

THE RELATIONSHIP BETWEEN GAIT SPEED AND DYNAMIC STABILITY
FOLLOWING A 4-WEEK INTERVENTION IN KNEE OSTEOARTHRITIS PATIENTS

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ABSTRACT

Kayla Vredevelde: The Relationship Between Gait Speed and Dynamic Stability Following a 4-week Intervention in Knee Osteoarthritis Patients
(Under the direction of Erik Hanson)

PURPOSE: This study explored the relationship of both gait speed and body composition to gait stability following knee osteoarthritis (KOA) treatment. **METHODS:** 53 diagnosed KOA patients completed 4 weeks of therapeutic rehabilitation with testing sessions immediately before and after. Testing assessed self-reported disability, body composition, muscle function, and gait mechanics. Paired sample t-tests were completed, followed by correlations comparing gait speed, center of pressure, and ground reaction forces with baseline and change score values. **RESULTS:** 20 meter gait speed significantly increased following intervention, while pain and self-reported function scores improved. Ground reaction forces showed increased acceleration and deceleration in the involved limb. Preliminary data showed correlation between lean mass and mediolateral center of pressure displacement. **CONCLUSIONS:** Current KOA treatments are able to not only improve function through increased walking speed, but also improve the ability to load the limb with greater ground reaction forces. Body composition data warrants further exploration.

To my friends and family who have instill in me the truth of who I am, whose I am, and where I
am going.

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TABLE OF CONTENTS

LIST OF ABBREVIATIONS.....	viii
CHAPTER 1: INTRODUCTION.....	1
Research Questions.....	4
Hypotheses.....	4
Limitations.....	4
Delimitations.....	5
Assumptions.....	5
Significance of Study.....	5
CHAPTER 2: LITERATURE REVIEW.....	6
CHAPTER 3: METHODOLOGY.....	12
Research Design Overview.....	12
Subjects.....	12
Procedures.....	13
Intervention Groups.....	14
Outcome Measures.....	15
Statistical Analysis.....	18
CHAPTER 4: RESULTS.....	19
CHAPTER 5: DISCUSSION.....	24
APPENDIX A (Informed Consent Form).....	28

REFERENCES34

LIST OF ABBREVIATIONS

AP	Anteroposterior
BIA	Bioelectrical impedance analysis
BMI	Body mass index
CAR	Central activation ratio
COP	Center of pressure
DEXA	Dual energy x-ray absorptiometry
FM	Fat mass
GRF	Ground reaction force
KOA	Knee osteoarthritis
LM	Lean mass
ML	Mediolateral
MVIC	Maximal voluntary isometric contraction
TE	Therapeutic exercise
TENS	Transcutaneous electrical nerve stimulation

CHAPTER 1: INTRODUCTION

Knee osteoarthritis (KOA) is a health condition of the musculoskeletal system that affects 12-16% of the population over 60 years old^{1 2}. The degenerative disease is associated with other health conditions including cardiovascular disease, chronic obstructive pulmonary disease, obesity, diabetes, and depression³⁻⁸ at a rate of 50% of the KOA population⁹. Collectively, these comorbidities along with KOA lead to an increased mortality⁶ and decreased quality of life⁹ due to the limitations in independently completing activities of daily living. The ability to complete daily tasks in KOA patients is negatively effected by the resulting loss of balance, which is amplified by the loss of strength, muscle activation, and the compromised body composition.

Falls are a prevalent issue in the healthy elderly, with studies reporting balance deficits as early as 50 years old¹⁰ and observations concluding that 1 in 3 adults over 65 years will fall over the course of a year¹¹. Overall, loss of balance and falls are not only more common in KOA patients¹²⁻¹⁴, but also have significantly greater deficits compared to the healthy elderly averages^{12 15}, with deficits increasing as the disease progresses¹³. Reliable measurements of dynamic balance are infrequent in KOA studies, but their direct relationship to the ability to complete activities of daily living and consequently quality of life^{12 15} demands that they are further explored.

To quantify balance more precisely than clinical tests and to detect minimal changes, balance can be measured using both the position and movement of the center of pressure (COP) while the foot is in contact with a force plate¹⁶⁻¹⁹. Studies show significant increases in

mediolateral (ML) COP velocity and a decreased anteroposterior (AP) COP velocity in an unhealthy population compared to healthy matches¹⁹. This suggests that COP velocity may also increase in the KOA population. COP velocity is influenced by gait speed with studies showing COP velocity decreases when gait speed decreases in elderly subjects^{19 20}. Although COP variables are altered based on foot structure, COP measurements have been shown to have moderate to good reliability¹⁸.

