

5-2-2016

The Effects of Locomotion-Induced Shock Loading on Tibiofemoral Bone Stress Response

Alexa Standerfer
University of Nevada, Las Vegas

Suzenna Ngo
University of Nevada, Las Vegas

Karen Daun
University of Nevada, Las Vegas

Follow this and additional works at: <https://digitalscholarship.unlv.edu/thesesdissertations>

 Part of the [Physical Therapy Commons](#)

Repository Citation

Standerfer, Alexa; Ngo, Suzenna; and Daun, Karen, "The Effects of Locomotion-Induced Shock Loading on Tibiofemoral Bone Stress Response" (2016). *UNLV Theses, Dissertations, Professional Papers, and Capstones*. 3547.

<http://dx.doi.org/10.34917/14871592>

This Dissertation is protected by copyright and/or related rights. It has been brought to you by Digital Scholarship@UNLV with permission from the rights-holder(s). You are free to use this Dissertation in any way that is permitted by the copyright and related rights legislation that applies to your use. For other uses you need to obtain permission from the rights-holder(s) directly, unless additional rights are indicated by a Creative Commons license in the record and/or on the work itself.

This Dissertation has been accepted for inclusion in UNLV Theses, Dissertations, Professional Papers, and Capstones by an authorized administrator of Digital Scholarship@UNLV. For more information, please contact digitalscholarship@unlv.edu.

THE EFFECTS OF LOCOMOTION-INDUCED SHOCK LOADING
ON TIBIOFEMORAL BONE STRESS RESPONSE

By

Alexa Standerfer

Suzenna Ngo

Karen Daun

A doctoral project submitted in partial fulfillment
of the requirements for the

Doctor of Physical Therapy

Department of Physical Therapy

School of Allied Health Sciences

Division of Health Sciences

The Graduate College

University of Nevada, Las Vegas

May 2016

Copyright by Alexa Standerfer, Suzenna Ngo, and Karen Daun, 2016
All Rights Reserved.



Doctoral Project Approval

The Graduate College
The University of Nevada, Las Vegas

May 13, 2016

This doctoral project prepared by

Alexa Standerfer

Suzenna Ngo

Karen Daun

entitled

The Effects of Locomotion-Induced Shock Loading on Tibiofemoral Bone Stress Response

is approved in partial fulfillment of the requirements for the degree of

Doctor of Physical Therapy
Department of Physical Therapy

Kai-Yu Ho, Ph.D.
Research Project Coordinator

Kathryn Hausbeck Korgan, Ph.D.
Graduate College Interim Dean

Kai-Yu Ho, Ph.D.
Research Project Advisor

Merrill Landers, Ph.D.
Chair, Department of Physical Therapy

ABSTRACT

Purpose/Hypothesis: Knee osteoarthritis (Coats, Zioupos, & Aspden) is a degenerative joint disease that negatively impacts the quality of life. About 9.3 million people in the U.S. population are affected. It has been suggested via magnetic resonance imaging (MRI) studies that bone marrow edema (i.e., indicative of bone stress response) and joint structure changes may be the main contributing factors of pain in OA. Frontal plane lower extremity (LE) alignment has been a topic of much interest regarding development of OA in the knee joint. It is hypothesized that varus alignment increases forces through the medial compartment of the knee, thereby leading to bone stress response and initiation of OA. The purpose was to investigate the effects of locomotion-induced shock loading and LE alignment on tibiofemoral bone stress response in older adults without knee OA.

Number of Subjects: Five male and five female subjects with no medical diagnosis of knee OA (57.9 ± 3.9 years; 84.2 ± 12.7 kg; 1.7 ± 0.1 m) participated.

Materials/Methods: Each subject underwent a clinical biomechanical testing session and an MRI assessment session. During the clinical biomechanical testing, static LE alignment was obtained by measuring the angle between the long axes of femur and tibia. Dynamic LE alignment, in particular the peak frontal plane LE angle during loading response of fast walking, was obtained using a 3-dimensional motion capturing system. During the MRI assessment session, a chemical-shift-encoded water-fat MRI protocol was applied to the dominant knee. MRI data was obtained before fast walking and immediately following a 30-minute fast walking session. Bone stress response was determined by quantifying the bone water content within the weight-bearing regions of

the medial and lateral compartments. Paired t-tests were used to compare bone water content before and after fast walking. Pearson correlation coefficient analyses were used to determine the associations between LE alignment and changes in water content after fast walking.

Results: The paired t-tests revealed no change in water content after fast walking within medial femur ($p = 0.671$), lateral femur ($p = 0.174$), medial tibia ($p = 0.461$), and lateral tibia ($p = 0.190$). Pearson correlation coefficient analyses revealed a significant moderate correlation between increased bone water content of the medial femur and increased static varus alignment ($R = 0.688$, $p = 0.027$). Additionally, a trend with moderate correlation was observed between increased bone water content of the medial tibia and increased static varus alignment ($R = 0.437$, $p = 0.206$). No association was found between changes in bone water content and dynamic alignment ($p < 0.05$).

Conclusions: This is the first study assessing the acute effects of locomotion on bone stress response in older adults without knee OA. Although there was no significant change in bone water content post locomotion, a greater varus alignment was associated with increased water content in the medial compartment.

Clinical Relevance: Our findings provide further understanding of the contribution of LE alignment and development of OA. This research can impact the early detection, prevention, and interventions for individuals at risk for joint deformity and knee OA.

Key Words: Alignment, Bone Water Content, Knee Osteoarthritis

ACKNOWLEDGEMENTS

This research study was made possible by the Graduate & Professional Student Association Grant and the University of Nevada, Las Vegas Physical Therapy Department Grant. The authors would like to thank Kai-Yu Ho, PT for her excellent guidance as principle investigator of this study. The authors would also like to thank Szu-Ping Lee for his additional help with this project.

TABLE OF CONTENTS

ABSTRACT.....	iii
ACKNOWLEDGEMENTS.....	v
LIST OF FIGURES	viii
INTRODUCTION	1
METHODS	3
RESULTS	14
DISCUSSION.....	18
CONCLUSION.....	22
REFERENCES	23
CURRICULUM VITAE.....	26

LIST OF TABLES

Table 1. The associations between static LE alignment and changes in bone water content. * indicates a statistical significance ($p < 0.05$).	17
Table 2. The associations between dynamic LE alignment and changes in bone water content. * indicates a statistical significance ($p < 0.05$).	17

LIST OF FIGURES

Figure 1. Locations of reflective markers were placed on the above anatomical landmarks in anterior, posterior, and sagittal views. 7

Figure 2. Measurement of frontal plane static LE angle. (A) Manual marking of anterior mid-thigh, center of the patella, and midpoint of the patellar tendon; (B) Measurement of frontal plane static LE angle with goniometer; (C) The acute angle highlighted in blue was measured. 8

Figure 3. Measurement of frontal plane dynamic LE angle. The peak frontal plane knee angle during stance phase was defined as the dynamic LE angle. 9

Figure 4. Output of IDEAL water-fat MRI: (A) water-only image; (B) fat-only image; (C) water fraction map. 10

Figure 5. Quantification of bone water content within medial femur, lateral femur, medial tibia, and lateral tibia. The lines connecting the epicondyles of the femur and tibia (solid lines) served as the superior and inferior borders of the subchondral bone. The center of the trochlear groove (top black arrow) was the landmark for dividing the medial and lateral compartments of the femur and the center of the tibial spine (bottom black arrow) was used to divide the medial and lateral compartment of the tibia. The dashed lines indicated the borders for medial and lateral compartments. Abbreviations: L = lateral; M = medial. 11

Figure 6. Comparison of bone water content values between pre and post walking condition. 15

Figure 7. Positive significant moderate correlation between static alignment and the change in bone water content of the medial femur ($R = 0.688$, $p = 0.028$). A greater LE angle indicates a more varus alignment. 16

Figure 8. Positive moderate correlation between static alignment and the change in bone water content of the medial tibia ($R = 0.437$, $p = 0.206$). A greater LE angle indicates a more varus alignment. 16

INTRODUCTION

Knee osteoarthritis is a degenerative joint disease that negatively impacts the quality of life (Guccione et al., 1994). Knee OA often develops around 40 years old, and about 9.3 million people in the U.S. population are affected (Murphy, 2012). It has been accepted that knee OA is the leading cause of disability in the elderly (Nuesch et al., 2011).

