 mm (anterior) and 0.64−2.47 mm (posterior). Mean (SD) thickness was 0.65 mm (0.39 mm) and 1.64 mm (0.52 mm) for the anterior and posterior cortex respectively.

Pearson correlation coefficients for all metric trabecular bone measures and PA failure load are presented in Table 6.2. BV/TV at the base or middle of the T7 spinous process (fracture sites) showed a strong significant correlation with PA failure load of T6 (base: $r=0.74$, $p=0.01$ (Figure 6.5A); middle: $r=0.73$, $p=0.01$). Mean Tb.N and mean Tb.Th at the spinous process base was significantly correlated with PA failure load (mean Tb.N: $r=0.64$, $p=0.03$, Figure 6.5B; mean Tb.Th: $r=0.65$, $p=0.03$, Figure 6.5C). Mean Tb.Sp at the middle of the spinous process was inversely correlated with PA failure load ($r=-0.61$, $p=0.048$) (Figure 6.5D). BV/TV of the vertebral body centrum was not significantly correlated with BV/TV of the spinous process base ($r=0.60$, $p=0.05$). Anterior cortical thickness (compressed side) of the spinous process base was more strongly correlated with PA failure load than cortical thickness of the posterior

compartment, but neither correlation was statistically significant (anterior: r=0.51, p=0.11; posterior: r=0.13, p=0.69).

Mean Tb.Th was significantly lower at the spinous process than at the lamina (p=0.003, ANOVA) (Figure 6.6). BV/TV between the three regions (spinous process base, middle and lamina) approached significance (p=0.06). There was a trend toward decreased BV/TV from the spinous process to the lamina (linear contrast p=0.03) Further comparison of Tb.Th with the paired t-test revealed a significant difference between the spinous process base and lamina (p=0.002).

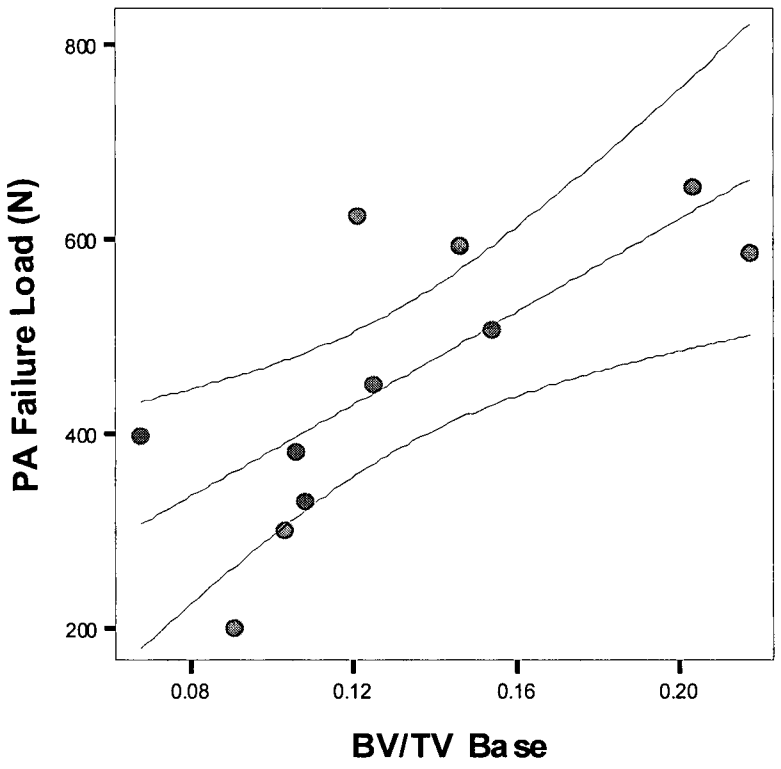


**Figure 6.5A.** *Pearson correlation for bone volume/total volume (BV/TV) of the base of the T7 spinous process and posteroanterior (PA) failure load (N) of T6 from eleven cadaveric spines. r=0.74, p=0.01*

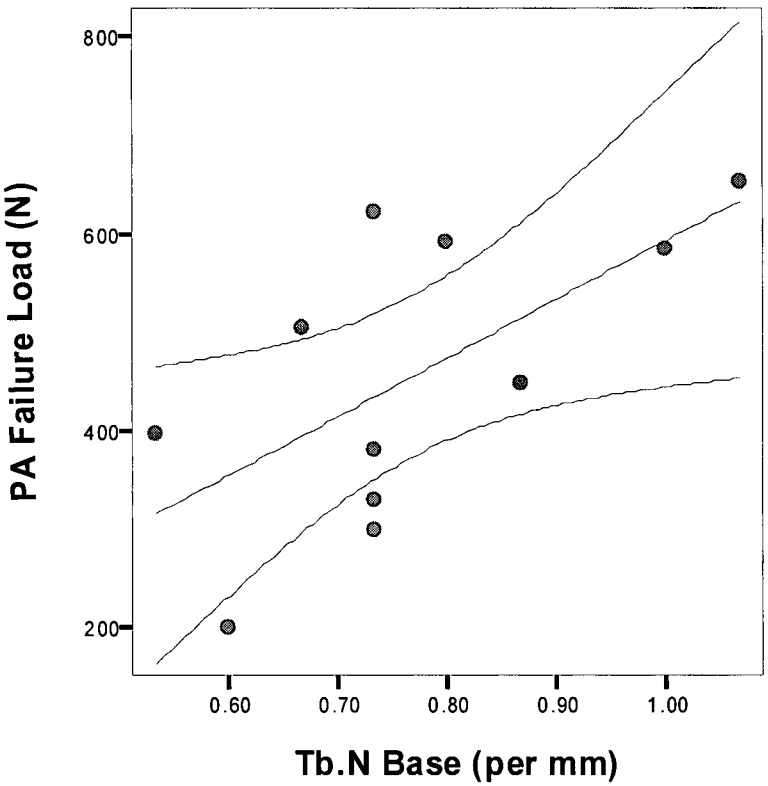


**Figure 6.5B.** *Pearson correlation for mean Tb.N (per mm) at the base of the T7 spinous process and posteroanterior (PA) failure load (N) of T6 from eleven cadaveric specimens. r=0.64, p=0.03*

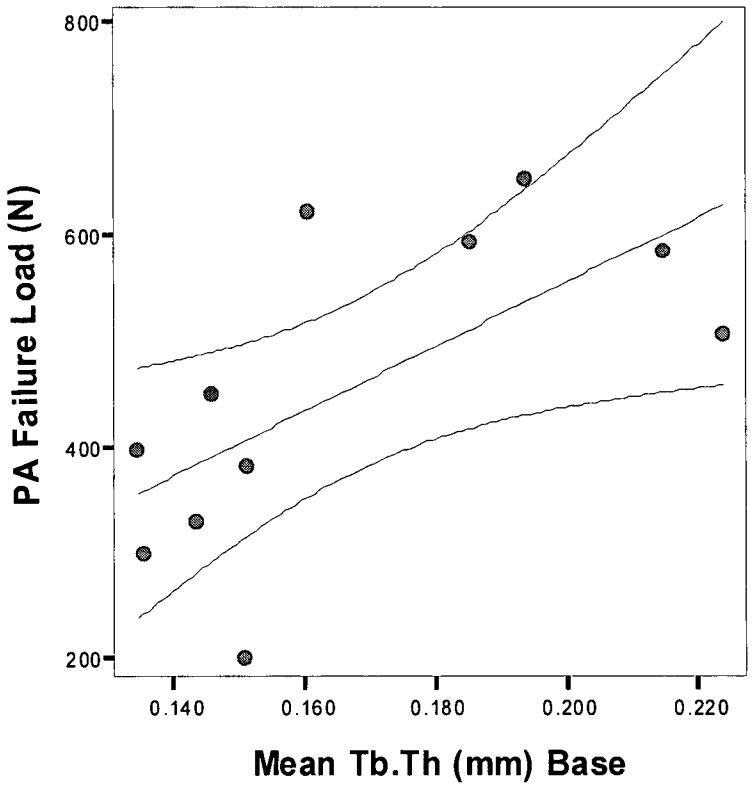


**Figure 6.5C.** *Pearson correlation for mean Tb.Th (mm) at the base of the T7 spinous process and posteroanterior (PA) failure load (N) of T6 from eleven cadaveric specimens. r=0.64, p=0.03*

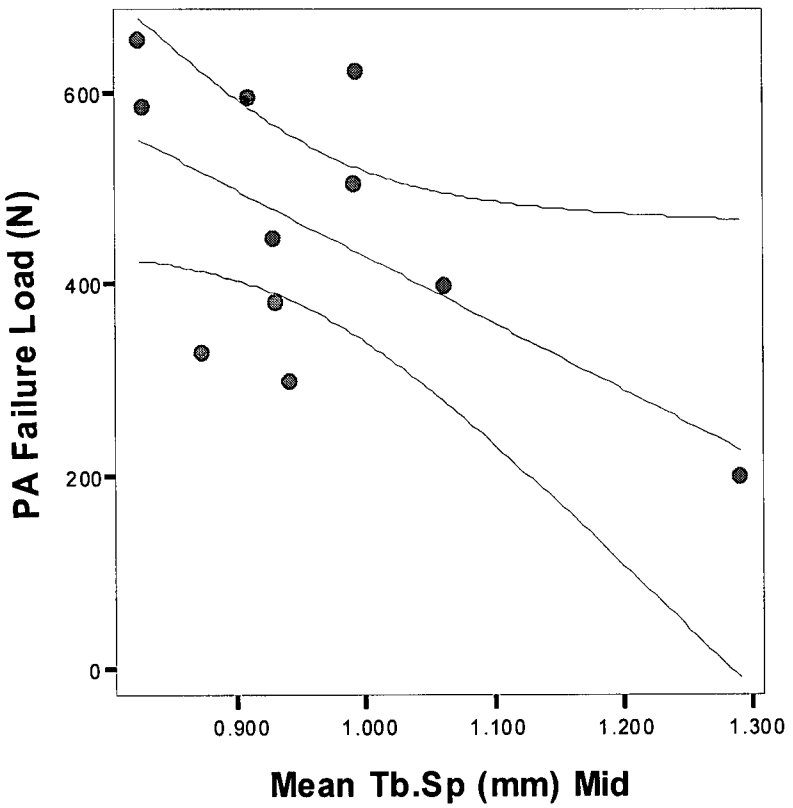


**Figure 6.5D.** *Pearson correlation for mean Tb.Sp (mm) at the middle of the T7 spinous process and posteroanterior (PA) failure load (N) of T6 from eleven cadaveric specimens. r= −0.61, p=0.048*