Although obesity has been identified as a comorbidity with KOA⁶, it has not been established if changes in body composition are a potential cause or the result of KOA. Studies have shown that the fat mass (FM) and lean mass (LM) are significantly different in KOA patients compared to healthy matched subjects, but the values could not differentiate between mild and severe level KOA subjects²¹. This suggests that body composition may be just one of several influencing factors. In comparing men and women with KOA, it has been suggested that increased FM more strongly correlates with KOA in women while decreased LM is more closely associated in men^{22 23}. Increased FM or decreased LM both reduce the relative force production of the muscles^{22 23} indicating that they are related to functional and balance measures, although KOA studies have not directly assessed these outcomes.

As suggested by the evident changes in body composition, KOA patients have a loss of muscle strength, measured through maximal voluntary isometric contraction (MVIC)²⁴. This loss of strength is due to both the loss of muscle mass^{21 23 25} and the activation of the motor units within the muscle²⁶⁻²⁹. The central activation ratio (CAR) measures the maximal strength capacity of the muscle by forcing a maximal contraction through electric stimulation, and comparing it to the MVIC to determine the ratio of motor units recruited. Decreased CAR in the quadriceps is common in KOA patients²⁶⁻²⁹, showing that even when the muscle mass is present,

the whole muscle is not being used. CAR of the rectus femoris has been able to differentiate between asymptomatic and moderate severity KOA²⁸, with moderate KOA patients having a CAR below 80%²⁷.

Balance measures are correlated to quadriceps strength in the KOA population, making quadriceps function an important factor to consider when looking at function ($r=0.37$)¹⁵. When compared to healthy controls, KOA subjects have lower balance, strength, and activation measures^{14 15}, confirming the existing relationship. Other studies have also shown that both decreased quadriceps strength and CAR are indicative of greater balance deficits in KOA patients^{15 30-32}. Within the KOA population, the strength deficit and number of falls are significantly greater in surgical candidates compared to non-surgical patients³², suggesting that strength and balance continue to decrease as the disease progresses.

To counteract the physical decline resulting from KOA, therapeutic exercise (TE) and transcutaneous electrical nerve stimulation (TENS) interventions have been used to not only attenuate pain, but also to increase quadriceps CAR with the aim of ultimately improving performance in activities of daily living^{27 33}. A combination of TE+TENS was shown to be significantly more effective at improving CAR than TE alone²⁷. Baseline testing measured a $78\pm 7\%$ CAR in KOA patients, with a 4 week TE+TENS intervention increasing the CAR to $94\pm 4\%$ ²⁷. Function and balance measures were not assessed in this study, but the literature suggests balance is related to CAR¹⁴. In a study that used only TE as an intervention, improvements for both the timed up and go test and the timed sit to stand test reached statistical significance³⁴. The timed up and go test has been shown to be a valid measure of dynamic balance¹³, indicating that the subjects' balance and lower extremity strength improved together.

To fully determine the results of treatment in KOA patients following an intervention, it must be determined not only if patients can move better, as determined by measures of strength, CAR, and gait speed, but also if patients are improving their dynamic stability mechanisms. COP measurements of sway velocity, sway path, and ML displacement can be used to quantify dynamic gait stability so they can be compared to other changes occurring as a result of intervention. An increase in dynamic stability and the ability to move must occur simultaneously to ensure that not only are the patients able to move better, but they can move safer.

Purpose

1. To determine if there is a relationship between the changes in gait speed and dynamic stability following a 4 week therapeutic intervention in KOA patients
2. To establish if there is a relationship between body composition and dynamic stability during KOA treatment

Research Questions

1. Is there an association between the change in gait speed and the change in COP measured immediately before and after a 4 week KOA treatment intervention?
2. Is COP trajectory post intervention associated with lean mass, fat mass, CAR, or pain level?

Hypotheses

1. An improved COP trajectory will be associated with an increase in 20 meter maximal walking speed following a 4 week intervention.
2. Improvement in COP trajectory after a 4 week intervention will be significantly correlated with an increase in lean body mass and decreased fat mass.