Although OA is characterized by the loss of cartilage initially, people who are affected often do not develop pain until a significant loss of cartilage has occurred (Sofat, Beith, Anilkumar, & Mitchell, 2011). In fact, it has been suggested via magnetic resonance imaging (MRI) studies that synovitis, bone marrow edema, and joint structure changes may be the main contributing factors of pain in OA (Sofat et al., 2011).

Lower extremity (LE) alignment has been a topic of much interest regarding the development of OA at the tibiofemoral joint. During the loading response in gait, LE alignment can determine the medial to lateral load distribution of the tibiofemoral joint (Shelburne, Torry, & Pandy, 2006). Particularly, as the mechanical axis of the tibiofemoral joint passes through the medial compartment of the knee, an adduction moment at the knee naturally translates force through the medial compartment of the tibiofemoral joint (Miyazaki et al., 2002). Studies have further shown that individuals with an increased knee adduction moment demonstrate a greater load on the tibiofemoral joint (Miyazaki et al., 2002). Excessive varus alignment is believed to increase the adduction moment of the knee, leading to elevated mechanical loading to the medial compartment of the tibiofemoral joint (Amin et al., 2004).

Given the fact that the medial joint bears more loading during locomotion, the medial compartment of the tibiofemoral joint has been hypothesized to be the site of initiation and development of bone stress injuries. Current literature has demonstrated that the medial tibial condyle has a greater amount of subchondral bone marrow edema (i.e., MRI-detected elevated bone water content within focal regions) and bony changes (i.e. osteophytes observed in radiographs) in older adults with OA (Felson et al., 2003). The observed bone marrow edema is thought to be the result of chronic overloading to the subchondral bone (Roemer et al., 2009). However, it remains unclear how an acute bout of locomotion-induced loading contributes to fluid accumulation within the subchondral bone in adults without knee OA. Additionally, there is little data to support the premise that genu varum is associated with an acute accumulation of bone fluid within the medial compartment.

The objectives of our study were 1) to investigate tibiofemoral bone stress response induced by an acute bout of fast walking and 2) to determine the correlation between LE alignment and bone stress response of the tibiofemoral joint. Specifically, we hypothesized that there would be an increase in bone water content (indicative of bone stress responses) of the tibiofemoral joint observed on a chemical-shift-encoded water-fat MRI protocol. Additionally, MRI-detected elevated bone water content within the medial compartment would be associated with a varus alignment in the LE.

METHODS

Subjects

We recruited 10 subjects (5 females and 5 males) between 50 to 65 years of age who were able to walk at brisk pace (2.5-4 mph) for at least 30 minutes. Both genders were recruited as it was found that there are no statistically significant differences in knee adduction moment between genders (Kerrigan, Riley, Nieto, & Della Croce, 2000). The data from an existing study was used to estimate the sample size for detecting transient fluid changes after a bout of mechanical loading (Ho, Hu, Colletti, & Powers, 2014). Using a two-sided paired t-test with 92% power and α value of 0.05, the analysis estimated that four individuals would be needed to detect the difference in bone water content before and after shock loading. However, as a larger sample size is critical for establishing correlation relation proposed in purpose 2, a total of 10 subjects were recruited.

Subjects were excluded from participation if they reported having any of the following: 1) medical diagnosis of knee OA, 2) history of knee surgery, or 3) implanted biological devices that could interact with the magnetic field. The reason to exclude those with clinical diagnoses of knee OA is to minimize the impact of potential confounding factors such as joint deformation and cartilage damage from an ongoing inflammatory process of the disease. Subjects' physical activity levels were determined based on the World Health Organization's Global Physical Activity Questionnaire (Bull, Maslin, & Armstrong, 2009). This questionnaire has been reported to provide a valid and reliable estimate of physical activity (Herrmann, 2013). Prior to participation, all subjects were informed of

the nature of the study and signed a consent form approved by the Institutional Review Board of the University of Nevada, Las Vegas (IRB#1312-4655).

Procedure

Subjects completed 2 phases of data collection: MRI assessment (Day 1) and biomechanical testing (Day 2). All testing was performed on the dominant side, determined by asking the subject which leg they prefer to land on from jumping or kick a ball with.

MRI Assessment

Upon arrival to the imaging center, patients were asked to complete the GPAQ questionnaire. The static LE alignment of the dominant leg was then measured. The static alignment was defined as the acute angle between the midpoint of the dominant anterior mid-thigh and the midpoint of the patellar tendon using the center of the patella as the fulcrum (Hinman, May, & Crossley, 2006). The measurement of static LE alignment was performed by the same investigator (AS).

MRI data was collected using a 3.0 Tesla General Electric (GE Healthcare, Milwaukee, WI, USA) scanner with a medium flex coil and 16 channels. Prior to a fast-walking session, 3-dimensional fast gradient echo (FGRE) iterative decomposition of water and fat with echo asymmetry and least-squares estimation (IDEAL) sequence was utilized to quantify bone water content. The scan parameters were: time to repetition (TR) = 7.592 ms, echo time (TE) = 2.972 ms, flip angle = 5 degrees, slice thickness = 2 mm, field of

view (FOV) = 160 x 160 mm, matrix = 512 x 512, pixel bandwidth (BW) = 122.07 kHz, scan time = 8 mins.

Immediately following the first MRI scan subjects were asked to walk briskly on the treadmill for 30 minutes. The fast walking speed was defined as the highest speed within 2.5 to 4.0 miles/hour (1.1 to 1.8 m/s) that a subject achieved without the presence of double limb swing and reported physical discomfort. Their highest speed during fast walking was also recorded, which was used to match their walking speed in the biomechanical testing (see below). Immediately following fast pace walking, the subjects received a second MRI on the dominant knee using the same MRI protocol as described previously. As moderate-intensity cardiorespiratory exercise training for 30-minute per day is recommended for maintaining physical fitness and health in general populations (Garber et al., 2011), a 30-minute walking protocol was used in this study. It has been reported that the average walking speed for individuals between 50 and 59 years old is 1.2 ± 0.1 m/s (Schimpl et al., 2011). Thus, we set up the lowest target speed as 1.1 m/s (lower limit of the population) and highest target speed as 1.8 m/s (50% increase) for this cohort. In addition, as Arnoldi and colleagues (Arnoldi, Linderholm, & Mussbichler, 1972) reported that experimentally-induced intraosseous fluid accumulations in the femur dissipated after only 30 minutes, we believe that it is important to detect the changes in water content immediately after loading.