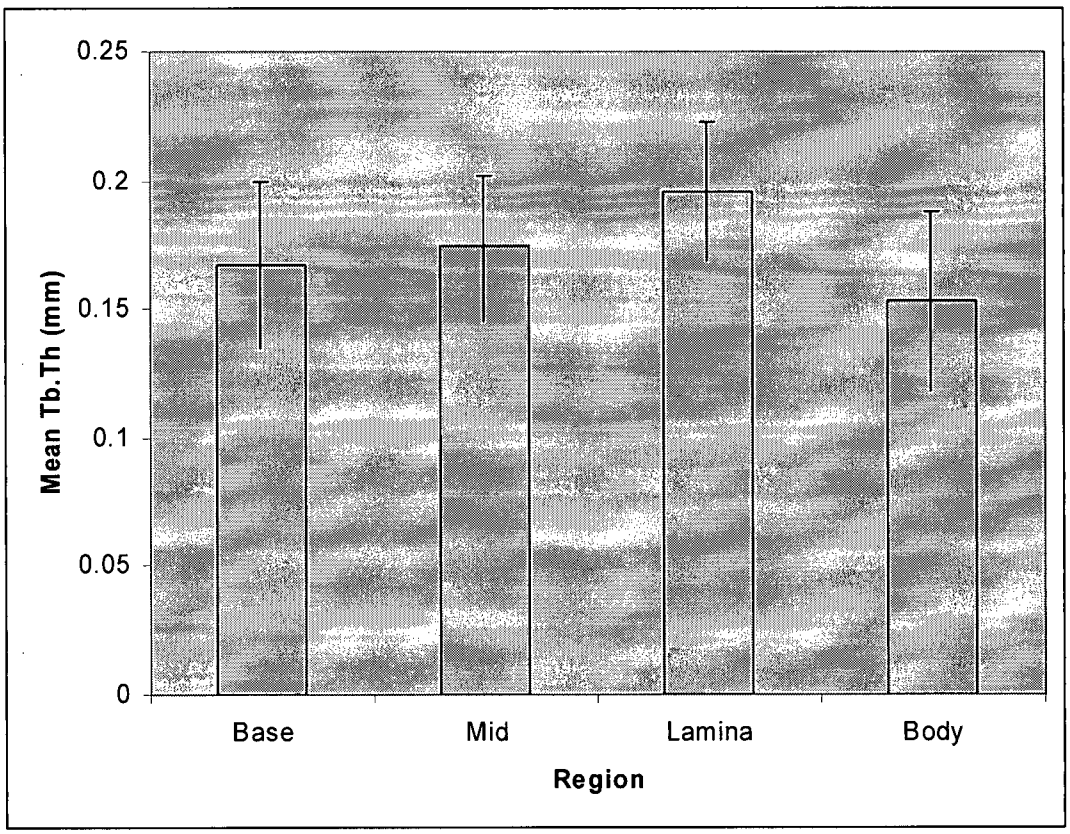


**Figure 6.6.** *Mean ± 1 standard deviation for Tb.Th (mm) in four regions: spinous process base (Base), spinous process mid (Mid), lamina and vertebral body (Body).*

**Table 6.1.** *Range, mean and standard deviation for trabecular BV/TV, Mean Tb.Th (mm), Mean Tb.N (per mm) and Mean Tb.Sp (mm) for each of the four trabecular regions analysed.*

| | BV/TV | | | Mean Tb.Th (mm) | | | Mean Tb.N (per mm) | | | Mean Tb.Sp (mm) | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Region** | **Range** | **Mean** | **SD** | **Range** | **Mean** | **SD** | **Range** | **Mean** | **SD** | **Range** | **Mean** | **SD** |
| **Base** | 0.068-0.217 | 0.131 | 0.046 | 0.134-0.224 | 0.167 | 0.032 | 0.533- 1.067 | 0.770 | 0.159 | 0.827-1.231 | 1.010 | 0.135 |
| **Middle** | 0.080-0.211 | 0.144 | 0.034 | 0.134-0.227 | 0.174 | 0.028 | 0.533- 1.000 | 0.836 | 0.161 | 0.824-1.291 | 0.961 | 0.130 |
| **Lamina** | 0.115-0.265 | 0.160 | 0.039 | 0.144-0.243 | 0.195 | 0.027 | 0.600- 1.333 | 0.818 | 0.202 | 0.710-1.276 | 0.991 | 0.141 |
| **Body** | 0.041-0.222 | 0.108 | 0.059 | 0.104-0.222 | 0.153 | 0.035 | 0.400- 1.133 | 0.667 | 0.237 | 0.591-1.203 | 0.929 | 0.202 |

**Table 6.2.** *Pearson correlations for the metric T7 trabecular bone measures (BV/TV, mean Tb.Th, mean Tb.N, mean Tb.Sp) in each region (Base= spinous process base; Mid= spinous process middle; Lamina= central lamina; Body= vertebral body centrum) and T6 PA failure Load (N), in cadaveric vertebrae. *significant at p< 0.05*

| Variable and Region | Correlation with PA Failure Load (N) | |
|---|---|---|
| **Base** | **r** | **p** |
| BV/TV | 0.74* | 0.01 |
| Mean Tb.Th | 0.65* | 0.03 |
| Mean Tb.N | 0.64* | 0.03 |
| Mean Tb.Sp | -0.40 | 0.23 |
| **Mid** | – | – |
| BV/TV | 0.73* | 0.01 |
| Mean Tb.Th | 0.50 | 0.12 |
| Mean Tb.N | 0.46 | 0.12 |
| Mean Tb.Sp | -0.61* | 0.048 |
| **Lamina** | – | – |
| BV/TV | 0.57 | 0.07 |
| Mean Tb.Th | 0.32 | 0.33 |
| Mean Tb.N | 0.43 | 0.19 |
| Mean Tb.Sp | -0.51 | 0.11 |
| **Body** | – | – |
| BV/TV | 0.44 | 0.10 |
| Mean Tb.Th | 0.55 | 0.08 |
| Mean Tb.N | 0.32 | 0.33 |
| Mean Tb.Sp | -0.52 | 0.10 |

## 6.4 DISCUSSION

This investigation using μCT suggests that BV/TV of the base and middle regions of the spinous process is correlated with failure when the spinous process is subjected to a PA load. Further, the lower mean Tb.Th of the spinous process base compared with the lamina may have influenced the site of fracture.

I remind the reader that integral vertebral body BMD measured by DXA was not correlated with failure load of the spinous process (Chapter 4). That finding, taken together with the results of this investigation, suggests that scientists and clinicians should not rely on bone mass measures from the vertebral body if they seek information about the posterior elements. My results are relevant in the case of spinal fixation and implant research, where DXA may be used to gain insights into bone strength. My results extend the findings of Coe et al. [19] who found a significant correlation between BMD and loads to failure for transpedicular screws and spinous process wires, but no significant correlation between BMD and load to failure for laminar hooks. Furthermore, the results of this study suggest that vertebral body trabecular BV/TV is not strongly correlated with trabecular BV/TV of the posterior elements.

A strength of this study was the use of three-dimensional image analysis by μCT which allowed direct measurement of trabecular thickness, number and separation that is model-independent. [15] This avoids model-dependent errors associated with two-dimensional analysis, [10,15] and avoids errors that occur with planar methods such as DXA.

Cortical thickness of the spinous process did not predict PA failure load. It is possible that other spinous process cortical measures, such as cortical porosity, may predict PA failure load even though cortical thickness did not. I could not measure cortical porosity because the large size of my samples provided inadequate resolution of cortical pores. Cortical thickness in the compressed anterior compartment was more strongly correlated with PA failure load than posterior cortical thickness, although this was not statistically significant, and warrants further investigation with a larger sample size. It is also possible that PA failure load is related to a combination of trabecular and cortical bone mass and structure, and this could be tested in a larger study. Finally, although my sample size was normally distributed, it was small and thus, conclusions must remain limited.

A limitation of this study was that I studied PA failure of T6 vertebrae and then investigated whether regional vertebral morphology of T7 vertebrae predicted T6 failure load. Clearly, mechanical testing and measures of morphology on the same vertebrae would have been ideal but this was not possible because T6 was damaged. The presence of this damage to the bone precluded a meaningful measurement of the bone morphology. Although vertebral compressive strength has been shown to increase caudally [2,20] due to the increase in the cross-sectional area of the vertebral end-plate, [20] there is no evidence to suggest that PA failure load would be significantly different between T6 and T7. BMC and BMD, by DXA, also gradually increases caudally in the midthoracic spine but, as I found in Chapter Four, lateral and AP DXA are not good predictors of spinous process failure load.

At present, our μCT scanner is unable to scan an entire cadaveric vertebra therefore I sectioned each vertebra and scanned each region individually. While quantitative computed tomography (QCT) can accommodate whole vertebrae and spine segments, the resolution (100-400 μm depending on the machine) is not sufficient for 3D analysis of trabecular microarchitecture. New high-resolution μCT scanners have recently become available (XtremeCT, Scanco Medical, Basserdorf, Switzerland) that will allow measurement of entire vertebral bodies at resolutions sufficient to establish trabecular morphology (30-40 micrometers).

Whereas previous data indicate that BMD by DXA is not a good predictor of PA failure load, [21] regional BV/TV of the spinous process base and middle regions, the sites of fracture, is strongly correlated with PA failure load. It is noteworthy that trabecular thickness differs significantly between the spinous process base and lamina regions, and may have influenced the site of fracture in Chapter Four.

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# Chapter Seven

## *Posteroanterior Stiffness as a Predictor of Intervertebral Motion in Cadaveric Thoracic Spine Segments*

## ABSTRACT

**Background.** Spinal joint mobilization is a mainstay of clinical assessment of individuals with back pain. The clinician manually assesses stiffness and joint motion relative to segments above and below. Although clinical theory suggests that manually performed techniques can predict or detect intervertebral motion, this hypothesis remains untested.

**Objectives.** To correlate stiffness measured during mechanically simulated central posteroanterior (PA) mobilization with (1) flexion and extension range of motion (ROM; Deg), (2) flexion/extension neutral zone (NZ) motion (Deg) and (3) flexibility (Deg/Nm) in three dimensions, in midthoracic cadaveric spine segments of older adults.