Limitations

1. COP data will be based on the single step that contacts the force plate.

Delimitations

1. Subjects were limited to those able to walk without an assistive device.
2. Subjects were excluded if they are obese (body mass index (BMI) >35).
3. Participation was limited to subjects with moderate to severe KOA.

Assumptions

1. Subjects did not intentionally alter gait pattern during the testing session
2. Subjects did not have medical problems, besides KOA, interfering with gait pattern
3. Subjects answered self-reported data truthfully
4. COP variables were representative of overall stability

Significance of Study

Since there is improved maximum gait speed and limb loading following treatment, maximum gait speed can be used as an outcome measure to determine if the gait pattern has improved in KOA patients. Likewise, the preliminary results between body composition and stability serves as a foundation for future studies.

CHAPTER 2: LITERATURE REVIEW

KOA is one of the top five causes of disability and is associated with an early onset of the inability to independently complete activities of daily living, making it as debilitating as heart disease^{9,34}. This separates those with KOA and the healthy aging. Risk of developing KOA increases with age¹, so the rising number of the elderly in the United States population, which is expected to double by 2050³⁵, demands that more attention is given to this manageable health condition. Up to 50% of KOA patients have at least one other medical condition⁹, including depression, cardiovascular disease, obesity, diabetes, and chronic obstructive pulmonary disease³⁻⁸. In most cases, it is unknown if KOA is the cause or effect of other diseases. However, a few research studies have concluded that KOA is shown to be the causative factor of cardiovascular disease, obesity, and diabetes⁶.

Falls are a prevalent issue in the healthy elderly, with studies reporting balance deficits as early as 50 years old¹⁰ and observations concluding that 1 in 3 adults over 65 years will fall over the course of a year¹¹. From early on in gait related research, it was noted that aging brought about changes in the gait cycle³⁶, usually finding a decrease in gait speed³⁷⁻³⁹. Conflicting results investigating the relationship between gait speed and stability have been published. Using similar methodology, some suggest that the decrease in walking speed is used to increase stability and prevent age associated falls⁴⁰, while others indicate that there may be no additional stability gained through this mechanism^{20,41}.

Similar to the general aging population, a significant decrease in gait speed has also been found in subjects with severe KOA²⁸. Additionally, balance deficits are shown to be significantly worse in KOA patients when compared to the healthy elderly^{12 15}, with half of KOA patients sustaining falls within the year prior to receiving surgical intervention³². Loss of balance and falls are more prevalent in KOA patients^{12 13} because they are exacerbated by changes in muscle strength and activation, especially of the quadriceps^{15 32 37}.

To quantify balance more precisely than clinical tests and to detect minimal changes, balance should be measured through COP. Not only should balance be measured using this method, but it should also be measured during a dynamic task, such as walking, so that the results are more applicable than static posture COP assessments. COP can be quantified by measures using both the position and velocity at any point during foot contact on the force plate and provide information about the dynamic stability of the individual. Although COP is influenced by foot structure, it has been determined that a healthy ML COP displacement covers 18% of the foot width¹⁸. COP measures are highly reliable with ICC between 0.65 and 0.82 ML, and between 0.69 and 0.93 AP, indicating moderate to good reliability for COP position, with similar values for COP velocity¹⁸. The lower ICC in ML COP was seen primarily in the middle of stance phase, which is when the foot structure has the highest influence on COP¹⁸.

Body composition changes in KOA patients are evident, but it is unclear whether they are the cause or effect of KOA²¹⁻²³. Although not a true assessment of body composition, BMI calculates the ratio of body weight to height and is commonly used to determine the obesity level in KOA patients⁴²⁻⁴⁶. Studies using this methodology indicate that a BMI over 30kg/m² increases KOA risk 7 to 8 times higher compared to those with a BMI less than 25kg/m²^{42 43 47}. Bioelectrical impedance analysis (BIA) is able to estimate fat mass and fat free mass and has the

advantage of simple testing procedures, encouraging its use in research^{45 46 48}. Multivariate analyses showed that BIA estimates of LM were better predictors of KOA presence and severity compared to BMI⁴⁶. However, in studies using both BMI and body fat percentage via BIA, an increased BMI indicated a greater risk of KOA compared to an increased body fat percentage⁴⁵. These inconclusive results in the literature regarding the influence of FM and LM on KOA may be due to the error introduced through BIA estimations, despite using pre-assessment guidelines.