Biomechanical Testing

All testing was performed at the Clinical Locomotion Neuromechanics Laboratory at the University of Nevada, Las Vegas. Ground reaction forces were collected at a rate of 2000 Hz using force plates instrumented in a dual-belt treadmill (Fully Instrumented Treadmill, Bertec Corp., Columbus, OH). A 10-camera motion analysis system (Vicon, Oxford Metrics Ltd., Oxford, UK) was used to capture kinematic data at 200 Hz. To allow for accurate placement of reflective markers (14-mm spheres), subjects wore sport shirts and tight shorts. In addition, the reflective markers were placed by the same investigator (SN).

Reflective markers were then placed on the following anatomical landmarks (Fig. 1): bilaterally over the 1st and 5th metatarsal heads, medial and lateral malleoli, medial and lateral femoral epicondyles, the joint space between L5–S1 and over the greater trochanters, iliac crests and anterior superior iliac spines (ASIS). The foot markers were placed on the shoes and all other markers were attached directly onto the skin. In addition, clusters of rigid reflective tracking markers were placed on the lateral surfaces of each subject's thigh, lower leg, and heel counter of the shoe. After obtaining a static calibration trial, all anatomical markers (with the exception of those attached to the pelvis) were removed. Subjects were then asked to walk on an instrumented treadmill at the same speed used in Day 1 data collection. Three 10-second walking trials were collected for each subject.



Figure 1. Locations of reflective markers were placed on the above anatomical landmarks in anterior, posterior, and sagittal views.

Data Analysis

Data Processing for LE Alignment

The static LE alignment was assessed using the goniometer method described earlier (Hinman et al., 2006). Static LE alignment was quantified by measuring the angle between the long axes of femur and tibia (Fig. 2). An angle of 180° is considered neutral alignment, and genu varum was defined as a LE alignment angle greater than 180° .

To quantify the dynamic LE alignment, reflective markers were labeled and digitized using Vicon Nexus software (Oxford Metric Ltd., Oxford, UK). Visual 3D software (C-

Motion, Rockville, MD) was used to quantify the peak frontal plane knee angle during the stance phase of fast walking (Fig. 3). Kinematic data were filtered using a 4th order, 6 Hz, low pass Butterworth filter with zero lag compensation. The researcher analyzed a total of 9 stance phases of gait (3 stance phases x 3 walking trials) for each subject to obtain the average value of the peak frontal plane LE angle. Stance phase of gait was characterized as the time between initial contact to pre-swing of the same leg detected by a force plate.

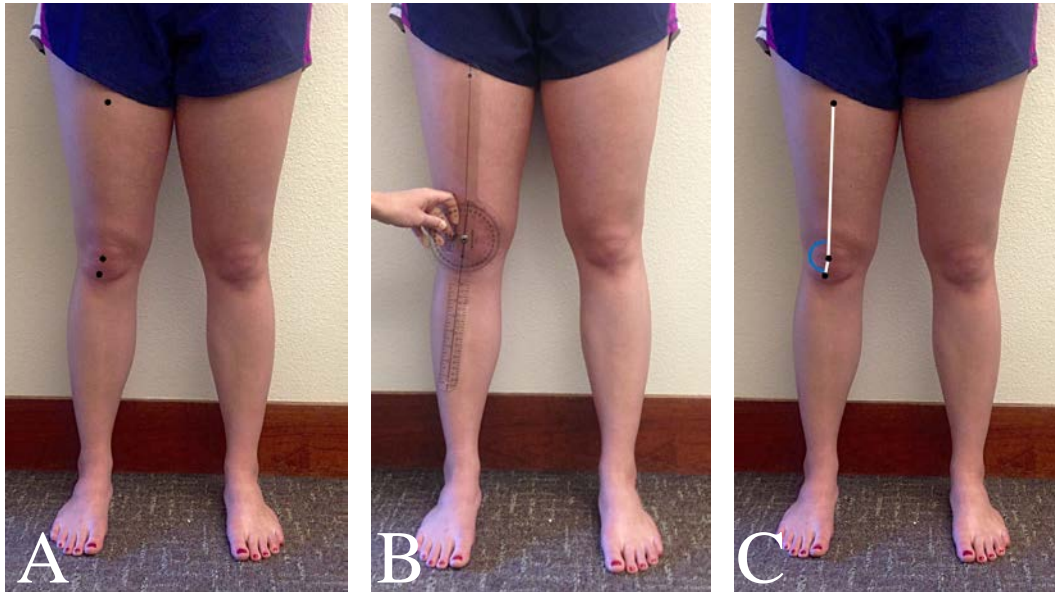


Figure 2. Measurement of frontal plane static LE angle. (A) Manual marking of anterior mid-thigh, center of the patella, and midpoint of the patellar tendon; (B) Measurement of frontal plane static LE angle with goniometer; (C) The acute angle highlighted in blue was measured.

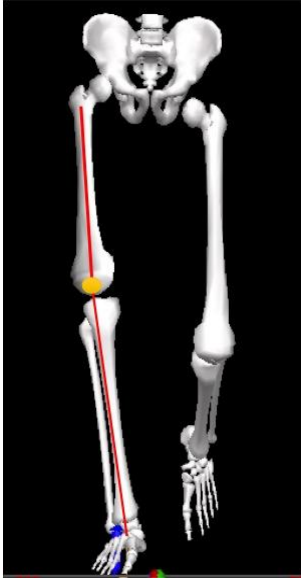


Figure 3. Measurement of frontal plane dynamic LE angle. The peak frontal plane knee angle during stance phase was defined as the dynamic LE angle.

MRI Data Processing

Bone stress response of the tibiofemoral joint was determined by quantifying the water content within the medial and lateral compartment of the tibiofemoral joint. The default reconstruction software provided by GE Healthcare automatically returns individual series of water-only and fat-only images (Fig.4 A & B). For purposes of this study, we performed additional post-processing analysis using ImageJ software (National Institutes of Health, Bethesda, MD, USA) to reconstruct water fraction ($\text{water}/[\text{fat}+\text{water}]\times 100\%$) maps (Fig.4 C).



Figure 4. Output of IDEAL water-fat MRI: (A) water-only image; (B) fat-only image; (C) water fraction map.

To detect walking-induced fluid fluctuations within the medial and lateral compartments of the tibiofemoral joint, 4 steps of analysis were performed. First, the image slices that contained weight-bearing regions of bones were identified (Blazek, Favre, Asay, Erhart-Hledik, & Andriacchi, 2014). Specifically, the weight-bearing area on each condyle was defined as the region bounded anteriorly by the medio-lateral line intersecting with the lowest point of the cartilage in the trochlea and extending 60% of the distance to the most posterior point of the articular cartilage covering each condyle (Blazek et al., 2014). Once the weight-bearing slices were identified, the lines that defined the 4 regions of subchondral bone (i.e., lateral femur, medial femur, lateral tibia, and medial tibia) were identified on each image slice (Peterfy et al., 2004). Specifically, the epicondyles of the femur and tibia served as the superior and inferior landmarks outlining the subchondral bone. The center of the trochlear groove was used to divide the medial and lateral compartments of the femur and the center of the tibial spine was used to divide the medial and lateral compartment of the tibia (Fig. 5). Third, to quantify the water content within each region of interest, the subchondral bone region on the water fraction maps (defined as the dark region under articular cartilage) was manually contoured (Fig. 5).