**Methods.** Using a precision opto-electronic camera system and a custom spine testing machine, I measured intervertebral ROM, NZ motion and three-dimensional flexibility in eight T5-8 cadaveric specimens (mean age 81 yrs). I then measured stiffness when a cyclic PA load was applied at the spinous process of T6 using a servohydraulic material testing machine (Instron 8874), simulating the PA spinal mobilization technique.

**Results.** There was a strong significant inverse relationship between stiffness during cyclic PA loading of T6 and flexion or extension ROM of T6 relative to T7 ($r = -0.88$, $p<0.01$, extension; $r = -0.81$, $p=0.01$, flexion), and T6-7 flexibility in all six directions.

**Conclusions.** Stiffness during simulated central cyclic PA mobilization in the cadaveric midthoracic spine is inversely correlated with flexion and extension ROM and three-dimensional flexibility at the level at which the technique is applied. These findings provide biomechanical support for the inclusion of specific joint mobilization in the assessment of older adults with back pain.

## INTRODUCTION

When evaluating patients with back pain, musculoskeletal health care practitioners including physiotherapists commonly use spinal joint mobilization to assess the stiffness and joint motion relative to segments above and below. [1] Stiffness is a term used to describe the force needed to achieve a certain deformation of a structure. One very common clinical spinal mobilization technique is PA mobilization. [2-4] It can be applied at an individual spinous process [5,6] to assess stiffness at a specific segmental level.

In the assessment of spine pain, studies have found that manual examination by a physiotherapist is highly accurate in detecting the segmental level responsible for a patient's complaint when compared against a spinal block, [7,8] and is correlated with disability. [9] Clinical dogma suggests that the diagnostic assessment technique of spinal joint mobilization also provides a measure of spinal motion [5,6,10] but this hypothesis has never been tested formally. Three studies have previously measured PA spinal stiffness in the thoracic spine by inferring vertebral translations from the motion of an indenter at the skin-surface, [11-13] but no previous study has examined the association between stiffness during PA mobilization and an objective measure of intervertebral motion.

For this reason, my primary objective was to correlate stiffness measured during mechanically simulated central PA mobilization of T6 with (1) flexion and extension range of motion (ROM; Deg), (2) flexion/extension neutral zone (NZ) motion (Deg) and (3) flexibility (Deg/Nm) in three dimensions (flexion, extension, right and left lateral

bending, right and left axial rotation), in midthoracic cadaveric spine segments of older adults.

## METHODS

Eight fresh-frozen (unembalmed) human cadaveric spines were obtained from the UBC Department of Anatomy. Donors included five females and three males. Age at death ranged from 70-93 years, mean 81 years. Each specimen was given a number for identification to maintain anonymity. This study was approved by the UBC Clinical Ethics Review Board.

### Specimen Preparation

Each specimen was dissected to isolate a segment consisting of T5-T8 with intact discs and ligaments (see Chapter Four, 'Specimen preparation'). The isolated segments were stored frozen at −20° C until testing.

Lateral and AP radiographs were taken of each specimen prior to testing.
No specimen showed any sign of malignancy. One specimen had a 20% wedge compression fracture of T8 and another specimen had signs of severe degenerative change (i.e. large osteophytes).

Steel (24 gauge) wire was secured to the pedicles of T5 and T8 of each spine segment. Each specimen was embedded in dental cement such that half of the vertebral bodies of T5 and T8 and the attached steel wire were fixed in cement. Thus, the T5 transverse processes were fully embedded and half of the T8 transverse processes were embedded. The T5-6 and T7-8 facet joints remained free, as did all parts of T6 and T7.

**Measuring Intervertebral Range of Motion, Neutral Zone Motion and Flexibility**

A custom spine testing machine [14] was used to load the specimens in flexion/extension, axial rotation and lateral bending (Figure 7.1). This machine consists of a DC motor, a planetary reduction gearhead, an articulated arm of two universal joints, a ball spline and a torque cell (model TRT-200, Transducer Techniques, CA, USA). Pure moments (no other external forces were applied to the spine) were applied to the upper vertebra at 2.0 degrees per second to a moment maximum of 4.0 Nm, so as to be non-destructive. I applied three complete loading cycles, as described by Wilke, [15] in flexion/extension, axial rotation and lateral bending. Marker carriers with four infrared light emitting diodes (LEDS) were secured to the vertebral body of T5 (middle) and the transverse processes of T6-8 with 3.5 mm cancellous bone screws. In cases where the transverse process was too weak to sufficiently secure the marker carrier, the middle of the vertebral body was used. Each marker carrier was positioned to be in clear view of the cameras while avoiding contact with dental cement or another marker carrier during the test. An opto-electronic camera system (Optotrak 3020, Northern Digital, Waterloo, Ontario, Canada) monitored the three-dimensional positions of the marker carriers. The accuracy of this system exceeds 0.1°. [16]

**Cyclic PA Loading (simulated PA mobilization)**

Next, the spine segment was oriented horizontally in the testing machine (Instron 8874, Instron Corp. Canton, MA) to facilitate the PA load application (Figure 7.2). The T5 and T8 specimen mounts were clamped rigidly, such that the T6 spinous process was aligned with the linear actuator of the machine. Load was applied through a circular delrin

indenter (20 mm diameter, Young's Modulus 3.1 GPa), mounted on the end of the actuator. I chose a 20 mm diameter to simulate pisiform hand contact (Figure 1.5) and to ensure that the load was only applied at the T6 spinous process. This indenter had a 7 mm diameter groove for the spinous process and 3 mm foam (PPT, Langer Biomechanics Group Inc, NY) was attached to the bottom of the indenter to enable a distributed load transmission and to prevent slipping of the spinous process. A very low load (5 N) functional test was used to verify that the intended PA load did not produce noticeable coupled axial rotation.

A cyclic PA load of 50-200 N was applied to the most posterior point of the T6 spinous process at 0.5 Hz for 30 seconds. Kinematic data were recorded during the test at 10 Hz using a precision opto-electronic camera system (Optotrak 3020, Northern Digital, Waterloo, Ontario). Figure 7.3 shows vertebral motion during PA mobilization at T6, as found in Chapter Four.

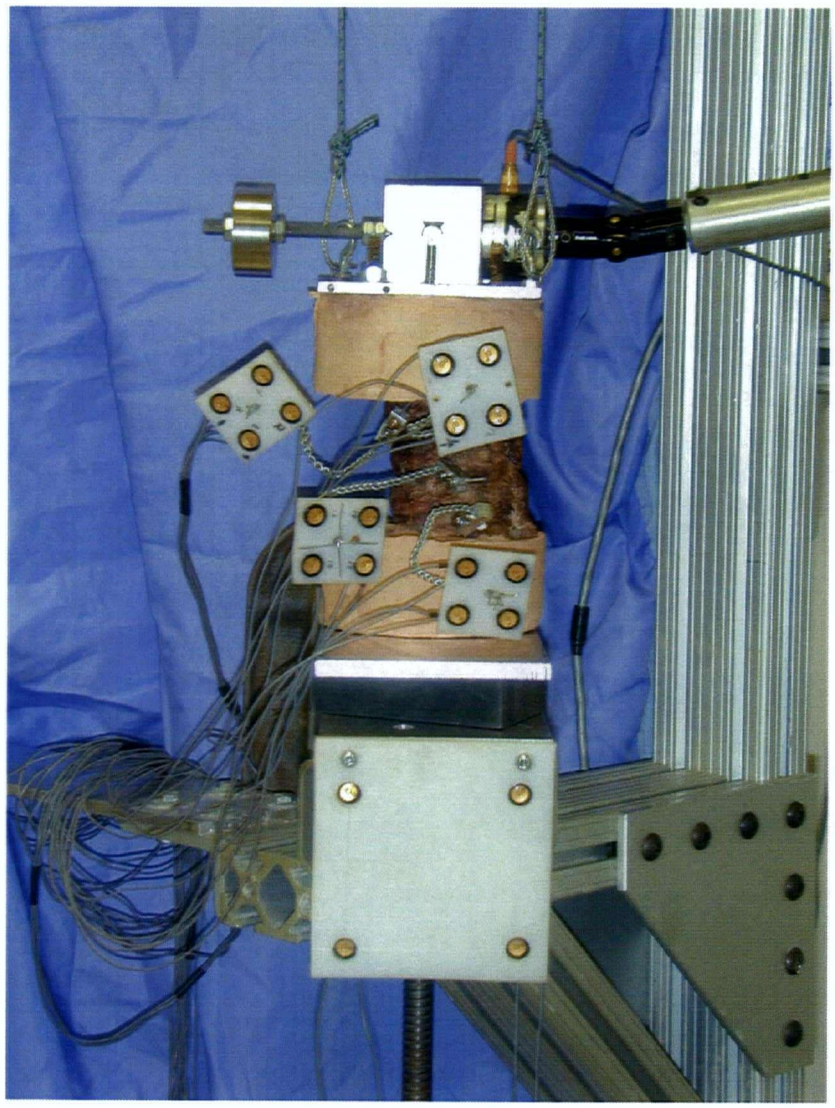

**Figure 7.1.** *A typical specimen set-up for the flexibility tests. This photo shows the base marker carrier (below the specimen), the marker carriers attached to the specimen, the specimen embedded in dental cement, fixed in the custom testing jig and secured to the spine flexibility machine.*