Dual energy x-ray absorptiometry (DEXA) has been shown to provide valid and reliable measures of bone mineral density, FM, and LM^{49 50}, making it the ideal method of assessing body composition. In the studies using DEXA in KOA, FM and LM are both significantly correlated with KOA, but neither could determine the severity of KOA^{21 22}. However, the correlation between KOA and LM is not consistent, as other studies found no correlation between them²³. Due to the small number of studies looking at the relationship between body composition and KOA, further study should be done using DEXA to quantify FM and LM to produce valid and reliable data.

Without measuring total body composition, muscle atrophy has been quantified using quadriceps cross sectional area, which was found to be 12% smaller in older women with KOA compared to healthy women of the same age⁵¹. Although comparisons of healthy old and young women show that older women without KOA battle against loss of muscle mass, KOA diagnosis significantly increased the loss⁵¹. Maintaining muscle mass is important because it determines the maximum capacity of strength production, which is shown to be strongly linked to physical function^{25 52 53}.

Although muscle mass is significant in determining function, it is not the sole factor. In a study by Mizner et al. (2005), KOA patients were compared before and after total knee

arthroplasty and it was found that muscle mass and muscle inhibition together explained 85% of the strength deficit, but muscle inhibition was twice as significant as the muscle mass⁵⁴. This shows that negating atrophy is important, but muscle inhibition must be addressed in order to receive the greatest benefits of therapeutic exercise and to gain the maximum pain free function³³.

A true maximal contraction can be produced through electric stimulation of the muscle during MVIC testing. The CAR is determined by comparing the MVIC to the stimulated maximal contraction^{26 27 29}. It is common for KOA patients to have a CAR below 80%, meaning that 20% of the muscle fibers are not voluntarily recruited²⁷. This inactivation leads to weakness in KOA patients that is evident in both isometric and isokinetic strength testing²⁴. It was observed that 50% of subjects with mild KOA were unable to fully activate the quadriceps⁵⁵. When muscle fibers are not voluntarily fired, they are not able to be recruited to complete daily activities. However, when quadriceps activation is increased through an exercise intervention, a significant increase in MVIC results²⁹.

This weakness that is due to both a loss of muscle mass and a loss of muscle activation alters the gait pattern in KOA patients^{24 28 29 33 51 54}. Just as weakness effects function, it also effects balance scores in KOA patients³¹. When compared to healthy controls, KOA subjects have lower static balance, strength, and activation measures¹⁴, confirming the existing relationship. Several studies have also shown that both decreased quadriceps strength and CAR are indicative of greater balance deficits in KOA patients^{15 30 31}. Within the KOA population itself, the quadriceps strength deficit is significantly greater in surgical KOA candidates compared to non-surgical KOA patients and increases their fall prevalence from 30% to 48%³².

KOA directly decreases physical function, specifically gait function, due to accompanying knee pain⁵⁶⁻⁵⁸. Pain levels are strongly associated with the severity of KOA⁵⁹. However, there is evidence that these pain levels, based on self-reported pain using a visual analog scale (VAS), are manageable because a hyaluronate injection intervention significantly decreased pain after 5 weeks⁵⁶. KOA pain inhibits a normal gait pattern, as the expectant double peak typically seen in the ground reaction forces of healthy individuals is not present in KOA patients⁵⁷. Instead, KOA patients exhibit a blunted ground reaction force response and alter their mechanics to reduce loading forces in the lower extremities, shown in both level ground walking⁵⁷ and during more demanding tasks such as descending stairs⁶⁰. Hyaluronate injections, used in KOA to reduce pain levels, allow the ground reaction forces to be restored to those of a healthy individual following a 5-week intervention of hyaluronate injections^{56 57}.

Current treatments for KOA include both TE and TENS interventions with the ultimate goal of increasing normal, pain free function in KOA patients. The focus of TE is typically to increase lower extremity strength, especially in the quadriceps³⁴. Although TE can increase the strength of the muscle by increasing the size and number of muscle fibers⁶¹, it may not increase the amount of muscle fibers voluntarily contracting, leaving the patient prone to both losses of muscular strength and muscular atrophy⁶². Traditionally, TENS was used in treatment to reduce pain⁶³⁻⁶⁵. However, more recent applications of TENS have been used to increase the CAR of the quadriceps^{27 29 33 63 66 67}. By applying TENS to increase CAR, the muscle's true potential may be able to be reached.

