BONE GEOMETRY AND AQUATIC EXERCISE IN OSTEOPOROTIC WOMEN

Assessment of Bone Geometry in Postmenopausal Women with Osteoporosis of the Spine Before and After a 6 Month Aquatic Exercise Program

by
Alison Bonnyman, B.Sc.P.T.

A Thesis Submitted to the School of Graduate Studies
in Partial Fulfilment of the Requirements for
the Degree Master of Rehabilitation Science

MASTER OF SCIENCE (2011)
(Rehabilitation Science)

McMaster University
Hamilton, Ontario

TITLE: Assessment of Bone Geometry in Women with Osteoporosis Before and After a 6 Month Aquatic Exercise Program

AUTHOR: Alison Bonnyman, B.Sc.P.T. (McMaster University)

SUPERVISOR: Dr N.J. MacIntyre

NUMBER OF PAGES: xvii, 147

CONTRIBUTIONS

The body of this thesis contains two separate papers, each formatted according to the style of the journal targeted for submission for peer review. Although multiple authors appear on each paper, Alison Mary Bonnyman was responsible for all aspects of the study, including the design, analysis and writing of the manuscripts. The co-authors on the papers had varying involvement ranging from securing funding, contributing to the study design, data collection and analysis and manuscript review

.

ABSTRACT

Background: Increased physical activity is associated with better physical and mental well-being. In postmenopausal women, land-based exercise has a modest effect on bone strength which is predominantly reflected in the spatial distribution (geometry) of bone mineral at the skeletal sites targeted by the exercise. However, the risks and benefits of exercise for women with osteoporotic vertebral fracture (VFs) who are at high risk for future fracture are not known. Women with established osteoporosis may prefer exercising in water where compressive loads are reduced. However, it is not known if the reduced compressive loading is detrimental to bone health. Also contributing to this evidence gap is the limited methods available for measuring vertebral bone geometry which may be expected to respond to exercises targeting the trunk. Bone geometry can be measured using computed tomography scans but this involves exposure to a substantial dose of radiation. Semi-automated analyses of dual energy X-ray absorptiometry (DXA) vertebral fracture assessment (VFA) scans provide measures of vertebral height (VH); however, the measurement properties of this outcome have not been established. Measures of mechanical bone strength and volumetric density also provide insight into bone adaptations to exercise. No research has yet investigated the effect of exercising in water on bone geometry in women with osteoporotic VFs.

Purpose: The overall purpose of this thesis was to investigate methods of measuring bone geometry in women with osteoporotic VFs that could be used in a future clinical trial to determine the effect of water exercises on bone in women with VFs. The first objective was to determine the relative and absolute intra-rater reliability of VHs in postmenopausal women with and without VFs. In the second study, protocols for recruitment of postmenopausal women with osteoporotic VFs for a 6 month water exercise intervention and protocols for assessing proposed outcome measures were piloted to determine the recruitment, adherence to the intervention, adherence to the assessment protocol, safety of the intervention and assessment and retention.

Methods: To address the first objective, DXA VFA scans were acquired for 32 women [mean (SD) age 70(7)] and analyzed on 2 occasions, 4 weeks apart, by a single rater using a predetermined protocol. Semi-automated software derived measures of anterior, middle, and posterior VH. Intra-rater relative reliability was estimated using the intraclass correlation coefficient (ICC) with 95% confidence intervals (95% CI). Absolute reliability was estimated using standard error of measurement (SEM) with 95% CI. To address the second objective, women 60 years and older with one or more VF were recruited through two osteoporosis clinics and poster advertisements over two months. Feasibility of recruitment was summarized using the CONSORT flow diagram. Adherence to the six month community-based aquatic exercise program (74 sessions) was evaluated by percentage of sessions attended. Adherence to the assessment protocol was evaluated based on the number of data points lost. The safety was assessed based on the occurrence of adverse events that were documented as major and minor. Retention was assessed as number of participants returning for follow-up.

Results: DXA-based VH intra-rater reliability could be estimated from T9 to L4, with reduced visibility from T4 to T8. The ICCs were > 0.80 and the SEM was less than 1.17 mm for all VH except for the posterior aspect of T9 (ICC = 0.62 (0.15, 0.84), SEM = 0.92 mm). For the feasibility study, 10 participants were recruited in 10 weeks by expanding the inclusion criteria. The average adherence to the intervention was 68%. No measures of VH were obtained for two participants. Movement during acquisition and unanticipated protocol changes resulted in loss of 46% of pQCT scans and 10% of physical performance measurement data. There was one major adverse event (fracture). Retention was 100% at 6 months and 89% at 12 months.

Conclusion: Intra-rater reliability was acceptable for VH between T10 and L4. Further study is needed to assess other measurement properties of DXA-based VH measures and to identify methods for assessing more proximal vertebral levels. Further study is needed to determine feasible protocols for recruitment and assessment of outcome measures. Screening tests for falls risk and protocol for implementing suitable safety precautions are recommended.

DEDICATION

To Steve, Blythe, Clare and James, with whom, I am complete,

To family & friends for believing I could,

ACKNOWLEDGEMENTS:

A heartfelt thanks to:

My supervisor Dr Norma MacIntyre and my committee members Dr Colin Webber and Prof. Paul Stratford;

Dr R Adachi and his staff for assistance with recruitment;

Rita, Cathy, Santokh, Jean, Margaret, Yula, Irena, Nadene and Josephine;

HHS Radiology Research Committee, School of Rehabilitation Science, NSERC and the City of Burlington for funding support;

Leslie Beaumont and the Dept of Nuclear Medicine, HHS, for supporting and performing the image acquisition;

My fellow graduate students for invaluable support, guidance and encouragement.

Table of Contents

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

aBMD – areal bone mineral density

ANOVA – analysis of variance

ATRI – Aquatic Therapy Rehab Institute

BES – isometric back extensor strength

CALA – Canadian Aquatic Leadership Alliance

CCT – clinical controlled trials

CI – confidence interval

coBMD – volumetric cortical bone mineral density

CPG – clinical practice guidelines

CT – computed tomography

CTT – classical test theory

CV – coefficient of variation

DXA- dual energy x-ray absorptiometry

EPOS - European Prospective Osteoporosis Study

HFS – isometric hip flexor strength

HHD – hand held dynamometer

HRQOL – health related quality of life

ICC – intra-class correlation coefficient

ICF – international classification system

KI – kyphotic index

L - lumbar vertebra

L.sp – lumbar spine

LI – lordotic index

MRI – magnetic resonance imaging

NOF – National Osteoporosis Foundation

P_{obs} – proportion of agreement

pQCT – peripheral quantitative computed

PSIS – posterior superior iliac spine

pSSI – polar strength-strain index

QCT – quantitative computed tomography

QOL – quality of life

RAPA – Rapid Assessment of Physical Activity

RCT – randomized controlled trials

RMSCV – root mean square coefficient of variation

RMSSD – root mean square standard deviation

RPE – rate of perceived exertion

SD – standard deviation

SEM – standard error of measure

SR – systematic review

T - thoracic vertebra

THR – total hip replacement

TKR – total knee replacement

trBMD – volumetric trabecular bone mineral density

TUGT – timed up and go test

vBMD – volumetric bone mineral density

VF – vertebral fracture

VFA – vertebral fracture assessment

VH – vertebral height

VHa – anterior vertebral height

VHm – middle vertebral height

VHp – posterior vertebral height

WHO – World Health Organization

CHAPTER 1: INTRODUCTION

1.1. Historical Perspective

Osteoporosis is a systemic skeletal disorder characterized by low bone mass and microarchitectural deterioration of bone tissue resulting in bone fragility and susceptibility to fracture (*1*). Low bone mass is based on the assessment of areal bone mineral density (aBMD, g/cm^2) in the femur or lumbar spine quantified using dual energy X-ray absorptiometry (DXA) and referenced to gender-matched, young, adult normative values. Clinical manifestation of bone fragility is fracture. The Canadian Radiologists Association endorses the use of key indicators to predict the 10 year absolute risk for osteoporotic fracture. In addition to aBMD, age, and gender (factors included in the DXA-based clinical diagnosis), glucocorticoid use and history of fragility fracture over the age of 40 years are considered (*2*). However, the microarchitectural factors in bone fragility have yet to be a clinical component of diagnosis.

One in four women over 50 years of age are diagnosed with primary osteoporosis in North America (*3*). Net bone loss occurs with increasing age and is elevated for women during menopause (*4*). The most common primary osteoporotic fracture sites are the wrist, hip and vertebra (*5*). In women, the lifetime risk of any osteoporotic fracture is approximately 40-50% (*5*). The incidence of vertebral fractures increases linearly with age, such that the incidence doubles every 10 years (*6*). The presence of any fracture elevates the risk two-fold however a vertebral fracture elevates the individual's risk for subsequent vertebral fracture four-fold (*7*). The factors that contribute to this "vertebral fracture cascade" include spinal posture, intervertebral disc integrity, neuromuscular control and the vertebral body size, shape and composition (*8*). Women with one or more vertebral fractures can have lower health related quality of life scores than those without fracture, and physical impairments of hyperkyphosis, back pain and impaired mobility (*9, 10, 11*). Despite the prevalence and elevated risk for fracturing again few studies have targeted this high risk population to evaluate the effectiveness of exercise interventions for reducing the impact on physical function and quality of life (*12, 13, 14*).

Areal BMD explains only a portion of vertebral bone strength (*15*). A more detailed understanding of bone strength includes the spatial orientation, amount of mineralization, damage accumulation and the rate of bone turnover. Mechanical stimulus is a primary determinant in the structural adaptation of bone material (*16*). The vertebral body is composed of a thin cortical shell and an inner matrix of trabecular bone, designed to withstand compressive forces while optimizing material strength in a lightweight structure. Presently fracture risk assessment is based on aBMD measures taken using the dual energy x-ray absorptiometry (DXA), a two-dimensional technology which is limited in the ability to measure bone quality.

Two-dimensional X-ray-based technology such as DXA is dependent on bone size and does not discriminate trabecular bone from the cortical bone. The imaging technology of peripheral quantitative computed tomography (pQCT) provides volumetric measures of trabecular and cortical bone properties separately at appendicular sites in the skeleton at a low radiation dose. Findings at the peripheral sites assessed using pQCT are correlated with aBMD measures at the femur and lumbar spine in the determination of fracture risk *(17)*. This technology has been used for research purposes in the evaluation of fracture risk in postmenopausal women (*17*). However, three dimensional assessment of the axial skeleton is limited by relatively high costs (magnetic resonance imaging) or high radiation dose (computed tomography). DXA-based vertebral fracture assessment (VFA) measures vertebral height (VH), at the anterior, middle and posterior aspects, mm, and provides information which is used to classify the severity and type of vertebral deformity (*18*). This two-dimensional measure of vertebral shape has been investigated in secondary analysis of data from a randomized controlled trial (RCT) investigating the effect of a home exercise program in postmenopausal women over 60 years of age with established osteoporosis of the spine (*19*). The rate of loss in VHs was slower in the group of women who participated in the exercise program than in the control group *(19)*. This was the only study to date which used VH as an outcome measure and further investigation into the measurement properties is needed. Given the limitations in obtaining 3-D measures of the spine, extending the measures acquired using 2-D technology or using a combination of 2-D and 3-D technologies may provide more insight into bone properties that contribute to bone strength.

Most often, the assessment of bone adaptations in response to exercise has been limited to the measure of aBMD at the femur and lumbar spine. The most recent systematic review of RCTs investigating the effect of exercise on femur and lumbar spine aBMD in postmenopausal women suggests a small but statistically significant effect (*20*). More recently, the pQCT has been used to measure bone properties in the radius and tibia in response to exercise interventions. Hamilton *et al* (2009), synthesized the findings from RCTs investigating the effects of exercise on bone geometry, measured using pQCT, in postmenopausal women and reported a modest, site-specific effect predominantly in the cortical bone (*21*). The pQCT measures, in combination with DXA measures, enhance the ability to assess changes in bone strength in response to exercise in postmenopausal women.

Land-based exercise studies have demonstrated that exercise programs of varying length and design improve balance, increase muscle strength and reduce the incidence of falls over a one to 10 year follow-up in older women with osteoporosis compared with control groups (*10, 22-24*). Four studies have investigated the effect of exercising in water for postmenopausal women and have reported improved balance, strength and quality of life compared to controls

(*25-28*). One aquatic exercise studied women diagnosed with osteoporosis (*25)* and two others studied women with osteopenia *(26, 28*). Two of the aquatic exercise studies included bone outcomes reporting aBMD at the hip and spine for a group of healthy *(27)* and osteopenic *(28)* postmenopausal women and the evidence is inconclusive. At present, the reduced weight bearing and concentric muscle contractions associated with aquatic exercise are perceived as a limitation for optimizing bone strength. It is known that bone mechanical strength is maximized by loading the target bone with repeated high peak forces and by a varied strain distribution (*29*). During movement in water, regional muscle stress and strain on the spine and upper extremities are multiplanar, engaging the trunk musculature in a reduced load environment which minimizes the negative forces associated with bending and twisting. There are no studies that have investigated adaptations in bone geometry in response to aquatic exercises in postmenopausal women with established osteoporosis.

1.2. Thesis Objectives

The assessment of bone geometry contributes to the understanding of mechanical bone strength and adaptation to exercise. Exercise recommendations are not well evidenced in women with osteoporotic vertebral fractures. The water environment can provide reduced spinal compression while strengthening muscles yet the reduced weight-bearing environment has been considered a limitation to bone response. The overall objective of this thesis was to examine methods of evaluating bone properties using DXA and pQCT technologies which may be useful to investigate the effect of aquatic exercise on bone geometry in postmenopausal women with osteoporosis of the spine and at high risk to fracture. This was achieved through the completion of two research studies. The specific objective of the first study was to estimate the intra-rater reliability of vertebral height measures of the anterior, middle and posterior aspects for each level from T4 to L4, using the DXA VFA in women 60 years of age or older. The specific objectives of the second study were to assess the feasibility of:

(i) recruitment of women over 60 years of age with osteoporosis and at high risk-to-fracture,
(ii) adherence of participants to a six month aquatic exercise intervention,
(iii) adherence to the protocol assessing body structure, body function and activity outcome measures
(iv) safety of the exercise intervention and assessment protocols
(v) retention of participants over a 12 month study period.

1.3. Organization of the Thesis

The relevant background knowledge regarding osteoporosis, exercise and bone imaging is presented in Chapter 2. Chapter 3 describes the intra-rater reliability study of the DXA-based VH measures and is prepared for submission to the Journal of Clinical Densitometry. Chapter 4 describes the feasibility study to address objectives required as a first step in the design of an RCT to investigate the effect of a six month aquatic exercise program with 12 month follow-up on bone properties and physical performance. The feasibility study is prepared for submission to the open access journal ISRN Rehabilitation. Chapter 5 is a discussion of the thesis findings as a whole and recommendations for future directions.

References

1. World Health Organization (WHO) Study Group. 1994 Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. *WHO Technical Report Series 843*.

2. Siminoski K, Leslie WD, Frame H et al. 2007 Recommendations for bone mineral density reporting in Canada: A shift to absolute fracture risk assessment. *J Clin Densitom* 10:120-123.

3. Hanley DA, Josse RG.1996 Prevention and management of osteoporosis: consensus statements from the Scientific Advisory Board of the Osteoporosis Society of Canada: 1.Introduction. *CMAJ* 155:921-3.

4. Samelson EJ, Hannan MT. 2006 Epidemiology of osteoporosis *Curr Rheumatol Rep* 8:76-83.

5. Johnell O, Kanis J. 2005 Epidemiology of osteoporotic fractures. *Osteoporos Int* 16:S3-S7.

6. Roy DK, O'Neill DW, Finn JD et al. 2003 Determinants of incident vertebral fracture in men and women: results from the European prospective osteoporosis study (EPOS). *Osteoporos Int* 14:19-26.

7. Klotzbuecher CM, Ross PD, Landsman PB et al. 2000 Patients with prior fractures have an increased risk of future fractures: a summary of the literature and statistical synthesis. *J Bone Miner Res* 15:721–739.

8. Christiansen BA, Bouxsein ML. 2010 Biomechanics of vertebral fractures and the vertebral fracture cascade. *Curr Osteoporos Rep* 8:198-204.

9. Salaffi F, Cimmino MA, Malavolta N et al. 2007The burden of prevalent fractures on health-related quality of life in postmenopausal women with osteoporosis: The IMOF study. *J Rheumatol* 34:1551-1560.

10. Madureira MM, Takayama L, Gallinaro AL et al. 2007 Balance training program is highly effective in improving functional status and reducing the risk of falls in elderly women with osteoporosis: a randomized controlled trial. *Osteoporos Int* 18:419-425

11. Silverman SL, Piziak VK, Chen P et al. 2005 Relationship of health related quality of life to prevalent and new or worsening back pain in postmenopausal women with osteoporosis *J Rheumatol* 32:2405-9.

12. Papaioannou A, Adachi JD, Winegard K et al. 2003 Efficacy of home-based exercise for improving quality of life among elderly women with symptomatic osteoporosis-related vertebral fractures. *Osteoporos Int* 14:677-682.

13. Gold DT, Shipp DM, Pieper CF et al. 2004 Group treatment improves trunk strength and psychological status in older women with vertebral fractures: Results of a randomized, clinical trial. *J Am Geriatr Soc* 52:1471-1478.

14. Bergland A, Thorsen H, Karesen R. 2011 Effect of exercise on mobility, balance, and health-related quality of lie in osteoporotic women with a history of vertebral fracture: a randomized, controlled trial. *Osteoporos Int* 22:1863-1871.

15. Delmas PD, Seeman, E. 2004 Changes in bone mineral density explain little of the reduction in vertebral or nonvertebral fracture risk with anti-resorptive therapy. *Bone* 34:599-604.

16. Lanyon LE. 1987. Functional strain in bone tissue as an object, and controlling stimulus for adaptive bone remodelling. *J Biomech* 20:1083-1093.

17. Melton III LJ, Christen D, Riggs BL et al. 2010. Assessing forearm fracture risk in postmenopausal women. *Osteoporos Int* 21:1161-1169.

18. Fuerst T, Wu C, Genant HK et al. 2009 Evaluation of vertebral fracture assessment by dual X-ray absorptiometry in a multicenter setting. *Osteoporos Int* 20:1199-1205.

19. Webber CE, Papaioannou A, Winegard KJ et al. 2003 A 6-mo home-based exercise program may slow vertebral height loss. *J Clin Densitom* 6:391-400.

20. Howe TE, Shea B, Dawson LJ et al. 2011 Exercise for preventing and treating osteoporosis in postmenopausal women. *Cochrane Database Syst Rev* 7. Art. No.: CD000333.

21. Hamilton CJ, Swan VJD, Jamal SA. 2009 The effects of exercise and physical activity participation on bone mass and geometry in postmenopausal women: a systematic review of pQCT studies. *Osteoporos Int* 8:92-95.

22. Carter ND, Khan KM, Petit MA et al. 2001 Results of a 10 week community based strength and balance training programme to reduce fall risk factors: a randomised controlled trial in 65-75 year old women with osteoporosis. *Br J Sports Med* 35:348-351.

23. Sinaki M, Itoi E, Wahner HW et al. 2002 Stronger back muscles reduce the incidence of vertebral fractures: a prospective 10 year follow-up of postmenopausal women. *Bone* 30:836-841.

24. Nelson ME, Fiatarone MA, Morganti CM et al. 1994Effects of High-Intensity Strength Training on Multiple Risk Factors for Osteoporotic Fractures: A Randomized Controlled Trial *JAMA* 272:1909-1914.

25. Arnold CM, Busch AJ, Schachter CL et al. 2008 A randomized clinical trial of aquatic versus land exercise to improve balance, function and quality of life in older women with osteoporosis. *Physiother Can* 60:296-306.

26. Devereux K, Robertson D, Briffa NK. 2005 Effects of a water-based program on women 65 years and over: A randomized controlled trial. *Aust J Physiother* 51:102-108.

27. Rotstein A, Harush M, Vaisman N. 2008 The effect of a water exercise program on bone density of postmenopausal women. *J Sports Med Phys Fitness* 48:352-359.

28. Bravo G, Gauthier P, Roy PM et al. 1997 A weight-bearing, water-based exercise program for osteopenic women: its impact on bone, functional fitness and well-being. *Arch Phys Med Rehabil* 78:1375-1380.

29. Jiang Y, Zhao J, Rosen C et al. 1999 Perspectives on bone mechanical properties and adaptive response to mechanical challenge. *J Clin Densitom* 2:423-433.

CHAPTER 2: LITERATURE REVIEW

2.1. Epidemiology of Osteoporosis and Vertebral Fracture

In Canada, one in four postmenopausal women will be diagnosed with osteoporosis (*1*). Osteoporosis is a systemic skeletal disorder characterized by compromised bone strength predisposing a person to increased risk of fracture; bone strength reflects the integration of two main features: bone density and bone quality (*2*). Areal bone mineral density (aBMD) is the amount of bone mineral per area of bone tissue (g/cm^2). The WHO study group, 1994, defined osteoporosis based on the T-score which is computed by comparing the individual's aBMD with the mean aBMD for young adults of the same gender and race (*3*). This T-score is the number of standard deviations (SD) from the matched young adult mean such that osteoporosis is defined as a T-score < -2.5 SD. The WHO classification of 'established' osteoporosis includes a documented fragility fracture as well as a T-score below -2.5 SD (*3*). Clinical practice guidelines (CPG) for diagnosis and management of osteoporosis in Canada categorize an individual's absolute 10 year risk-to-fracture based on age, gender, fracture history, parental fracture history, use of glucocorticoids and aBMD at the femur or lumbar spine sites (*5*).This tool stratifies the 10 year absolute fracture risk as low (<10%), moderate (10-20%) or high (>20%). The incident of one fracture or use of glucocorticoids elevates one's risk to fracture by one stratification level (low to moderate or moderate to high) regardless of T-score. The most common sites of fracture are at the wrist, hip and spine (*6*). Osteoporotic fracture at the wrist and hip typically occur as a result of a low impact fall, however, vertebral fractures (VFs) occur in response to a low strain producing a compressive spinal load sufficient to compromise the strength of the vertebral body. VFs are the most common osteoporotic fracture occurring in 30% of women over 50 years of age (*7*). The presence of a VF elevates that individual's risk for a subsequent fracture four-fold (*8*). The National Osteoporosis Foundation reported 700,000 VFs occur each year in the USA (*2*). Diagnosis requires a spinal X-ray and analysis of vertebral morphometry to classify the grade of fracture as normal, mild, moderate or severe, based on height ratios (*9*). The severity of the fracture influences the therapeutic intervention. Bone quality is not yet addressed in the clinical diagnosis of osteoporosis or fracture risk assessment as the measurement of bone turnover rate, mineralization, accumulated damage and architecture are not yet clinically accessible. However, effective management of osteoporosis has shifted from a focus on aBMD to the avoidance of fragility fractures and prevention of falls (*10*). Management of osteoporosis must include accurate identification of an individual's fracture risk as related to bone strength and factors related to the complexity of fracture avoidance.

Bone is composed of organic and inorganic tissue, in a constant state of remodeling in response to physiology, endocrinology and mechanobiology. The vertebral body has a thin cortical shell encasing a trabecular matrix. Cortical bone is compact bone tissue, highly structured and mineralized. Trabecular bone is a more porous structure, designed to optimize bone strength while minimizing weight. Peak bone mass in the lumbar spine is accrued between the ages of 20 and 29 years (*11*). Age-related bone loss is expected such that 6% of total lifetime cortical bone loss and 37% of total lifetime trabecular bone loss is projected for women by 50 years of age (*12*). In the ten years after menopause women experience a rapid loss of bone mass due to changes in estrogen levels. The estrogen depletion increases the resorption of bone, particularly in trabecular bone as it is more sensitive than cortical bone to hormonal influences (*13*). The result is less mineralization and lower bone mineral density. In anti-resorptive therapy trials investigating VF risk, changes in aBMD did not explain the changes in fracture risk such that the reduced resorption rate increased the mineralization, elevating aBMD, but this in itself was not enough to reduce the incidence of fracture (*14*). Bone strength also depends on the spatial arrangement of the bone material which functions to resist specific loading directions. In the vertebral body, the trabeculae are primarily oriented vertically to resist compressive forces and despite age-related bone loss it has been shown that the vertical struts are maintained, even thickened, while the horizontal struts are reduced (*15*). The bone spatial adaptation has been demonstrated in computer modeling which has shown that the number of vertical trabeculae resorbed critically reduces the vertebral bone strength five times more than the same amount of mineral loss through thinning of all trabeculae (*16*). Study findings suggest that in women with a VF even the healthy vertebrae were more vulnerable to fracture due to an increased wedging of each vertebral body (*17*). Studies of age-related morphometric decline have demonstrated vertebral height decline in postmenopausal women from 0.5 mm/year to 1.1 mm/year (*18, 19*). Vertebral body composition as well as structure, on a micro and macro level, contributes to bone strength and defects may lead to increased fracture risk.