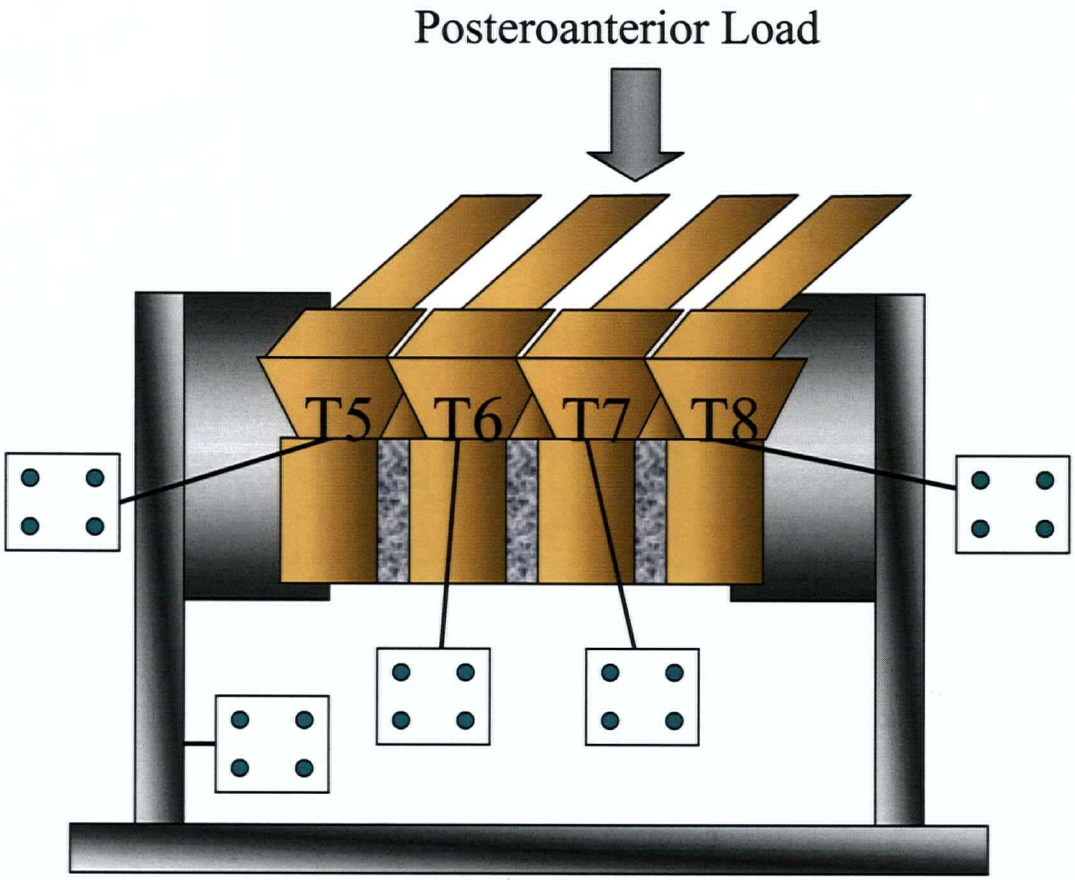


**Figure 7.2.** *Schematic of posteroanterior (PA) loading at the T6 spinous process in T5-T8 cadaveric spine segments. The five opto-electronic marker carriers are shown.*

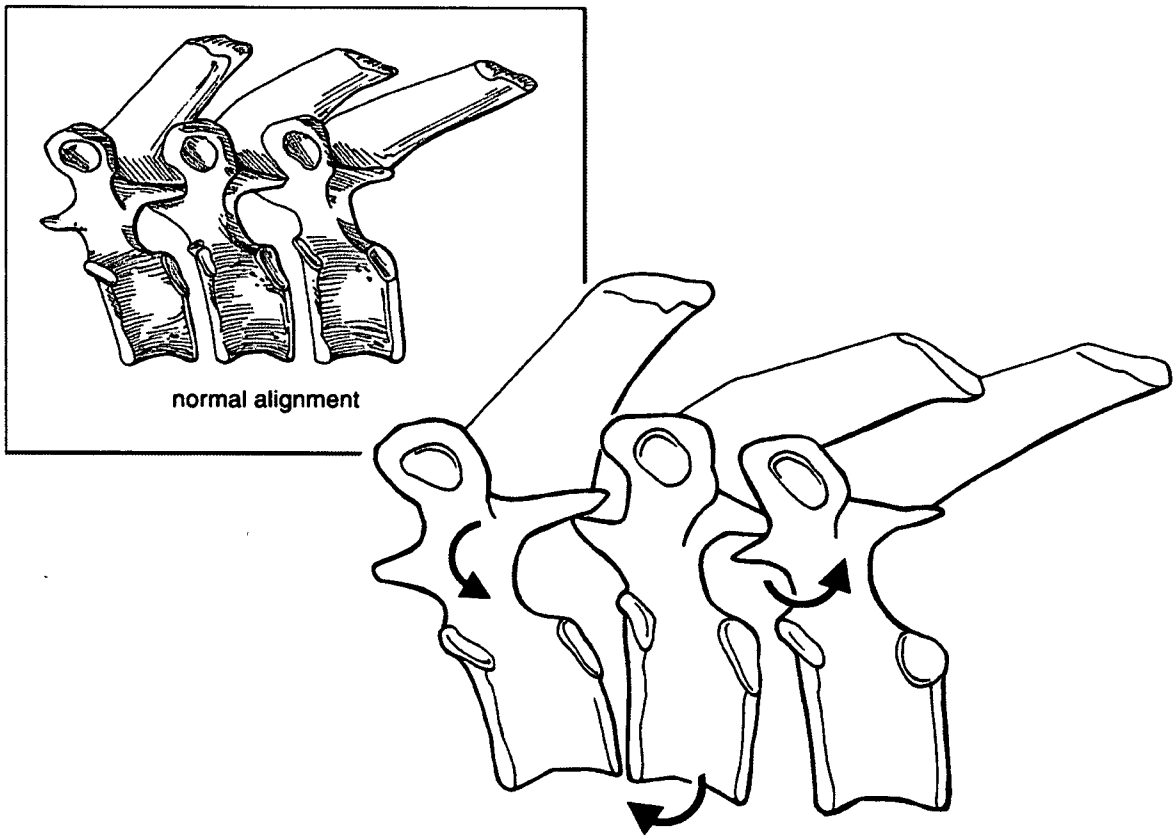


**Figure 7.3.** *Diagram of normal alignment of T5, T6 and T7 (top left) and vertebral motion during PA mobilization at T6, where T6 moves into extension relative to T5, and T5 and T7 flex relative to T6 and T8.*

**Data Analysis**

For each spinal level, I determined vertebral kinematics via the opto-electronic marker carriers. The anterior-inferior point on the vertebral body was the origin and a global coordinate system that was aligned with a base marker fixed to the machine (Figure 7.1 and 7.2) was used for all tests. The x-axis was in the anterior-posterior direction in the cyclic PA mobilization tests and the positive x-axis was to the left in the flexibility tests

(Figure 1.7). The y-axis was in the cephalad-caudad direction in all tests and the z-axis was the cross-product of the x and y axes. I assumed each vertebra to be a rigid body for measurement and I used custom software (KIN 2000, written in LabVIEW 6.0, National Instruments, USA).

For the tests conducted with the spine machine, kinematic data were collected from three cycles, but only the third cycle was used for statistical analysis. The ROM was defined as angular deformation in flexion and extension at the peak moments [15,17] (Figure 7.4). NZ motion was defined as the maximum difference in rotation within the moment-rotation curve between moment magnitudes of ± 0.2 Nm (Figure 7.4). Flexibility was calculated as the slope of the motion (Deg) versus moment (Nm) curve during the loading portion of the curve in each direction, using all points on that portion of the curve (Figure 7.5). I calculated flexibility at all three spinal levels (T5-6, T6-7 and T7-8).

Stiffness (kN/Deg) during PA mobilization was determined as the slope of the PA force versus T6-7 rotation angle curve for the loading portion of the curve between the two force limits (50-200 N). The slope was calculated using a simple linear regression using all points on the curve. I also determined PA stiffness using indenter motion (mm) (with PA force, as above) for comparison with previous studies of PA stiffness in the midthoracic spine.

One specimen had signs of severe degenerative change and was found to have small flexibility values (Table 7.2). However, this specimen's ROM and flexibility values fell within ± 3 SD of the group mean so I did not remove it from the statistical analysis.

**Statistical Analysis**

Pearson correlation coefficients were used to assess the relationship between T6-7 stiffness during cyclic PA loading of T6 and (1) flexion and extension ROM of the T5-6, T6-7, and T7-8 functional spinal units, (2) NZ motion in flexion/extension at T6-7, and (3) flexibility (Deg/Nm) of T5-6, T6-7 and T7-8 in extension, flexion, left and right axial rotation, and left and right lateral bending. Statistical significance was set at $p<0.05$.

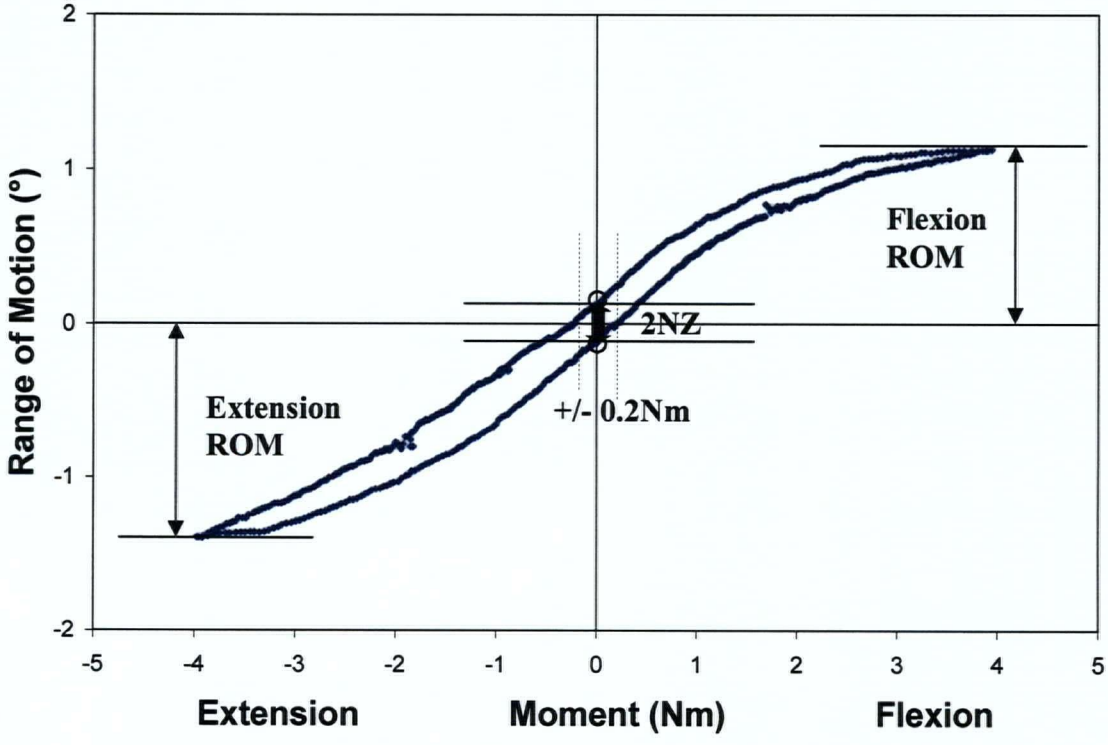


**Figure 7.4.** *Graphical representation of Range of Motion (ROM; Deg), Neutral Zone (NZ) motion (Deg). Dashed line (---) represents the moment magnitudes of ± 0.2 Nm.*