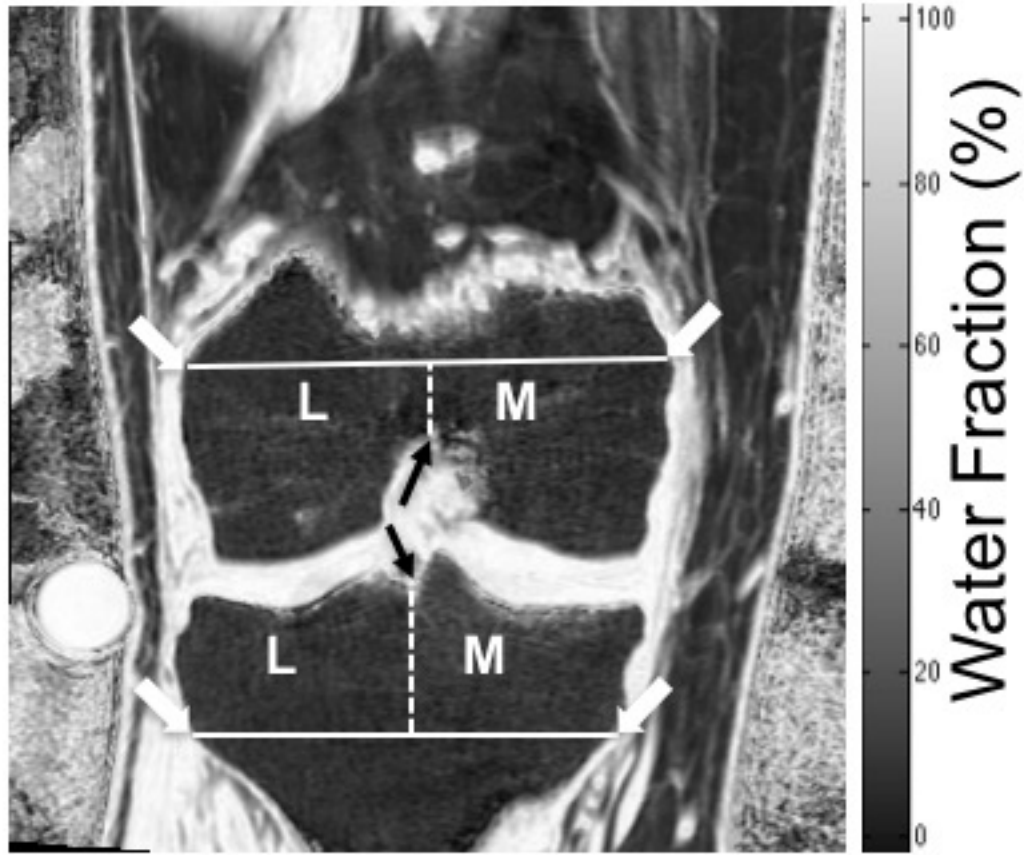


Figure 5. Quantification of bone water content within medial femur, lateral femur, medial tibia, and lateral tibia. The lines connecting the epicondyles of the femur and tibia (solid lines) served as the superior and inferior borders of the subchondral bone. The center of the trochlear groove (top black arrow) was the landmark for dividing the medial and lateral compartments of the femur and the center of the tibial spine (bottom black arrow) was used to divide the medial and lateral compartment of the tibia. The dashed lines indicated the borders for medial and lateral compartments. Abbreviations: L = lateral; M = medial.

Lastly, the average water fraction of each region of interest was then obtained by averaging the signal intensities of all voxels within the regions of interest using Equation 1 (Ho, MRI 2014)

$$\text{Eq. 1. Water Content (\%)} = \frac{\sum_1^n (\text{Water Fraction (n)} \times \text{Area Measured (n)})}{\sum_1^n \text{Area Measured (n)}}$$

, where n is number of images.

Reliability of Outcome Measures

To establish intra-rater reliability of each outcome measure, the data evaluator performed repeated measurement of 5 subjects at 2 days (with 7 days apart). Intraclass correlation coefficients (ICCs) and standard errors of measurement (SEM) were used to assess the reliability of the investigator between day 1 and 2. For static LE alignment, the investigator demonstrated an excellent measurement reliability (ICC = 0.952) with a low SEM (1.629 degrees). Excellent intra-rater reliability was also established in the measurement of dynamic LE alignment with an ICC of 0.919 and SEM of 1.137 degrees. Additionally, the investigator showed excellent intra-rater reliability in the measurement of bone water content within the medial and lateral compartments (ICC ranging from 0.937-0.968 and SEM ranging from 0.241-0.391%).

Statistical Analysis

The outcome variables of the current study include static LE alignment, dynamic LE alignment, and MRI-detected bone water content within 4 sub-regions (i.e., medial femur, lateral femur, medial tibia, and lateral tibia). Prior to statistical analysis, all variables were assessed for normality and found to be normally distributed based on obtainment of $p > 0.05$ in the Shapiro-Wilk test. To analyze MRI-detected bone water content before and after the fast walking, a paired t-test was used. Pearson correlation coefficient analyses were used to determine the associations between LE alignment (i.e., static and dynamic alignment angles) and the changes in tibiofemoral bone stress response (i.e., changes in bone water content of each sub-region) after fast walking. All statistical analyses were

performed with use of SPSS 22.0 statistical software (International Business Machines Corp., Armonk, NY, USA). A significance level was set as 0.05.

RESULTS

Subject Characteristics

The age, height, and weight for this cohort were 57.9 ± 3.9 years, $1.7 \text{ m} \pm 0.1 \text{ m}$ and $84.2 \text{ kg} \pm 12.7 \text{ kg}$, respectively. The average cadence for subjects was 114.8 ± 10.7 steps per minute and the average velocity was $1.5 \text{ m/s} \pm 0.2 \text{ m/s}$. The subjects had an average static frontal plane knee angle of 174.7 ± 5.0 degrees and an average dynamic frontal plane knee angle of 180.7 ± 5.2 degrees. The average activity level was 2220 ± 1503.6 MET min/week, indicating that this cohort is moderately active (Herrmann, 2013).

Changes in Bone Water Content after Fast Walking

The findings of paired t-tests showed that there were no changes in water content after fast walking within medial femur (Pre-walking = $22.22 \pm 1.47\%$; Post-walking = $22.00 \pm 1.33\%$; $p = 0.671$), lateral femur (Pre-walking = $21.59 \pm 1.65\%$; Post-walking = $22.56 \pm 1.30\%$; $p = 0.174$), medial tibia (Pre-walking = $23.20 \pm 1.50\%$; Post-walking = $23.86 \pm 2.10\%$; $p = 0.461$), and lateral tibia (Pre-walking = $21.76 \pm 1.91\%$; Post-walking = $22.94 \pm 2.18\%$; $p = 0.190$) (Fig 6).