There are other factors influencing VF risk. The complexities of events that lead to a VF are not well defined. Mechanical loads on the vertebrae are influenced by body biomechanics, the individual's height and weight, muscle forces, spinal curvature, intervertebral disc integrity and neuromuscular control (*11*).Spinal hyper-kyphosis has been correlated with a decrease in balance and agility (*20*) and an increased VF incidence (*21*) affecting the skeletal integrity and neuromuscular control. Paraspinal muscle activity in those with a VF is compromised by latent muscle activation (*22*). As a result, the slower response to loading by the muscles transfers the load to the skeleton, which can result in bone failure if the load exceeds the strength of the bone. Longitudinal studies have demonstrated back extensor strengthening exercises can reduce VF incidence (*23, 24*). Increased weight decreases risk for low bone density and fracture such that heavy individuals benefit from increased mechanical load on the skeleton that promotes structural adaptive responses in bone tissue (*13*). However, a cross-sectional study in Korea demonstrated much higher percentages of body fat and waist circumference in the VF group than the non-fracture group (*25*). The histological study of fat and bone tissue interaction suggests an inhibitory relationship (*26*). The increased severity of osteoporosis is associated with co-morbid conditions of inflammatory disease, however, the mechanism is not well understood (*27*). Other factors increasing the risk of fractures may include lack of awareness and knowledge regarding lifestyle changes for fracture prevention. There are many physiological intrinsic factors associated with VF risk.

Clinically, osteoporotic VFs are associated with height loss, hyperkyphosis, chronic pain and reduced quality of life (*11*). The diagnosis of VF relies on radiographic identification, however, it is estimated that 30% of VFs are not clinically diagnosed; either the individual dismisses these symptoms or there is an absence of symptoms, or absence of health care (*6*). The physical effects of VFs have great potential to negatively affect the psycho-social functioning of an individual, reducing their quality of life (*28*). In summary, the presence of a VF affects a significant proportion of individuals, diagnosed or not, and can lead to progressive impairment of function.

2.2. Evaluation of Bone Properties Associated with Fracture Risk

Studies, in vivo, investigating bone properties predictive of fracture risk routinely utilize measures of DXA aBMD at the femur and lumbar spine (*29*). More recent studies have utilized the peripheral quantitative computed tomography (pQCT) technology which is able to provide 3D measures of bone properties in trabecular and cortical bone at the peripheral skeleton (*30, 31*). The bone strength determinants of fracture risk are bone density and bone quality; utilization of both DXA and pQCT technologies will provide a more complete picture of the association between bone strength and fracture.

The DXA scan is a routine procedure in Canada for women over the age of 50 years to assess for bone loss, estimate fracture risk and, if necessary, to make decisions about therapeutic management to avoid fracture (*5*).It is used in the clinical assessment of osteoporosis to quantify aBMD (g/cm^2) at the femur and lumbar spine using standardized acquisition protocols and a database of normative values. Advantages to DXA are the relatively low cost, accessibility to testing, and a low radiation dose compared to computed tomography or plain X-ray at the same sites. The disadvantages are low resolution, soft-tissue image artefacts, two-dimensional assessment and the subsequent dependence on bone size. Low aBMD is a strong predictor of fracture however, clinical investigations have indicated that 50% of fractures occur in individuals with aBMD above the osteoporotic threshold (*32*). In the CPG, the DXA aBMD measure is only a part of the fracture risk assessment along with clinical risk factors.

DXA-based vertebral fracture assessment (VFA) involves the acquisition of a lateral spine scan for VF identification and diagnosis. It requires semi-automatic placement of six points on each imaged vertebra, three on each endplate in the lumbar and thoracic spine to generate anterior, middle and posterior vertebral heights (VH). Reliability estimates of VH measures have been investigated using the coefficient of variation (CV) in studies correlating the DXA VFA with the established standard of radiographic fracture identification (*33, 34*). The established categorization of fracture identification is based on VH ratios and interpretation is based percent categorization, standard deviation from norms or sum of height ratios (35-*38*). Using the percent categorization method, fractures are identified as wedge, biconcave and crush, and the severity is graded normal (<20%), mild (20-25%), moderate (25-40%) or severe (>40%) (*35*). Used as a screening tool, the VFA can discriminate non-fractured and mild fractures (<25% grade) from the moderate and severe fractures and its clinical utility is being investigated (*39*). DXA VFA provides a two-dimensional measure of shape of the vertebral body. Relative and absolute reliability of each VH using the DXA VFA has not been reported at each level. Relative reliability has not been reported using intraclass correlation coefficient (ICC), to identify the sources of error. Three-dimensional properties of the axial skeleton are limited to technologies associated with high cost (magnetic resonance imaging) and high radiation dose (computed tomography). The utilization of DXA-based VH may contribute to the understanding of vertebral bone geometry as it contributes to axial bone strength.

The pQCT utilizes a series of rotating X-rays to produce a three dimensional image of bone volume. Advantages of pQCT are the nominal radiation dose, the standardized acquisition protocol, the assessment of trabecular and cortical bone compartments separately and the assessment of bone mechanical strength (including polar strength-strain index, pSSI, and Section Modulus). Disadvantages would include the limited access to pQCT, the acquisition requires no movement over several minutes and axial sites cannot be measured using the pQCT. Apparent trabecular bone properties measured at the distal radius with the pQCT were able to differentiate between women with radial fractures and those without fractures (*40*). High resolution pQCT trabecular volumetric bone mineral density (vBMD) at the distal radius was correlated with low aBMD measures at the femur and lumbar spine differentiating postmenopausal women with wrist fracture from those without (*30*). The measures of bone volume and mechanical strength at the appendicular sites contribute to the understanding of fracture risk.

The evaluation of bone properties predictive of fracture risk increases the ability to identify, manage and prevent fractures. Bone density and bone structure contribute to bone strength and the ability to resist fracture. Areal BMD is limited in its assessment of fracture risk and the evaluation of other bone properties as clinical risk factors have been identified and combined with aBMD for more effective management.

2.3. Effects of Exercise on Bone in Postmenopausal Women

The mechanical stimulus of exercise on bone can be evaluated using measures of bone density and quality. Adaptive remodelling explains the bone response to optimize strength in reaction to specific loads imposed (*41*). The evaluation of the bone adaptation in response to exercise has primarily utilized DXA-based measures of aBMD. Randomized controlled trials (RCTs) investigating bone response to exercise have mixed results, varying in the site-specific changes of aBMD and the dosage and type of exercises, and the time-course of final measures. Earlier systematic reviews (SR) reported nominal response in DXA bone measures in response to exercise in postmenopausal women (*42, 43*). However, a recent prospective study investigated the association between physical activity, measured using an accelerometer, over two years and aBMD and reported an increased number of steps positively correlated with greater hip and spine aBMD and that this effect increased with age (*44*). The most recent SR of 43 RCTs investigating aBMD in response to exercise in postmenopausal women suggested a small but statistically significant increase in aBMD at the femur (total, neck and trochanter) and lumbar spine in postmenopausal women in response to exercise and that exercise may slow bone loss (*45*). The population criteria varied such that 10 studies had women with osteopenia/osteoporosis and the others described the subjects as women with low bone mass, calcium depletion, at high risk to fracture or with no diagnosis of osteoporosis. One RCT investigated women with vertebral fractures. The exercise duration varied from 10 weeks to two years, the frequency varied from one to five times per week and the sessions from 10 to 60 minutes. Subgroup analyses compared the effect of different types of exercise: static weight bearing, dynamic weight bearing low force (walking, Tai Chi Chun), dynamic weight bearing high force (jogging, jumping), non-weight bearing low force (high repetition strength training), non-weight bearing high force (progressive resisted strength training) and a combination of more than one type of these exercises. The total hip and femoral neck aBMD responded best to non-weight-bearing resistance loading, while the lumbar spine aBMD responded best to a combination of exercises compared with control groups. In the SR the synthesis of RCTs indicated that the mean lumbar spine aBMD change (95% CI) in the intervention groups was 0.85% (0.62-1.07) higher than those who didn't exercise, concluding a small but statistically significant, positive effect of exercise on lumbar spine aBMD (*45*). Table 2.1 outlines a variety of studies investigating the bone response to different types of exercise in postmenopausal women outlining the total dosage of exercise and participant adherence. The ages of the participants enrolled are generally 50 to 70 years of age. All but one study focussed on upright exercises, two studies were walking only, while a combination of strengthening and aerobic work is outlined in three studies. The results are mixed and assessment of each program's intensity, population ethnicity and the confounding variables of medication make it difficult to interpret the findings. Further study is warranted in order to determine the optimal dosage and provide evidence based guidelines for exercise to address the health status of postmenopausal women.

Table 2.1. RCTs of various dosage and type of exercise to assess the response of the axial and peripheral skeleton in postmenopausal women.

First author and year publication, ethnicity	Sample size N, [mean age (yr)]	Meds	Length of training (months)	Max dose x adherence (minutes)	Exercise description	Bone Measurement Methods and Sites	Bone measures taken (months from start of exercise)	Adherence (%)	Bone measures % change in EX compared to C
Chan K. et al., 2004, Chinese (46)	EX67 [54] C65 [54]	None	12	9828	Tai Chi Chun	aBMD fem neck/troch aBMD L.sp (L2-L4) pQCT tibia, trBMD and cortical BMD	12	84	Reduced loss in EX 0.1% aBMD fem troch 0.6% vBMD tibia
Nelson et al,1994, American (47)	EX21 [60] C19 [60]	None	12.5	8800	Supervised resistance training	aBMD, BMC fem neck and L.sp (L2-L4)	12	87	↑0.9 – 4.5% aBMD & BMC at fem neck and L.sp in EX
Ebrahim et al., 1997, British(48)	EX49 [67] C48 [69]	yes	24	6240	Brisk walking	aBMD fem neck aBMD L.sp	24	60	↑2% , p=0.056 for aBMD fem neck in EX
Karinkanta et al, 2007, Finnish (49)	EX_R37 [73] EX_B37 [73] EX_C38 [73] C37 [72]	None	12	5226	EX_R- Resistance EX_B Balance EX_C Combination	Fem neck BMC, aBMD pQCT radius, tibia-distal and shaft	12	67	No Δ aBMD,BMC at fem neck No Δ at radius and tibia
Uusi-Rasi et al., 2003, Finnish (50)	EX37 [53] C739 [53]	None	12	5200	Jumping Non-impact	aBMC fem neck aBMC L.sp. Tibia BSI, cortical BMC	12	54	aBMC L.sp.0.9% (-0.4–2.2) Tibia pSSI 3.6% (0.3–7.1) in EX
Chien et al., 2000, Taiwanese (51)	EX18 [57] C24 [57] Chinese	HRT	6	3168	Treadmill, stepping	aBMD fem aBMD L.sp (L2-L4)	6	88	aBMD ↑6.8% fem, p<0.05, aBMD ↑ 2.0% L.sp, p >0.05

EX – exercise group; C – control group; fem – femur; fem neck – femoral neck; fem troch – femoral trochanter L.sp – lumbar spine; BMC – bone mineral content; aBMD – areal bone mineral density; NR – not reported; Δ - change

In a SR of pQCT RCTs investigating the effects of physical activity on vBMD in postmenopausal women concluded that the effect is modest, site-specific and influences coBMD and trBMD at the appendicular sites (*52, 53*). Six RCTs were cited and exercises varied from five to 12 months duration; the type of exercise included site-specific resistance exercises for the wrist, agility training such as jumping, and balance training such as Tai Chi Chun. The synthesis of the findings indicated a mean vBMD % change (95% CI) in the trabecular bone of the distal tibia in the intervention groups was 0.87% (0.37-1.37) higher than the control groups. The SR did not assess bone strength indices in response to exercise due to the variation of outcome measures reported in the RCTs. RCTs of longer duration and specification of the subject's stage of menopause were recommended in future research utilizing the pQCT to assess the effects of exercise on bone (*53*).

The evaluation of bone geometry in the spine is challenging relying on CT or MRI. The DXA VFA generates a measure of vertebral shape (described in section 2.2, p.18). Presently there is only one study that has utilized the DXA-based VH measure as an outcome in secondary analysis in women with osteoporosis and one or more VF. This analysis demonstrated a slower rate of decline in VH (T9 to L4) in those who participated in a home exercise program compared to the control group (*54*). Although the DXA-based VH measure is two-dimensional, it may contribute to understanding vertebral bone site-specific response to exercise.

Engaging in physical activity can expose an individual to an increased risk of fracture however, epidemiological studies suggest higher levels of physical activity reduce the likelihood of sustaining a fracture (*55*). In the SR investigating exercise and aBMD, adverse events were synthesized such that exercisers reported 25% more falls and 10 times more minor aches and pains than the non-exercisers, however, the number of fractures was the same for both groups (*45*). A study investigating the intervention of Tai Chi Chun exercise reported that one exerciser fractured the fibula and three non-exercisers sustained a VF, wrist fracture and fifth metacarpal fracture due to falls or work related spinal overloading (*46*). A study investigating brisk walking reported one exercise related trauma but had a 41% drop-out rate in the first year of this two year study (*48*). The study by Karinkanta et al, 2007, evaluated different resistance and balance exercise regimes for non-osteoporotic, postmenopausal women, mean age 73 years, and reported a large falls incidence of 30% to 50% in all groups including controls, resulting in two fractures in the resistance group and two fractures in the control group (*49*). The fracture rate in RCTs when reported, do not appear to be elevated for those women who participated in the exercise intervention compared to controls. A SR of RCTs investigating exercise interventions to reduce fall-related fractures concluded exercise can reduce falls, fall-related fractures and several risk factors for falls in individuals with low BMD (*56*).

The effect of exercise on bone in postmenopausal women has been evaluated using measures of DXA aBMD at the femur and lumbar spine, compartment specific measures using pQCT and VH measures from the DXA VFA. Recent SRs conclude that exercise reduces fall risk and has a modest effect on bone properties in postmenopausal women. There are no RCTs yet that have investigated the effect of exercise on pQCT derived bone properties or vertebral geometry in postmenopausal women with established osteoporosis.

2.4. Effect of Exercise on Bone in Women with Vertebral Fractures

There are few studies investigating the effectiveness of exercise interventions in postmenopausal women with VF. A recent SR identified nine studies, both RCTs and one CCT, involving women with osteoporotic vertebral fractures and concluded there was not enough evidence to recommend any physical guidelines for therapeutic intervention (*57*). This author did not source studies in other languages and chose studies recruiting women with existing fractures; these are outlined in Table 2.2. However, the conclusion is the same, such that there is little evidence to make clinical decisions about the effect of exercise as a therapeutic intervention for women with VFs. The RCTs investigating the effect of exercise in this high risk group report consistent positive outcomes in self-report measures of quality of life (QOL) and pain (*58-64*). Posture, dynamic and static balance and strength were measured and shown to improve in the exercise group compared to the control group, however, statistical significance was not always achieved.

The duration of the studies varied from 10 weeks to 12 months. Exercise prescription varied from a community based, group of 20, participating in a comprehensive conditioning program to a single home exercise for back extensors (*62, 64*). Two of the studies measured aBMD at the femur and lumbar spine and reported no statistical differences (*60, 62*). The lack of evidence could be attributed to the challenges in conducting an adequately powered RCT in this patient group or a longer follow-up that would provide increased time for bone adaptive remodelling and mineralization yet could potentially reduce the retention rate. None of these studies measured bone geometry in response to exercise, except for secondary subgroup analysis of data from the RCT by Papaioannou *et al*. (*60*) investigating the effect of a home exercise program in postmenopausal women with at least one VF (*54).* As mentioned previously, the secondary analysis of available VH data suggested a slower rate of decline in VH in those participating in the home-exercise program compared to the control group. The benefits of exercise have been shown to enhance the quality of life and address issues associated with elevated fracture risk such as poor balance and hyperkyphosis in this population. Further study is required to understand the influence of exercise on bone strength in women with osteoporotic VFs.

Table 2.2. Studies that assess the response of the axial and peripheral skeleton in women with vertebral fractures to land-based exercises.

First author and year of publication, ethnicity	Sample size N, [mean age (yr)]	Meds	Length of exercise training (months)	Dosage = max minutes x adherence% (minutes)	Intervention	Measurement Methods	Adherence (%) - EX Retention (%) – EX,C	Outcomes for EX
Bennell et al, 2010, Australian (58)	EX10 C9 Age range 53-90	NR	2.5	2520	Taping, Manual therapy, education, home exercises	NPS, QOL, , Thoracic kyphosis, TUGT 3m Timed Load Standing test	73 100, 100	Improved pain and standing test No Δ in TUGT or kyphotic index
Bergland et al, 2011, Norwegian (59)	EX38 [71] C32 [72]		3	1300	3 hr education Walking, balance, trunk strength	QOL, Walking Speed, TUGT 3m, Functional reach	75 64, 60	Improved in all measures, p<0.05
Papaioannou et al, 2003, Canadian (60)	EX37 [72] C37 [72]	NR	6 supervised; 6 unsupervised	2902	Home exercises monthly visits, biweekly phone	QOL, Sway test TUGT 3m, aBMD L.sp.(L2-L4) and femoral neck	62 at 6 mo 46 at 12mo 81, 81	Improved OQLQ and postural sway No Δ in BMD
Gold et al, 2004, American (61)	EX185 [81]	yes	6	2250	Coping classes, Resistance U/E, L/E, trunk	NPS 90 item psych BES	64 77	Improved BES p<.001 No Δ in pain
Lord SR et al, 1996 Australian (62)	EX90 [72] C89 [72]	HRT	12	5040	General aerobics, strengthening, stretching	Quads strength Postural sway aBMD L.sp (L2-L4) aBMD femur	73 76, 83	improved quads strength, p<0.01 and sway, p<0.05 No Δ in BMD
Malmros et al, 1998, Danish (62)	EX27 [65] C25 [68]	yes	2.5	1200	Balance, strength, trunk isometrics	QOL, pain scale, sway index, BES, quads strength	90 85, 88	Improved pain p=0.02
Hongo et al, 2007, Japanese (64)	EX38 [67] C36 [67]	None	4	480	Home exercise BES prone lying	QOL Isometric BES	NR	Improved BES, p 0.028, and posture p 0.02

EX – exercise group; C – Control group; Meds – medication; NR – not reported; HRT – hormone replacement therapy; U/E – upper extremity; L/E – lower extremity; BES – back extensor strength; NPS – Numeric Pain Scale; QOL – quality of life; TUGT – timed up and go test; L.sp.- lumbar spine; quads – quadriceps muscle;; Δ - change

Adverse events were reported in some studies and indicated no difference in the incidence between the exercisers and controls. On review of the studies investigating exercise interventions for women with vertebral fractures, a 10 week exercise program reported 11% of exercisers and 8% of non-exercisers dropped out due to adverse events not related to the training (*64*). Falls occurred in both the control group (n=37) and exercise groups (n=37) of women age mean 72 years participating in a one year RCT (*49*). A pilot RCT investigating exercise and manual therapy for men and women with osteoporotic VFs reported minor soft tissue injuries in 50% of the treatment group (n=11). A low impact study assessing back extensor strengthening exercises (n=38) in women with established osteoporosis reported one radial fracture in the exercise group (*64*). All studies followed exercise recommendations for women with VFs avoiding flexion, twisting and loading of the spine. All studies documented falls history and subjects were deemed able to participate in an exercise program. Adverse events that have been reported in the literature are variable and can involve both the exercise group and the control group.

Exercise has been shown to enhance quality of life and address physical factors associated with elevated fracture risk. An increased fracture risk is also associated with reduced bone strength. Measures to assess bone geometry adaptation in response to exercise in this population may provide insight into the effectiveness of exercise. The CPG recommend physical activity to reduce fracture risk (5*)*. Further investigation into the exercise type, intensity and duration best suited to this high-risk population would be beneficial.

2.5. Aquatic Exercise for Women with Osteoporosis

Benefits of exercise must outweigh the risks and the type of exercise is best tailored to the individual's health status and preference. There is consensus on the positive benefits of physical activity for women with established osteoporosis in physical performance outcomes and self-reported quality of life (*58-64*). Community programming offers many types of exercise including pool based exercise programs offered in warm water pools targeting those with arthritis (*6*). The hydrostatic properties of buoyancy, viscosity and turbulence are used to challenge balance and improve strength while reducing the compression on the joints. Aquatic exercise is a viable alternative for strength and balance training while reducing the joint load and falls impact.

Three RCTs have investigated aquatic exercise for women with osteopenia or osteoporosis and demonstrated improved balance, strength and quality of life in those that participated in the exercise program compared to the control group of non-exercisers (*66-68*). Four RCTs investigated aquatic exercise benefits in postmenopausal women (*69-72*). Two of these RCTs investigated resistance exercises in water reporting significant strength gains over three and eight week programs (*71, 72*). The other exercise programs included a warm-up, resistance and aerobic training, and a cool-down, with the duration of programming variable (five to 12 months). In two of the studies aBMD was measured at the hip and lumbar spine in response to a 12 month aquatic exercise program for osteopenic women *(67)* and a seven month aquatic program for healthy postmenopausal women *(69*). Bravo *et al*. (1997) reported aBMD at the lumbar spine decreased significantly ($p<0.001$) over the year in osteopenic women mean age(SD) 59(5) years, however, this was a test-retest, prospective study and had a 25% drop-out rate (*67*). Rotstein *et al*. (2008) reported a general trend towards maintenance or improvement of bone status in the healthy women mean age (SD) 55(4) years compared to a bone loss in the control group; low sample size and short study duration (seven months) were cited as limitations for achieving statistical significance (*69*). The two studies differed in exercise program duration, intensity and the water depth (waist versus chest). As in land-based exercise studies, those who participated in the exercise class improved in functional capacity and psychological well-being compared to the control group. Compartment specific and geometrical bone properties have not been investigated in response to aquatic exercise. RCTs to evaluate the effectiveness of aquatic exercise in women with established osteoporosis that investigated the bone geometry, would help to clarify outcomes and develop exercise guidelines for this particular group at high risk to fracture.

For a fracture to occur the load on the bone must overcome the bone strength. Anterior wedge fractures are the most common type of osteoporotic vertebral fracture (*73*). The anterior vertebral body load is increased when the spine is in a position of forward flexion. Aquatic exercise reduces compressive loading which may potentially reduce VF risk. In RCTs investigating the effects of aquatic exercise on physical performance outcomes in women with osteoporosis there was one report of an adverse skin reaction to chlorine, and complaints of muscle cramping in the water exercise group more than the land exercise group (*66, 68*). Devereux et al, 2005, investigated balance reactions (Step Test) as well as fear of falling (Modified Falls Efficacy Scale) in osteopenic and osteoporotic women mean age(SD) 73(3) years, after a 10 week water exercise program (*68*). Although balance measures improved, the fear of falling did not. The viscosity of water increases the reaction time available allowing more time for muscle retraining however, the degree to which balance skills are transferred to land is unclear. Aquatic exercise is commonly described as vertical water training and requires recruitment of trunk musculature to maintain the head out of water during movement execution. The reduction of spinal compression, isometric trunk muscle engagement and reduced falls impact may provide a viable exercise environment for individuals with established osteoporosis.

2.6. Summary

The assessment of bone geometry may contribute to understanding bone response to exercise. There are no studies that have yet investigated adaptations in bone geometry in response to exercise in postmenopausal women with established osteoporosis. Aquatic exercise is a viable alternative to gain strength, balance and QOL. Utilizing both DXA VH measures and pQCT imaging, we can evaluate the effect of aquatic exercise on bone geometry in women with established osteoporosis of the spine in a reduced weight-bearing environment. Prior to using VH as an outcome measure the measurement properties need to be established. The feasibility of using DXA and pQCT to assess bone response to aquatic exercise needs to be determined. Furthermore, methods for recruitment, adherence and retention need to be feasible in order to conduct an RCT to investigate the effectiveness of exercise in the aquatic environment on musculoskeletal outcomes in women with osteoporosis at high risk to fracture.

References

1. Wade JP. 2001 Rheumatology: 15. Osteoporosis. *CMAJ* 165:45-50.
2. National Institutes of Health.2000 Osteoporosis prevention, diagnosis, and therapy. NIH consensus statement. United States Department of Health and Human Services Public Health Service. v17:1-45. http://consensus.nih.gov.libaccess.lib.mcmaster.ca/cons/111/111_intro.html. Accessed 2011, April 16, 2011.
3. World Health Organization. 1994 Assessment of fracture risk and its application to screening for postmenopausal osteoporosis.Geneva:*WHO Technical Report Series*.

4. Melton JL III, Riggs BL, Keaveny TM et al. 2011 Relation of vertebral deformities to bone density, structure, and strength. *J Bone Miner Res* 25:1922-1930.
5. Papaioannou A, Morin S, Cheung AM et al. 2010 Efficacy of home-based exercise for improving quality of life among elderly women with symptomatic osteoporosis-related vertebral fractures. *CMAJ* 182:1864-1874.
6. Cummings SR, Melton LJ III. 2002 Epidemiology and outcomes of osteoporotic fractures. *Lancet* 359:1761-1767.
7. Melton LJ 3rd, Lane AW, Cooper C et al. 1993 Prevalence and incidence of vertebral deformities. *Osteoporos Int*. 3:113-9.
8. Ross PD, Genant HK, Davis JW et al. 1993 Predicting vertebral fracture incidence from prevalent fractures and bone density among non-black, osteoporotic women. *Osteoporos Int* 3:120-126.
9. Genant HK, Wu CY, van Kuijk C et al. 1993 Vertebral fracture assessment using a semiquantitative technique. *J Bone Miner Res* 8:1137-1148.
10. Järvinen TL, Sievänen H, Khan KM et al. 2008 Shifting the focus in fracture prevention from osteoporosis to falls. *BMJ*. 336:124-6.
11. Christiansen BA, Bouxsein ML. 2010 Biomechanics of vertebral fractures and the vertebral fracture cascade. *Curr Osteoporos* Rep 8:198-204.
12. Riggs BL, Melton LJ, Robb RA et al. 2008 A population-based assessment of rates of bone loss at multiple skeletal sites: evidence for substantial

trabecular bone loss in young adult women and men. *J Bone Miner Res.* 23:205-14.