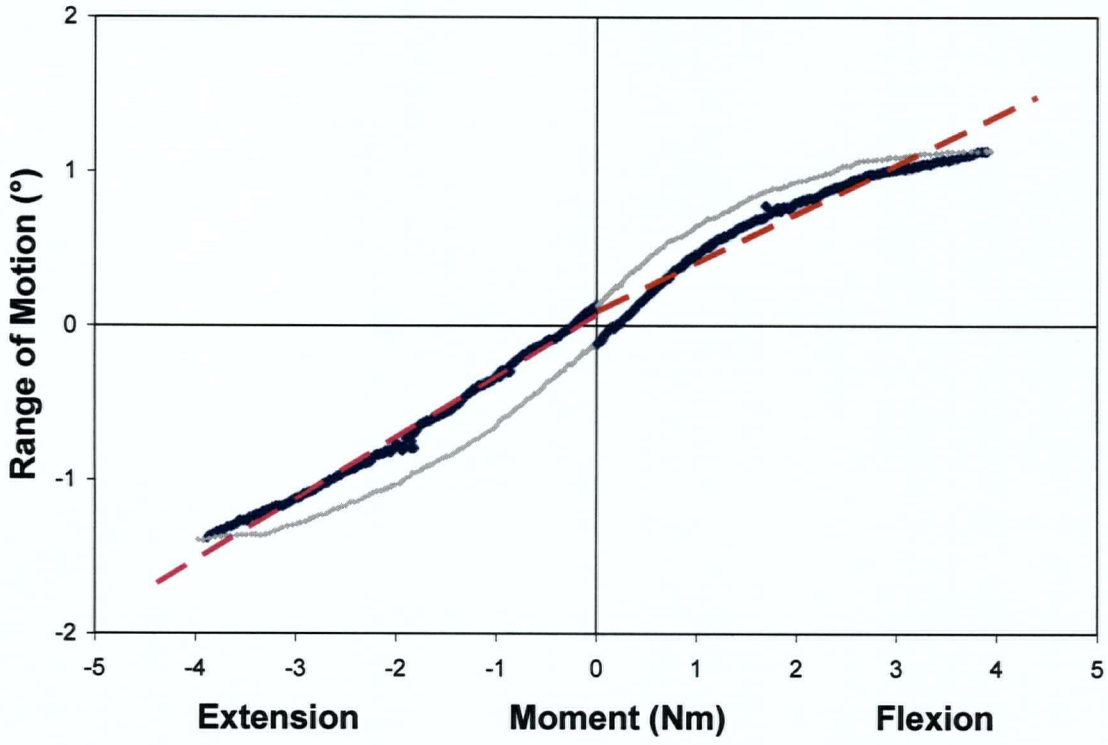


**Figure 7.5.** *Flexibility was calculated as the slope of the motion (Deg) versus moment (Nm) curve during the loading portion of the curve in each direction (dark solid lines), using all points on that portion of the curve. Dashed line represents the slope.*

## RESULTS

T6-7 PA stiffness ranged from 0.25 to 2.02 kN/Deg (mean 0.99, SD 0.70). Mean, range and SD for flexion and extension ROM at T5-6, T6-7 and T7-8 are presented in Table 7.1. The mean, range, and SD flexibility for extension, flexion, axial rotation, and lateral bending of T5-6, T6-7, and T7-8 (average of all three intervertebral levels) is presented in Table 7.2. There was a strong significant inverse relationship between stiffness during cyclic PA loading of T6 and flexion or extension ROM of T6 relative to T7 [$r = -0.88$, $p < .01$, extension; $r = -0.81$, $p = 0.01$, flexion]. The relationship between T6-7 PA stiffness and T6-7 NZ motion in flexion/extension was not statistically significant ($r = -0.60$, $p = 0.11$). There was a strong statistically significant relationship between T6-7 PA stiffness and T6-7 flexibility (Deg/Nm) in all directions (extension, flexion, left and right axial rotation, left and right lateral bending). There was no relationship between T6-7 PA stiffness and flexion/extension ROM or three-dimensional flexibility at T5-6 or T7-8 (Table 7.3). One specimen's right lateral bending flexibility data were excluded due to contact with dental cement during the test.

PA stiffness (N/mm) using the motion of the indenter at the surface of the spinous process (mm), ranged from 91-245 N/mm (mean= 148, SD= 42).

**Table 7.1.** *Mean, range and standard deviation range of motion (Deg) in flexion and extension at T5-T6, T6-T7 and T7-T8.*

| | Flexion | | | Extension | | |
|---|---|---|---|---|---|---|
| | T5-T6 | T6-T7 | T7-T8 | T5-T6 | T6-T7 | T7-T8 |
| **Mean** | 0.69 | 1.25 | 0.83 | 0.80 | 1.31 | 0.99 |
| **Range** | 0.02-2.06 | 0.17-2.54 | 0.17-2.31 | 0.07-1.92 | 0.15-2.24 | 0.28-2.52 |
| **Standard Deviation** | 0.66 | 0.87 | 0.66 | 0.73 | 0.81 | 0.74 |

**Table 7.2.** *Mean, range and standard deviation (average of T5-6, T6-7 and T7-8) flexibility (Deg/Nm) for extension, flexion, rotation and lateral bending in T5-T8 cadaveric spine segments. Rotation and lateral bending include motion to the left and right.*

| T5-T8 Flexibility (Deg/Nm) | Extension | Flexion | Axial Rotation | Lateral Bending |
|---|---|---|---|---|
| **Mean** | 0.31 | 0.27 | 0.62 | 0.43 |
| **Range** | 0.00-0.88 | 0.01-0.67 | 0.04-1.58 | 0.03-1.02 |
| **Standard Deviation** | 0.25 | 0.18 | 0.43 | 0.26 |

**Table 7.3.** *Pearson correlation coefficients for T5-T6, T6-T7 and T7-T8 extension and flexion range of motion (Deg), and flexibility (Deg/Nm) in three dimensions [extension, flexion, right and left axial rotation (Rotn.), right and left lateral bending (Lat.Bend)] with posteroanterior (PA) stiffness (kN/Deg).* ^ *: n = 7* * *= significant at p<0.05*

| ***Range of Motion (Deg)*** | ***Stiffness (kN/Deg)*** |
|---|---|
| T5-6 Extension | r= −0.45, p= 0.26 |
| T5-6 Flexion | r= −0.48, p= 0.22 |
| T6-7 Extension | **r= −0.88*, p< 0.01** |
| T6-7 Flexion | **r= −0.81*, p= 0.01** |
| T7-8 Extension | r= −0.38, p= 0.35 |
| T7-8 Flexion | r= −0.32, p= 0.43 |
| ***Flexibility (Deg/Nm)*** | – |
| T5-6 Extension | r= −0.65, p= 0.08 |
| T5-6 Flexion | r= −0.62, p= 0.10 |
| T5-6 Right Lat. Bend | r= −0.17, p= 0.69 |
| T5-6 Left Lat. Bend | r= −0.32, p= 0.44 |
| T5-6 Right Axial Rotn. | r= −0.31, p=0.45 |
| T5-6 Left Axial Rotn. | r= −0.26, p=0.53 |
| T6-7 Extension | **r= −0.90*, p< 0.01** |
| T6-7 Flexion | **r= −0.87*, p< 0.01** |
| T6-7 Right Lat. Bend | **r= −0.78*, p= 0.02** |
| T6-7 Left Lat. Bend | **r= −0.82*, p= 0.01** |
| T6-7 Right Axial Rotn. , | **r= −0.82*, p= 0.01** |
| T6-7 Left Axial Rotn. | **r= −0.79*, p= 0.02** |
| T7-8 Extension | r= −0.43, p= 0.28 |
| T7-8 Flexion | r= −0.53, p=0.18 |
| T7-8 Right Lat. Bend | r= −0.68^, p= 0.09 |
| T7-8 Left Lat. Bend | r= −0.21, p= 0.62 |
| T7-8 Right Axial Rotn. | r= −0.51, p= 0.20 |
| T7-8 Left Axial Rotn. | r= 0.04, p= 0.92 |

## DISCUSSION

My findings suggest that stiffness during simulated central cyclic PA mobilization in the cadaveric midthoracic spine is inversely correlated with flexion and extension ROM (Deg) at that spinal level. Further, I found that T6-7 PA stiffness is a strong predictor of flexibility (Deg/Nm) in all six directions (flexion, extension, left and right lateral bending, left and right axial rotation) at T6-7 (Table 7.3). The significant results at T6-7 only may be related to T5-6 and T7-8 intervertebral motion being somewhat limited by my methodology, which may account for the lower mean ROM at these levels compared with T6-7 (Table 7.1). Intervertebral motion is also influenced by differences in intervertebral disc height [18] and morphology and orientation of the facet joints from one spinal level to the next . [19] In Chapter Four I found that the mobilized thoracic vertebra moves into extension under a PA load (Figure 7.3). This may explain the slightly stronger relationship between T6-7 extension ROM (Deg) and flexibility (Deg/Nm) with T6-7 PA stiffness (kN/Deg), as compared with flexion ROM or flexibility.

Many clinicians and scientists consider NZ motion to be analogous to joint laxity. [20,21] My results suggest that PA stiffness is not a good predictor of NZ motion thus clinicians should likely use other techiniques, [22] rather than PA mobilization, if the aim is to assess laxity in the midthoracic spine.