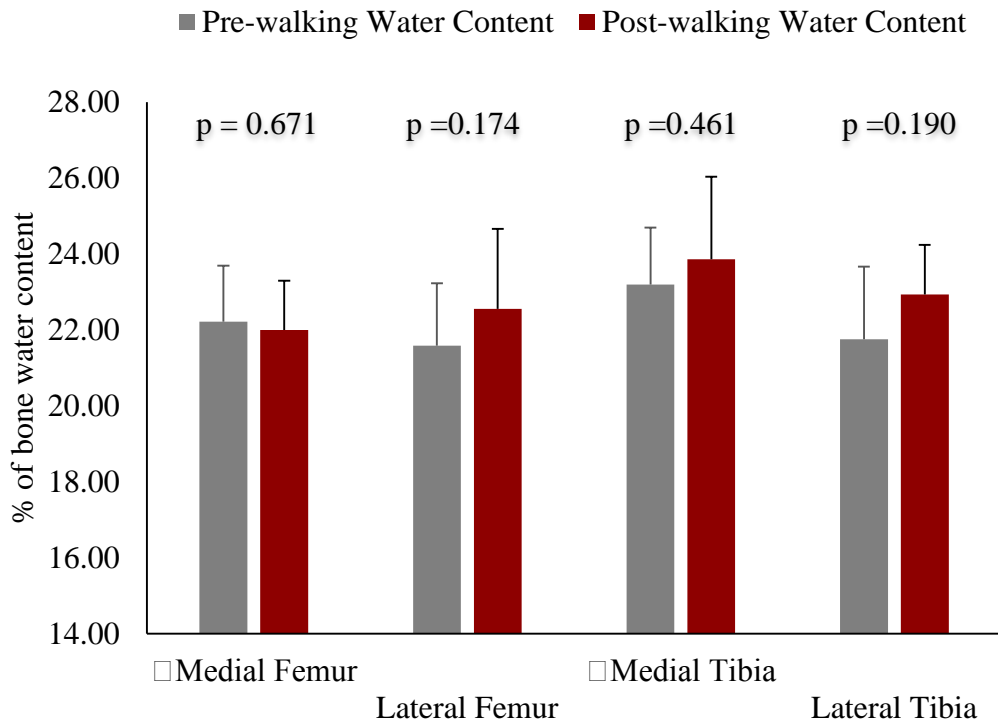


Figure 6. Comparison of bone water content values between pre and post walking condition.

Associations between Altered Bone Water Content and Frontal Plane LE Alignment

Pearson correlation coefficient analyses revealed a significant moderate correlation between increased bone water content of the medial femur and increased static varus alignment ($R = 0.688$, $p = 0.028$), as shown in Fig. 7. Although not significant, a trend with moderate correlation was observed between increased bone water content of the medial tibia and increased static alignment ($R = 0.437$, $p = 0.206$) (Fig. 8). No statistically significant relationships were found between static alignment and lateral femur/lateral tibia. Table 1 shows the Pearson correlations between static LE alignment and the change in bone water content found in each compartment of the tibiofemoral joint.

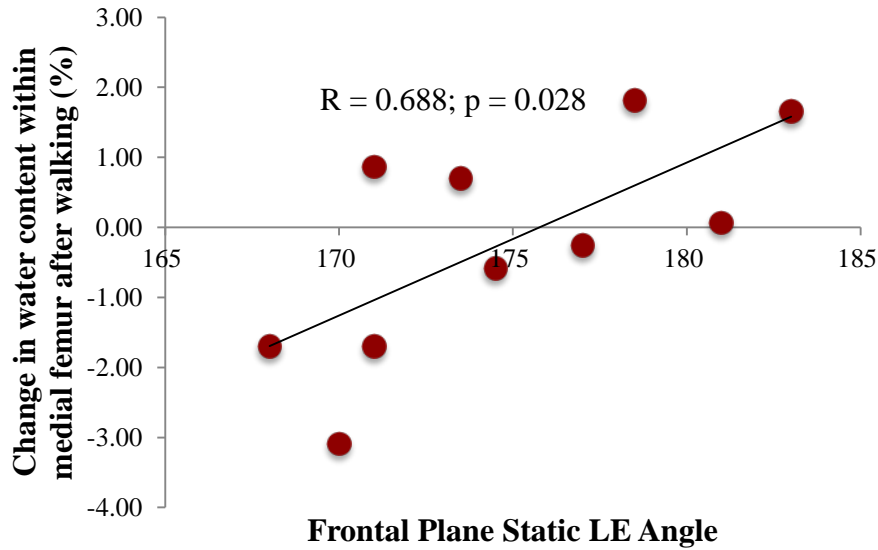


Figure 7. Positive significant moderate correlation between static alignment and the change in bone water content of the medial femur ($R = 0.688$, $p = 0.028$). A greater LE angle indicates a more varus alignment.

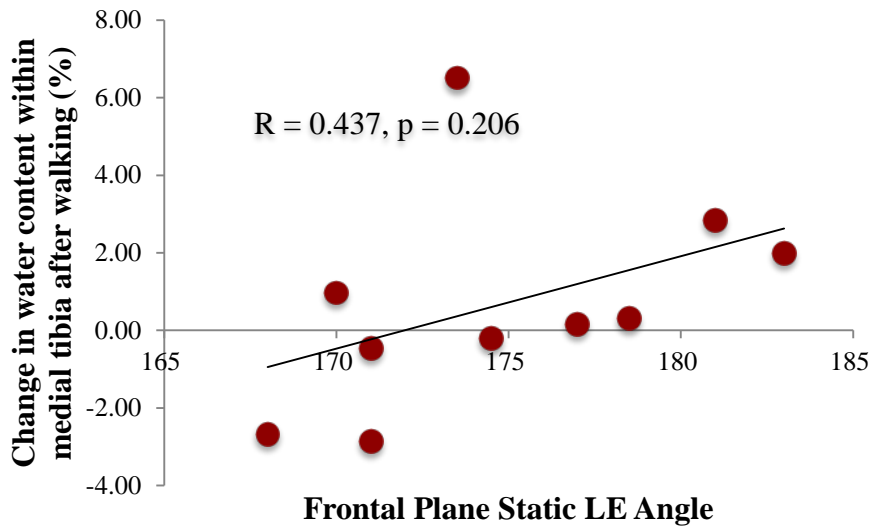


Figure 8. Positive moderate correlation between static alignment and the change in bone water content of the medial tibia ($R = 0.437$, $p = 0.206$). A greater LE angle indicates a more varus alignment.

	R	P value
Medial Femur	0.688	0.028*
Lateral Femur	0.238	0.509
Medial Tibia	0.437	0.206
Lateral Tibia	0.366	0.298

Table 1. The associations between static LE alignment and changes in bone water content. * indicates a statistical significance ($p < 0.05$).

No statistically significant relationships were found between dynamic LE alignment and the following compartments: medial femur, lateral femur, medial tibia, and lateral tibia.

Table 2 shows the Pearson correlations between dynamic alignment and the change in bone water content found in each compartment of the tibiofemoral joint.

	R	P value
Medial Femur	0.101	0.782
Lateral Femur	0.371	0.291
Medial Tibia	0.566	0.088
Lateral Tibia	0.495	0.146

Table 2. The associations between dynamic LE alignment and changes in bone water content. * indicates a statistical significance ($p < 0.05$).