13. Samelson EJ, Hannan MT. 2006 Epidemiology of osteoporosis.*Curr Rheumatol Rep* 8:76-83.
14. Delmas PE, Rizzoli AE, Cooper C et al. 2005 Treatment of patients with postmenopausal osteoporosis is worthwhile. The position of the International Osteoporosis Foundation. *Osteoporos Int* 16: 1–5.
15. McDonnell P, McHugh PE, O' Mahoney D. 2007 Vertebral Osteoporosis and Trabecular Bone Quality. *Ann Biomed Eng* 35:170–189.
16. Wegrzyn J, Roux JP, Arlot ME et al. 2010 Role of Trabecular microarchitecture and Its heterogeneity parameters in the mechanical behaviour of ex vivo human L3 vertebrae. *J Bone Miner Res* 25:2324–2331.
17. Morosano ME, Menoyo I, Caferra DA et al. 2011 Vulnerability of healthy vertebrae in patients with and without previous vertebral fracture. *Bone* 48:820-827.
18. Rea JA, Steiger P, Blake GM et al. 1998 Morphometric x-ray absorptiometry: reference data for vertebral dimensions. J *Bone Miner Res* 13:464-474.
19. Diacinti D, Acca M, D'Erasmo E et al. 1995 Aging changes in vertebral morphometry. *Calcif Tissue Int* 57:426-429.

20. Katzman WB, Vittinghoff E, Kado DM. 2011 Age-related hyperkyphosis, independent of spinal osteoporosis, is associated with impaired mobility in older community-dwelling women. *Osteoporos Int* 22:85–90.
21. Huang MG, Barrett-Connor E, Greendale GA et al. 2006 Hyperkyphotic posture and risk of future osteoporotic fractures: the Rancho Bernardo study. *J Bone Miner Res* 21:419-423.
22. Briggs AM, Greig AM, Bennel KL et al. 2007 Paraspinal muscle control in people with osteoporotic vertebral fracture. *Eur Spine J* 16:1137-1144.
23. Sinaki M, Itoi E, Wahner HW et al. 2002 Stronger back muscles reduce the incidence of vertebral fractures: a prospective 10 year follow-up of postmenopausal women. *Bone* 30:836-841.
24. Borgo MJ, Sinaki M. 2010 Back progressive resistive exercise program to reduce risk of vertebral fractures. *J Miner Stoffwechs* 17:66-71.
25. Kim KC Shin DH, Lee SY et al. 2010 Relation between obesity and bone mineral density and vertebral fractures in Korean postmenopausal women. *Yonsei Med J* 51:857-863.
26. Rosen CJ, Bouxsein ML. 2006 Mechanisms of disease: is osteoporosis the obesity of bone? *Nat Clin Pract Rheumatol* 2:35-43.
27. David C, Confavreux B, Mehsen N et al. 2010 Severity of osteoporosis: what is the impact of co-morbidities? *Joint Bone Spine* 77:S103-S106.
28. Gold DT. 1996 The clinical impact of vertebral fractures: Quality of life in women with osteoporosis. *Bone* 18:185S-189S.

29. Marshall D, Johnell, O, Wedel H. 1996 Meta-analysis of how well measures of bone mineral density predict occurrence of osteoporotic fractures. *Br Med J* 312:1254-1260.
30. Melton III LJ, Christen D, Riggs BL et al. 2010 Assessing forearm fracture risk in postmenopausal women. *Osteoporos Int* 21:1161-1169.
31. Mueller TL, van Lenthe GH, Stauber M et al. 2009 Regional, age and gender differences in architectural measures of bone quality and their correlation to bone mechanical competence in the human radius of an elderly population. *Bone* 45:882-891.
32. Schuit SCE, van der Klift M, Weel, AEAM et al. 2004 Fracture incidence and association with bone mineral density in elderly men and women: the Rotterdam Study. *Bone* 34:195-202.
33. Steiger P, Cummings SR, Genant HK et al. 1994 Morphometric X-ray absorptiometry of the spine: Correlation in vivo with morphometric radiography. *Osteoporos Int* 4:238-244.
34. Rea JA, Chen MB, Li J et al. 1999 Morphometric X-ray absorptiometry and morphometric radiography of the spine: a comparison of analysis precision in normal and osteoporotic subjects. *Osteoporos Int* 9:536-544.
35. Genant HK, Wu CY, van Kuijk C et al. 1993 Vertebral fracture assessment using a semiquantitative technique. *J Bone Miner Res* 8:1137-1148.
36. Estell R, Cedel SL, Wahner HW et al. 1991 Classification of vertebral fractures. *J Bone Miner Res* 6:207-215.

37. McCloskey EV, Spector TD, Eyres KS et al. 1993 The assessment of vertebral deformity: a method for use in population studies and clinical trials. *Osteoporos Int* 3:138-147.

38. Diacinti D, Pisani D, Barone-Adesi F et al. 2010 A new predictive index for vertebral fractures: the sum of the anterior vertebral body heights. *Bone*46:768-73.

39. Jager PL, Slart RH, Webber CL et al. 2010 Combined vertebral fracture assessment and bone mineral density measurement: a patient-friendly new tool with an important impact on the Canadian Risk Fracture Classification. *Cdn Assoc Rad J* 61:194-200.

40. MacIntyre NJ, Adachi JD, Webber CE. 2003 In vivo measurement of apparent trabecular bone structure of the radius in women with low bone density discriminates patients with recent wrist fracture from those without fracture. *J Clin Densitom* 6:35-43.

41. Lanyon LE. 1987 Functional strain in bone tissue as an object, and controlling stimulus for adaptive bone remodelling. *J Biomech* 20:1083-1093.

42. Wolff I, van Croonenborg JJ, Kemper HCG et al. 1999 The effect of exercise training programs on bone mass: a meta-analysis of published controlled trials in pre- and postmenopausal women. *Osteoporos Int* 9:1-12.

43. Berard A, Bravo G, Gauthier P. 1997 Meta-analysis of the effectiveness of physical activity for the prevention of bone loss in postmenopausal women. *Osteoporos Int* 7:331-337.

44. Foley S, Quinn S, Jones G. 2010 Pedometer determined ambulatory activity and bone mass: a population-based longitudinal study in older adults. *Osteoporos Int* 21:1809-1816.

45. Howe TE, Shea B, Dawson LJ et al. 2011 Exercise for preventing and treating osteoporosis in postmenopausal women. *Cochrane Database Syst Rev* 7. Art. No.: CD000333.

46. Chan K, Qin L, Lau M et al. 2004 A randomized, prospective study of the effects of tai chi chun exercise on bone mineral density in postmenopausal women. *Arch Phys Med Rehabil* 85:717-722.

47. Nelson ME, Fiatarone MA, Morganti CM et al. 1994 Effects of high-intensity strength training on multiple risk factors for osteoporotic fractures: A randomized controlled trial *JAMA* 272:1909-1914.

48. Ebrahim S, Thompson PW, Baskaran V et al. 1997 Randomized placebo-controlled trial of brisk walking in the prevention of postmenopausal osteoporosis. *Age and Ageing* 26:253-261.

49. Karinkanta S, Heinonen A, Sievanen H et al. 2007 A multi-component exercise regimen to prevent functional decline and bone fragility in home-dwelling elderly women: randomized, controlled trial. *Osteoporos Int* 18:453-462.

50. Uusi-Rasi K, Kannus P, Cheng S et al. 2003 Effect of alendronate and exercise on bone and physical performance of postmenopausal women: A randomized controlled trial. *Bone* 33 132–143.

51. Chien MY, Wu YT, Hsu AT et al. 2000 Efficacy of a 24-Week aerobic exercise program for osteopenic postmenopausal women. *Calcif Tissue Int* 67:443-448.

52. Hamilton CJ, Swan VJD, Jamal SA. 1998 The effects of exercise and physical activity participation on bone mass and geometry in postmenopausal women: a systematic review of pQCT studies. *Osteoporos Int* 8:92-95.

53. Polidoulis I, Beyene J, Cheung AM. 2011 The effect of exercise on pQCT parameters of bone structure and strength in postmenopausal women—a systematic review and meta-analysis of randomized controlled trials. *Osteoporosis Int* epub 03 August 2011. doi 10.1007/s00198-011-1734-7

54. Webber CE, Papaioannou A, Winegard KJ et al. 2003 A 6-mo home-based exercise program may slow vertebral height loss. *J Clin Densitom* 6:391-400.

55. Gregg EW, Pereira MA, Caspersen CJ. 2000 Physical activity, falls and fractures among older adults: a review of the epidemiological evidence. *J Am Geriatr Soc*. 48:1-18.

56. de Kam D, Smulders E, Weerdesteyn V et al. 2009 Exercise interventions to reduce fall-related fractures and their risk factors in individuals with low

bone density: a systematic review of randomized controlled trials. *Osteoporos Int* 20:2111-2125.

57. Dusdall K., Grundmanis D, Luttin K, Ritchie P. et al. 2010 Effects of therapeutic exercise for persons with osteoporotic vertebral fractures: a systematic review. *Osteoporos Int* 22:755-769.
58. Bennell KL, Matthews B, Greig A et al. 2010 Effects of an exercise and manual therapy program on physical impairments, function and quality-of-life in people with osteoporotic vertebral fracture: a randomised, single-blind controlled pilot trial. *BMC Musculoskel Dis* 11:36.
59. Bergland A, Thorsen H, Karesen R. 2011 Effect of exercise on mobility, balance, and health-related quality of lie in osteoporotic women with a history of vertebral fracture: a randomized, controlled trial. *Osteoporos Int* 22:1863-1871.
60. Papaioannou A, Adachi JD, Winegard K et al. 2003 Efficacy of home-based exercise for improving quality of life among elderly women with symptomatic osteoporosis-related vertebral fractures. *Osteoporos Int* 14:677-682.
61. Gold DT, Shipp DM, Pieper CF et al. 2004 Group treatment improves trunk strength and psychological status in older women with vertebral fractures: Results of a randomized, clinical trial. *JAGS* 52:1471-1478.

62. Lord SR, Ward, JA, Williams P et al. 1996 The effects of a community exercise program on fracture risk factors in older women. *Osteoporos Int* 6:361-367.

63. Malmros B, Mortensen L, Jensen MB et al. 1998 Positive effect of physiotherapy on chronic pain and performance in osteoporosis. *Osteoporos Int* 8:215-221.

64. Hongo M, Itoi, E, Sinaki M et al. 2007. Effect of low-intensity back exercise on quality of life and back extensor strength in patients with osteoporosis: a randomized controlled trial. *Osteoporos Int* 18:1389-1395.

65. Becker BE. 2009. Aquatic therapy: Scientific foundations and clinical rehabilitation applications. *Phys Med Rehab* 1:859-872.

66. Arnold CM, Busch AJ, Schachter CL et al. 2008. A randomized clinical trial of aquatic versus land exercise to improve balance, function and quality of life in older women with osteoporosis. *Physiother Can* 60:296-306.

67. Bravo G, Gauthier P, Roy PM et al. 1997 A weight-bearing, water-based exercise program for osteopenic women: its impact on bone, functional fitness and well-being. *Arch Phys Med Rehabil* 78:1375-1380.

68. Devereux K, Robertson D, Briffa NK. 2005 Effects of a water-based program on women 65 years and over: A randomized controlled trial. *Aust J Physiother* 51:102-108.

69. Rotstein A, Harush M, Vaisman N. 2008 The effect of a water exercise program on bone density of postmenopausal women. *J Sports Med Phys Fitness* 48:352-359.

70. Tsourlou T, Benik A, Dipla K et al. 2006. The effects of a twenty-four-week aquatic training program on muscular strength performance in healthy elderly women. *J Strength Cond Res* 20:811-818.

71. Graef FI, Pinto RS, Alberton CL et al. 2010 The effects of resistance training performed in water on muscle strength in the elderly. *J Strength Cond Res* 24:3150-3156.

72. Katsura Y, Yoshikawa T, Ueda SY et al. 2010 Effects of aquatic exercise training using water-resistance equipment in elderly. *Eur J Appl Physiol* 108:957-964.

73. Black DM, Cummings SR, Stone K et al. 1991 A new approach to defining normal vertebral dimensions *J Bone Miner Res* 6:883-892.

CHAPTER 3

Intra-Rater Reliability of Dual Energy X-Ray Absorptiometry-Based Measures of Vertebral Height in Postmenopausal Women

The following paper has been formatted for submission to Journal of Clinical Densitometry.

Intra-Rater Reliability of Dual Energy X-Ray Absorptiometry-Based Measures of Vertebral Height in Postmenopausal Women

Alison M Bonnyman, MSc Student[1]

Colin E Webber, PhD[2]

Paul W Stratford, PT, MSc[1]

Norma J MacIntyre, PT, PhD[1]

1. School of Rehabilitation Science, McMaster University, Hamilton, ON, Canada.
2. Nuclear Medicine Department, McMaster Health Sciences, Hamilton, ON, Canada.

Please address all correspondence to:

Alison Bonnyman

School of Rehabilitation Science.IAHS-403 1400 Main St., Hamilton, ON, Canada, L8S 1C7. Phone (905) 525-9140, ext: 26410. Email: bonnymam@mcmaster.ca

Running Title: Reliability of DXA-based Vertebral Height Measures

Abstract

The purpose was to estimate intra-rater reliability of dual-energy X-ray absorptiometry vertebral fracture assessment measures of vertebral body height (VH) based on manual placement of endplate markers and intra-rater reliability of duplicate analysis in the classification of fractures in postmenopausal women. VFA images were acquired for 32 women, mean age (SD) 70(7) years, using the Hologic Discovery A. Each image was analyzed on two occasions (4 weeks apart) by a single rater using a predetermined protocol. The semi-automated software derived measures of anterior, middle, and posterior VH and classified vertebral deformity as normal, mild, moderate or severe. Intra-rater reliability was assessed using the intraclass correlation coefficient (ICC) with 95% confidence intervals (95% CI). Overall reliability of vertebral deformity classification was assessed using unweighted *kappa* (κ, with 95% CI). For levels T9 to L4, intra-rater reliability varied from 0.87 (0.74, 0.94) at L2 posterior VH to 0.98 (0.95, 0.99) at L1 anterior VH, except for T9 posterior VH [0.62 (0.15, 0.84)]. Overall agreement for vertebral deformity classification was 0.50 (0.28, 0.72). Intra-rater reliability for VH measures in these postmenopausal women was acceptable from T9 to L4 with the exception of T9 posterior VH. Reliability for duplicate classification of vertebral deformity was poor.

Key Words: DXA, vertebral height, reliability, postmenopausal women

3.1. Introduction

Confidence in a measured value translates into confidence in clinical decisions based on a measured value. Typical clinical decisions include differentiating among patients and assessing change within a patient over time. The ability to accomplish these objectives increases as the reliability of the measurement process increases. We use the term measurement process to include all aspects of measurement including the sample composition, rater characteristics, instrumentation and setting. We use measures in a context and it is a measure's score that has reliability, not the test itself. Reliability is the measurement property that quantifies measurement error, and within the context of Classical Test Theory (CTT), the measurement error is considered to be random.

Two quantifications of reliability are of interest to those who apply measured values to shape clinical decisions. Relative reliability considers the ability of scores to differentiate among patients and is quantified by the intra-class correlation coefficient (ICC). There are many types of ICC, all of which contain the true variance in the numerator (in this context, the variance among patients), and true variance plus relevant sources of error variance in the denominator. As such, an ICC can take on values from 0 to 1 with higher values representing greater reliability in the measurement process. CTT denominator contains a single, all-encompassing error term. Other ICCs, typically associated with Generalizability Theory *(1)* which is an extension of CTT, allow the partitioning of error variances dependent on the study design. Reliability can also be quantified in terms of absolute measurement error. In contrast to relative reliability, absolute reliability quantifies measurement error in the same units as the original measurement. Absolute measurement error is quantified by the standard error of measurement (SEM)—not to be confused with the standard error of the mean. The SEM is calculated as the square-root of the residual error term from a repeated measures study design where the main effects are patients and other relevant factors (e.g., raters, occasion, etc., depending on the research question and study design).

Dual energy X-ray absorptiometry (DXA) vertebral fracture assessment (VFA) generates measures of vertebral body height (VH) in the thoracic and lumbar spine (T4 to L4) based on operator placement of markers on a lateral scan. Ratios of these measures are used to classify the type and severity of vertebral deformity according to Genant's semiquantitative method *(2)*. These classifications guide clinical decisions regarding further testing and initiation of treatment for osteoporosis. To date, the sources of error in VH measures have not been well described. Information about reliability of VH measures is imbedded in previous research. Age-specific normative data for women and the rates of decline in VH have been reported *(3, 4).* A number of studies have validated classification of vertebral deformity grades derived from DXA with the established standard of radiographically defined vertebral fracture grades *(3-14).* In preparation for these validation studies, intra-rater reliability has been described based on duplicate analyses with relative reliability reported as the coefficient of variation (CV%). The CV varied from 1.8%, pooled VHs, in 12 postmenopausal women without osteoporosis (*5)* to 5.1% for the anterior VH at T9 in 41 postmenopausal women with osteoporosis (*6)*. Absolute reliability has been reported as the root mean square standard deviation (RMSSD) for pooled VH, varying from 0.39 mm to 1.0 mm in the same studies just discussed (*5,6*). One study has utilized VH as an outcome measure, demonstrating a slower rate of decline in postmenopausal women randomly assigned to a six month exercise program compared to the control group of non-exercisers, and characterized measurement error using regression analyses (*15)*. Variations in the study design, pooling of data, diverse statistical approaches and lack of detail in reporting the protocol for analysis make it difficult to compare previous estimates of reliability.

Fracture classification using DXA VFA has been compared to the established standard of radiographic fracture classification. Studies vary in classification categories and the frequency of analysis. Intra-rater reliability of classification of vertebral deformity (normal, mild, moderate or severe) by three expert radiologists on duplicate analyses of VFA images from 203 women with osteoporosis and a mean(SD) age of 68(10) years, was reported in terms of agreement with weighted *kappa* from 0.73 – 0.88 (*16*). Consensus readings generated a lower *kappa* (0.64) when all readable vertebrae were included in comparison to the *kappa* = 0.80 for moderate and severe fracture categories alone (*16*). Agreement between the classification of vertebrae as fractured or non-fractured in 80 Caucasian, post-menopausal women was moderate, *kappa* = 0.545 (*8*). In this study agreement of classification based on single analyses of VFA, as read by two non-radiologist clinicians was compared to single analysis of a spinal X-ray, read by an expert radiologist. Reported agreement was 94% between moderate and severe grades and 50% for mild fracture grades *(8)*. Overall, VFA has demonstrated reduced agreement for the mild fracture identification in comparison to spinal radiographs however VFA has the advantage of single scan acquisition and a lower radiation dose (*8, 9, 12, 16*).

The primary purpose of this study was to estimate the intra-rater reliability of anterior, middle, and posterior VH measures at each level, based on duplicate analyses of single DXA VFA images from postmenopausal women using a standardized protocol. A secondary purpose was to determine the consistency in VFA classification of vertebral deformity by a novice rater on duplicate analyses.

3.2. Materials and Methods

3.2.1. Images

Images were randomly selected from a database of 464 VFAs acquired between March 2009 and February 2010 as part of ongoing studies approved by the institutional research ethics board. Inclusion criteria for this study were images acquired in postmenopausal women 60 years of age or older. The scans were acquired by six trained technologists using DXA (Hologic Discovery A, Waltham, MA) following the manufacturer's standardized acquisition protocol. The long term precision of the DXA was determined based on daily scans of a lumbar spine phantom (Hologic #12221) and the *in vitro* CV during this time was 0.56% for areal bone mineral density (aBMD, g/cm^2).

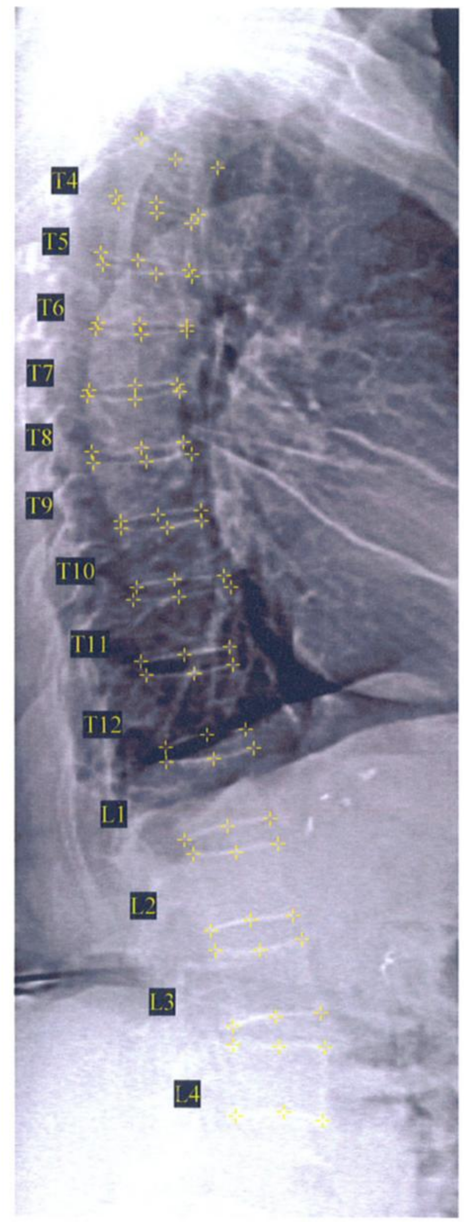
3.2.2. Image Analysis

Semi-automatic analysis of each image was completed by a single, novice rater using the manufacturer's software (Hologic Apex v.2.3:1, n = 24; Hologic Apex v.13.0:03, n = 8). The novice rater was a physiotherapist with training that consisted of reading the user manual and receiving instructions from an experienced technologist. The protocol described in Table 3.1 was developed based on five practice trials to guide consistent placement of markers identifying the anterior, middle and posterior points of each visible endplate of the 13 vertebrae imaged in each VFA (Figure 3.1).

Table 3.1. Protocol for image analysis of a vertebral fracture assessment.

Step	Task	Procedure
1	Open Image	Identify L4, using sacrum and ribs to guide.
2	Magnify image to 200%	Confirm identification of 4th lumbar vertebra
3	Identify vertebral outline for marker placement	a) One right mouse click per vertebra provides 6 markers to drag into position. b) Six marker placements should follow sequential order on the superior and inferior endplates: Superior-Anterior, Superior-Posterior, Inferior-Anterior, Inferior-Posterior, Superior-Middle, Inferior-Middle. c) Place markers on each visible vertebra in distal to proximal order. d) Check that the vertebral label is correct (software generated).
4	Marker placement in the presence of unclear landmarks	a) Anterior Landmarks: for bony thickening at the endplate, place the marker in the center of the thickening, aligned vertically with the cortex. b) Posterior Landmarks: use the outline of intervertebral foramen to confirm placement of the superior-posterior marker above the inferior posterior marker c) Middle Landmarks: for multiple lines at the middle of the endplate, the vertebral height is to be defined as the minimum distance between the superior and inferior endplates.
5	Quality Control	a) Note the original gray scale setting and adjust the gray scale to enhance visualization of the vertebral outline. b) If any of the vertebral landmarks are not visible, stop analysis at that level. Analysis of proximal levels not continued.
6	Extract vertebral heights	a) Left mouse click on Print and select print preview on the pop up menu. b) Review the report displaying the calculated vertebral heights and check for missing data. c) In the case of missing data, cancel print preview, return to step 5 and re-label the vertebral levels. d) Print a hard copy (the marker placement is not saved).

Figure 3.1. Vertebral fracture assessment image of a 75 year old woman with visible landmarks for marker placement from T4 to L4.



The operator performed a single analysis of each image on two occasions separated by four weeks and remained blinded to previous results. Time to complete the semi-automatic analysis varied from 8 to 15 minutes depending on the number of vertebral levels visible. The outcome measures generated by the commercial software were anterior VH (VHa), middle VH (VHm), and posterior VH (VHp) in millimeters (mm).

The Hologic Apex v.2.3:1 software classifies vertebral deformity in terms of type (normal, wedge, biconcave, crush) and severity (normal, mild, moderate or severe) for each visible vertebra. Percent deformation was quantified and categories of grades were computed based on Genant's semiquantitative classification (*2*).

3.2.3. Statistical Analyses

For the intra-rater reliability study of DXA-based VH measures, a minimum sample size of 22 VFA images was required to estimate an intraclass correlation coefficient (ICC) of 0.80 with a lower 1-sided 95% confidence interval (CI) width of 0.10. A previous study reported that vertebral markers could not be positioned on T4 in 41% of the images acquired in a patient group similar to ours *(15).* To estimate the intra-rater reliability of VHs L4 to T4, 32 VFA images were analyzed.

The Bland and Altman method was used to test the assumption that the error was independent of the measured value, to characterize the measurement bias

(*18)*. For each vertebral level, the difference in VH (Occasion 1 – Occasion 2) was plotted as a function of the mean VH for VHa, VHm and VHp.