In this study I measured PA stiffness, intervertebral ROM, NZ motion and three-dimensional flexibility in cadaveric midthoracic spine segments consisting of four vertebrae. A previous study [23] measured flexibility of the cadaveric thoracic spine using

a two-vertebra construct that included intervening ligaments and the head and neck of articulating ribs. Despite these methodological differences, our extension and lateral bending results are similar except that I found greater flexibility in axial rotation and less in flexion. The greater flexibility in axial rotation may be related to my having removed the ribs [24] or anatomical differences between the thoracic regions tested in the two studies. Note that I studied 24 motion segments from the *midthoracic* region of eight thoracic spines, while Panjabi et al. tested 11 motion segments, one for *each thoracic level* from five thoracic spines. [23]

Three previous studies have measured PA spinal stiffness in the thoracic spine by inferring translation from the motion of an indenter at the skin-surface [11-13] and reported T7 mean PA stiffness measures of 10.7 N/mm [11] and 12.5 N/mm [12]; T4 PA stiffness of 13.6 N/mm. [13] For comparison only, I also determined PA stiffness using motion of the indenter (mm) at the surface of the spinous process and the PA force data. I reported much higher stiffness than these previous studies (mean 148 N/mm) using this method. This can be attributed to methodological differences between the studies. I studied midthoracic cadaveric spine segments consisting of four vertebrae and their intervening discs and ligaments. With a longer specimen (i.e. more than four vertebrae) I would expect lower stiffness and increased flexibility. Further, measuring PA stiffness by inferring vertebral translation from the motion of an indenter, which is separated from the bone by 3 mm thick foam, similar to the skin and soft tissues in vivo studies, is likely to affect the accuracy of the stiffness measure. Thus I would expect PA stiffness, in vivo, to be reduced due to the length of the spine (compared to my study) and increased by the rib

cage. Another important difference between the studies, which might explain some of the variability in PA stiffness measures, is that my specimens were much older than the individuals included in previous investigations (mean age 28.6 years, [11] mean age 26.6 years, [12] age range 20-42 years [13]).

There are a number of strengths of this study. First, I measured vertebral motion using bone pins, whereas previous studies calculated stiffness based on vertebral translations inferred from the motion of an indenter at the skin surface. [11-13] Further, the accuracy of the motion measurement system used in my study exceeds 0.1°, I applied cyclic PA mobilization with loads similar to those applied in vivo, [2,25,26] and at a frequency of 0.5Hz, consistent with clinical guidelines. [6]

I used a moment maximum of 4 Nm to avoid damage to the specimen during testing. Panjabi et al. [23] used a moment maximum of 5 Nm but they also tested the lower thoracic spine. Studies of the cervical and lumbar (and thoracolumbar) spine have typically used maximum moments between 1.5-2.0 Nm and 7.5-10.0 Nm respectively, so the 4.0 Nm used in my study falls in between these values and is similar to a previous study in the thoracic spine. [23]

**Clinical Implications**

These novel data provide biomechanical support for a technique that clinicians use in daily practice to assess spinal joint motion. [4-6,10-12,25,27-33] I found that stiffness under a cyclic PA load, simulating the PA mobilization technique in cadaveric midthoracic spine

segments of older adults, reflects spinal ROM and flexibility at the particular level at which it is applied. These data support the clinical practice of PA mobilization in the assessment of patients with spine pain, if the goal is to gain specific information about intervertebral motion.

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# Chapter Eight

## *General Discussion, Summary and Conclusions*

## GENERAL DISCUSSION

In this final chapter I discuss and summarise the findings of the six studies that comprise this thesis. I discuss the results of my studies on (1) the effectiveness of manual therapy for spinal pain, (2) physiotherapists' perceptions and practice patterns with respect to the management of individuals with osteoporosis, (3) the safety of manual therapy in older spines with low bone density, (4) the accuracy of DXA in the thoracic spine and differences between three methods of estimating vBMD, (5) μCT measures of regional bone volume ratio and trabecular microarchitecture as predictors of vertebral failure under a PA load, and (6) PA stiffness as a predictor of intervertebral motion. For each study, I also discuss limitations and recommend future studies that would be a logical extension of my research to date. I close this chapter with a summary, conclusions and my contributions to the field.

### 8.1 Evidence for the Effectiveness of Manual Therapy for Spinal Pain

My systematic review (Chapter Two) suggested that there were clinically relevant differences between studies reporting positive results of manual therapy and those reporting no significant difference over other conservative treatments. In particular, key aspects of the manual therapy intervention had received little research attention to date. My analysis indicated that: (1) manual therapy techniques, rather than joint manipulation alone, appeared to yield better results; (2) interventions in which the treatment protocol reflected clinical practice appear to be consistently more successful (i.e. protocols where a number of manual therapy techniques were used or manual therapy was combined with

another mode of treatment; (3) interventions based on 'best practice' guidelines were successful; (4) physiotherapy including manual therapy at a dose of 30-45 minutes per session for 4-8 weeks was effective in reducing pain and improving function. My conclusions differ from previous systematic reviews and meta-analyses that included older studies and failed to critically assess the elements of the manual therapy intervention itself. [1,2] I limited my review to a recent six year period to reflect the dramatic changes in clinical practice, and thus clinical trials, due to research published in the late 1990s.

To extend this research, a future review might include all clinical trials published on the topic, but also include a further subanalysis within the years I studied to scrutinize the impact of changes in clinical practice and an increase in relevant physiotherapy research. However, at present there may be insufficient data to warrant such a study. Also, this type of review will likely be confounded by improvements in methodological factors over time.

A limitation of my review is the lack of statistical analysis. Further information may be gained by conducting a meta-analysis, but the large variability of the manual therapy interventions used in clinical trials (i.e. type, dose), as identified in my review, should be taken into consideration.

Future research should seek to better identify those patients who have a high likelihood of improving with manual therapy treatment. For example, Flynn et al [3] identified five

variables to form a clinical prediction rule for patients with low back pain who are likely to respond favorably to a specific manipulative technique.

Manual therapy is not only used in the treatment of low back and neck pain. Pilot studies have been conducted in individuals with thoracic pain [4] and cervico-brachial pain syndrome. [5] The next step is for researchers to conduct well designed RCTs to determine the effectiveness of manual therapy for pain and disability in individuals with these conditions, or patients with pain in other regions or with different diagnoses.

To date, clinical trials of manual therapy have been conducted in adults. Future studies should consider investigating the effectiveness of manual therapy in other age groups (i.e. teenagers, older adults) and special populations, such as those with osteoporosis.

### 8.2 Physiotherapy and Osteoporosis: Clinicians' Perceptions and Practice Behaviors

I found that physiotherapists reported using evidence-based therapies when treating individuals with osteoporosis. A number also reported using manual therapy in this population. Physiotherapists reported concern about fracture as a complication of manual therapy treatment, in particular vertebral fracture and rib fracture.

The brief questionnaire used in this study provides novel information on clinical practice but also has limitations. I did not measure how often manual therapy was used, nor did I provide an opportunity for therapists to clarify or expand on their concerns. I surveyed

physiotherapists working in all areas of practice (public and private workplaces) with or without any specific postgraduate qualifications. A survey of only those with postgraduate qualifications in manual therapy may provide different data and insights. It is not unreasonable to speculate that physiotherapists may also have concerns about other modes of treatment in those with osteoporosis, such as exercise prescription. A further survey would need to be administered to investigate this question. As my research focused on manual therapy, I asked the specific question about the use of manual therapy.

In the opening question I stated that the individual had osteoporosis, but did not state what the individual was being treated for (i.e. osteoporosis or an unrelated condition), or whether treatment was being given in an area where osteoporotic fractures commonly occur. While this may have been helpful for the participants, I felt that this additional information could have alerted therapists that I was interested in their knowledge of osteoporosis (i.e. it is a systemic condition mainly affecting trabecular bone) and common sites of osteoporotic fracture (Appendix I, Question 3).

Using quantitative research alone was a limitation. I met my specific objectives but this small survey justifies further investigation of therapists' beliefs and concerns using qualitative methodology. For example, it is possible that barriers to care exist, such as treatment time, which could limit a clinician's ability to provide optimal care. Specifically, conventional appointment times may be relevant for younger adults attending physiotherapy but may not be adequate for older individuals who present with various comorbidities and/or restricted mobility.

### 8.3 Safety of Posteroanterior Spinal Mobilization

There were five key findings from my study in Chapter Four: (1) vertebral body injury is an unlikely complication of PA mobilization in the midthoracic spine; (2) failure load, in vitro, and applied load, in vivo, were significantly different for most specimens, however the lowest fracture thresholds were around the same force as the upper range of the applied loads; 3) PA failure typically occurs at the spinous process; (4) plain radiography and CT scan have poor sensitivity for that spinous process fracture; and (5) vertebral kinematics in the midthoracic spine during PA mobilization differ from previous reports in the lumbar spine.

The limitations of this study relate to the spine segment model, which is devoid of muscle contraction, the rib cage, intraabdominal organs and intraabdominal pressure. All of these are likely to increase spinal stiffness in vivo. Nevertheless, my purpose was to investigate the failure load and failure site of midthoracic vertebrae under a PA load and there is no evidence to suggest that the associated skeleton and organs would increase strength of the spinous process, in vivo. Further, I validated my spine segment kinematics with an intact cadaver and found both the magnitude and direction of vertebral motion to be similar. I could not find any reports of spinous process fracture associated with mobilization and my data suggest that if this pathology were to exist then traditional methods of fracture diagnosis, such as plain radiography and CT scan, would have poor sensitivity to detect it. The inability of two radiological methods to detect anatomically proven fractures suggests that a trial of more intensive investigation (bone

scan, MRI) may be warranted in patients who present with a clinical history that strongly suggests vertebral fractures but in whom x-ray is normal.

Bone is a viscoelastic material and thus its biomechanical behavior varies with the rate of loading. Bone is stiffer and is able to sustain a higher load to failure when loads are applied at a higher rate. However, at very high strain rates (>1 per second) [6] bone becomes more brittle, such as in impact trauma. Clinically, the loading rate influences the fracture pattern and the amount of soft tissue damage that occurs. Stored energy is released when a bone fractures. At a low loading rate, such as that used in my study, the energy can dissipate through the formation of a single crack so bone and soft tissues remain relatively intact. This is consistent with the fractures produced in my study. At a high loading rate, as occurs in impact trauma, the greater stored energy cannot dissipate quickly enough through a single crack, and thus a comminuted fracture and extensive soft tissue damage is often the result. [6] I used a loading rate of 2 mm/second. Manual therapy techniques can be applied slowly or more quickly, as with high velocity thrust techniques (manipulation). My aim was to study the PA spinal mobilization technique that can often be applied at a faster rate but it is still slow as compared with manipulation. However, my aim was not only to measure the failure *load* but also to investigate the *site* of failure under a PA load. Due to the short delay in stopping the test once fracture occurred, a faster loading rate would have resulted in further damage between the time of initial failure and the time that the machine was stopped. Thus, my loading rate allowed for simulation of the mobilization technique but also allowed sufficient control of the experiment.