DISCUSSION

To the authors' knowledge, this is the first study assessing the acute effects of locomotion on bone stress response in older adults without knee OA. The primary purpose of the current study was to test the hypothesis that a 30-minute session of fast walking would result in acute fluid accumulation within the subchondral bone of the tibiofemoral joint. Our findings demonstrated that the bone water content within the medial and lateral compartments did not change after fast walking. In support of our secondary hypothesis, a significant association between increased static LE angle and increased bone water content within medial femur was observed. Although an insignificant correlation between genu varum and increased bone water content within the medial tibia was noted, we speculated that such a correlation might be affected by a participant whose data point was outlying (Fig. 8). Interestingly, the dynamic LE angle during loading response in gait did not correlate with altered bone water content of any compartment.

The acute effects of locomotion (primarily running) have been studied using MRI. With the application of IDEAL imaging technique, Ho et al. has reported that completion of a 40-minute running session with moderate exertion effort resulted in significant increases in patella water content in individuals with patellofemoral pain (Ho et al., 2014). Lazzarini et al. and Trappeniers et al. (Lazzarini, Troiano, & Smith, 1997; Trappeniers et al., 2003) have suggested that 50-80% of runners developed focal bone marrow lesions of the ankle bones 3-7 days following running. Conflicting findings were reported by Hohmann and colleagues (Hohmann, Wortler, & Imhoff, 2004), who found that running does not increase the presence of bone marrow lesions in the tibiofemoral joint 24-48

hours post-running. The lack of change in the current study may indicate that 30 minutes of fast pace walking was not a sufficient amount of time to cause stress that would elicit significant change in the water content of the tibiofemoral joint. Additionally, walking may not have been a highly strenuous activity that would create a large enough ground reaction force through the compartments of the knee to show an increase in bone water content. Also our study did not look at the peak knee adduction moment, and it could be possible that the peak frontal plane knee angle and knee adduction moment did not occur at the same phase of gait (Barrios, Higginson, Royer, & Davis, 2009). Knee adduction moment may be a better indicator of bone stress response during gait.

Our study agrees with previous studies that a varus alignment is associated with pathological changes in the medial compartment of the tibiofemoral joint. Janakiramanan et al. found that for every 1° increase towards genu varum, an individual has an increased risk for the development of medial compartment cartilage defects (Janakiramanan et al., 2008). They further reported that for every 1° increase in a valgus direction, there was an associated reduced risk of the presence of cartilage defects in the medial compartment (Janakiramanan et al., 2008). In accordance with our findings, it was found that knee valgus alignment did not correlate with increased risk of the presence of lateral cartilage defects in persons without knee OA (Janakiramanan et al., 2008). A similar finding was reported by Brouwer et al. who demonstrated that a varus alignment was associated with a 2-fold increased risk of OA (Brouwer et al., 2007). Sharma et al. further suggested that genu varum but not valgus was associated with incident OA (Sharma et al., 2010).

Although it was speculated that elevated dynamic varus alignment would affect knee loading/knee adduction moment, our study did not find any association between dynamic alignment and change in bone water content. It has been found that knee adduction moment during gait is related to elevated medial compartment loading. Multiple factors determine the magnitude of knee adduction moment, including dynamic LE alignment, body mass, walking velocity, trunk posture, and ground reaction force magnitude and direction (Amin et al., 2004; Harding, Hubley-Kozey, Dunbar, Stanish, & Astephen Wilson, 2012; Miyazaki et al., 2002; Mundermann, Dyrby, & Andriacchi, 2005; Shelburne et al., 2006). Thus, we believe that it would be important to take into account of these factors when analyzing the effects of walking on changes in bone water content. Additionally, we found that the dynamic LE alignment obtained using a motion capture system did not correlate with the static LE alignment in several subjects. This may be associated with the displacement of markers on the skin due to vibration from fast walking in the biomechanical analysis session.

The role of subchondral bone in OA and its mechanism in disease progression was first proposed by Radin et al. (Radin, Paul, & Rose, 1972; Radin & Rose, 1986). Based on the data of stiffness and thickness in early degenerated bone, it has been suggested that trabecular micro-damage due to impulsive loading initiates bone remodeling in subchondral bone plate (Day et al., 2004; Imhof, Breitenseher, Kainberger, Rand, & Trattig, 1999; Radin & Rose, 1986). This consequently results in focal stiffening of subchondral bone that leads to an increase in cartilage stress, thereby causing cartilage breakdown (Day et al., 2004; Radin et al., 1972; Radin & Rose, 1986). As articular

cartilage plays a critical role in transferring load across the joint, the altered cartilage absorption ability due to bone remodeling and cartilage damages can further accelerate the progression of OA (Goldring & Goldring, 2010). Murray et al. (Murray, Vedi, Birch, Lakhani, & Goodship, 2001) reported that subchondral bone thickness increased after 19 weeks of high intensity treadmill exercise in a horse model. Current in vivo studies suggest that increased compression load causes the trabeculae to respond by increasing the number of trabeculae, however the quality of the new trabeculae is weak and thin (Woloszynski et al., 2012). It has also been found that with medial compartment OA there is relative unloading of the lateral compartment therefore bone resorption occurs (Woloszynski et al., 2012). Based on our results and the existing literature, it is speculated that varus alignment may be associated with subchondral bone micro-damage induced by mechanical stress such as the repetitive impact locomotion. Such damage may be a precursor to the development of knee OA and the associated bone remodeling and subsequent osseous alterations (e.g., increased volume and altered trabecular texture) in the medial compartment of the tibiofemoral joint. Over time, this can lead to tibiofemoral varus deformity and progressive degeneration of the medial compartment later in life (Felson et al., 2003; Miyazaki et al., 2002).

With respect to the findings of the current study, four major limitations should be recognized. First, the goniometer method used in our study for quantifying LE angle tended to underestimate the static LE alignment by 4°-5°, although it has been identified as a reliable approach (Hinman et al., 2006). This may be due to the fact that the measuring axis for the lower leg was aligned with the patellar tendon, instead of the axis

of the mid-tibia. Second, as the presence of clinical symptoms served as the criteria for diagnosing knee OA (Altman et al., 1986), we did not employ radiography-based criteria (i.e., Kellgren and Lawrence grading on X-ray) in the current study. Third, only middle-aged individuals without knee OA were evaluated in this study. Although those with knee OA were excluded to prevent bias from existing bone injuries, the response from our relatively healthy subjects may be different from those with knee OA. Additionally, the subjects in this study self-reported to have an active lifestyle, as reflected in the GPAQ. As such, caution should be taken when generalizing our results to other populations.

CONCLUSION

This is the first study assessing the acute effects of locomotion on bone stress response in older adults without knee OA. Although there was no significant change in bone water content post locomotion, there was a correlation between static varus alignment and bone water content in the medial femur. A trend was found for the correlation of static varus alignment and bone water content in the medial tibia. Our findings provide further understanding of the contribution of LE alignment and development of OA. This research can impact the early detection, prevention, and interventions for individuals at risk for joint deformity and knee OA.