Descriptive statistics and relative reliability were computed using SPSS software (SPSS v18, SPSS Inc, Chicago, IL, USA). The ICCs with 95% CI were determined based on repeated measures analysis of variance (ANOVA) for average measures with absolute agreement according to the following equation:

$$ICC\ (2,1) = \frac{\text{subject variance}\ (\sigma_s^2)}{subject\ variance\ (\sigma_s^2) + rater\ variance\ (\sigma_r^2) + error\ variance\ (\sigma_e^2)}$$

We calculated corresponding estimates of absolute intra-rater reliability, standard error of measurement (SEM) with 95% CI, reported in the same units of measurement as the VH measures (mm). SEM is equal to the square root of the residual error variance, from the ANOVA. Our criteria for acceptable intra-rater reliability for VH measures was an ICC ≥ 0.80 with a lower 95% CI ≥ 0.70 in combination with an acceptably low SEM as compared to previous studies and proportional to the height measured, for example < 1.0mm or < 5% of mean VH.

For comparison with previously reported estimates of relative reliability, we calculated the RMSCV as the ratio of the root mean square standard deviation (RMSSD) to the average VHa, VHm and VHp at each vertebral level. RMSSD is defined as:

$$\text{RMSSD} = \sqrt{\frac{\sum_{i=1}^{N}(VH1-VH2)^2}{2N}}$$

where VH1 and VH2 are the VH values on occasion 1 and occasion 2 respectively, and N is the total number of measurements.

Grades of vertebral deformity (normal, mild, moderate, severe) were generated in duplicate for 192 vertebrae. Level of agreement across all grades and for fractured and non-fractured categories (≤ 25% deformation/non-fractured, > 25% deformation/fractured) was characterized using Cohen's unweighted kappa (κ) calculated using the VassarStats website *(19)*. The observed proportion of agreement (P_{obs}) was used to characterize agreement for each grade separately. For both statistics, perfect agreement = 1.

3.3. Results

The 32 images included in this study were acquired in women with a mean (SD) age of 70 (7) years and a mean (SD) body mass index of 27.9 (7.3) kg/cm^2. The mean (SD) T-score was -1.3 (1.6) at the spine and -1.3 (1.3) at the hip.

Vertebral body heights of T11 to L4 could be analyzed in all 32 images. Markers could be positioned and heights measured at T10 for 28 images and at T9 for 24 images. The number of thoracic vertebrae visible for marker placement decreased as the analysis progressed proximally (T8 = 21, T7 = 17, T6 = 11, T5 = 7 and T4 = 6).

Bland-Altman plots confirm that the error was independent of the mean VH value (Figure 3.2). In the 24 women, VHp at T9 demonstrated low variability around the mean VH value (Figure 3.2A). In contrast, VHm at L1 for 32 women had greater variability between subjects (Figure 3.2B). For all levels, there was no bias suggesting VH mean influenced the measure difference and there was no systematic error. Bland-Altman plots for VHa, VHm and VHp at levels T9 to L4 are shown in Appendix 1.

Figure 3.2. Bland-Altman plots of the difference versus the mean of the vertebral body heights at A) the posterior aspect of T9 for 24 postmenopausal women and B) the middle aspect of L4 for 32 postmenopausal women.

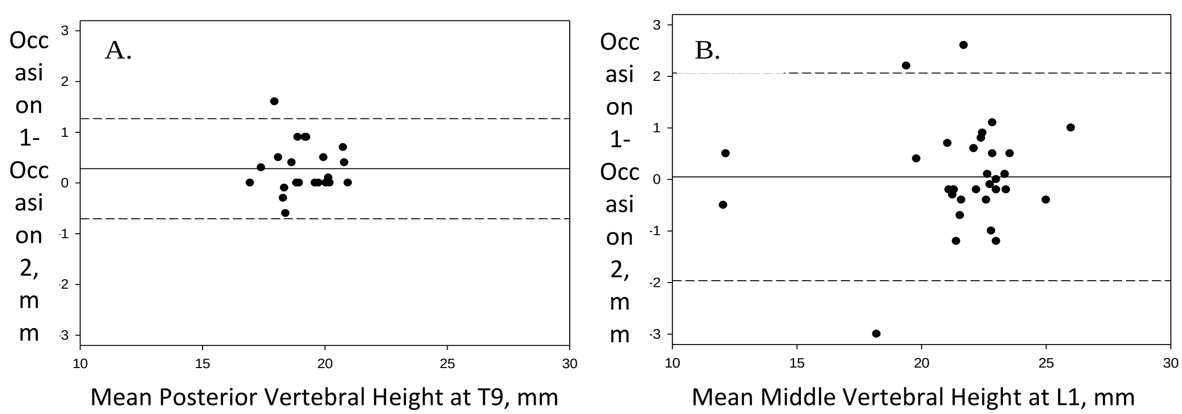


Table 3.2 summarizes the mean VHa, VHm and VHp for T9 to L4 obtained on occasions 1 and 2 and the average of the two measures. As expected, VHs are greater for the lumbar vertebrae than thoracic vertebrae. For individual subjects, the between-occasion difference in VH measures varied from 0.0mm (VHp at L1, n = 2; VHm at T12, n = 1) to 7.1mm (VHa at L4, n = 1).

Table 3.2**.** Vertebral height (mm) at Occasion 1 (1), Occasion 2 (2) and mean vertebral height, measured one time on two occasions, 4 weeks apart in postmenopausal women 60 years of age and older.

	Anterior			Middle			Posterior		
Level[a]	1	2	Grand Mean	1	2	Grand Mean	1	2	Grand Mean
T9[b]	17.26	17.09	17.17	16.67	16.75	16.71	19.40	18.91	19.16
T10[c]	19.41	19.29	19.35	18.25	18.11	18.18	20.74	20.43	20.58
T11 [a]	20.18	20.18	20.18	19.34	18.98	19.16	22.21	22.13	22.17
T12 [a]	21.84	21.75	21.79	20.42	20.23	20.32	23.77	23.72	23.74
L1 [a]	23.32	23.43	23.38	21.58	21.53	21.56	24.69	24.70	24.70
L2 [a]	24.6	24.60	24.60	22.68	22.54	22.61	25.64	25.83	25.74
L3 [a]	26.26	26.34	26.29	23.52	23.32	23.42	25.88	26.02	25.95
L4 [a]	25.83	25.57	25.69	22.95	22.55	22.75	24.65	24.68	24.66

[a] n = 32; [b] n = 24; [c] n = 28

Intra-rater reliability of VHa from T9 to L4 is summarized in Table 3.3. All ICCs were ≥ 0.88 with lower 95% CI ≥ 0.73 and all RMSCV are ≤ 4.89%. The SEM varied from 0.50mm at T11 to 1.17mm at L4.

Table 3.3. Relative and absolute intra-rater reliability of anterior height measures for thoracic (T) and lumbar (L) vertebra in postmenopausal women 60 years of age and older.

Level[a]	Relative Reliability		Absolute Reliability	
	ICC (average)[d]	RMSCV[e] (%)	SEM[f] (mm)	RMSSD[g] (mm)
T9[b]	0.88 (0.73, 0.95)	4.89	0.80 (0.64, 1.07)	0.84
T10[c]	0.92 (0.84, 0.96)	3.54	0.67 (0.54, 0.89)	0.66
T11	0.95 (0.90, 0.98)	2.48	0.51 (0.41, 0.67)	0.50
T12	0.96 (0.91, 0.98)	2.63	0.57 (0.46, 0.76)	0.57
L1	0.98 (0.95, 0.99)	3.16	0.62 (0.49, 0.82)	0.61
L2	0.95 (0.90, 0.98)	2.99	0.74 (0.59, 0.99)	0.73
L3	0.94 (0.87, 0.97)	2.49	0.65 (0.52, 0.86)	0.64
L4	0.93 (0.85, 0.96)	4.87	1.17 (0.93, 1.55)	1.16

[a]n=32; [b]T9: n=24; [c]T10: n = 28; [d] ICC (average):Intraclass correlation coefficient type 2,1 for average measures; [e] RMSCV: coefficient of variation; [f] SEM: standard error of the measurement; [g] RMSSD: root mean square standard deviation

Intra-rater reliability of VHm from T9 to L4 is summarized in Table 3.4. All ICCs were ≥ 0.90 with lower 95% CI ≥ 0.81 and all RMSCV are ≤ 3.88%. The absolute reliability varied from 0.42mm at T9 to 0.73mm at L4.

Table 3.4. Relative and absolute intra-rater reliability of middle height measures for thoracic (T) and lumbar (L) vertebra in postmenopausal women over the age of 60 years of age and older.

	Relative Reliability		Absolute Reliability	
Level[a]	ICC (average)[d]	RMSCV[e] (%)	SEM[f] (mm)	RMSSD[g] (mm)
T9[b]	0.95 (0.87, 0.98)	2.57	0.47 (0.38, 0.62)	0.42
T10[c]	0.93 (0.85, 0.97)	4.13	0.72 (0.57, 0.95)	0.71
T11	0.90 (0.77, 0.95)	3.06	0.55 (0.44, 0.73)	0.60
T12	0.96 (0.92, 0.98)	2.59	0.49 (0.40, 0.66)	0.50
L1	0.97 (0.94, 0.99)	3.49	0.71 (0.57, 0.95)	0.70
L2	0.96 (0.92, 0.98)	2.93	0.68 (0.55, 0.91)	0.68
L3	0.90 (0.81, 0.95)	2.79	0.65 (0.52, 0.87)	0.66
L4	0.97 (0.93, 0.99)	3.88	0.69 (0.55, 0.92)	0.73

[a]n=32; [b]T9: n=24; [c]T10: n = 28; [d] ICC (average):Intraclass correlation coefficient type 2,1 for average measures; [e] RMSCV: coefficient of variation; [f] SEM: standard error of the measurement; [g] RMSSD: root mean square standard deviation

Intra-rater reliability of VHp from T9 to L4 is summarized in Table 3.5. All ICCs were ≥ 0.87 with lower 95% CI ≥ 0.74 with the exception of T9 (ICC = 0.62). All RMSCV are ≤ 4.90%. The absolute reliability varied from 0.54mm at T12 to 0.92mm at T9.

Table 3.5. Relative and absolute intra-rater reliability of posterior height measures for thoracic (T) and lumbar (L) vertebra in postmenopausal women 60 years of age and older.

Level[a]	Relative Reliability		Absolute Reliability	
	ICC (average)[d]	RMSCV[e] (%)	SEM[f] (mm)	RMSSD[g] (mm)
T9[b]	0.62 (0.15, 0.84)	4.90	0.91 (0.73, 1.21)	0.92
T10[c]	0.91 (0.80, 0.96)	3.62	0.69 (0.56, 0.92)	0.72
T11	0.94 (0.88, 0.97)	2.55	0.57 (0.45, 0.75)	0.56
T12	0.95 (0.89, 0.97)	2.41	0.55 (0.44, 0.73)	0.54
L1	0.95 (0.90, 0.98)	2.90	0.62 (0.50, 0.83)	0.61
L2	0.87 (0.74, 0.94)	2.82	0.73 (0.58, 0.97)	0.73
L3	0.94 (0.88, 0.97)	2.38	0.61 (0.49, 0.81)	0.61
L4	0.95 (0.90, 0.98)	3.13	0.74 (0.59, 0.98)	0.72

[a]n=32; [b]T9: n=24; [c]T10: n = 28; [d] ICC (average):Intraclass correlation coefficient type 2,1 for average measures; [e] RMSCV: coefficient of variation; [f] SEM: standard error of the measurement; [g] RMSSD: root mean square standard deviation

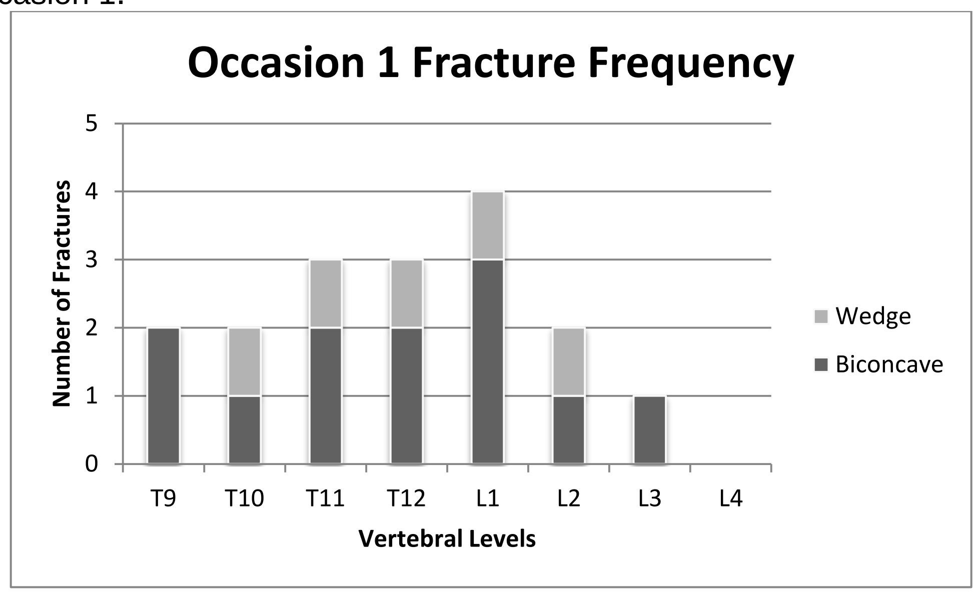
Table 3.6 shows the classification of grades of vertebral deformity for the 192 vertebrae (T9 to L4) on occasion one and two. Consistent classification was observed for 174 vertebrae (165 normal, 4 mild, 4 moderate, and 1 severe). Overall, *kappa* (95%CI) = 0.50 (0.28, 0.72). Agreement of classification for each specific grade was P_{obs} (95%CI) for normal, mild fracture, moderate fracture, and severe fracture was 0.92 (0.86, 0.95), 0.24 (0.08, 0.50), 0.36 (0.12, 0.68) and 0.50 (0.03, 0.97), respectively. When classified as no fracture (grades normal and mild) and fracture (grades moderate and severe), *kappa* = 0.65 (0.34, 0.91), and P_{obs} = 0.97 (0.93, 0.99).

Table 3.6. Number of vertebrae, by fracture severity, on each occasion from T9 to L4, in 24 images.

		Occasion 2				
		Normal	Mild	Moderate	Severe	Total
Occasion 1	Normal	165	7	3	0	175
	Mild	4	4	0	0	8
	Moderate	1	2	4	0	7
	Severe	0	0	1	1	2
	Total	170	13	8	1	192

Figure 3.3 illustrates the distribution and types of fractures. On occasion 1, 17 fractures (5 wedge, 12 biconcave) were identified in 13 images (two images had 2 or more vertebral fractures). On occasion 2, 22 fractures (7 wedge, 15 biconcave) were identified in 17 images (seven images had 2 or more vertebral fractures).

Figure 3.3. Number of biconcave and wedge fracture types using Hologic software from T9 to L4 in images from 24 postmenopausal women analyzed on occasion 1.



3.4. Discussion

In the measurement process, scores must be reliable, enabling confident clinical decisions based on the context. Reliability is a measurement property that determines the extent to which patients can be categorized and partitions out the error, random and attributable. In this study we show that a rater with minimal training can follow our protocol and obtain VH measures with acceptable reliability from T9 to L4 with the exception of VHp at T9, based on duplicate analyses. A secondary objective was to assess the extent of agreement beyond chance alone in the consistency of the classification of grades of vertebral deformity by duplicate VFA analyses. Reliability of the grade classification was good for distinguishing vertebrae with deformity in the normal range.

The measurement process is defined by the instrumentation, the specific population, rater characteristics and the methodology. This study group was a cross-section of individuals with variable bone health. The ICC quantified the measure's score and partitioned out the subject variability. The desired outcome is a high relative reliability, the error-free portion of the measure approaching one, and a small absolute reliability proportional to the magnitude of VH. For VHp at T9, the RMSCV was acceptable at 4.9% whereas the ICC was unacceptable at 0.62, with a lower 95% CI = 0.15. The homogeneity of VHp at T9 (Figure 3.2A) indicated that the error-free portion of this measure is small potentially due to the lack of between-subject and between-occasion variability. A larger and more varied population may have yielded different results. The relative reliability using RMSCV was 4.9% and similar to previous results for VHp at T9 of CV 4.3% (*6*) suggesting a CV below 5% acceptable reliability, however the calculation of relative intra-rater reliability using the RMSCV does not discriminate the subjects or occasions as sources of error. The SEM was below 0.80mm in 92% of all VHs from T9 to L4. Similarly, the average precision value for T9 to L4 was 0.85mm based on duplicate analyses for a similar population (*6*). There was no trend to suggest that the SEM value was proportional to the height of the vertebra. The ICC and SEM values generated suggest that use of our standardized analysis protocol yields good relative and absolute intra-rater reliability from T10 to L4 in postmenopausal women.

Grading of vertebral deformity on duplicate analyses identified 85.9% of the vertebrae from T9 to L4 as normal. This frequency compares favorably with a validation study of fracture identification from T7 to L4 in similar a population, which identified 87.9% normal based on lateral spine X-ray (*5)*. Validity studies comparing single analysis of DXA-based vertebral fracture classification with gold standard radiographic assessment of vertebral fracture report that moderate and severe grades of fracture are more consistently identified than mild fractures *(6-14).* In our study, the observed proportion of agreement for grades of vertebral deformity representing fractures was poor. The low prevalence of fractures, while comparable to previous reports (*3-14*), may have contributed to the low observed level of agreement. The 11 vertebrae that were identified as normal and then classified as mild between occasion 1 and occasion 2 had a difference in mean percent deformation (software generated) of 5.6%. This may be interpreted in the context of Genant's classification for mild deformity which is 20% to 25% deformation. In comparison, the four fractures that changed classification from normal to moderate had a mean difference of 17.5% deformation. Collapsing the data into two categories, non-fractured with < 25% deformation and fractured with ≥ 25% deformation, resulted in *kappa* = 0.65 (0.34, 0.91), and P_{obs} = 0.97 (0.93, 0.99). A previous study of 80 postmenopausal women reported the intra-rater reliability *kappa* = 0.81 (*9*). Through duplicate analyses of the same images, we suggest that this protocol did not produce acceptable agreement for mild, moderate or severe fracture identification.

While fracture location was consistent with that reported previously *(10-14),* fracture type differed*.* The majority of factures in our study were biconcave and no crush fractures were identified. This contrasts with previous reports of a higher proportion of wedge and crush fractures *(3, 10, 11).* Biconcave fractures are defined as an abnormal decline (>20%) in VHm relative to VHp and wedge fractures are defined as an abnormal decline in the VHa (>20%) relative to VHp (*2)*. The VHp mean was comparable to a group similar in age and geographic location (*15*). Previous studies have reported middle height marker placement at the midpoint between multiple endplate projections whereas our analysis protocol placed the marker at the lowest midpoint on the superior endplate and the highest midpoint on the inferior endplate (*2*). This definition of a minimum middle height may have contributed to the higher prevalence of biconcave fractures. Subjects were not eliminated due to scoliosis or disc space osteoarthritis which is reported to decrease anterior and middle vertebral body heights (*20*). This may also have accounted for the increased biconcave fracture prevalence. However, it is the severity of the vertebral deformation that is used to determine therapeutic intervention and this protocol marking minimal middle height still yielded highly reliable VHm for T9 to L4 (ICCs > 0.90, lower 95% CI ≥ 0.81).

The findings of this study need to be considered in the context of the following limitations. First, we report intra-rater reliability of VFA image analyses based on duplicate measures. Clinically, each VFA image would be analyzed once. Analysis of variance using single measure analysis (SPSS v.19) generated moderate ICCs (≥ 0.82) from T10 to L4 however, lower bounds of 95% CI were unacceptable (≤ 0.67) for VHm at L3 and T11 and for VHp at T10 and L2 (data not shown). Reliability could be better if readers complete the duplicate analyses on a single occasion. Second, we underestimated the loss of visibility in the thoracic spine and were unable to estimate intra-rater reliability of VH above T9 with adequate confidence. Previous studies suggest that artefacts of motion of the diaphragm and rib overlay explain the reduced visibility *(4, 11).* This methodological limitation is of particular concern when aiming to classify vertebral deformity or monitor change over time in the thoracic region. Earlier studies report from 10% to 94% loss of visibility at T4 and report various exclusion criteria and methodology to control scan visibility *(9-11).* Further investigation is necessary to determine if the loss of analysis above T9 could be reduced by omitting poorly outlined vertebra yet continuing the analysis more proximally. Third, our analysis protocol for defining the middle points of the endplates may have underestimated VHm producing a bias of biconcave fracture type and an increased prevalence of fractures in this group of postmenopausal women. Our study was designed to investigate reliability and the accuracy of the measures is not known. Fourth, two different versions of Hologic VFA analysis software were used and the contribution of this factor to measurement error was not investigated. This study focused on the intra-rater reliability of VFA image analysis using Hologic software and was not designed to investigate sources of error such as patient repositioning, repeat scanning, or analyses by different raters.

DXA-based VH can be reliably measured from L4 to T9 (except VHp at T9) in postmenopausal women over 60 years of age by a novice rater following a standardized protocol. By reporting the relative and absolute reliability at each vertebral level and height we were able to identify that the error-free portion of VHp at T9 was small in this population. Further investigation is required to identify strategies for improving reliable assessment of the thoracic spine. The low radiation dose and accessibility of the VFA scan support its use for the identification of vertebral deformity, fractured and nonfractured, and for further inquiry of DXA-based VH as an outcome measure. Duplicate analyses of each image by the same rater would optimize reliability. Further research is needed to estimate reliability above T9 and establish responsiveness of VH measures to change. Finally, the loss of visibility in the mid to upper thoracic spine and the poor reliability for identifying mild fractures requires attention. These factors may not preclude the clinical utility of VFA as a screening tool but may limit the use of VH as an outcome measure for assessing change in response to interventions targeting the spine.

1. Cronbach LJ, Nageswari R, Gleser GL. 1963 Theory of generalizability: a liberation of reliability theory. *Br J Stat Psych* 16:137-163.
2. Genant HK, Wu CY, van Kuijk C et al. 1993 Vertebral fracture assessment using a semiquantitative technique. *J Bone Miner Res* 8: 1137-1148
3. Black DM, Cummings SR, Stone K et al. 1991 A new approach to defining normal vertebral dimensions *J Bone Miner Res* 6:883-892.
4. Rea JA, Steiger P, Blake GM et aI. 1998 Morphometric X-ray absorptiometry: reference data for vertebral dimensions. *J Bone Miner Res* 13:464-474.
5. Rea JA, Chen MB, Li J et aI. 1999 Morphometric X-ray absorptiometry and morphometric radiography of the spine: a comparison of analysis precision in normal and osteoporotic subjects. *Osteoporos Int* 9:536-544.
6. Steiger P, Cummings SR, Genant HK et al. 1994 Morphometric X-ray absorptiometry of the spine: Correlation in vivo with morphometric radiography. *Osteoporos Int* 4:238-244.
7. Rea JA, Chen MB, Li J et al. 2000 Morphometric X-ray absorptiometry and morphometric radiography of the spine: A comparison of prevalent vertebral deformity identification. *J Bone Min Res* 15:564-574.

8. Binkley N, Krueger D, Gangnon R et al. 2005 Lateral vertebral assessment: a valuable technique to detect clinically significant vertebral fractures. *Osteoporos Int* 16:1513-1518.

9. Vokes TJ, Dixon LB, Murray JF. 2003 Clinical utility of dual-energy vertebral assessment (DVA) *Osteoporos Int* 14:871-878. DOI 10.1007/s00198-003-1461-9.

10. Schousboe JT, DeBold CR. 2006 Reliability and accuracy of vertebral fracture assessment with densitometry compared to radiography in clinical practice. *Osteoporos Int* 17:281-289.

11. Jager PL, Slart RH, Webber CL et al. 2010 Combined vertebral fracture assessment and bone mineral density measurement: a patient-friendly new tool with an important impact on the Canadian Risk Fracture Classification. *Cdn Assoc Rad J* 61:194-200.

12. Chapurlat RD, Duboeuf F, Marion-Audibert HO et al. 2006 Effectiveness of instant vertebral assessment to detect prevalent vertebral fracture. *Osteoporos Int* 17:1189-1195.

13. Rea JA, Chen MB, Li J et al. 2001 Vertebral morphometry: A comparison of long-term precision of morphometric X-ray absorptiometry and morphometric radiography in normal and osteoporotic subjects. *Osteoporos Int* 12:158-166.

14. Eastell R, Cedel SL, Wahner HW et al. 1991 Classification of vertebral fractures. *J Bone Miner Res* 6:207-215.

15. Webber CE, Papaioannou A, Winegard KJ et al. 2003 A 6 mo home-based exercise program may slow vertebral height loss. *J Clin Densitom* 6:391-400.
16. Fuerst t, Wu C, Genant HK, von Ingersleben G et al. 2009 Evaluation of vertebral fracture assessment by dual X-ray absorptiometry in a multicenter setting. *Osteoporos Int* 20:1199-1205.
17. Norman GR, Streiner DL. 2008 Biostatistics The Bare Essentials 3rd Edition. BC Decker Inc. Hamilton, Ontario.
18. Bland JM, Altman DG. 1986 Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1:307-310.
19. Lowry R. Vassar Stats: website for statistical computation. Richard Lowry, Poughkeepsie, NY; 2009. http://faculty.vassar.edu/lowry/kappa.html
20. Osman A, Bassiouni H, Doutri R et al. 1994 Aging of the thoracic spine: distinction between wedging in osteoarthritis and fracture in osteoporosis – a cross-sectional and longitudinal study. *Bone* 15:437-442

.

CHAPTER 4

The Feasibility of Potential Methods to Evaluate the Effect of a Six Month Aquatic Exercise Program on Bone Geometry in Women with Established Osteoporosis

The following paper has been formatted for submission to ISRN Rehabilitation Online Access Journal.