While TENS as an intervention for increasing CAR and strength shows potential and should continue to be developed, there is also evidence suggesting that TENS may directly increase balance. In a healthy population, TENS applied to the gastrocnemius was shown to have

an immediate acute effect on balance, quantified by a pressure mat⁶⁸. Park et al. compared TE+TENS to a TE+shamTENS group of stroke patients, finding that the TENS group had greater improvements in balance after a 6 week intervention⁶⁹. The influence of TENS on balance needs to be further explored and tested in the KOA population because of its potential to decrease fall risk and increase safe participation in activities of daily living.

Research shows that KOA patients are negatively effected by balance deficits, which are related to the compromised body composition and strength. Treatments targeting strength may result in an improvement in body composition as well as physical function. However, in order to benefit KOA patients to the greatest extent, dynamic stability must also increase to lower fall risk while completing these tasks. By ensuring KOA patients are functioning at a higher level physically and are more stable during these activities, the quality of life with KOA can improve greatly.

CHAPTER 3: METHODOLOGY

Research Design Overview

The primary purpose of this study was to determine if a relationship exists between the change in gait speed and the change in dynamic stability following an intervention. The secondary purpose was to establish if there is a relationship between body composition and dynamic stability following KOA treatment. Subjects went through a 4 week intervention with baseline and post-intervention testing sessions.

Subjects

All subjects in this study were diagnosed radiographically with moderate to severe KOA on the Kellgren-Lawrence (KL) scale. Subjects were recruited through referral by their orthopaedic physician at the Orthopaedic Clinic. Subjects were eligible for inclusion if they meet all of the following criteria:

- Between the ages of 40 and 75 years old
- Exhibit symptomatic KOA, which we will define as a normalized, person based, Western Ontario and McMaster Universities Arthritis Index (WOMAC) function subscale score ≥ 31
- Radiographic evidence of tibiofemoral osteoarthritis (2-4 on the KL scale)
- Neuromuscular activation deficits, defined as central activation ratio of less than 90% $\pm 2\%$ in the involved leg

Subjects were excluded from the study if any of the following were present:

- Diagnosed with a cardiovascular condition restricting exercise
- Have had a corticosteroid or hyaluronic acid injection in the involved knee in the previous 14-days
- Have a pacemaker
- Have a neurodegenerative condition
- Have rheumatoid arthritis
- Have cancer
- Have a neural sensory dysfunction over the knee
- Have a BMI over 35
- Have a history of lower extremity orthopaedic surgery in the past year
- Have a history of a traumatic knee injury in the past 6 months
- Have any history of a total knee arthroplasty in either extremity
- Have a diagnosed, non-reconstructed knee ligament tear
- Need an assistive device to walk
- Currently pregnant or planning to become pregnant while enrolled in the study

Prior to data collection, subjects signed an informed consent form (Appendix A) which was approved by the University of North Carolina Biomedical Institutional Review Board.

Procedures

After a physician confirmed the OA diagnosis, a member of the research team explained the goals of the study. Subjects were also recruited through the Carolina Data Warehouse for Health and UNC-Hospital's Database. These subjects were contacted via mail with an informational packet. A research team member then called them to follow-up. If subjects were interested in participating in the study, they were screened either in the lab or over the phone for

demographic information and self-reported function based on the Functional subscale of the WOMAC Questionnaire. Subjects were also able to ask any questions related to involvement in the study. If interested subjects were still eligible for the study, an appointment in the Neuromuscular Research/Sports Medicine Research Laboratory was made. At this appointment, subjects signed the informed consent, and completed the baseline testing before their first appointment at UNC Meadowmont Physical Therapy Clinic.

Intervention Groups

The subjects were randomized into 1 of 3 treatment groups before the first PT visit.

Therapeutic Exercise

Subjects in this group completed all 10 visits at UNC Meadowmont, participating in TE with the goal of increasing lower extremity strength and function. Each visit lasted approximately 45 minutes, and subjects completed 2-3 sessions a week, totaling 10 over a 4 week period. TE included flexibility exercises, lower extremity strengthening exercises, and balance training, with all subjects receiving the same protocol, but progressing on an individual basis.