REFERENCES

- Altman, R., Asch, E., Bloch, D., Bole, G., Borenstein, D., Brandt, K., . . . et al. (1986). Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. *Arthritis Rheum*, 29(8), 1039-1049.
- Amin, S., Luepingsak, N., McGibbon, C. A., LaValley, M. P., Krebs, D. E., & Felson, D. T. (2004). Knee adduction moment and development of chronic knee pain in elders. *Arthritis Rheum*, 51(3), 371-376. doi:10.1002/art.20396
- Arnoldi, C. C., Linderholm, H., & Mussbichler, H. (1972). Venous engorgement and intraosseous hypertension in osteoarthritis of the hip. *J Bone Joint Surg Br*, 54(3), 409-421.
- Barrios, J. A., Higginson, J. S., Royer, T. D., & Davis, I. S. (2009). Static and dynamic correlates of the knee adduction moment in healthy knees ranging from normal to varus-aligned. *Clin Biomech (Bristol, Avon)*, 24(10), 850-854. doi:10.1016/j.clinbiomech.2009.07.016
- Blazek, K., Favre, J., Asay, J., Erhart-Hledik, J., & Andriacchi, T. (2014). Age and obesity alter the relationship between femoral articular cartilage thickness and ambulatory loads in individuals without osteoarthritis. *J Orthop Res*, 32(3), 394-402. doi:10.1002/jor.22530
- Brouwer, G. M., van Tol, A. W., Bergink, A. P., Belo, J. N., Bernsen, R. M., Reijman, M., . . . Bierma-Zeinstra, S. M. (2007). Association between valgus and varus alignment and the development and progression of radiographic osteoarthritis of the knee. *Arthritis Rheum*, 56(4), 1204-1211. doi:10.1002/art.22515
- Bull, F. C., Maslin, T. S., & Armstrong, T. (2009). Global physical activity questionnaire (GPAQ): nine country reliability and validity study. *J Phys Act Health*, 6(6), 790-804.
- Coats, A. M., Zioupos, P., & Aspden, R. M. (2003). Material properties of subchondral bone from patients with osteoporosis or osteoarthritis by microindentation testing and electron probe microanalysis. *Calcif Tissue Int*, 73(1), 66-71.
- Day, J. S., Van Der Linden, J. C., Bank, R. A., Ding, M., Hvid, I., Sumner, D. R., & Weinans, H. (2004). Adaptation of subchondral bone in osteoarthritis. *Biorheology*, 41(3-4), 359-368.
- Felson, D. T., McLaughlin, S., Goggins, J., LaValley, M. P., Gale, M. E., Totterman, S., . . . Gale, D. (2003). Bone marrow edema and its relation to progression of knee osteoarthritis. *Ann Intern Med*, 139(5 Pt 1), 330-336. doi:139/5_Part_1/330 [pii]
- Garber, C. E., Blissmer, B., Deschenes, M. R., Franklin, B. A., Lamonte, M. J., Lee, I. M., . . . American College of Sports, M. (2011). American College of Sports Medicine position stand. Quantity and quality of exercise for developing and maintaining cardiorespiratory, musculoskeletal, and neuromotor fitness in apparently healthy adults: guidance for prescribing exercise. *Med Sci Sports Exerc*, 43(7), 1334-1359. doi:10.1249/MSS.0b013e318213fefb
- Goldring, M. B., & Goldring, S. R. (2010). Articular cartilage and subchondral bone in the pathogenesis of osteoarthritis. *Ann N Y Acad Sci*, 1192(1), 230-237. doi:NYAS5240 [pii]

10.1111/j.1749-6632.2009.05240.x

- Guccione, A. A., Felson, D. T., Anderson, J. J., Anthony, J. M., Zhang, Y., Wilson, P. W., . . . Kannel, W. B. (1994). The effects of specific medical conditions on the functional limitations of elders in the Framingham Study. *Am J Public Health, 84*(3), 351-358.
- Harding, G. T., Hubley-Kozey, C. L., Dunbar, M. J., Stanish, W. D., & Astephen Wilson, J. L. (2012). Body mass index affects knee joint mechanics during gait differently with and without moderate knee osteoarthritis. *Osteoarthritis Cartilage, 20*(11), 1234-1242. doi:10.1016/j.joca.2012.08.004
- Herrmann, S. D. H., K. J.; Der Ananian, C. A.; Ainsworth, B. E. . (2013). Validity and Reliability of the Global Physical Activity Questionnaire (GPAQ). *Measurement in Physical Education and Exercise Science*. doi:10.1080/1091367X.2013.805139
- Hinman, R. S., May, R. L., & Crossley, K. M. (2006). Is there an alternative to the full-leg radiograph for determining knee joint alignment in osteoarthritis? *Arthritis Rheum, 55*(2), 306-313. doi:10.1002/art.21836
- Ho, K. Y., Hu, H. H., Colletti, P. M., & Powers, C. M. (2014). Running-induced patellofemoral pain fluctuates with changes in patella water content. *Eur J Sport Sci, 14*(6), 628-634. doi:10.1080/17461391.2013.862872
- Hohmann, E., Wortler, K., & Imhoff, A. B. (2004). MR imaging of the hip and knee before and after marathon running. *Am J Sports Med, 32*(1), 55-59.
- Imhof, H., Breitenseher, M., Kainberger, F., Rand, T., & Trattnig, S. (1999). Importance of subchondral bone to articular cartilage in health and disease. *Top Magn Reson Imaging, 10*(3), 180-192.
- Janakiraman, N., Teichtahl, A. J., Wluka, A. E., Ding, C., Jones, G., Davis, S. R., & Cicuttini, F. M. (2008). Static knee alignment is associated with the risk of unicompartmental knee cartilage defects. *J Orthop Res, 26*(2), 225-230. doi:10.1002/jor.20465
- Kerrigan, D. C., Riley, P. O., Nieto, T. J., & Della Croce, U. (2000). Knee joint torques: a comparison between women and men during barefoot walking. *Arch Phys Med Rehabil, 81*(9), 1162-1165.
- Lazzarini, K. M., Troiano, R. N., & Smith, R. C. (1997). Can running cause the appearance of marrow edema on MR images of the foot and ankle? *Radiology, 202*(2), 540-542.
- Miyazaki, T., Wada, M., Kawahara, H., Sato, M., Baba, H., & Shimada, S. (2002). Dynamic load at baseline can predict radiographic disease progression in medial compartment knee osteoarthritis. *Ann Rheum Dis, 61*(7), 617-622.
- Mundermann, A., Dyrby, C. O., & Andriacchi, T. P. (2005). Secondary gait changes in patients with medial compartment knee osteoarthritis: increased load at the ankle, knee, and hip during walking. *Arthritis Rheum, 52*(9), 2835-2844. doi:10.1002/art.21262
- Murray, R. C., Vedi, S., Birch, H. L., Lakhani, K. H., & Goodship, A. E. (2001). Subchondral bone thickness, hardness and remodelling are influenced by short-term exercise in a site-specific manner. *J Orthop Res, 19*(6), 1035-1042. doi:10.1016/S0736-0266(01)00027-4