Abstract

Background: Randomized controlled trials (RCT) investigating exercise in postmenopausal women with established osteoporosis have demonstrated positive gains in balance, strength and quality of life. For women with vertebral fractures (VFs), exercising in water provides reduced spinal compressive load, reduces fall impact and engages trunk muscles isometrically. Investigations of bone properties in response to exercise in women with VFs are limited to measures of areal bone mineral density (aBMD) at the hip and lumbar spine using DXA and the evidence is inconclusive. Evaluation of bone geometry may reflect site-specific skeletal adaptations to exercise, however these have not been investigated in women with established osteoporosis. One RCT investigated aquatic exercise intervention in women with osteoporosis but did not assess bone outcomes. If feasible, an RCT investigating bone properties in response to aquatic exercise for women with established osteoporosis would help to determine best practice guidelines for women at high risk to fracture. The purpose of this feasibility study was to assess i) recruitment rate ii) adherence to intervention iii) adherence to assessment protocol iv) intervention and outcome measure safety and v) retention rate.

Study Design: Before and after community-based 6 month aquatic exercise intervention with 12 month follow up.

Methods: The criteria for a successful recruitment rate was set at 16 participants over the 10 week recruitment time. Successful adherence to the intervention was set at >60% and adherence to the assessment protocol was set at 100% data collected and analyzed. The intervention and assessment were considered safe if no adverse event occurred. Retention was judged successful if all participants attended the 12 month follow-up.

Results: Recruitment rate was 10 over the 10 weeks. Average adherence to intervention was 68%. Adherence to the assessment protocol averaged 84% for DXA and VH imaging and physical performance measures. Adherence to acquisition protocol was 54% for pQCT. One adverse event after class resulted in a fracture. Retention was 89% at 12 months.

Conclusion: Adherence to the intervention and retention rate was considered acceptable. To improve adherence to the assessment protocol, better management of resources, additional exclusion criteria and better follow-up on data collection is required. Implementation of a screening test and enhanced safety precautions to avoid adverse outcomes is recommended. This study identified further piloting strategies required to plan a pilot RCT.

Key Words: hydrotherapy, osteoporosis, DXA, pQCT, vertebral morphometry

4.1. Introduction

Osteoporosis is defined as “a disease characterized by low bone mass and structural deterioration of bone tissue, leading to bone fragility and an increased risk of fractures of the hip, spine, and wrist. (*1*).The clinical diagnosis includes the measure of bone mass (areal bone mineral density, aBMD, g/cm^2) at the femur or lumbar spine using dual energy X-ray absorptiometry (DXA) and factors associated with fracture risk (age, gender, glucocorticosteroid medication, history of a fragility fracture over the age of 40 years) (*2*). In Canada, the clinical practice guidelines (CPG) recommend diagnosis based on the 10-year absolute risk to fracture assessment (3). Fracture risk is categorized as low (<10%), moderate (10% - 20%) and high (>20%) (*3*). The history of a fragility fracture after age 40 years and use of glucocorticoids elevates a person’s risk to fracture one level. Studies have reported the presence of any fragility fracture elevates a person’s 10 year absolute fracture risk two-fold and the presence of a vertebral fracture elevates the risk of second fracture four-fold; this risk increases with every subsequent fracture (*4*).The three most common sites of osteoporotic fractures are at the wrist, hip and spine (*5*). The most common type is the vertebral fracture (VF) which is frequently not reported by the patient and is consequently underdiagnosed (*6*). Osteoporotic VFs occur in response to a low strain and/or compressive spinal load sufficient to compromise the strength of the vertebral body. At present, measures of the microarchitecture of bone are not available clinically to include in the evaluation of fracture risk.

Studies investigating the effect of exercise on bone properties in postmenopausal women have assessed changes utilizing the DXA aBMD assessment. A recent systematic review concluded there was a statistically small but significant effect of exercise on aBMD at the femur and lumbar vertebrae sites in postmenopausal women compared to controls (*7*). However, only two studies have investigated aBMD at the hip and lumbar spine in response to exercise in women with established osteoporosis and these were unable to show a difference between the exercisers and controls (*8, 9*). The DXA is limited such that it is a two-dimensional image that is dependent on bone size and does not differentiate the trabecular and cortical compartments. DXA can generate measures of vertebral height (VH, mm) using the vertebral fracture assessment (VFA). Secondary analysis of a subset of data from an RCT reported a slower rate of decline in DXA-based VH measures in women with VF who completed a home exercise program compared with women randomized to the non-exercising control group (*10*). Assessment of VH may provide further information about how the bone adapts to exercises targeting the spine.

Peripheral quantitative computed tomography (pQCT) assesses bone properties in the trabecular and cortical bone compartments separately and generates measures of bone geometry that are associated with the mechanical strength of bone (such as cross-sectional area, polar strength-strain index, section modulus). Two systematic reviews concluded that pQCT studies investigating the effect of exercise on bone mass and geometry in postmenopausal women demonstrate positive, modest, site-specific changes dependent on the type of exercise (*11, 12*). For example, Lui-Ambrose *et al*, (2007), tailored a six month exercise program to induce maximum mechanical stress at the wrist joint (closed-kinetic chain and open kinetic chain exercises) and was able to demonstrate an increase in cortical volumetric bone mineral density (coBMD), bone mineral content (BMC) and cross-sectional area in the distal radius (*13*). The assessment of pQCT derived bone properties at peripheral sites differentiate trabecular and cortical bone adaptations to exercise and evaluate mechanical strength indices which contribute to understanding the influence of exercise on bone health.

Seven randomized controlled trials (RCTs) were reviewed that have investigated the effectiveness of exercise interventions in women with vertebral fractures (VFs) at high risk for further fracture (*8, 9, 14-18*). The individuals participating in the land-based exercises, varying in frequency and duration, demonstrated improved posture, muscle strength, aerobic conditioning, balance and agility, and quality of life in comparison to the individuals in the control group. A recent systematic review concluded the evidence is not yet available to determine the benefits of therapeutic exercise for women with VFs (*19*). The CPG for management of osteoporosis suggest exercises to enhance core stability for individuals with VFs and exercises that focus on balance and gait training for those at higher risk for falls (*3*). For exercise and physical activity to be effective it must be maintained and for individuals with VFs, the exercise type, dose and risk for injury must be considered carefully. Aquatic exercise is an increasingly popular exercise choice due to the advantages of warmth and reduced joint compression addressing the symptoms of arthritic conditions which are common comorbidities for women with VF (*20*). The aquatic environment provides resistance in all planes of movement engages the trunk musculature to maintain vertical alignment and primarily facilitates concentric muscle action. The biological effects of water immersion are related to the fundamental principles of hydrodynamics as outlined in Table 4.1.

Table 4.1. Properties of water and application in vertical water exercise

Properties	Definition	Application of Trunk Extension Exercises
Buoyancy	The upward force generated by the volume of water displaced	Arms buoyant and out to sides, push water behind body, facilitating back extension with shoulder horizontal abduction; vary arm abduction angle. Supine, supported with noodles at neck and waist, double or single leg extension in downward motion resisting buoyancy - isometric
Thermodynamics	A body immersed in a mass of water becomes a dynamic system to equilibrate	Earlier muscle warm up; increases available range of motion
Viscosity	The magnitude of internal friction specific to a fluid during motion. Increases as a log function of velocity	Walking backwards maintaining upright posture Increased speed of movement will increase the resistance
Turbulence	Water motion, slow to stop as movement stills. Pressure drag is the negative pressure behind the rock or moving person	Anchor feet to floor of pool and rapidly move arms (alternating), front and back at sides with no motion in trunk and while maintaining upright posture. Walking forward, negative pressure posteriorly increases erect posture

Five studies investigating the effect of aquatic exercise on musculoskeletal outcomes in postmenopausal women have demonstrated improvement in balance, strength, neuromuscular and functional fitness performance (*21-25*).

The studies are outlined in Table 4.2. Study participants were diagnosed with osteoporosis in one study, osteopenia in two studies and were not diagnosed with osteoporosis in the other 2 studies. Study duration varied from 10 weeks to one year. All programs were comprehensive, including a warm-up, resistance and aerobic training, and a cool-down. Rotstein *et al*, (2007), investigated the effect of aquatic exercise on aBMD at the hip and lumbar spine in healthy, postmenopausal women, mean age (SD) 54 (4) years, and reported no significant differences between the exercise group, n = 20, and the control group, n = 10, pre and post a seven month aquatic intervention, in chest deep water (*23*). Bravo *et al*, (1997) reported a 2% loss of aBMD (0.009 g/cm^2) in the lumbar spine and no loss in the hip, in 77 osteopenic women in a test-retest, cross-sectional, prospective study (no control group) after a 12 month aquatic exercise program, in waist deep water (*24*). Evidence to date suggests women with osteoporosis participating in aquatic exercise can improve physical performance however the benefits to bone health remain unknown. The challenges in evaluating the site-specific bone properties that adapt to exercise, time-course of measurement, the parameters of the exercise program and sample size limit the interpretation of the results of these studies.

Table 4.2. Studies investigating the effects of aquatic exercise in postmenopausal women

First author and year publication	Sample Characteristics N, (Age), Bone Health Status	Length of training (months)	Aquatic Exercise progression, Education, Exertion Total dose (min)	Number of people per class	Outcome Measures	Adverse events	Adherence (%)	Results
Devereaux et al, 2005 (21)	EX23 (73) C24 (73) Healthy	2.5	Progression NR, 100 minutes of education, Moderate 800 min	23	Step Test Modified Falls Efficacy Scale SF36	Chlorine reaction, n=1	80	Improved step test p<0.001) Mental health,vitality improved p<0.05
Arnold et al, 2008 (22)	EX31 (68) C_{LB}33 (69) C_{NE}27 (67) LB = land based EX NE = no EX Osteoporosis	5	Equipment for progression, no education, Moderate 2250 min	10 to 17	Berg Balance Scale functional Reach Test Backward Tandem Walking Osteoporosis QOL	Muscle cramping, n=8, Joint pain, n=9	75	Improved functional reach test and Backward tandem walking p=0.006
Rotstein et al, 2008 (23)	EX25 (55) C10 (56) Healthy	7	Repetition ↑ No education, Moderate + 4400 min	20	aBMD fem neck, aBMD L.sp (L2-L4)	NR	NR	No ∆ BMD L.sp Increased BMC hip, (p<.01)
Bravo et al, 1997 (24)	EX77 (59) Osteopenic	12	Progression of jumps from 30% to 60% max heart rate 7000 min	12 to 30	aBMD (L2-L4) aBMD fem neck Functional fitness test	NR	75	No change in aBMD Improved fitness tests, p<0.001
Tsourlou et al, 2006 (25)	EX12 (69) C10 (68) Healthy	6	Velocity progression, no education, Moderate + 3888 min	6 to 8	Peak isometric knee extensor strength, handgrip strength, squat jump height, TUGT	NR	90	Increased peak strength, p<0.05 Improved TUGT and squat jump height

EX – exercise group; C – control group; aBMD – areal bone mineral density; NR – not reported; L.sp – lumbar spine; fem neck – femoral neck; moderate+ - 60-80% of max heart rate;

The effect of aquatic exercise has not yet been investigated in women with osteoporosis VFs despite the elevated risk to sustain further fracture. Utilization of both the DXA and pQCT technologies may contribute to understanding how the bone adapts to exercise. The primary purpose of this study was to assess the recruitment rate, adherence to the intervention, adherence to the assessment protocol, safety of the intervention and outcome measures and the retention in order to properly plan a methodologically rigorous pilot RCT designed to assess the effectiveness of aquatic exercise on the bone geometry of postmenopausal women with osteoporotic vertebral fractures.

4.2. Methods

4.2.1. Study Design

This was a before-after feasibility study with a 12 month follow-up. The study timeframe is outlined in Figure 4.1. All tests were completed in the Hamilton Health Sciences Department of Nuclear Medicine, and the study protocol was approved by the McMaster University Faculty of Health Sciences/Hamilton Health Sciences Research Ethics Board. All participants provided written informed consent prior to the start of the study.

Figure 4.1. Study design and timeline.

ASSESSMENT

Recruitment January-March 2010	Screen for Eligibility
Baseline Assessment February-March	DXA, pQCT, Back Extensor Strength, Hip Flexor Strength, 8foot TUGT, Kyphotic index, Lordotic Index, Tragus-to-Wall, Hip Girth, Height, Weight, Rapid Assessment of Physical Activity
6 Months Pool Exercise 74 Sessions	3 times per week for 60 minutes per session
6 Month Follow-up August 2010	pQCT, Back Extensor Strength, Hip Flexor Strength, 8foot TUGT, Kyphotic index, Lordotic Index, Tragus-to-Wall, Hip Girth, Height, Weight, Rapid Assessment of Physical Activity
12 Month Follow-up February 2010	DXA, pQCT, Back Extensor Strength, Hip Flexor Strength, 8foot TUGT, Kyphotic index, Lordotic Index, Tragus-to-Wall, Hip Girth, Height, Weight, Rapid Assessment of Physical Activity

4.2.2. Recruitment Rate

4.2.2.1. Recruitment Protocol

The target sample was community dwelling, postmenopausal women over the age of 60 years, diagnosed with osteoporosis and having at least one VF and living within a 20 km radius of the pool site. Vertebral fractures were identified through chart review. The exclusion criteria was 1) any fracture within the past three months, 2) unable to participate in water exercise (open wounds, incontinence, skin disease), 3) living within 20 kilometres of the pool site and 4) medical history of secondary causes of bone loss, primary cardiac disease, uncontrolled hypertension and cognitive impairment limiting the ability to follow instructions for assessment and/or exercise.

Participants were recruited by letter of invitation from two university affiliated osteoporosis clinics and through poster advertisements distributed to four rheumatology clinics in Burlington, Oakville and Hamilton as well as the Hamilton chapter of the Osteoporosis Society, the YMCA in downtown Hamilton, the Department of Nuclear Medicine, HHS, and a local homecare physiotherapist specializing in osteoporosis. Follow-up phone interviews were conducted to provide study details and verify inclusion criteria.

4.2.2.2. Criteria for Judging Successful Recruitment Rate

Feasibility of recruitment was determined for the two recruitment strategies and summarized using a participant flow diagram. Rate of recruitment through the osteoporosis clinics was assessed by the number of individuals that enrolled in the study over the 10 week recruitment period. Recruitment through the poster was quantified by the number of responses and participants recruited. The criteria for success was a class size of 16.

4.2.3. Adherence to a Six Month Aquatic Exercise Intervention Protocol

4.2.3.1. Setting for Intervention

Community, institution and hotel pools were contacted to determine accessibility, availability, temperature, depth, facilities (change rooms, safety), rental cost and parking. Criteria for pool utilization was appropriate accessibility to the building and the pool (steps), available parking and disabled parking allocation and public transit within one block. The class required three one hour time slots at a consistent time each week for six consecutive months. The water temperature was to be a minimum 30 degrees Celsius (termed warm water pool). The depth was to be no less than one meter with a sloped shallow end. The facilities were to be clean, allow for showering and free of obstructions. The rental cost was also considered.

4.2.3.2. Exercise Intervention Protocol

All participants attended a one-hour supervised aquatic group exercise class scheduled three days per week for 26 weeks and totalling 74 sessions. The exercise class was designed and instructed by a physiotherapist specializing in aquatic therapy. Post-graduate courses attended included “Evidence-based Aquatic Therapy” – Level 1 & 2 at Aquatic Therapy University in Minneapolis, the Aquatic Therapy Research Institute (ATRI) conference and seminars in Chicago, certification for group aquatic training through WaterArt in Toronto, and advanced group training through Canadian Aquatic leadership Alliance (CALA) in Toronto.

She is presently a master trainer for CALA and has taught the “Healing Waters” course.

Class format included a 10 minute warm-up, 35 minutes of targeted exercises, 10 minutes of aerobic exercise and a five minute cool-down. All movement was executed in a vertical position. The primary components aimed to challenge trunk, arm and leg musculature in multiple planes of movement to produce novel loading directions on the skeleton. Surface area and speed was altered to generate maximal muscle effort and load. Exercise progression was related to the speed of execution, length and surface area of the moving limb and the use of buoyant and resistive equipment. Participants were required to anchor feet and maintain core stability when executing upper extremity work. Posture was constantly corrected with verbal cues. Exercises are listed and progression is outlined in Appendix 2. Twisting and forward bending were avoided to prevent high-risk loading of the spine. Walking patterns, running and bounding in the chest deep water were performed to challenge dynamic balance. The instructor modified the exercises as needed in response to reported difficulty or pain by reducing the repetitions, speed, lever arm and/or focussing on trunk stability. Participants were instructed to work at a moderate effort level (“your heart beats faster, you can talk but not sing”). Education about posture, muscles and proper breathing were discussed throughout the class to ensure safe and proper execution of the exercises.

4.2.3.3. Criteria for Judging Successful Adherence to the Exercise Intervention Protocol

Adherence to the intervention was determined by recording attendance and the reason for absence at each aquatic exercise class. Adherence for each participant was characterized as the ratio of attended sessions to scheduled sessions multiplied by 100 (%), assessed for all sessions and on a monthly basis. Adherence was deemed successful if the participant completed >60% of the classes over the six months.

4.2.4. Adherence to the Assessment Protocol

Outcome measures are categorized under the ICF framework of body structure, function and activity. The outcome measures acquired at each assessment time point are shown in Figure 4.1.

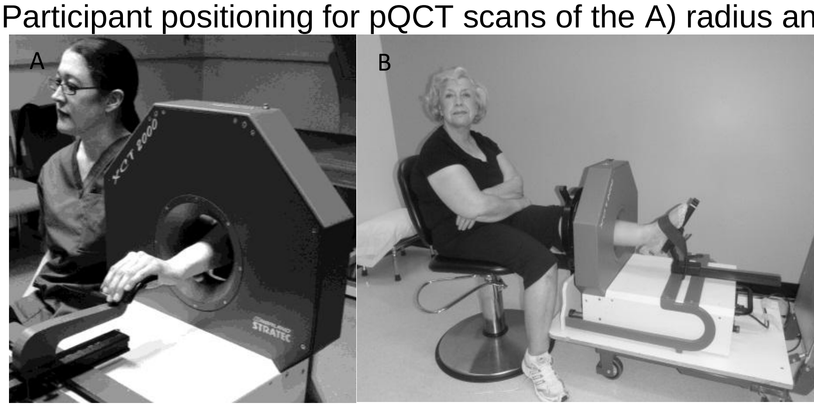
4.2.4.1. Body Structure and Function Outcome Measures

Lumbar Spine and Hip Bone Variables. DXA was performed by the same technician using the Hologic Discovery A (Waltham, MA, USA) and required approximately 20 minutes. For the hip scan, the participant was in a supine position with the non-dominant leg extended and fixed in slight internal rotation. For the lumbar scan, the participant was in supine with hip and knees supported at 90˚ flexion. Analyses were completed using the Hologic Apex v.13.0:03 software to provide measures of aBMD (g/ cm^2), BMC (g) and area (cm^2) of the total hip and lumbar spine (L1-L4) sites, measured to the nearest 0.01 unit.

Vertebral Heights. The VFA scan was performed immediately following the DXA lumbar spine scan while the participant remained lying in supine with hips and knees supported at 90˚ flexion. The scan required approximately five minutes to complete and was analyzed in duplicate, two weeks apart, by the same reader using semi-automatic marker placement which followed the protocol described in chapter 3, table 3.1, p.52. Based on the marker placement, the Hologic Apex v.13.0.03 software generated measures of anterior, middle and posterior vertebral height (VH), measured to the nearest 0.01mm. VHs were measured from levels T9 to L4 only, due to uncertainty as determined by the intra-rater reliability estimates above T9 (chpt. 3, pp 59-61). The long term precision of the DXA was determined based on daily scans of a lumbar spine phantom (Hologic #12221) and the *in vitro* CV during this time was 0.56% for aBMD. Intra-rater reliability of vertebral height (VH) measures in postmenopausal women mean age (SD) 70(7) years was ICC (95% CI) ≥0.87 (0.73, 0.95) from T9 to L4, excluding the posterior VH at T9 as described in chpt. 3, pp 59-61.

Radius and Tibia Volumetric Trabecular and Cortical Bone Variables. pQCT scans of the nondominant radius and tibia were taken by the same technician using the XCT 2000 (manufactured by Stratec Medizintechnik, Germany, and distributed in North America by Orthometrix, White Plains, NY, USA) and required approximately 30 minutes using standard image acquisition protocols with Stratec XCT software (v.5.5). Two sites in the non-dominant radius were scanned: 4% and 30% of the total length of the ulna. The length of the ulna was measured (mm) as the distance from the ulnar styloid process to the olecranon process with the elbow resting on a table and the forearm in a vertical position. The participant was then seated comfortably with the forearm stabilized in the arm rest of the scanner (Figure 4.2A). A 30 mm scout scan was used to identify the radio-ulnar joint to define the anatomic reference line for the distal radius. Cross-sectional images were taken in a proximal to distal sequence in order to minimize the effect of movement. Two sites in the non-dominant tibia were scanned: 4% and 38% of the total length of the tibia. The length of the tibia was measured (mm) as the distance from the medial malleolus to the medial tibial plateau while in a seated position. The participant was seated comfortably with their lower leg positioned in the gantry and the foot stabilized in the footrest (figure 4.2B). A 30 mm scout view at the tibia-fibular joint defined the anatomic reference line. Cross-sectional images were taken in a proximal to distal sequence in order to minimize the effect of movement.

Figure 4.2. Participant positioning for pQCT scans of the A) radius and B) tibia.



All images were acquired with an in-plane resolution of 0.32 mm², a slice thickness of 2.4 mm, SV speed of 40.00 mm/s and CT speed of 15.00 mm/s. The radiation dose for each scan was approximately 0.3 μSv. The long term precision of the pQCT device was determined based on daily scans of a phantom to ensure the machine's calibration for volumetric density was within 0.5% of the initial factory setting.

pQCT scans were analyzed using the manufacturer's software (Stratec v5.5). Analyses at the 4% sites of the radius and tibia required definition of the region of interest (ROI) around the cross-sectional image of the radius or tibia. A standard filter was applied to the image. The contour algorithm, contour mode 2 (C2) based on a threshold of 280 mg/cm³, separated the soft tissue and established the periosteal boundary. Peel mode 1 (P1) was used to isolate the inner 45% of bone comprising the trabecular bone compartment. Measures of total vBMD (mg/cm³), trabecular vBMD (trBMD), total content BMC (mg), trabecular BMC (trBMC), total area (totA, cm³) and trabecular area (trA) were used in the analyses.

For analyses of cortical bone properties at the 30% radius site and the 38% tibia site, the ROI was defined around the bone perimeter. Cortical bone was defined using P2, C3, and separation mode 4 with the inner and outer thresholds set at 710 mg/cm³ (*26*). Measures of cortical vBMD (mg/cm³), cortical BMC (coBMC), and cortical area (CoA) and indices of mechanical strength (section modulus, polar moment of resistance and polar moment of inertia) were used in the analyses.

Muscle Cross-Sectional Area and Density. A pQCT scan at the 66% site of the nondominant tibia was taken following the image acquisition protocol described above. The protocol specified an in-plane resolution of 0.32 mm^2,slice thickness of 2.4mm, and a CT speed of 15 mm/s. Image analyses followed the method described in detail elsewhere (*27*). An ROI was set around the entire calf to determine the total cross-sectional area. To separate the subcutaneous fat from bone and muscle, the ROI was set around the calf muscle, a median filter was applied to the image and the iterative edge detection algorithm was used (C3, P1, threshold = 40 mg/cm^3). To separate bone from muscle, ROIs were set around the tibia and fibula and C1, P2 (threshold of 280 mg/cm3), separation mode 4 (inner threshold 100) were used. Muscle mass (mg/mm) was calculated as the total mass of the tibia and fibula subtracted from the total mass of the muscle and bone. Muscle cross-sectional area (mm^2) was calculated as the tibia and fibula cross-sectional area subtracted from the muscle and bone cross-sectional area. Muscle density (mg/cm^3) was calculated by dividing muscle mass (g) by muscle area (cm^3) and multiplying by 0.001.

Body Habitus. Body mass index (BMI, kg/m^2) was calculated from the height (m) and weight (kg) measured to the nearest 0.1 unit using a stadiometer (SECA, Germany). Whole body lean mass (kg) and fat mass (kg) were obtained using the DXA whole body scan. The participant lay supine for approximately five minutes as per the standard scan acquisition protocol. For hip girth measurement, the participant stood unsupported with clothes on. The rater landmarked the greater trochanter bilaterally, then measured, with a cloth tape, the circumference of the hip at the greater trochanter to the nearest 0.1 cm. Three measures were taken within approximately five minutes, and the average value was used in the analysis. Intra-rater reliability in 49 men and women, mean age (SD) 44(13) years was CV% = 1.8% (*28*).

Back Extensor Muscle Strength (BES). BES was measured as peak force to the nearest 0.1 Newtons, using a dynamometer (Microfet 2, Sammonds Preston). Participants were positioned on a plinth in prone lying, with the head in a neutral position (pillows or a rolled towel(s) were used if required for comfort) and arms were at the sides. The dynamometer was placed at the T3/4 interspace and a strap was secured tightly around the bed, dynamometer and participant (Figure 4.3).

Figure 4.3. Participant position for isometric back extensor strength.