Therapeutic Exercise + TENS

This group completed the same TE as the control group, but also used a TENS unit (EMPI, Inc., St. Paul, MN; TENS Manual). Subjects were educated on how to use the system during the first physical therapy visit and given an instruction manual for increasing dosage throughout the 4 weeks. Subjects were instructed to apply TENS for approximately 8 hours per day, when they are most active.

Therapeutic Exercise +shamTENS

Subjects in this group completed the same TE program, and were given a TENS unit programmed to discontinue current output after 20 seconds. Subjects were instructed similarly to the TENS group, but were told that it is normal to not feel the current output after application. No instructions for increasing dosage were given.

Outcome Measures

At all lab visits, subjects underwent the same testing procedures, completed by a blinded member of the research team.

Visual Analog Scales (VAS) were used for current level of knee pain. A solid line from 0 to 100 was shown to the subject, and they were asked to mark how they currently felt. A score of 100 indicated “worst pain imaginable”, and a score of 0 indicated “no pain”. Distance was measured from 0 to the line drawn and reported in centimeters.

Body Composition

A subpopulation in the study completed body composition testing via DEXA (DEXA; GE Lunar DEXA, GE Medical Systems Ultrasound & Primary Care Diagnostics, Madison, WI, USA), using the encore software for analysis (enCORE Software Version 16). Subjects adhered to the following pre-assessment guidelines:

- Remove shoes and any jewelry prior to testing
- Two hours fasted and adequately hydrated

A member of the research team positioned each patient in a straight line within the table boundaries. Subjects were asked to lie still for approximately 10 minutes while the scan was completed. Measurements of total body and lower extremity total mass, fat mass, fat percentage, and lean mass were recorded for analysis.

Muscle Function

Subjects were positioned on the isokinetic dynamometer, using straps to secure their torso, thigh, and lower leg to the device. The knee was in 90° of flexion and the movement arm was in a fixed position to test strength isometrically. Two electrodes were placed over the quadriceps. The subjects were instructed to ‘kick out’ in order to flex the quadriceps as quickly and as strongly as possible while keeping their arms crossed over their chest to prevent accessory movement. A practice trial was done at approximately 25, 50, and 75% of the subject’s perceived maximum, then three maximal trials were completed and the average score was recorded. For the next 2 trials, an electrical stimulus was given after the torque plateaus at the previously determined average MVIC. The CAR was calculated by comparing the voluntary force to the electrically stimulated force production.

Gait Biomechanics

Subjects walked along a 6m walkway at a comfortable, self-selected speed. A minimum of 5 practice trials were done to determine the average preferred speed given in real time through 2 sets of timing gates (TF100, Trac Tronix, Lenexa, Kansas, United States). Five valid trials for each limb were completed for data collection. For a trial to be valid, subjects had to fully contact the force plate and be within $\pm 5\%$ of their preferred gait speed.

Force Plates

While walking at their preferred speed, subjects crossed over embedded Bertec force plates (40x60cm, FP406010, Bertec Corporation, Columbus, Ohio, United States). Ground reaction forces were sampled at 1200Hz, filtered using a dual pass 4th order Butterworth filter with a 12Hz cut off, using Vicon Nexus v1.7.1 motion capture software (Vicon Motion Systems, Los Angeles, CA, USA). This data was uploaded to The Motion Monitor v9.0 software system

(Innovative Sports Training, Inc., Chicago, IL, USA) for analysis. The x -axis indicated anteroposterior and the y -axis indicated mediolateral movement of the COP relative to the participant. Once the data was verified and analyzed in The Motion Monitor, the exported results were run through Matlab (The Mathworks, Inc., R2016a) where the mean for each of the following variables was determined using the 3 middle trials. Trials were substituted if there were ground reaction forces (GRF) on both plates, indicating their foot was not fully on the plate.

- Stance time
- COP ellipse area
- COP sway path
- COP sway velocity
- ML excursion
- M displacement
- L displacement
- Vertical ground reaction force (VGRF) maximum
- Anteroposterior ground reaction force (APGRF) maximum and minimum
- Mediolateral ground reaction force (APGRF) maximum and minimum

All GRF variables were calculated for the first and second 50% of stance phase. Initial contact was defined as the point at which the ground reaction force is greater than 10N, and the toe off was the point at which the force is less than 10N.