- Nuesch, E., Dieppe, P., Reichenbach, S., Williams, S., Iff, S., & Juni, P. (2011). All cause and disease specific mortality in patients with knee or hip osteoarthritis: population based cohort study. *BMJ*, *342*, d1165. doi:10.1136/bmj.d1165
- Peterfy, C. G., Guermazi, A., Zaim, S., Tirman, P. F., Miaux, Y., White, D., . . . Genant, H. K. (2004). Whole-Organ Magnetic Resonance Imaging Score (WORMS) of the knee in osteoarthritis. *Osteoarthritis Cartilage*, *12*(3), 177-190. doi:10.1016/j.joca.2003.11.003
- S1063458403002917 [pii]
- Radin, E. L., Paul, I. L., & Rose, R. M. (1972). Role of mechanical factors in pathogenesis of primary osteoarthritis. *Lancet*, *1*(7749), 519-522.
- Radin, E. L., & Rose, R. M. (1986). Role of subchondral bone in the initiation and progression of cartilage damage. *Clin Orthop Relat Res*, *213*(213), 34-40.
- Roemer, F. W., Guermazi, A., Javaid, M. K., Lynch, J. A., Niu, J., Zhang, Y., . . . investigators, M. S. (2009). Change in MRI-detected subchondral bone marrow lesions is associated with cartilage loss: the MOST Study. A longitudinal multicentre study of knee osteoarthritis. *Ann Rheum Dis*, *68*(9), 1461-1465. doi:10.1136/ard.2008.096834
- Schimpl, M., Moore, C., Lederer, C., Neuhaus, A., Sambrook, J., Danesh, J., . . . Daumer, M. (2011). Association between walking speed and age in healthy, free-living individuals using mobile accelerometry--a cross-sectional study. *PLoS One*, *6*(8), e23299. doi:10.1371/journal.pone.0023299
- Sharma, L., Song, J., Dunlop, D., Felson, D., Lewis, C. E., Segal, N., . . . Nevitt, M. (2010). Varus and valgus alignment and incident and progressive knee osteoarthritis. *Ann Rheum Dis*, *69*(11), 1940-1945. doi:10.1136/ard.2010.129742
- Shelburne, K. B., Torry, M. R., & Pandy, M. G. (2006). Contributions of muscles, ligaments, and the ground-reaction force to tibiofemoral joint loading during normal gait. *J Orthop Res*, *24*(10), 1983-1990. doi:10.1002/jor.20255
- Sofat, N., Beith, I., Anilkumar, P. G., & Mitchell, P. (2011). Recent clinical evidence for the treatment of osteoarthritis: what we have learned. *Rev Recent Clin Trials*, *6*(2), 114-126.
- Trappeniers, L., De Maeseneer, M., De Ridder, F., Machiels, F., Shahabpour, M., Tebache, C., . . . Osteaux, M. (2003). Can bone marrow edema be seen on STIR images of the ankle and foot after 1 week of running? *Eur J Radiol*, *47*(1), 25-28. doi:S0720048X02002218 [pii]
- Woloszynski, T., Podsiadlo, P., Stachowiak, G. W., Kurzynski, M., Lohmander, L. S., & Englund, M. (2012). Prediction of progression of radiographic knee osteoarthritis using tibial trabecular bone texture. *Arthritis Rheum*, *64*(3), 688-695. doi:10.1002/art.33410

Curriculum Vitae

Alexa Standerfer, SPT

EDUCATION

- University of Nevada, Las Vegas – Las Vegas, NV
Doctorate of Physical Therapy – Expected graduation date May 2016
- University of Nevada, Reno – Reno, NV
Bachelor of Science in Community Health Sciences 2012

CLINICAL EXPERIENCE

- Physiotherapy Associates, Outpatient Clinic – Austin, TX (1/2016-4/2016)
- Renown Rehabilitation Hospital, Inpatient Setting – Reno, NV (10/2015-12/2015)
- Mountain View Hospital, Acute Care Setting – Las Vegas, NV (7/2015-9/2015)
- Carson Valley Medical Center, Outpatient Clinic – Gardnerville, NV (6/2014-8/2014)

CONTINUING/SUPPLEMENTAL EDUCATION

- Combined Sections Meeting of the American Physical Therapy Association – Anaheim, CA 2016
- Combined Sections Meeting of the American Physical Therapy Association – Las Vegas, NV 2014
- “Therapeutic Neuroscience Education” Dr. Adrian Lowe 2014
- “Biomechanical Basis for Conservative Treatment of Patello-Femoral Disorders” Dr. Chris Powers 2013

PROFESSIONAL MEMBERSHIP

- American Physical Therapy Association 2013 – Present

DOCTORAL DISSERTATION

- Ho, Kai-Yu., Standerfer, Alexa., Ngo, Suzenna., Daun, Karen. *The Effects of Locomotion-Induced Shock Loading on Tibiofemoral Bone Stress Injury*. April 2014 – May 2016.

Suzenna Ngo, SPT

EDUCATION

- University of Nevada, Las Vegas – Las Vegas, NV
Doctorate of Physical Therapy – Expected graduation date May 2016
- University of Nevada, Las Vegas – Las Vegas, NV
Bachelor of Science in Kinesiological Sciences: Allied Health 2012

CLINICAL EXPERIENCE

- Summerlin Hospital Medical Center – Las Vegas, NV (1/2016 – 4/2016)
- North Las Vegas VA Medical Center – Las Vegas, NV (10/2015 – 12/2015)
- HealthSouth Rehabilitation Hospital of Las Vegas – Las Vegas, NV (7/2015 – 9/2015)
- Henderson Physical Therapy – Las Vegas, NV (6/2014 – 8/2014)

CONTINUING/SUPPLEMENTAL EDUCATION

- Combined Sections Meeting of the American Physical Therapy Association – Anaheim, CA 2016
- Combined Sections Meeting of the American Physical Therapy Association – Las Vegas, NV 2014
- “Therapeutic Neuroscience Education” Dr. Adrian Lowe 2014
- “Biomechanical Basis for Conservative Treatment of Patello-Femoral Disorders” Dr. Chris Powers 2013

PROFESSIONAL MEMBERSHIP

- American Physical Therapy Association 2013 – Present

DOCTORAL DISSERTATION

- Ho, Kai-Yu., Standerfer, Alexa., Ngo, Suzenna., Daun, Karen. *The Effects of Locomotion-Induced Shock Loading on Tibiofemoral Bone Stress Injury*. April 2014 – May 2016.

Karen Daun, SPT

EDUCATION

- University of Nevada, Las Vegas – Las Vegas, NV
Doctorate of Physical Therapy – Expected graduation date May 2016
- University of Nevada, Reno – Reno, NV
Bachelor of Science in Public Health 2013

CLINICAL EXPERIENCE

- Cleveland Clinic, Lou Ruvo Center for Brain Health – Las Vegas, NV (1/2016 – 4/2016)
- University Medical Center – Las Vegas, NV (10/2016 – 12/2015)
- Desert Springs Hospital – Las Vegas, NV (5/2015 – 9/2015)
- Orthosport Physical Therapy – Las Vegas, NV (5/2014 – 8/2014)

CONTINUING/SUPPLEMENTAL EDUCATION

- September 2013: Dr. James Navalta “Exercise Immunology: A matter of Life and Death”
- November 2013: Dr. Chris Powers “Biomechanical Basis for Conservative Treatment of Patello-Femoral Disorders”
- December 2013: Dr. Shawn Sorensen “No Train, No Gain: Lifetime Exercise and Health Among Elite Competitive Athletes”
- January 2014: Dr. Pat Camp “Physical Activity in Hospitalized Patients with an acute exacerbation of COPD”
- February 2014: Combined Sections Meeting – Las Vegas, NV
- August 2014: Dr. Mark Guadagnoli “Challenge Point Theory”
- February 2016: Combined Sections Meeting – Anaheim, CA

PROFESSIONAL MEMBERSHIP

- American Physical Therapy Association 2013 – Present

DOCTORAL DISSERTATION

- Ho, Kai-Yu., Standerfer, Alexa., Ngo, Suzenna., Daun, Karen. *The Effects of Locomotion-Induced Shock Loading on Tibiofemoral Bone Stress Injury*. April 2014 – May 2016.