Participants were instructed to raise their head and shoulders off the bed exhaling and pushing up into the dynamometer with maximum effort, and hold for a count of 5 seconds. Three trials were recorded with a one minute rest between; the average of the three measures was used in the analysis. The test took 10 minutes to complete. Test-retest reliability of BES measures acquired in 68 healthy, postmenopausal women using a similar testing protocol with a fixed rod to stabilize the dynamometer rather than a strap, has been reported CV% = 8.7%

(*29*). Intra-rater reliability of the triplicate BES measures for this rater was $ICC_{(2,1)}$, (95% CI) = 0.94 (0.83, 0.99).

Isometric Hip Flexor Muscle Strength (HFS). Lower extremity muscle strength is associated with functional performance and independence. We hypothesized that the HFS peak force would reflect psoas muscle strength and, since this muscle is attached to the anterior aspect of the lumbar spine, may affect the geometry of the lumbar vertebrae. Isometric hip flexor strength (HFS) was measured to the nearest 0.1 Newtons using a dynamometer (Microfet 2, Sammonds Preston). Participants were seated comfortably in a straight backed chair with hands resting on their lap and the knees flexed to 90 degrees (Figure 4.4). A strap was secured tightly around the participant's non-dominant foot, the tester's foot and the participant's knee fixing the dynamometer approximately two inches above the superior aspect of the patella, on the quadriceps muscle of the non-dominant leg.

Figure 4.4. Participant positioning for hip flexor strength testing.

Participants were instructed to raise their thigh upward, foot off the floor, exhaling and pushing up into the dynamometer with maximum effort, and hold for a count of five seconds. Three trials were recorded with a 30 second rest between; the average of the three measures was used in the analysis. The test took six minutes to complete. Reliability has not been determined for this population. Test-retest reliability for 23 community dwelling women fallers with a mean (SD) age of 76(9) years was ICC = 0.99 (*30*). Intra-rater reliability for 14 women and 4 men, mean age 74, was ICC (95% CI) = 0.92 (0.80, 0.97) (*31*).

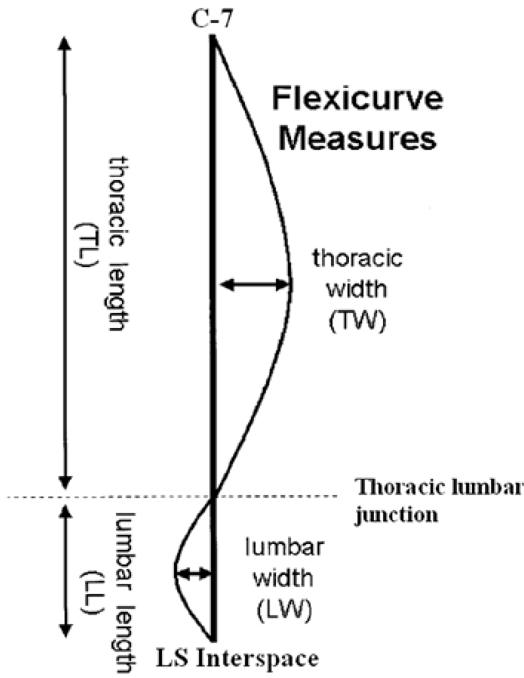
Spine Curvatures. The kyphotic index (KI) and lordotic index (LI) outcomes were measured using the flexicurve ruler according to the instructional CD distributed by the American Physical Therapy Association Geriatrics Division (*32*). Participants were instructed to stand, without footwear and with hands at their side, to maintain ‘best posture’ while the rater molded the flexicurve ruler against the skin along the midline of the spine. The cranial end of the ruler was marked at the level of the inferior tip of the C7 spinous process and the caudal end was marked at the level of the posterior superior iliac spine (PSIS). Then the side of the flexicurve ruler that was molded against the spine was traced onto grid paper along with the marks representing the C7 and PSIS landmarks (Figure 4.5). The *KI* and *LI* were calculated according to the following formulas:

$$KI = \frac{thoracic\ width\ (mm)\ x\ 100}{thoracic\ length\ (mm)}$$

$$LI\ = \frac{lumbar\ width\ x\ 100}{lumbar\ length}$$

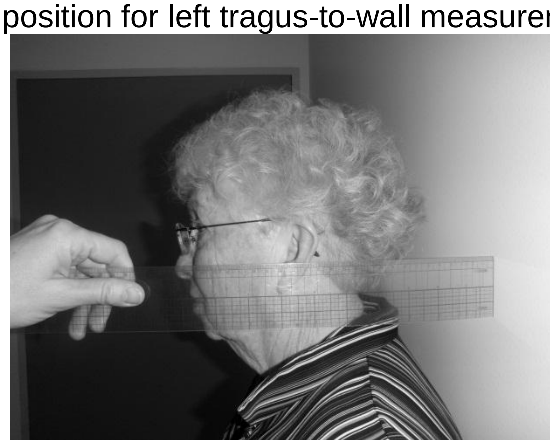
The measurement protocol was repeated three times, taking approximately 25 minutes, and the average values for *KI* and *LI* were used in the analysis. Intra-rater reliability for this rater, estimated using generalizability theory, was R = 0.96 and 0.84 for *KI* and *LI*, respectively (*33*).

Figure 4.5. Flexicurve ruler measures used to calculate the kyphotic index and lordotic index.



Tragus-to-wall Distance (TWD). Measures were taken to the nearest 0.1 cm using a rigid ruler. The participant was positioned standing (no shoes) with heels and buttocks touching the wall and knees straight. The participant was instructed to look straight ahead, keep the chin parallel to the floor and maintain 'best posture' (Figure 4.6).

Figure 4.6. Participant position for left tragus-to-wall measurement.



The distance between the tragus, prominent bony protuberance above the earlobe, and the wall was measured on the right and left. Three trials were recorded with a 30 second rest between; the average of the three measures was used in the analysis. The test took 10 minutes to complete. Reliability has not been determined for this population. The test-retest reliability of TWD measured by a physiotherapist in 52 males mean age (SD) of 45(11) years with AS was ICC = 0.89 (*34*).

4.2.4.2. Activity Outcome Measures

Balance. Participants reported any falls, from standing or a low height, in the last year. Time was measured to the nearest 0.1 seconds using a stop watch. A chair with arms and a seat height of 27 cm was placed in a hallway with a large cone placed eight feet away. The rater demonstrated the task of sitting with hands on thighs and feet flat on the floor, rising, walking briskly forward, around the cone and back to the chair, and sitting down. Participants were instructed to avoid pushing off from arms of the chair if possible, to walk at a safe but quick pace and not to flop into the chair. The participants were timed from when their buttocks left the chair seat to when their buttocks contacted the chair seat again. Three trials were completed with a one minute rest between; the average of the three measures was used in the analysis, taking approximately five minutes to complete. Test-retest reliability for the eight foot TUGT in 48 community dwelling postmenopausal women with a mean age(SD) of 69(5) years was ICC (95% CI) = 0.90 (0.83, 0.95) (*35*).

Self-Reported Physical Activity. The Rapid Assessment of Physical Activity (RAPA) is a nine-item self-report questionnaire that was developed to assess levels of physical activity among adults older than 50 years (*35*). It was used in this study to determine the frequency and duration of the participant's level of physical activity at each assessment time point. The RAPA is easy to score and interpret, scores six to 10 represent an active lifestyle, two to five is under-active and one is sedentary. The RAPA has demonstrated good construct validity to the Community Healthy Activities Model Program for Seniors (CHAMPS) questionnaire, r = 0.54, which is an objective measure of physical activity for research into caloric expenditure that has shown to be valid, reliable and sensitive to change in community dwelling seniors (*36*).

4.2.4.3. Criteria for Judging Successful Adherence to the Assessment Protocol

Successful adherence to the assessment protocol was determined by recording the frequency of missing data at each time point for each outcome measure. The assessment protocol would be feasible if there were no missing data.

4.2.4.4. Parameter Estimations for Outcome Measures

Descriptive statistics (mean, standard deviation, range) were used to summarize bone properties, body structure and activity outcome measures. VH differences were explored on a per vertebrae, per height and average height basis.

4.2.5. Safety of the Exercise Intervention and Assessment Protocols

Procedures were taken to minimize risk. During assessments, standard safety protocol was in place, supervising the balance measures and remaining in close proximity to participants getting on and off the plinth. During the exercise sessions there was a lifeguard present as well as the instructor. During the first two months, a volunteer with lifesaving training assisted participants and the introductory sessions focussed on acclimatization to movement in the water environment. Stairs with railings were present for pool entry and exit; benches and chairs were available for resting 10 feet from the poolside; railings and benches were present in the dressing room; the cleaning protocol ensured no puddling of water on deck or in change areas. Participants were informed of pool deck rules. The community pool building was accessible by a ramp with a railing outside and disabled parking spaces were available.

4.2.5.1. Criteria for Judging Safety of the Exercise Intervention and Assessment Protocols

Major and minor adverse events were to be documented with corrective action and follow-up recorded. Major adverse events were defined as requiring hospitalization. Minor adverse events were defined as “still able to attend exercise sessions” or “missing less than six sessions” (for example, muscle or joint pain). This would inform the instructor regarding exercise tolerance and modifications for the participants in this group. Minor adverse events of respiratory illness or skin reaction to chlorine were to be documented in order to assess the setting (management of air and water circulation in community pool). Criteria for success was no major adverse event(s).

4.2.6. Retention Rate

Retention is defined as the adherence to testing over the 12 month period and was expressed as the ratio of tests attended to the total number of tests planned for each of two time points, six months and 12 months, multiplied by 100 (%) and the ratio of tests attended to the total number of tests planned for the total study multiplied by 100 (%).

4.2.6.1. Criteria for Judging Successful Retention

Retention was deemed successful if 100% of the participants returned for testing at six months and 12 months.

4.3. Results

4.3.1. Recruitment Rate

Nine women were recruited. Figure 4.3 describes the recruitment process and results. One participant was recruited in a direct interview with a rheumatologist (no chart review). The recruitment process continued with the first mailing January 12, 2010. The follow-up phone calls yielded questions regarding allowable absence, schedule and location. At that time potential participants were told the maximum absence was eight weeks (34% of 26 weeks). The reasons for declining participation included poor health (cardiac, bronchitis, LBP), family caregiver responsibilities (grandchildren, spouse), water phobia, access and transportation difficulties and scheduling conflicts. At eight weeks, seven women with vertebral fractures were recruited from the chart review therefore the inclusion criteria was modified to include women without vertebral fractures but at a high 10-year absolute risk to fracture determined using the clinical practice guidelines (*2*). Two more individuals were then recruited in a two week timeframe.

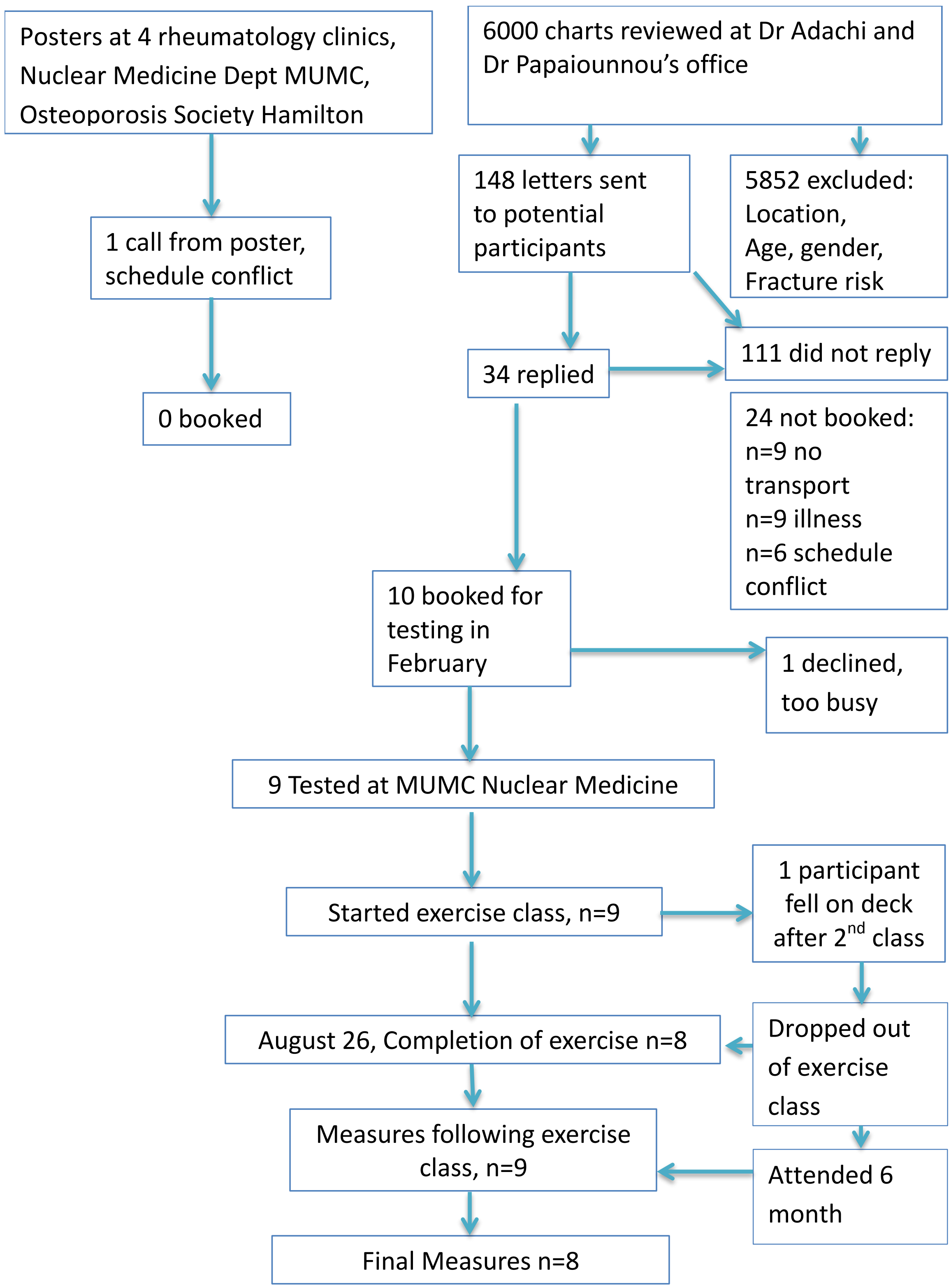
The characteristics of the participants are reported in Table 4.3. All were living within a 12 km radius of the pool, eight were married and all participants had children. One woman walked with a single cane, one woman walked with a quad cane. Five participants drove themselves to the pool, two were driven by their husband and two carpooled with others or could walk as they lived less than one kilometer away. All participants were taking bone-building medication as prescribed by a rheumatologist. Two women did not have a VF, one was taking glucocorticoids and one was a frequent faller and had fractured her hand and ankle. Using the CPG, they were categorized at a high 10-year absolute risk for fracture. Four participants had a normal BMI for persons 65 years of age and older (*37*) with the median 27.1 kg/m^2 and one individual was categorized class II obese. From the doctor's report, seven participants had one or more VFs (see Table 4.3). Scores on the RAPA indicated that six individuals were 'active' and three were 'under-active'. One participant had fractured her wrist three months prior. Seven of the nine women reported medication for comorbidities including systemic lupus erythematosus, rheumatoid arthritis, osteoarthritis, angina and high blood pressure.

Table 4.3. Clinical characteristics of patients (n=9)

	Median	Min – Max
Age (y)	73	64 - 78
Height (cm)	158	147 - 162
Weight (kg)	64.3	59 - 94
BMI (kg/m^2)	27.3	24 - 42
T-score (L.sp)	-2.0	-2.6 – 0.4
Physical Activity Self Report, max 10	6	3 - 9
Falls in last year	6 of 9 reported a fall	
Medications:	Number	
Actonel	5	
Fosovance	3	
Vitamin D	8	
Fractures*	Thoracic 6,7,8,9(x2),11,12 Lumbar 2,3 (x2)	Wedge - 7 Biconcave - 3
Comorbidity	Systemic Lupus Erythematosus, n=1, High Blood Pressure/Angina, n=4 Rheumatoid Arthritis, n=3	

*n=7

Figure 4.7.Participant flow.



4.3.2. Adherence to a Six Month Aquatic Exercise Intervention Protocol

4.3.2.1. Setting for Intervention

Seven pools were contacted to determine accessibility, availability, temperature, depth, facilities (change rooms, safety) and parking. Four sites were visited. Two pools (YMCA on Rymal Rd, Hamilton and St. Josephs Villa, Dundas) were not available for three one hour time slots in the weeks from March to August. The pool depth was less than one metre at two sites in Burlington and parking was difficult and costly at the YMCA in downtown Hamilton. The Aldershot community pool in Burlington could offer three sessions at the same time each day, The warm water pool ($9m^2$, 31˚C) was accessible (ramps and free parking), and had a sloping shallow end with a minimum depth of 1.15 m. The pool provided one lifeguard on deck and pool equipment and was one block from a mainline bus stop. The initial quote for pool rental was $125/hour. The City of Burlington accepted the application for a fee waiver and pool rental was negotiated to include only the shallow end in order to cut costs. Class was scheduled on Monday, Tuesday and Thursday at 1:30pm from March to June and in July and August the group voted to take the opportunity to change the class time to 9:30 am. Over the course of six months, the pool was shared with free swim, private swimming lessons and scuba lessons. We used the first six meters of the shallow end. The pool was closed due to a chemical imbalance for one class and there were three statutory holidays resulting in a total of 74 completed aquatic exercise sessions over the 26 weeks.

4.3.2.2. Rate of Adherence to Exercise Intervention Protocol

Exercise adherence average was 68%. Four women attended over 84% of the sessions, three women attended 68% of the sessions. One participant with chlorine-aggravated bronchitis attended 47% of the time and one dropped out due to a fall after the second session (3% adherence). The reasons for absence included planned vacations, illness, comorbidity exacerbation, family responsibilities (helping out with grandchildren, spousal support). The months of June and August had the least number of absences, 16% and 19%, respectively, while March was the poorest attended at 32% absenteeism. No seasonal patterns emerged. There was no correlation between age, comorbidity or falls history in the eight participants who completed the intervention and their number of absences.

All participants were able to work in the water for one hour and execute all components of the class. The music was chosen by the group and cadence averaged 120 bpm (range 72 – 176 bpm). The pulse was not taken, however, rubor and respiratory rate was observed and feedback was immediate. Rate of perceived exertion (RPE) was based on the participant's ability to "talk but not sing". Water depth varied from the xiphoid process to the sternoclavicular joint and depended on the height of the participant and position in the shallow end. Participants reported functional gains after eight weeks such as "able to climb stairs without use of railing", "able to function with minimal hip or back pain", "able to lift pots and pans", "sleeping better". Buoyant and resistive equipment (noodles, dumbbells, paddles, flutter boards) were introduced after week six, using one piece of equipment for approximately 10 minutes per class to progress strength and challenge balance (Appendix 2). Participants reported that the consecutive Monday and Tuesday classes produced residual muscle fatigue in the upper extremity therefore we instigated 'no wrist' Tuesdays, reducing specific wrist exercise dosage to 50 sessions. However, constant use of the arms as levers with the hand shape a slice, fist or paddle required consistent isometric wrist contraction. The class size enabled effective education and individualized exercise modifications and progressions but did not allow evaluation of adherence to intensity and duration of specific exercises.

4.3.3. Adherence to Assessment Protocol

4.3.3.1. Rate of Adherence to Assessment Protocol

The assessment took approximately two hours to complete. Table 4.4 summarizes the missing data as a function of the measures and the assessment time point. Some data was lost due to deviations from the assessment protocol due to changes in accessibility of manpower, space and equipment resources. A different rater took the height and weight measures on a different stadiometer at six months. This data was not comparable with that obtained at baseline and 12 months and was excluded (Table 4.8). The BES was measured at baseline on a hard plinth while the six and 12 month BES was tested on a soft plinth - six and 12 month BES data could not be compared to baseline (Table 4.9). Adherence to the pQCT image acquisition protocol was variable. The protocol specified an in-plane resolution of 0.50 mm^2 at the 66% site of the tibia but these images were acquired with an in-plane resolution of 0.32 mm^2 at baseline and six months. The final pQCT images acquired at all sites with an in-plane resolution of 0.20 mm^2 resolution could not be compared to the earlier data. Other reasons contributing to missing pQCT data included factors related to the participant - motion artefact at the tibia 38% site (n = 1) and inability to fit the tibia 66% site in the gantry (n=1)). Reasons for missing DXA data included the presence of hardware in the lumbar spine (inability to perform lumbar spine and VFA scan, n=1) and operator deviance from the assessment protocol (hip scan not completed, n=1).

Table 4.4. Data collected according to time point and outcome measures.

Variables		Baseline (n=9)	6 months (n=9)	12 months (n=9)
Body Mass Index (kg/m2)		9/9	0/9	8/9
Isometric Back Extensor Strength		0/9	9/9	8/9
pQCT scans, 5 per person		43/45	43/45	0/45
DXA	Hip	8/9	Not assessed	8/9
	Lumbar	8/9	Not assessed	7/9
Vertebral Height		8/9	Not assessed	7/9
Total Lost Data		14/90 = 16%	11/63 = 17%	52/90 = 58%

4.3.3.2. Bone Outcomes Parameter Estimates

Lumbar Spine and Hip Bone Variables. Table 4.5 summarizes the DXA total hip and lumbar spine measures of aBMD, BMC and area at baseline and 12 months.

Table 4.5. The DXA bone variables at baseline and 12 months, n=7

DXA Site	Bone Variables	Time points: Baseline Mean (SD) Min, Max	Time points: 12 months Mean (SD) Min, Max
Total Hip	aBMD (mg/cm^3)	0.76 (0.08) 0.67, 0.87	0.75 (0.07) 0.66, 0.88
	BMC (mg)	24.1 (2.6) 22.2, 28.2	24 (2.7) 20.2, 27.9
	Area (cm^3)	32.7 (2.4) 30.5, 36.9	32.1 (2.4) 28, 35.5
Lumbar (L1-L4)	aBMD (mg/cm^3)	0.84 (0.16) 0.71, 1.09	0.82 (0.13) 0.69, 1.01
	BMC (mg)	45.1 (10) 33.2, 61.1	44.81 (9.52) 31.3, 57.5
	Area (cm^3)	54 (7.2) 42.1, 65.2	54.5 (7.6) 42.4, 65.8

Vertebral Heights. Table 4.6 summarizes the baseline and 12 month DXA-based vertebral height (VH) measures, anterior (VHa), middle (VHm) and posterior (VHp), from T9 to L4.

Table 4.6. Average vertebral heights at baseline and 12 months for each level, n=7

	VH anterior (mm) Mean (SD)		VH middle (mm) Mean (SD)		VH posterior(mm) Mean (SD)	
Vertebra	Baseline	12 months	Baseline	12 months	Baseline	12 months
T9	17.4 (6.5)	17.3 (2.8)	16.5 (1.7)	16.6 (1.9)	19.7 (0.9)	19.6 (1.3)
T10	18.9 (1.6)	18.6 (1.3)	18.2 (1.2)	17.6 (1.4)	20.6 (1.2)	19.4 (2.0)
T11	19.4 (1.8)	19.7 (2.4)	18.6 (1.0)	18.7 (1.3)	21.8 (1.8)	21.7 (1.4)
T12	20.8 (2.7)	19.9 (4.5)	19.3 (2.2)	19.8 (3.9)	23.2 (1.6)	22.5 (2.7)
L1	23.6 (1.9)	23.3 (1.4)	21.1 (1.2)	21.4 (0.8)	23.9 (2.5)	24.6 (1.5)
L2	24.0 (2.8)	24.8 (1.6)	21.2 (2.8)	22.3 (0.9)	25.5 (1.3)	25.9 (0.9)
L3	25.9 (1.8)	24.2 (5.1)	22.6 (1.5)	21.8 (3.4)	25.6 (1.6)	24.4 (2.6)
L4	24.7 (4.7)	24.8 (2.3)	20.6 (4.3)	22.1 (2.2)	24.1 (1.9)	23.4 (1.3)

Radius and Tibia Volumetric Trabecular and Cortical Bone Variables. Table 4.7 summarizes the pQCT trabecular and cortical bone variables at the 4% distal radius and 4% distal tibia.

Table 4.7. Bone properties at baseline and 6 months in the 4% radius and 4% tibia sites, n = 9

		Time points	
		Baseline	6 months
pQCT site	Bone Variables	Mean (SD) Min, Max	Mean (SD) Min, Max
Radius 4%	Total Density (mg/cm³)	289 (46) 236, 364	303 (55) 229, 394
	Trabecular Density (mg/cm³)	144 (11) 129, 162	145 (11) 131, 162
	Total Content (mg)	79.9 (13) 52.7, 92.3	80.5 (14.5) 52.1, 96.2
	Trabecular Content (mg)	18.3 (4.4) 11.4, 25.9	17.6 (4) 11.0, 24.7
	Total Area (cm³)	282 (63) 193, 371	271 (58) 187, 372
	Trabecular Area (cm³)	127 (28) 87, 167	122 (26) 84, 167
Tibia 4%	Total Density (mg/cm³)	233 (38) 174, 278	230 (38) 174, 273
	Trabecular Density (mg/cm³)	186 (31) 139, 235	185 (30) 139, 234
	Total Content (mg)	235 (27) 209, 292	234 (28) 205, 295
	Trabecular Content (mg)	83 (10) 75, 111	83 (12) 72, 114
	Total Area (cm³)	1023 (114) 901, 1219	1033 (127) 817, 1222
	Trabecular Area (cm³)	461 (51) 405, 549	465 (57) 367, 550

Table 4.8 summarizes the pQCT trabecular and cortical bone variables for the 30% radius and 38% tibia sites.