The World Health Organization classification of osteoporosis is based on a history of fragility fractures or DXA based BMD values obtained from the proximal femur and lumbar spine. Thus, it is not appropriate to classify my specimens as being osteoporotic based on their thoracic spine BMD. Also, the WHO classification applies to in vivo scans, which clearly differs from scanning cadaveric specimens. Nevertheless, the lumbar spines of the specimens used in all of my cadaveric studies were also scanned by DXA at UBC. The t-scores for the lumbar vertebrae of these specimens were all below −2.5.

Of note, German researchers found that both in situ and ex situ lumbar AP DXA BMC and BMD were similarly correlated with the failure load of L3. [7] This suggests that DXA scan results from spine segments are unlikely to show significantly different correlations with failure load than scan results from intact cadavers.

I measured the load applied by two experienced physiotherapists, one male and one female, both trained in the same undergraduate and postgraduate programs. The range of applied loads in my study (106-223 N) was smaller than some previous studies (i.e. 60-230 N [8]). Differences in the number of participants, the region studied and the experience and training of the therapists can contribute to variability in applied force.

I used the Tekscan system to measure applied load in the intact cadaver tests. Calibration of the Tekscan unit with a six-axis load cell revealed consistent underestimation of

applied load data (Appendix II). In future, other alternatives to the Tekscan should be considered for such research. For example, Herzog and colleagues used a thin flexible pressure mat to measure applied load. [9] Future studies requiring this type of load measurement may consider comparing the accuracy of such a system with that of the Tekscan system.

The result of my Chapter Four research has implications for physiotherapy practice and training. My results provide an indication of typical loads applied by experienced therapists and the failure load of vertebrae under a PA load and suggests that there is only a small amount of overlap between physiotherapists' applied load and the failure load in the cadaveric specimens. My study provides specific data that could be used to help train physiotherapists so they can be made aware of the loads they are applying. A previous study found that physiotherapists can be trained to apply specific forces. [10] This type of training may improve therapist confidence for the use of manual therapy in individuals with osteoporosis, and increase the safety margin.

The pattern of fracture can provide valuable information about the forces involved in this loading mode. I photographed the failure site after each failure test. A limitation of this method was that the poor resolution in some photos made it difficult to clearly see the whole fracture line. High resolution CT could be used to better assess fracture patterns. High-resolution CT images may help guide researchers on which bone measures (i.e. cortical thickness, which region of the cortex) might be associated with this fracture pattern.

The information gained through this study, specifically the applied load and PA failure load data, could be used to develop accurate mathematical models so that the influence of anatomical variations could be investigated. For example, a common postural fault in individuals with osteoporosis is an excessive midthoracic kyphosis. Modeling a spine with an increased kyphosis, along with structural and material characteristics of the vertebrae, such as the spinous process length, the size of the vertebral body, and the bone mineral density of the vertebra, may provide additional information on the effect of these factors on PA failure load. Such biomechanical findings could then be correlated with clinical measures of kyphosis, to provide a guide to clinicians as to what degree of kyphosis constitutes a major risk for vertebral compression fracture. The analytical process of Receiver Operator Curve development could be used to identify appropriate thresholds for risk, and with that, potential interventions. Interventions could include strength training, spinal orthoses [11] or manual therapy, but each of these would need to be tested in the relevant population.

### 8.4 Accuracy of DXA Scanning of the Thoracic Spine

In Chapter Five I found that lateral or AP BMC of spine segments by DXA was highly correlated with the ash weight of the vertebral body. My research extended the one previous study of DXA accuracy in thoracic vertebrae by evaluating both AP and lateral DXA scans. Also I scanned spine *segments*, as this is often the unit tested in thoracic spine research, rather than the vertebral body itself. Previously published methods of estimating vBMD have never been tested against an ash weight gold standard. I tested

the two previous published methods and I also proposed a new method of calculating vBMD (elliptical cylinder). I found that calculations of vBMD assuming that vertebral body geometry resembles an elliptical cylinder, cube, or cylinder, as may be used in mathematical models, were all highly correlated with vBMD measured by ash weight and CT. However the mean difference was lowest when using the new elliptical cylinder method.

### 8.5 Regional Vertebral Trabecular Bone Morphology

In Chapter Four I reported that bone mineral density of the whole vertebra was not a good predictor of PA failure load, despite its known correlation with axial compressive failure load. [12,13] I then hypothesized that this may be due to BMD being an integrated measure of the entire vertebra, whereas the fractures from PA loading occurred in the spinous process. Thus the purpose of the study reported in Chapter Six was to test whether *regional* trabecular bone morphometry, measured using μCT, could predict failure at this site. I found that bone volume fraction of the base and middle regions of the spinous process predicted failure at those sites. Further, the lower mean trabecular thickness of the spinous process base compared with the lamina may have influenced the site of fracture. Whether a difference in trabecular thickness influences *vertebral body* fracture warrants future consideration. The question of what causes vertebral bodies to fail remains a germane question in the field. As mentioned previously (Chapter Six), it is only recently that μCT scanners have become able to scan whole vertebral bodies.

I measured cortical thickness from two-dimensional images due to limitations of the SkyScan software. Future studies of cortical thickness and its relationship with failure load should consider using a scanner and software which allows for three-dimensional cortical thickness measures. Beyond their interest in my study, these findings provide important evidence for the role of trabecular bone in maintaining structural strength.

### 8.6 Posteroanterior Stiffness as a Predictor of Intervertebral Motion

Although clinical theory has long suggested that manually performed spinal techniques can predict or detect intervertebral motion, this hypothesis has not been previously tested. I found that stiffness during central cyclic PA mobilization in the cadaveric midthoracic spine of older adults was a strong predictor of flexion and extension ROM and three-dimensional flexibility at that spinal level. My findings provide biomechanical support for the inclusion of specific joint mobilization in the assessment of older individuals with back pain.

However, the limitations of this study must also be acknowledged. First, the cadaver specimens were all from older adults, so the generalizability of my findings to younger clinical populations must be considered with caution. Also, my cadaveric study results do not account for muscle contraction, the rib cage, intraabdominal organs and intraabdominal pressure, all of which are likely to increase spinal stiffness, in vivo. [14-17] I did, however, previously validate the cadaveric spine segment kinematics against those of an intact cadaver (Chapter Four) and found both the magnitude and direction of vertebral

motion was similar. Further, the length of the specimen can also influence PA stiffness, but this was kept constant for all specimens and tests. However, use of longer spine segments (i.e. six vertebrae) may provide a better indication of whether PA stiffness at one level can predict ROM and flexibility at adjacent levels.

Although my results suggest that PA stiffness is correlated with intervertebral motion at the spinal level at which the technique is applied, I did not address the extent to which therapists can perceive spinal stiffness. Maher and colleagues investigated therapist inter- and intrarater reliability in measuring PA stiffness. In one study they found therapists had much better ability to judge spring stiffness than the PA stiffness of human spines [18] but another study showed that therapists can accurately judge spinal stiffness using a matching task. [19] Future research might consider whether there is a threshold between degrees of stiffness (mild, moderate, severe) which therapists can detect and other more subtle variations in stiffness that are difficult to perceive with manual testing.

## 8.7 Summary and Conclusions

Summary

1. Interventions based on 'best practice' guidelines or textbooks written by experts appear to be more successful, and physiotherapy including manual therapy at a dose of 30-45 minutes per session, for 4-8 weeks is effective in adult populations with back or neck pain.

2. Many physiotherapists practicing in British Columbia, Canada use evidence based methods (i.e. strength training) when treating individuals with osteoporosis. A large number use manual therapy and most have concerns about its use in individuals with osteoporosis. Physiotherapists are concerned about fracture as a complication of treatment, in particular vertebral fractures. Studies on the safety and effectiveness of manual therapy in this population are needed to guide clinical practice.

3. Although there was a reasonable margin between the vertebral failure load, in vitro, and the applied PA mobilization load, in vivo, for most specimens, the lowest fracture thresholds were around the same force as the upper range of the applied loads. Vertebral body injury is an unlikely complication of PA mobilization in the midthoracic spine. Plain radiography and CT scan had poor sensitivity for the spinous process fractures produced. Kinematic data suggest that the mobilized thoracic vertebra moves into extension as a result of the mobilization.

4. DXA scanning is an appropriate surrogate measure for thoracic spine segment bone mineral measurement. Calculations of vBMD assuming that vertebral body geometry resembles an elliptical cylinder, cube, or cylinder, as may be used in mathematical models, were all highly correlated with vBMD measured by ash weight and CT but the mean difference was lowest when using the novel elliptical cylinder method.

5. BMD measures by DXA did not correlate with failure load of the spinous process. However, further regional investigation using μCT showed that BV/TV of the base and middle regions of the spinous process correlated with failure at those sites. The lower mean Tb.Th of the spinous process compared with the lamina may have influenced the site of fracture.

6. Stiffness under a cyclic PA load in vitro, simulating the PA mobilization technique in the midthoracic spine, reflected spinal ROM and flexibility at the particular level at which it was applied. These data support the clinical practice of specific PA mobilization in the assessment of patients with spine pain, if the goal is to gain specific information about intervertebral motion.

Conclusions

1. Physiotherapy including manual therapy at a dose of 30-45 minutes per session, for 4-8 weeks is effective in adult populations with back or neck pain. There are clinically relevant differences between the manual therapy interventions used in clinical trials that may influence the outcomes.

2. Many physiotherapists in British Columbia, Canada use manual therapy in patients with osteoporosis and most have concerns about its use in this population. Physiotherapists are concerned about fracture as a complication of treatment, in particular vertebral fracture.

3. Vertebral body injury is an unlikely complication of PA mobilization in the midthoracic spine. PA mobilization produces spinous process fractures. Areal BMD of the whole vertebra is not a good predictor of PA failure load, despite its strong correlation with axial compressive failure load in previous studies. The mobilized thoracic vertebra moves into extension as a result of the mobilization.

4. DXA scanning is an appropriate surrogate measure for thoracic spine segment bone mineral measurement. The elliptical cylinder method should be used when calculating vBMD of the vertebral body.