Table 4.8. Bone properties at baseline and 6 months in the 30% radius and 38% tibia sites, n = 9.

		Time points	
		Baseline	6 months
pQCT site	Body Structure Variables	Mean (SD) Min, Max	Mean (SD) Min, Max
Radius 30%	Cortical Density (mg/cm³)	1188 (45) 1107, 1262	1190 (37) 1110, 1236
	Cortical Content (mg)	71 (12) 50, 83	71 (12) 50, 86
	Cortical Area (cm³)	59(10) 45, 73	59 (10) 45, 72
	Section Modulus (mm³)	171 (35) 128, 243	172 (35) 128, 244
	Polar Strength/Strain Index (mm³)	168 (34) 133, 240	171 (35) 130, 240
	Polar Moment of Resistance (mm⁴)	1137 (280) 810, 1537	1131 (272) 796, 1541
Tibia 38%	Cortical Density (mg/cm³)	1116 (36) 1066, 1160	1110 (43) 1034, 1161
	Cortical Content (mg)	252 (44) 181, 310	247 (43) 179, 300
	Cortical Area (cm³)	225 (38) 166, 273	223 (37) 163, 268
	Section Modulus (mm³)	1312 (233) 1038, 1705	1301 (237) 964, 1680
	Polar Strength/Strain Index (mm³)	1202 (240) 965, 1629	1187 (232) 934, 1602
	Polar Moment of Resistance (mm⁴)	17.1 (3.2) 13.2, 22.4	16.9 (3.0) 12.5, 21.8

4.3.3.3. Body Structure Parameter Estimates

Body Habitus. At six month measures one participant had sustained a VF due to a fall one participant had fallen from a chair, one participant continued to report controlled falls from a standing height at least biweekly. BMI and hip girth remained stable however one participant lost 10 kg over the six months and was able to maintain that weight loss at 12 months. At 12 months, three participants were no longer on bone medication (Fosovance) but remained on Vitamin D. Descriptive statistics for all body structure and activity outcome measures are summarized in the tables in Appendix 3.

Muscle Cross-sectional Area and Density. Table 4.9 summarizes the pQCT muscle variables for the tibia 66% site.

Table 4.9. Muscle properties at baseline and 6 months in the 66% tibia sites, n = 9.

		Time points	
		Baseline	6 months
pQCT Site	Muscle Variables	Mean (SD) Min, Max	Mean (SD) Min, Max
Tibia 66%	Muscle Area cm^3	575 (142) 420, 704	577 (168) 371, 704
	Muscle Density mg/cm^3	69.9 (8.4) 58.8, 75.2	69.9 (6.5) 61.4, 74.1

4.3.4. Safety of the Exercise Intervention and Assessment Protocols

At the end of the second class, March 2, 2010, one participant raised her left foot to explain a foot problem, lost her balance and fell backwards onto the deck. She complained of immediate back pain. Her husband was present and an ambulance was called. Follow up by telephone determined that the X-rays taken at the hospital showed a thoracic spine fracture. She was examined by her rheumatologist, received homecare, returned for the six month assessment and did not return for 12 month assessment. On March 8th, one individual reported a backwards fall off a chair at home resulting in a soft tissue injury and low back pain but reported it felt better in the water and continued with aquatic exercise classes. One participant was a frequent faller but reported no injury or cessation of activities due to falls. During the first three weeks, two participants did lose their balance in the water but regained their footing and had a lifeguard by their side immediately. There were no adverse effects from the loss of balance during the aquatic exercise classes. Two participants reported knee pain due to a gardening injury and osteoarthritis. Exercises were modified in response to the participants discomfort by changing range, speed and positioning for that day and that specific movement. One participant reported a mild facial skin reaction to the pool water which was managed with a barrier cream and this did not impact her attendance or performance. Another participant attended only 47% of the classes due to repeated bouts of bronchitis of which the attending physician suggested were aggravated by the pool environment.

4.3.5. Retention Rate

The average time between baseline and mid measures was seven months. The average follow up for final measurement was 14 months from baseline. Retention of participants was 100% for the six month testing and 89% for the 12 month testing because the one participant that fell in March, 2010, did not return for the final measure. On completion of the 26 weeks, one participant reported that she continued with a community-based aquatic exercise program 3x/week closer to her home and another reported that she returned to land-based exercises with her spouse.

4.4. Discussion

The feasibility objectives and criteria for success were met with respect to the adherence to the intervention, outcome measure safety and the retention rate. However, issues around the recruitment rate, adherence to the assessment protocol and participant safety must be addressed prior to planning a pilot randomized control trial assessing the effect of aquatic exercise on bone geometry in women with osteoporosis and at high risk to fracture.

Recruitment was most efficient through two busy osteoporosis clinics servicing a populated region of southern Ontario. In this study, the assessment of the 10-year absolute risk to fracture category was defined using the lowest aBMD of the hip or lumbar spine, however, future study may benefit from using the lumbar spine aBMD only in order to focus on the assessment of spinal geometry. Another means to improve the recruitment rate may be to expand the geographical boundaries of recruitment. However, the exercise program did require a substantial time commitment, therefore, proximity to the site was thought to be an advantage and positively influence the adherence. The premise of limiting the inclusion criteria by distance was reinforced by the call-back response from women in the neighbouring city, citing “too far” as the reason for not participating. A multi-sited study would address the issue of proximity to class as well as enable recruitment from a larger catchment area. The DXA aBMD and VH measures were not completed in one person due to metal implants in the lumbar spine. Future study would require exclusion of individuals with metal implants that would prevent the acquisition of bone outcome measures. Recruitment is limited by the smaller proportion of women that have VFs and the increased age and comorbidities of this group, yet this does not diminish the necessity to determine guidelines for effective exercise interventions for this group.

Adherence to the assessment protocol was poor and could be better managed with closer supervision on image acquisition and advanced organization of assessment equipment and space. The pQCT data lost was primarily due to misguided protocol however, movement during image acquisition was an issue in two participants rendering 7% of scans unreadable. The loss of physical performance measurement data was not acceptable and although testing was completed in two hours in the same location, the resources for consistent methodology were not in place. For example, the loss of BES data was due to inconsistent methodology, with a hard plinth at baseline and a soft surface plinth used at six and 12 months. Future study must balance the burden of testing and the available resources for consistent measurement.

Physical performance measures were safely completed in a reasonable timeframe. The 8-foot TUGT was used to assess dynamic balance in a small space. The TUGT was not sensitive to change before and after the intervention for seven of the nine participants. The participant who fell after the second session had a moderate fall risk based on the 8-foot TUGT and had reported a fall in the last year. This individual was under-active (RAPA score was 5/10), was dependent on spousal support to attend and used a quad cane. Although this individual may have benefitted from the exercise program, her level of independence was potentially inadequate for an active, group exercise program. The fall history and the TUGT could be used as a screening tool in recruitment and to guide the level of supervision during dressing and pool deck access for safety. In a larger trial with a similar community-dwelling population, the assessment of balance pre and post the exercise intervention may best be assessed using a test more responsive to change. This requires further investigation in order to plan for a larger trial.

Limitations to this study would include the participant bias since all women were recruited to participate in the exercise program and aware of the perceived benefits of exercise. A previous RCT indicated a 7% drop-out rate in the control group due to disappointment in their allocation to the control group (*16*). Instructor bias was not controlled and may have contributed to the exercise adherence rate and retention rate. The rater was also the researcher and this may have affected measurement bias. Two of the exercise classes were scheduled on consecutive days. The lack of a recovery day resulted in reported wrist fatigue and required a modification to the exercise program on Tuesdays. Recovery is an important factor in strength gains and effort therefore it is a recommendation to schedule future interventions on alternating days. Confounding factors such as medication were not controlled and may have impacted the retention rate however all participants were being followed by the same rheumatologist thereby assuming a similar treatment regime and standard of care. It is expected that women with established osteoporosis are on active treatment and the high incidence of comorbidities further complicates the attempts to control for medication. A recent RCT investigating exercise and manual therapy for participants with osteoporotic vertebral fractures did not control for medication but required the participant to be on a stable dose of medication for treatment of osteoporosis for at least six months prior to the exercise intervention (*14*). Informal change room chat and on deck education would be best addressed in a formal educational session(s) to properly address all the aspects of osteoporosis and exercise. Future study should include participant and assessor blinding, allowance for recovery days, medication criteria and formal education sessions. This study has drawn attention to some limitations which can be managed in future studies.

The gaps in the literature are both in the assessment of bone geometry as well as the assessment of the effectiveness of aquatic exercise in women with established osteoporosis. A recent systematic review investigating aBMD in response to exercise for postmenopausal women concluded there are small but significant positive changes at the hip and lumbar spine *(7)*. There is less evidence of the response of bone in women who are already compromised with low aBMD or fracture. Measures of aBMD and vBMD have been utilized to assess the bone response to exercise providing information about bone mineralization and composition however bone structural strength has not yet been assessed in this population. The lack of evidence in bone response to exercise encourages the exploration of measures of bone structure. pQCT indices of mechanical strength and bone geometry, although limited to the peripheral sites, contribute to the understanding of bone response to exercise. Accessibility of the DXA VFA enables the exploration of VH measures as an outcome measure of the geometry of the lumbar and thoracic vertebral bodies. Water buoyancy, turbulence and the increased viscosity create a unique environment for joint decompression, promotion of trunk muscle recruitment, and multiplanar limb resistance. Aquatic exercise is a viable exercise choice for women with vertebral fractures and comorbidities offering a supportive environment while providing gains in strength and function. Use of accessible imaging technologies would enable further understanding of the bone response to aquatic exercise in women with osteoporotic VFs.

The success of a pilot RCT study, with a control group, would require changes to the inclusion and exclusion criteria, more stringent management of assessment protocol, and screening for suitable independence in participants to ensure safety when engaging in community-based exercise programming. A questionnaire to detect change in the constructs of self-efficacy, pain and function would provide better detail in the participant's self-reported outcome measures. It would also be valuable to assess for falls and fracture incidence beyond the 12 month study period to understand the influence of the intervention on fracture prevention. Prior to future pilot study, measurement properties of VH and BES measures need to be established in postmenopausal women with osteoporosis.

In conclusion, based on the findings of this study it is not feasible at present to effectively plan a pilot RCT to investigate bone geometry in women with established osteoporosis before and after an aquatic exercise intervention. Further piloting of strategies for recruitment, assessment protocol and safety are required.

References

1. National Institute of Arthritis and musculoskeletal and skin disease. National Institute of Health – Osteoporosis and Related Bone Disease National Resource Center. Osteoporosis Overview. January 2011.http://www.niams.nih.gov/Health_Info/Bone/Osteoporosis/overview.asp. Accessed 2011, April 16, 2011

2. Siminoski K, Leslie WD, Frame H et al. 2007 Recommendations for bone mineral density reporting in Canada: A shift to absolute fracture risk assessment. *J Clin Densitom* 10:120-123.

3. Papaioannou A, Morin S, Cheung AM, et al. 2010 Clinical practice guidelines for the diagnosis and management of osteoporosis in Canada: summary. *CMAJ* 182:1864-1874.

4. Lunt M, O'Neill TW, Felsenberg D et al. 2003 Characteristics of a prevalent vertebral deformity predicts subsequent vertebral fracture: results from the European Prospective Osteoporosis Study (EPOS). *Bone* 33:505–513.

5. Cooper C. 1993 Epidemiology and public health impact of osteoporosis. *Bailliere's Clin Rheumatol* 7:459-477.

6. Fink HA. 2005 What proportion of incident radiographic vertebral deformities is clinically diagnosed and vice versa? *J Bone Miner Res* 20:1216 -1222.

7. Howe TE, Shea B, Dawson LJ et al. 2011 Exercise for preventing and treating osteoporosis in postmenopausal women. *Cochrane Database Syst Rev* 7. Art. No:CD000333.

8. Papaioannou A, Morin S, Cheung AM et al. 2010 Efficacy of home-based exercise for improving quality of life among elderly women with symptomatic osteoporosis-related vertebral fractures. *CMAJ* 182:1864-1874.

9. Lord SR, Ward, JA, Williams P et al. 1996 The effects of a community exercise program on fracture risk factors in older women. *Osteoporos Int* 6:361-367.

10. Webber CE, Papaioannou A, Winegard KJ et al. 2003 A 6-month home-based exercise program may slow vertebral height loss. *J Clin Densitom* 6:391-400.

11. Hamilton CJ, Swan VJD, Jamal SA. 1998 The effects of exercise and physical activity participation on bone mass and geometry in postmenopausal women: a systematic review of pQCT studies. *Osteoporos Int* 8:92-95.

12. Polidoulis I, Beyene J, Cheung AM. 2011 The effect of exercise on pQCT parameters of bone structure and strength in postmenopausal women—a systematic review and meta-analysis of randomized controlled trials. *Osteoporosis Int* epub 03 August 2011. doi 10.1007/s00198-011-1734-7

13. Liu-Ambrose TYL, Khan KM, Eng JJ et al. 2004Both Resistance and Agility Training Increase Cortical Bone Density in 75- to 85-Year-Old Women With Low Bone Mass: A 6-Month Randomized Controlled Trial. *J Clin Densitom* 7:390-398.

14. Bennell KL, Matthews B, Greig A et al. 2010 Effects of an exercise and manual therapy program on physical impairments, function and quality-of-life in people with osteoporotic vertebral fracture: a randomised, single-blind controlled pilot trial. *BMC Musculoskel Disord* 11:36.

15. Malmros B, Mortensen L, Jensen MB. 1998 Positive effect of physiotherapy on chronic pain and performance in osteoporosis. *Osteoporos Int* 8:215-221.

16. Bergland A, Thorsen H, Karesen R. 2011 Effect of exercise on mobility, balance, and health-related quality of lie in osteoporotic women with a history of vertebral fracture: a randomized, controlled trial. *Osteoporos Int* 22:1863-1871.

17. Hongo M, Itoi, E, Sinaki M, Miyakoshi N, Shimada Y, Mackawa S et al. 2007. Effect of low-intensity back exercise on quality of life and back extensor strength in patients with osteoporosis: a randomized controlled trial. Osteoporos Int 18:1389-1395.

18. Gold DT, Shipp DM, Pieper CF et al. 2004 Group treatment improves trunk strength and psychological status in older women with vertebral

fractures: Results of a randomized, clinical trial. *J Am Geriatr Soc* 52:1471-1478.

19. Dusdall K., Grundmanis D, Luttin K, Ritchie P. et al. 2010 Effects of therapeutic exercise for persons with osteoporotic vertebral fractures: a systematic review. *Osteoporos Int* 22:755-769.
20. David C, Confavreux B, Mehsen N, Paccou J, Leboime A, Legrand E. 2010. Severity of osteoporosis: what is the impact of co-morbidities? Joint Bone Spine 77 S103-S106

21. Arnold CM, Busch AJ, Schachter CL et al. 2008 A randomized clinical trial of aquatic versus land exercise to improve balance, function and quality of life in older women with osteoporosis. *Physiother Can* 60:296-306.

22. Devereux K, Robertson D, Briffa NK. 2005. Effects of a water-based program on women 65 years and over: A randomized controlled trial*. Aust J Physiother* 51:102-108.

23. Rotstein A, Harush M, Vaisman N. 2008 The effect of a water exercise program on bone density of postmenopausal women. *J Sports Med Phys Fitness* 48:352-359.

24. Bravo G, Gauthier P, Roy PM, Payette H, Gaulin P. 1997. A weight-bearing, water-based exercise program for osteopenic women: its impact on bone, functional fitness and well-being. *Arch Phys Med Rehabil* 78:1375-1380.

25. Tsourlou T, Benik A, Dipla K, Zafeiridis A, Kellis S. 2006. The effects of a twenty-four-week aquatic training program on muscular strength performance in healthy elderly women. *J Strength Cond Res* 20:811-818.

26. Rittweger J, Beller G, Ehrig J, Jung C, Koch U, Ramolla J et al. 2000 Bone-muscle strength indices for the human lower leg *Bone* 27:319-326.

27. MacIntyre NJ, Rombough R, Brouwer B. 2010 Relationships between calf muscle density and muscle strength, mobility and bone status in the stroke survivors with subacute and chronic lower limb hemiparesis. J *Musculoskelet Neuronal Interact* 10:249-255.

28. Nordhamm K, SoÈdergren E, Olsson E et al. 2000 Reliability of anthropometric measurements in overweight and lean subjects: consequences for correlations between anthropometric and other variables. *Intl J of Obesity* 24:652-657

29. Sinaki M, Itoi E, Wahner HW, Wollan P, Gelzcer R, Mullan BP, Collins DA, Hodgson SF. 2002 Stronger back muscles reduce the incidence of vertebral fractures: a prospective 10 year follow-up of postmenopausal women. *Bone* 30:836-841.

30. Wang CY, Olson SL, Protas EJ. 2002 Test-retest strength reliability: Hand-held dynamometry in community-dwelling elderly fallers. Arch Phys Med Rehabil 83:811-815.

31. Xue Q-L, Beamer BA, Chaves PHM, Guralnik JM, Fried LP. 2010. Heterogeneity in rate of decline in grip, hip and knee strength and the risk

of all-cause mortality: The women's health and aging study II. *J Amer Geriatr Soc* 58:2076-2084.

32. Lindsey, C., Bookstein, N. (2007). Kypholordosis Measurement Using a Flexible Curve [Instructional CD]. American Physical Therapy Association Section on Geriatrics.

33. MacIntyre NJ, Bennett L, Bonnyman AM, et al. 2011 Optimizing reliability of digital inclinometer and flexicurve ruler measures of spine curvatures in postmenopausal women with osteoporosis of the spine: An illustration of the use of generalizability theory. *ISRN Rheumatol* Article ID 571698.

34. Viitanen JV, Kokko ML, Heikkilä S et al. 1998 Neck mobility assessment in ankylosing spondylitis: a clinical study of nine measurements including new tape methods for cervical rotation and lateral flexion. *Br J Rheumatol* 37:377-81.

35. Rikli RE, Jones CJ. 1999 The development and validation of a functional fitness test for community-residing older adults *J Aging Phys Act* 7:129-161.

36. Topoloski TD, LoGerfo J, Patrick DL, et al. 2006 The rapid assessment of physical activity (RAPA) among older adults. *Prev Chronic Dis* 3. http://www.cdc.gov/pcd/issues/2006/oct/06_0001.

37. Health Canada Website: http://www.hc-sc.gc.ca – Accessed March 27, 2011.

CHAPTER 5: DISCUSSION

The assessment of bone strength in response to exercise is presently limited to axial aBMD (DXA) and appendicular volumetric properties and mechanical strength indices (pQCT). The results are mixed and provide some evidence that the pQCT-based measures are more responsive to site-specific skeletal adaptations to exercise, however, pQCT is not an option for imaging bone geometry in vertebral bodies. Vertebral morphometry may be able to contribute to the understanding of structural strength at the axial site by assessing bone shape. Measurement properties need to be established for vertebral height (VH) measures. Therapeutic management for women with osteoporotic DXA-based vertebral fractures (VFs) includes strengthening the core muscles and improved balance reactions to reduce the risk of further fractures (*1*). To date, only a few studies have investigated exercise programs for women with VFs, demonstrating gains in strength, balance and quality of life but unable to show bone response using DXA aBMD at the hip or lumbar spine (*2-8*). This thesis set out to address the measurement of vertebral bone geometry and pilot its use as an outcome measure investigating aquatic exercise for women with osteoporotic vertebral fractures. The feasibility study identified further strategies required to plan a methodologically rigorous pilot RCT suggesting changes to inclusion criteria and resource management and recommending the use of safety screening measures for participants. Methodological changes and measurement property estimates are to be addressed prior to a larger pilot RCT.

The VH intra-rater reliability estimates suggested VHs can be reliably measured by a novice rater. Although the measures of vertebral height have been used almost exclusively for fracture identification, they have been used in the assessment of the vertebral response to age (*9, 10*) and exercise (*11*). Previous reliability estimates (RMSCV, RMSSD) had not detailed the relative and absolute reliability for each height (anterior, middle and posterior) at each vertebra and partitioning out the error sources. Accessible measures of spinal bone geometry are limited by cost, accessibility and radiation dose. The DXA VFA is positioned to be an effective screening tool for fracture identification during a routine aBMD assessment (*12*). Bone geometry is a factor in bone strength not addressed in measures of aBMD. The VH analyses protocol outlined in chapter two, that measured the minimal middle height may have influenced the higher incidence of biconcave fractures however estimates of reliability at the middle VH were good. This protocol is not suitable for fracture identification but provides acceptable reliability estimates for anterior, middle and posterior VHs from L4 to T9, except for T9 posterior VH. Further studies must manage the reduced thoracic image visibility. This may be addressed by changing the protocol to allow for continued marker placement if the endplates are visible above, as opposed to the exclusion of VFAs of individual's with clinical presentations common with increased age such as arthritis. Duplicate analysis (using average measures) of the VFA scan is recommended to improve the reliability of VH as an outcome measure in research, although this is unlikely to be adopted in the clinical setting. Protocol changes to allow reading proximal to an inadequately visible vertebra must be considered. Inter-rater reliability and test-retest reliability of the VH measures still need to be established prior to utilization as an outcome measure in an RCT investigating the response of the spine to exercise.

All imaging measurements, four DXA and five pQCT sites, took approximately one hour and were not deemed burdensome. The time required to complete duplicate analyses of the VHs was no more than the other imaging analyses. Access and cost of imaging technology is a factor in the study of bone properties. Acquisition of the images was standardized however the parameters of acquisition are variable for the pQCT and require careful consideration and execution at each site. Research into bone requires imaging appropriate to the population. Psychometric testing of the reliability of pQCT measurements specific to this population, need to be completed. There are limitations to aBMD measures in the understanding of bone response to exercise and limitations of site accessibility in the utilization of the pQCT. Use of these three imaging methods may provide more insight into bone properties that contribute to bone strength and detect changes in bone strength in response to exercise.

The feasibility study indicated that further study is required prior to planning a pilot RCT to detect the response of bone to aquatic exercise in women with vertebral fractures. The inclusion criteria were expanded to include those without vertebral fractures who are still at a high risk to fracture, using the clinical practice guidelines. Factors of age, gender, medication, genetics, onset of early menopause, crohn’s disease and smoking elevate the risk for an osteoporotic fracture (*13*). In particular, the presence of an osteoporotic fracture elevates an individual a whole risk category. Ultimately, the goal is fracture prevention and high risk-to-fracture individuals are just an 'event' away from their first fracture. Mild fracture identification is poor yet these individuals have been shown to have compromised bone strength properties (*14*). Preservation of bone strength and increased physical activity is associated with decreased fracture risk (*15, 16*). Broadening the inclusion criteria to include women at a moderate 10-year absolute risk to fracture may improve recruitment rate and still address women with compromised bone strength. The broader inclusion criteria may provide the power to stratify results controlling for medication, age, comorbidity or menopausal stages (*1, 17, 18*). Medication as standard care necessitates detailed documentation of the type and dose in future study. Stratification by medication type requires a larger sample size but would allow an estimate of the effect of medication as a confounding variable.

The loss of data was unacceptable and better management of image acquisition and resources for physical tests would improve this outcome in future. The occurrence of a fall by one participant after the second exercise class was an event associated with fatigue and misjudgement. Future studies would be advised to include a screening tool in order to identify participants at increased fall risk to inform the instructor and enable increased safety measures (wheeled walker while on deck) or exclusion from the study.

Outcome measures were evaluated for ease of testing and comfort of measurement. The primary focus of this thesis is bone outcomes, however, pilot work is still needed to establish the measurement properties of back extension strength, hip flexor strength and tragus-to-wall measures in the assessment of physical function in women with osteoporosis at high risk to fracture. The concerns regarding testing back extensor strength in the prone lying position in women with VFs were unfounded. The advantages of testing isometric BES in the prone position is i) the neutral spine position mimicking an erect posture, ii) prone lying initiates movement at a grade three strength and iii) it is the standard clinical method (*19*). Formal education sessions addressing the principles of self-efficacy and goal setting would standardize the information exchanged during ‘change room chat’ and exercise instruction and provide an avenue for reiteration of safety precautions. The addition of a self-report questionnaire to capture informally reported functional gains and psychosocial benefits would help to characterize the participants, track the time-course of reported changes and assess the effectiveness of the program. Further study of exercise on bone strength and fracture risk needs to document fractures as an outcome and continue to follow the participants for several years to evaluate fracture incidence. This author would recommend the use of other balance measures that can capture change in the active participants and not just in the least active participants. The evaluation of other outcome measures in this target group is required in order to plan an effective pilot RCT.

The WHO’s ‘Active Aging’ policy encourages exercise for the preservation of health and ongoing participation in physical activity is the goal (*20*). Aquatic exercise is one of many exercise programs offered in the community and its appropriateness for targeted age groups and individuals with chronic disease is presently understudied. Participation in an aquatic exercise class does require the extra task of changing attire however this inconvenience is a personal decision, believing the benefits outweigh the task burden. Presently the National Osteoporosis Foundation (NOF) categorizes water aerobics as non-weight bearing and non-impact stating there is no effect on bones. However, NOF endorses muscle strengthening, balance and posture exercises (categorized as non-weight bearing and non-impact, respectively) for reducing falls risk (*21*). Understanding the risks and benefits of the exercise and tailoring the physical activity to the individual is most effective in engaging people in physical activity (*22*).

In conclusion, continued exploration of the bone's response to the mechanical stimulus of exercise is warranted. The muscle-bone interaction at the spine can be challenged safely in the water environment and trunk muscle strength has been associated with decreased fracture risk and improved quality of life in women with established osteoporosis. There is a lack of evidence to guide best exercise practices for this group of at-risk individual's and there are perceived limitations of the reduced weight bearing environment of the water. Prior to planning an RCT investigating the bone response to aquatic exercise in women with established osteoporosis, the issues of recruitment criteria, outcome measurement properties, management of assessment protocol and safety identified in this thesis must be addressed.

References

1. Papaioannou A, Morin S, Cheung AM, et al. 2010 clinical practice guidelines for the diagnosis and management of osteoporosis in Canada: summary CMAJ 182(17):1864-1874.

2. Papaioannou A, Morin S, Cheung AM et al. 2010 Efficacy of home-based exercise for improving quality of life among elderly women with symptomatic osteoporosis-related vertebral fractures. *CMAJ* 182:1864-1874.

3. Lord SR, Ward, JA, Williams P et al. 1996 The effects of a community exercise program on fracture risk factors in older women. *Osteoporos Int* 6:361-367.

4. Bennell KL, Matthews B, Greig A et al. 2010 Effects of an exercise and manual therapy program on physical impairments, function and quality-of-life in people with osteoporotic vertebral fracture: a randomised, single-blind controlled pilot trial. *BMC Musculoskel Disord* 11:36.

5. Malmros B, Mortensen L, Jensen MB. 1998 Positive effect of physiotherapy on chronic pain and performance in osteoporosis. *Osteoporos Int* 8:215-221.

6. Bergland A, Thorsen H, Karesen R. 2011 Effect of exercise on mobility, balance, and health-related quality of lie in osteoporotic women with a

history of vertebral fracture: a randomized, controlled trial. *Osteoporos Int* 22:1863-1871.

7. Hongo M, Itoi, E, Sinaki M, Miyakoshi N, Shimada Y, Mackawa S et al. 2007. Effect of low-intensity back exercise on quality of life and back extensor strength in patients with osteoporosis: a randomized controlled trial. Osteoporos Int 18:1389-1395.

8. Gold DT, Shipp DM, Pieper CF et al. 2004 Group treatment improves trunk strength and psychological status in older women with vertebral fractures: Results of a randomized, clinical trial. *J Am Geriatr Soc* 52:1471-1478.

9. Rea JA, Steiger P, Blake GM et al. 1998 Morphometric X-ray absorptiometry: reference data for vertebral dimensions. *J Bone Miner Res* 13(3):464-474.
10. Briot K, Kolta S, Fechtenbaum J et al. 2010 Increase in vertebral body size in postmenopausal women with osteoporosis. *Bone* 47:229-234.
11. Webber CE, Papaioannou A, Winegard KJ et al. 2003 A 6-mo home-based exercise program may slow vertebral height loss. *J Clin Densit* 6(4):391-400.
12. Jager PL, Slart RH, Webber CL et al. 2010 Combined vertebral fracture assessment and bone mineral density measurement: a patient-friendly new tool with an important impact on the Canadian Risk Fracture Classification. *Cdn Assoc Rad J* 61:194-200.

13. Samelson EJ, Hannan MT. 2006. Epidemiology of osteoporosis *Curr Rheumatol Rep* 8:76-83.

14. Melton JL III, Riggs BL, Keaveny TM et al. 2011 Relation of Vertebral Deformities to Bone Density, Structure, and Strength. *J Bone Miner Res* 25(9):1922-1930.

15. Marshall D, Johnell, O, Wedel H. 1996. Meta-analysis of how well measures of bone mineral density predict occurrence of osteoporotic fractures. Br Med J 312(7041):1254-1260.

16. Gregg EW, Pereira MA, Caspersen CJ. 2000. Physical activity, falls and fractures among older adults: a review of the epidemiological evidence. *J am Geriatr Soc*. 48(8):

17. Mueller TL, van Lenthe GH, Stauber M, Gratzke C, Eckstein F, Muller R. 2009 Regional, age and gender differences in architectural measures of bone quality and their correlation to bone mechanical competence in the human radius of an elderly population. Bone 45:882-891.

18. Polidoulis I, Beyene J, Cheung AM. 2011. The effect of exercise on pQCT parameters of bone structure and strength in postmenopausal women—a systematic review and meta-analysis of randomized controlled trials. Osteoporosis Int epub 03 August 2011.

19. Kendall FP & McCreary EK, Provance PG et al. 5th ed 2005. Muscles Testing and Function with Posture and Pain. Lippincott Williams & Wilkins. Philadelphia.

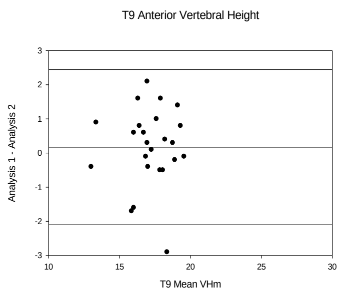
20. WHO. 2002 Active Ageing – A Policy Framework. Geneva: World Health Organization.

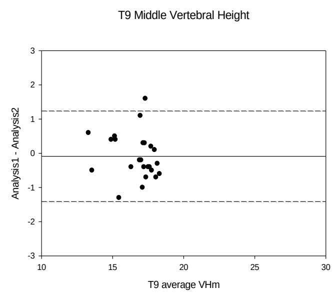
21. National Institute of Arthritis and musculoskeletal and skin disease. National Institute of Health – Osteoporosis and Related Bone Disease National Resource Center. Osteoporosis Overview. January 2011.http://www.niams.nih.gov/Health_Info/Bone/Osteoporosis/overview.asp. Accessed 2011, August 24, 2011

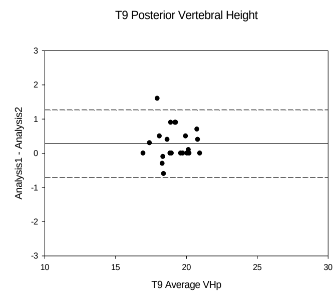
22. Moreland J, Richardson JA, Chan DH et al. 2003 Evidence-based guidelines for the secondary prevention of falls in older adults *Gerontology* 49:93-116.

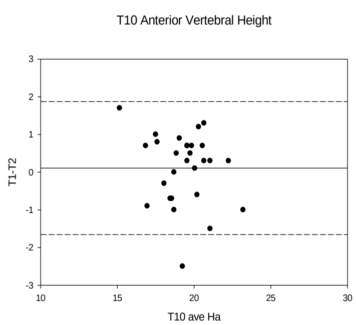
Appendix 1. Bland-Altman Plots

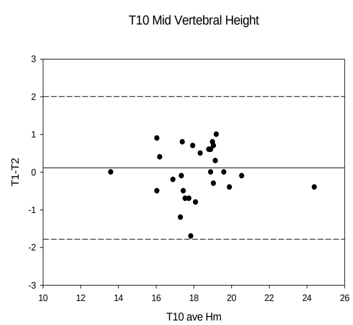
For each vertebral level, the difference in vertebral height (Analysis T1 – Analysis T2) was plotted as a function of the mean vertebral height for anterior, middle, posterior from T9-L4.

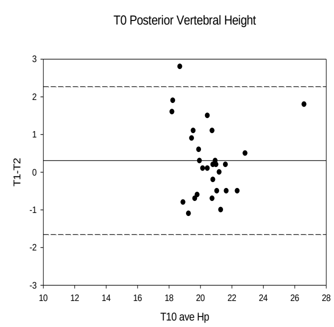


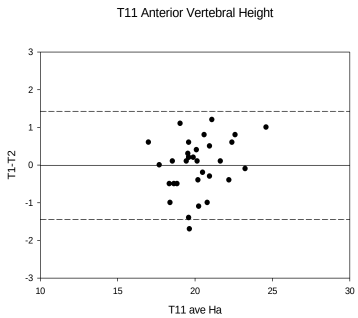


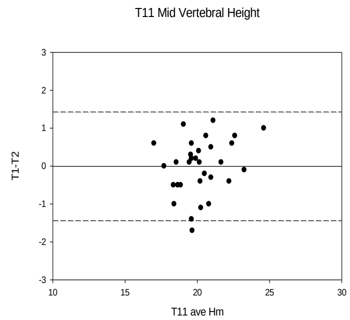


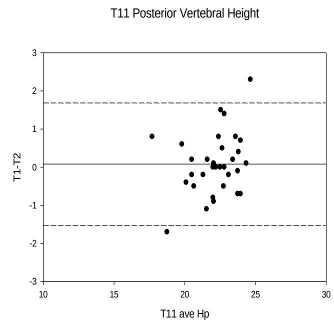


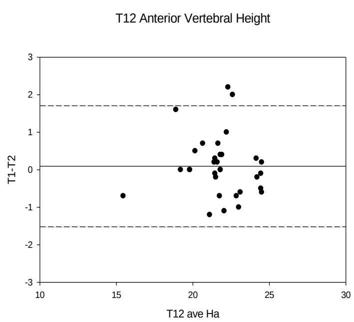


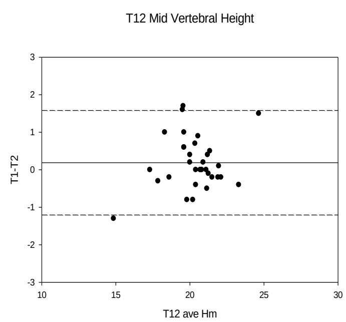


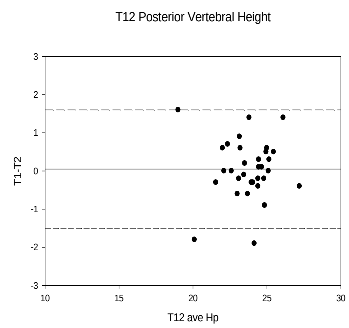

T11 Anterior Vertebral Height
T1-T2
T11 ave Ha

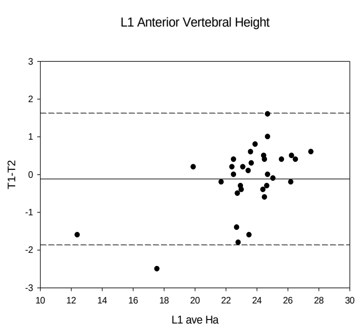

T11 Mid Vertebral Height
T1-T2
T11 ave Hm

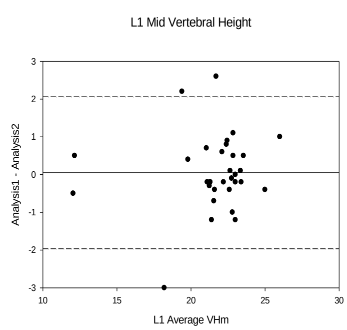

T11 Posterior Vertebral Height
T1-T2
T11 ave Hp

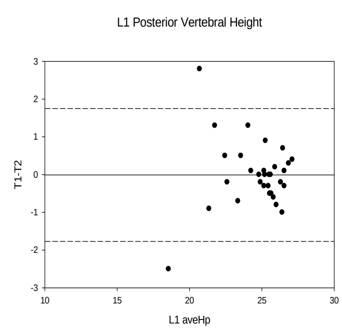

T12 Anterior Vertebral Height
T1-T2
T12 ave Ha

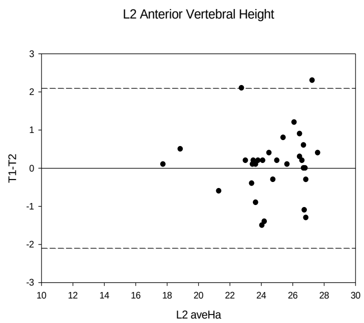

T12 Mid Vertebral Height
T1-T2
T12 ave Hm

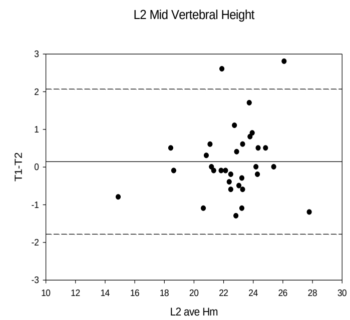

T12 Posterior Vertebral Height
T1-T2
T12 ave Hp

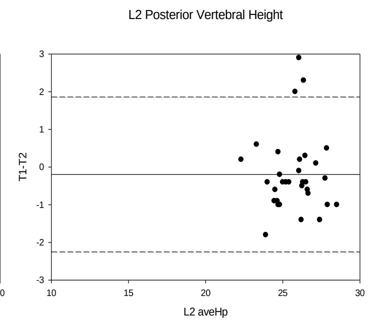

L1 Anterior Vertebral Height
T1-T2
L1 ave Ha

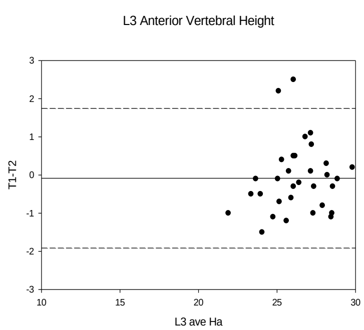

L1 Mid Vertebral Height
Analysis1 - Analysis2
L1 Average VHm

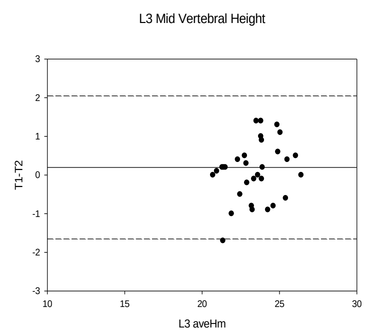

L1 Posterior Vertebral Height
T1-T2
L1 aveHp

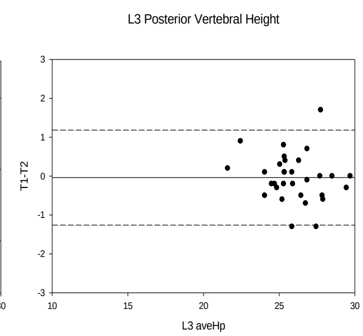

L2 Anterior Vertebral Height
T1-T2
L2 aveHa

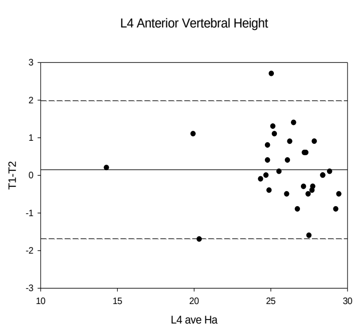

L2 Mid Vertebral Height
T1-T2
L2 ave Hm

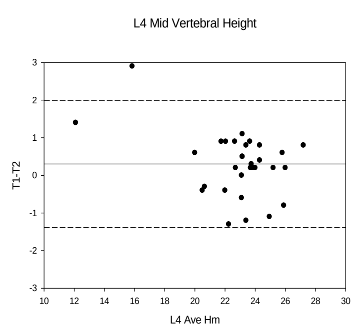

L2 Posterior Vertebral Height
T1-T2
L2 aveHp

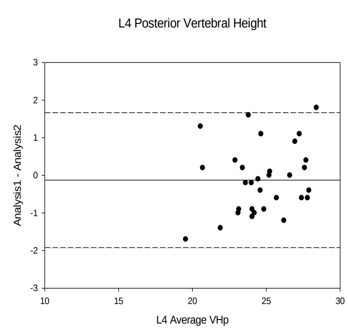

L3 Anterior Vertebral Height
T1-T2
L3 ave Ha


L3 Mid Vertebral Height
T1-T2
L3 aveHm


L3 Posterior Vertebral Height
T1-T2
L3 aveHp


L4 Anterior Vertebral Height
T1-T2
L4 ave Ha


L4 Mid Vertebral Height
T1-T2
L4 Ave Hm


L4 Posterior Vertebral Height
Analysis1 - Analysis2
L4 Average VHp

Appendix 2. Aquatic Exercise List and Progression Table

WARM-UP and CARDIOVASCULAR EXERCISES: Standing upright, maintain good posture.

Progression:

a. Walking using arms for propulsion
b. Walking speed increased in all directions
c. Walking stride length altered
d. Walking with arms trailing behind.

1. Forward Walking: bend the hip and knee exaggerating hip and knee flexion. Lower the foot down to the ground, landing on the heel. Gently push off with the toe. Emphasis on movement sequence
2. Backwards Walking: bend the hip and knee while stepping the leg behind your body. Press the foot down to the ground landing on the toe. Gently roll onto the heel.
3. Side stepping: step to one side bringing feet together with a straight leg.
4. Cross-over walking: Stepping sideways then bring trailing leg across midline to cross in front or behind the lead leg.
5. Lunge walking: walk forward using large steps, knee bent of leading leg and knee straight in trailing leg. Cue abdominals and back extensors for upright trunk.
6. Tandem walking: place lead foot directly in front of trailing foot; walk on a tightrope.
7. Stiff leg walking: forward walking with little or no knee flexion
8. Hopping: Standing upright, flex at the both hips and knees. Jump forward using arms for balance. Land on both feet, bending at knees for gentle impact.
9. Bounding: Hopping from one leg to the other in a wide stance moving forward or backward.
10. Jogging: Jogging action in water with immersion to sternal notch. and upright position, move forward and backward.
11. X-country Skiing: position of alternate arm with forward leg; arms and legs are straight, jump to alternate forward arm, mimicking ski action. For cardiovascular training. Immersion to sternum as comfortable.

TRUNK STRENGTH: Stand upright, looking forward, keep trunk still.

Progression:

a. Small amplitude movements
b. Short lever arm movements
c. Large amplitude movements
d. Long lever arm movements

12. Anchor feet on the floor, arms straight down by side; alternate movement of arms forward and backward, do not twist the trunk
13. Anchor feet on the floor, arm movement like windshield wipers across body and folding into body, do not move the trunk
14. Anchor feet on the floor, arms at sides, bend and straighten arms at the elbows working biceps and triceps, do not twist the trunk
15. Abdominals: lift knee up and press down with the ipsilateral hand, switch legs, repeat. Breathe out with touch.
16. Abdominals: lift knee up and press down with the contralateral hand, switch legs, repeat. Breathe out with touch.
17. Abdominals: push flotation equipment down below surface with arms while exhaling and thinking of curling ribs slightly towards pelvis, maintaining tall stance and feet on floor (cue – not to kiss the water).

UPPER EXTREMITY: maintain good trunk posture.

Progression:

a. Small to large amplitude, choose range
b. Short to long lever
c. Slow to fast speed
d. Hand shape – slice, fist, open palm

18. Shoulder flexion/extension – straight arm pull: keeping elbow straight, reach forward and pull back and down sweeping sides; alternating or together
19. Shoulder abduction/adduction arms – arms raise outwards from sides to water surface and back
20. Shoulder internal/external rotation – elbows bent, tucked into sides, do windshield wiper motion with forearms
21. Shoulder horizontal abduction/adduction – arms just under surface of the water, together in front of the body, pull out to sides, extend as comfortable
22. Shoulder combination arm movements: circular, diagonal and figure 8 arm movements to front and sides of the body.
23. Open the door - reach forward and pull back with bent elbow, emphasis on pulling back. Unilateral or alternating.
24. Punch out – emphasis on forward thrust. Unilateral or alternating.
25. Breast Stroke: Reach forward with both arms elbows bent, abduct horizontally until arms are in the same plane as the body, then return to forward reaching position (focus on scapular retraction).

Wrist progression:

a. hand shape
b. gripping 6 inch noodles

26. Wrist flexion/extension – elbows bent or straight (more difficult), cue waving motion
27. Wrist supination/pronation – elbows bent, cue “flipping pancakes” motion
28. Wrist ulnar/radial deviation – elbows bent, cue “hammering” motion

LOWER EXTREMITY: maintain good trunk posture.

Progression:

a. Small to large amplitude/ROM
b. Short to long lever
c. Slow to fast speed
d. Foot shape – plantar flexed, dorsiflexed

29. Hip flexion/extension: one leg swings in front and behind in sagittal plane
30. Hip abduction/adduction: one leg swings away from the body and back to touch knees
31. Hip internal/external rotation: feet together then step heel-toe to sides and back in (comfortable range)
32. Hip circumduction: one leg moves in circles, diagonal leg patterns, figure eights
33. Knee flexion/extension: squatting (close kinetic chain)
34. Knee flexion/extension: one-legged stance, kicking (flutter style), open kinetic chain
35. Knee flex/ext: sitting against wall (touch sacrum and scapula), semi squat position - unilateral kicking of foot forward and backward, comfortable range
36. Ankle ROM: one-legged stance, arms assist for balance, circle motions at ankle
37. Toe raises in standing, arms to balance, good base of support

BALANCE EXERCISES: Stand upright, looking forward, keep trunk still or maintain good trunk posture.

Progression:

a. Wide base of support
b. narrow base of support
c. one-legged stance

38. Upper extremity challenges with anchored feet, arm movement: paddle as turbine in front (creating own turbulence)
39. Walking patterns of square, figure eight, steps to side and back
40. One-legged stance – other leg swinging or ankle rolling movements
41. Tandem Walking progress to arms out of water
42. Circle of turbulence – walk around anchored person (create turbulence); stationary person tries not to move.
43. Semi-squat position, eyes following arm movement, open arms out to left then back to centre, open to right, breath

COOL DOWN AND STRETCHING

44. Slow walking across pool – long strides, arms dragging behind
45. Arm crossover: arm comes across body, below chin, lower shoulder and breathe
46. Gentle forward hug then open into extension position for upper torso.
47. Balance with arm assist while allowing the water to elevate one leg in front, stretching back of leg.
48. Balance with arm assist while allowing the water to elevate one leg behind (can hold side) allow knee to bend for quads stretch, tuck tummy.
49. Legs wide apart, feel gentle inner thigh stretch, then bend one knee and lean towards that side, straighten; bend other knee and lean
50. Hip Extension: stand tall, allow one knee to float behind the body, tuck tummy and feel stretch in front of thigh.
51. Hip Flexion: stand tall, lift one knee as high as you can, grasp it with your hands under the knee and gently pull it to your body. Hold 5 sec, do other side.

Table A2.1. Progression of exercises.

Primary Purpose of Exercises	**Exercise by # - Progression** **0 months ----- → 3 months ---- → 6 months**	**Repetitions** **0 ---- 3----6**
Warm Up	1, 2, 3, 4, 5→	8x1,8x2,8x3
Trunk Stability	12, 13, 14, 15, 16, 17	10 s to 30 s
Trunk Extension Strength	12 → 21 → 23 → 25 43	5 reps to 12 reps
	UPPER EXTREMITY	
Arm Flex/Extension Strength	18, 22, 23, 24,25 →	8x1,8x2,8x3
Arm Abb/Adduction Strength	19, 21, 22, → → 25 →	8x1,8x2,8x3
Scapular Retraction	21, 23, 25, 43, 46 →	8x1,8x2,8x3
Shoulder Strength	18 to 25 →	8x1,8x2,8x3
Wrist/Forearm Strength	26, 27, 28 →	Mon+Thurs 8x1 ---- 8x2
	LOWER EXTREMITY	
Hip Ext/Flex Strength	30 →	8x1,8x2,8x3
Hip Abd/Adduction Strength	31, 32, 33 →	8x1,8x2,8x3
Knee Flex/Extension Strength	34, 35, 36 →	8x1,8x2,8x3
Ankle Flex/Extension Strength	36, 37, 40 →	8x1,8x2,8x3
Balance	38, 39, 40, 41, 42, 43 →	10s – 1 minute
Cardiovascular	8, 9, 10, 11, 12 →	30s on, 30s off →2min on, 30s rest
Cool Down/Stretch	44, 45, 46, 47, 48, 49, 50, 51 →	As tolerated

Appendix 3: Descriptive Statistics of Body Function and Activity Variables.

Table A3.1. Descriptive statistics for body structure and body function variables at two time points.

	Time points	
	Baseline (n = 9)	12 months (n = 8)
Body Function Variables	Mean (SD) Min, Max	Mean (SD) Min, Max
BMI (kg/m^2)	28.9 (5.4) 24.2, 41.7	28.5 (5.0) 23.1, 38.1
Lean Mass (kg)	41.4 (3.9) 36.7, 48.2	38.6 (4.0) 32.6, 45.3
Fat Mass (kg)	30.9 (9.2) 22.7, 47.9	31.6 (8.3) 22.7, 47.7
Hip Girth (cm)	109.8 (9.9) 100.4, 129.5	109.9 (10.2) 99.2, 127.7

Table A3.2. Descriptive statistics for body function and activity variables at three time points.

	Time points		
	Baseline (n = 9)	6 months (n = 9)	12 months (n = 8)
Variables	Mean (SD) Min, Max	Mean (SD) Min, Max	Mean (SD) Min, Max
BES (Newtons)	74 (38) 37, 145	57 (32) 25, 125	79 (29) 35, 126
HFS (Newtons)	100 (46) 17, 170	86 (41) 33, 146	113 (32) 59, 149
Kyphotic Index	13.7 (5) 6, 20	12.1 (5) 5.5, 19.8	12.1 (7) 7.4, 21.2
Lordotic Index	13.9 (3) 9.9, 17	14.7 (4) 6.6, 20.2	13.4 (6) 9.8, 20.3
TWD Right (cm)	14.6 (3) 10.6, 18.8	15.2 (2.4) 12.4, 20.1	13.3 (5.2) 13.2, 17.9
TWD Left (cm)	14.9 (3) 10.0, 19.2	15.6 (2.5) 12.0, 20.0	15.2 (1.6) 12.3, 17.2
TUGT (sec)	7.1 (2.4) 5.3, 13.1	7.6 (3.0) 5.3, 15.1	7.8 (3.0) 5.8, 15.