5. Regional BV/TV of the spinous process base and middle regions, the sites of fracture, is strongly correlated with PA failure load. Trabecular thickness differs significantly

between the spinous process and lamina regions, and may have influenced the site of fracture.

6. In midthoracic spine segments, PA stiffness predicts segmental ROM and flexibility at the level at which the PA mobilization is applied.

### 8.8 Contributions

I made the following novel contributions to the field:

1. My systematic review (Chapter Two) identified four factors that differed among the interventions that constituted 'manual therapy' that may explain the conflicting outcomes in clinical trials and previous reviews.

2. My survey of clinicians' perceptions and practice behaviors with respect to the management of individuals with osteoporosis (Chapter Three) is the first study published on this topic. This study provides quantitative data on the most common treatment modes used by physiotherapists in the province of British Columbia, Canada when treating individuals with osteoporosis, including the percentage that are using manual therapy and are concerned about its use in this population. This survey also highlights the type of injuries clinicians are concerned about.

3. My biomechanical study on the safety of PA mobilization in the midthoracic spine (Chapter Four) provides novel data on the safety of manual therapy in older spines with low bone density. The results suggest that some manual therapy techniques may be safe for treating back pain in individuals with low bone density and that vertebral body injury is unlikely with this technique. The imaging techniques used in this study were not sensitive to the fractures produced and bring to the surface the issue of possible false negatives with plain radiography and CT scan when imaging vertebral fractures. My kinematic analysis, both in spine segments and an intact cadaver, provide accurate data on the magnitude and direction of motion during PA mobilization in the midthoracic spine—which has not been previously measured using bone pins.

4. My methodological study on the accuracy of DXA scanning of thoracic spine segments (Chapter Five) will allow researchers to base their interpretation of AP and lateral thoracic DXA scan accuracy on data rather than relying on assumptions based upon lumbar spine experiments. I proposed a new accurate method of calculating vBMD based on the results of quantitative three dimensional anatomical studies which suggest that thoracic vertebral endplate dimensions are best approximated as an ellipse.

5. The results of my regional investigation of vertebral bone volume fraction and trabecular microarchitecture (Chapter Six), using μCT, explain the poor association between PA failure load and BMD by DXA. To my knowledge, this is the first investigation of cadaveric regional bone microarchitecture to include regions outside the vertebral body.

6. My novel data (Chapter Seven) indicate that PA stiffness can predict intervertebral motion. This provides support for a technique that clinicians use in daily practice to assess intervertebral motion in patients with back pain.

## 8.9 REFERENCES

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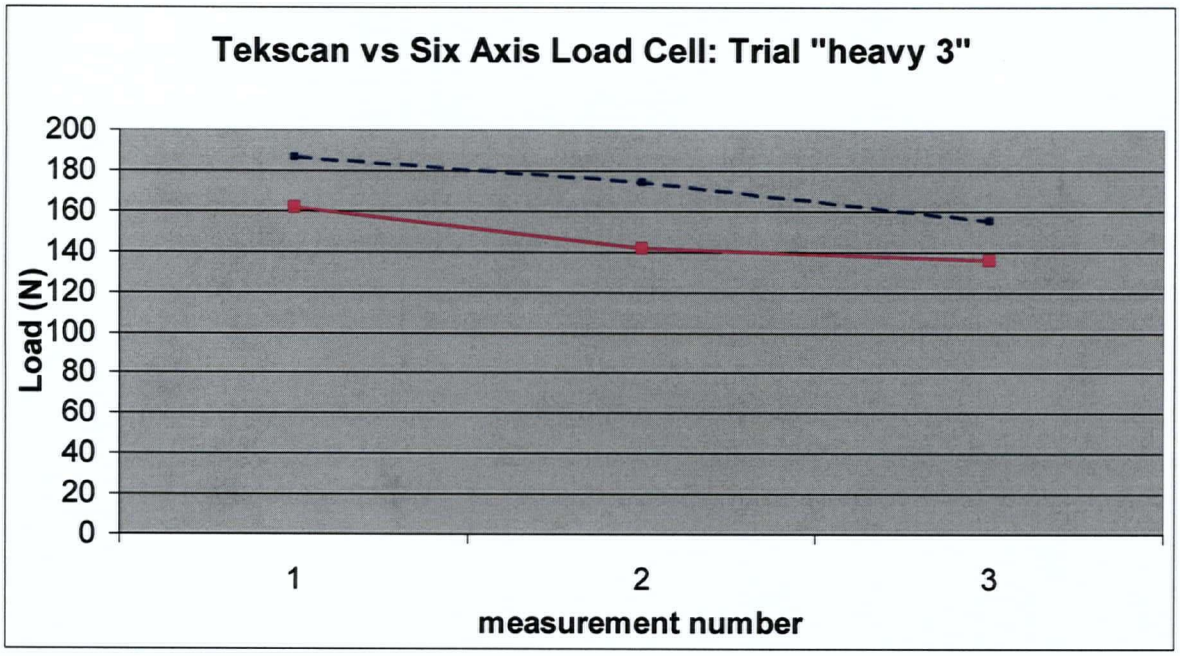
# Appendix I

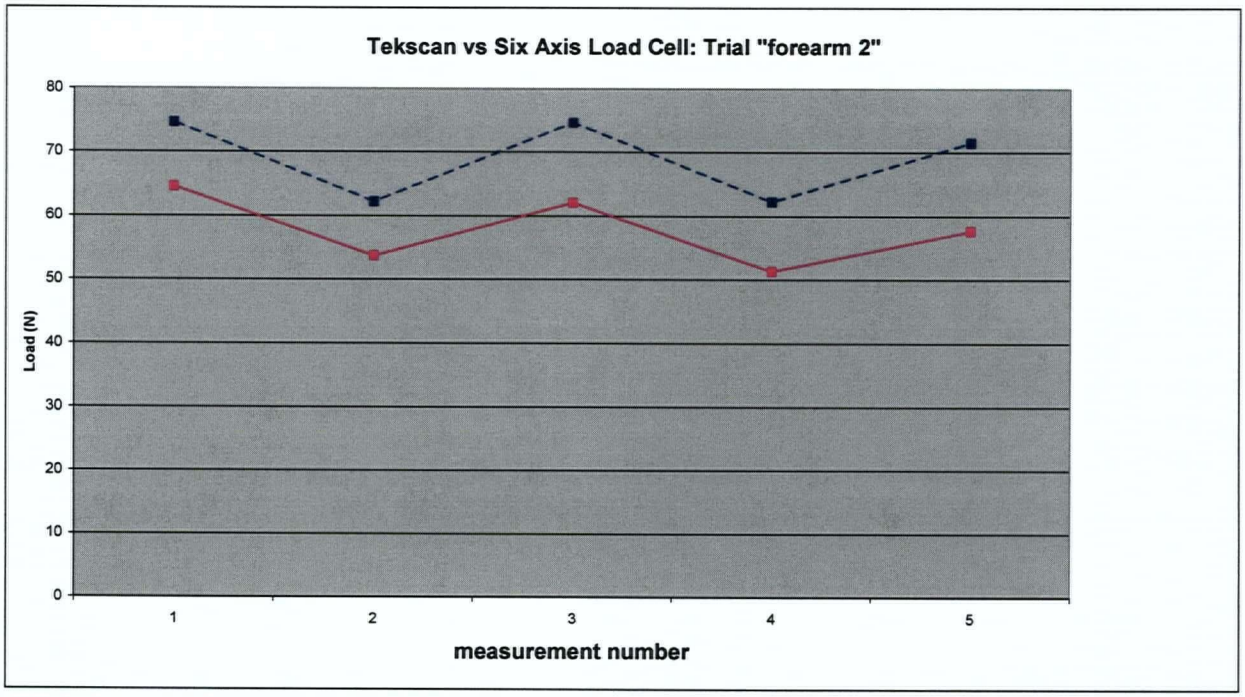
## *Questionnaire and Cover Letter*

# Appendix II

## *Tekscan Calibration with a Six Axis Load Cell*




*Load for three trials (measurement numbers 1-3) during manual loading of a human forearm, as measured by Tekscan and a six axis load cell. Dashed line represents the six axis load cell and the solid line represents Tekscan.*



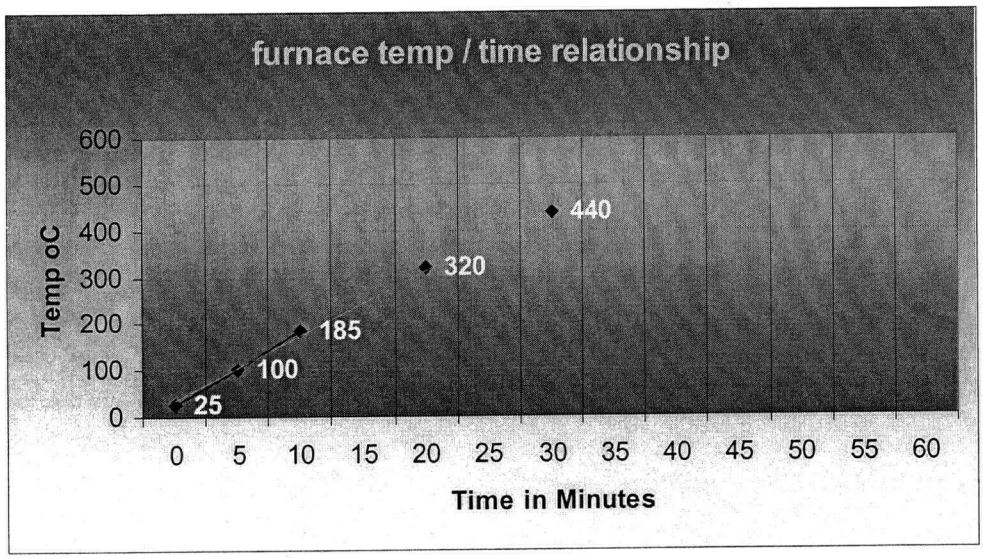

*Load (N) for five trials (measurement numbers 1-5) during manual loading of a human forearm, as measured by Tekscan and a six axis load cell. Dashed line represents the six axis load cell and the solid line represents Tekscan.*

# Appendix III

## *Thermolyne Muffle Furnace: Temperature vs. Time Profile*

Temperature versus time. Profile

Thermolyne muffle furnace in room 148 C




Gilles Galzi
Tuesday, July 23, 2002
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