Maximum Gait Speed

20 meter walk test was completed at the subject's maximum speed. Subjects were instructed to walk from the starting line to the cones placed 20 meters away as quickly as they

safely could without running. Three trials were completed and the average score was used in the data analysis.

Statistical Analysis

SPSS 23.0 (SPSS INC, Chicago, Ill) was used for all statistical calculations with statistical significance set a-priori at $p < 0.05$. Analysis for outliers was completed by determining the interquartile range for the 20 meter walk test. One outlier was found and removed for all statistical analysis. The descriptive characteristics were reported as the mean \pm standard deviation. A series of T-tests were run to determine if there were significant changes following intervention. In order to answer research question one, a correlation analysis was done comparing baseline and change scores of gait speed and the COP variables. A partial correlation was then completed controlling for the baseline maximum gait speed. For the second research question, a correlation analysis was done for the DEXA subjects between the COP variables and the subject characteristics.

CHAPTER 4: RESULTS

Fifty three older subjects participated in this study who were, on average, overweight, diagnosed radiographically with moderate to severe KOA and experiencing mild to moderate pain and dysfunction (Table 1), one subject was removed as an outlier upon statistical analysis. In a sub-group of individuals with body composition scans (N=7), subjects were found to be obese. No significant differences between the DEXA and no DEXA groups were found.

Table 1. Participant characteristics (N=53)

	Total	No DEXA	DEXA*
	Mean (SD)	Mean (SD)	Mean (SD)
Age (y)	62 (7)	62 (7)	61 (10)
Sex (% female)	25 (47)	23 (51)	3 (43)
Height (cm)	173.7 (10.5)	173.8 (10.5)	173.5 (12.1)
Mass (kg)	85.5 (15.2)	85.5 (15.6)	84.3 (14.1)
BMI (kg/m ²)	28.3 (3.8)	28.3 (4.0)	27.9 (2.6)
KOA condition (% bilateral)	39 (73.6)	34 (75.6)	71.4
KL Scale Score	2.8 (0.6)	2.8 (0.6)	2.7 (0.4)
WOMAC Score	48.1 (13.1)	48.5 (13.8)	43.9 (7.9)
CAR	0.77 (0.13)	0.77 (0.12)	0.74 (0.16)
Fat Mass (kg)	-	-	64.4 (13.2)
Body Fat (%)	-	-	36.3 (8.8)

*subpopulation of N=7

DEXA=dual energy x-ray absorptiometry; BMI=body mass index; KOA=knee osteoarthritis; KL=Kellgren-Lawrence; WOMAC=Western Ontario and McMaster Universities Arthritis Index; CAR=central activation ratio

Table 2. Gait characteristics before and following a 4 week intervention				
	Baseline	4 Week	% Change	p value
Pain (VAS; cm)	4.1 (2.6)	2.9 (2.5)	-27.9	0.008
20 meter walk test (s)	11.6 (2.1)	11.1 (2.1)	-4.4	<0.001
WOMAC Score	48.1 (13.2)	30.7 (15.2)	-34.9	<0.001
Stance Time (s)	0.76 (0.07)	0.74 (0.06)	-2.7	0.004
Ellipse Area (cm ²)	72.8 (24.2)	73.1 (21.1)	0.4	0.908
Sway Path (cm)	72.5 (9.6)	75.9 (9.6)	4.3	0.047
Sway Velocity (cm/s)	96.9 (15.6)	103.5 (16.3)	6.8	0.013
ML Excursion (cm)	5.6 (1.5)	5.8 (1.6)	2.6	0.490
M Displacement (cm)	3.3 (1.7)	2.8 (1.9)	-13.1	0.156
L Displacement (cm)	-2.3 (1.6)	-2.9 (2.1)	24.4	0.015
VGRF Maximum 1 (kg/N)	1.067 (0.072)	1.080 (0.075)	1.2	0.089
VGRF Maximum 2 (kg/N)	1.023 (0.058)	1.024 (0.069)	0.2	0.938
MLGRF Maximum 1(kg/N)	0.064 (0.018)	0.064 (0.018)	1.0	0.853
MLGRF Maximum 2 (kg/N)	0.058 (0.019)	0.057 (0.017)	-1.2	0.542
MLGRF Minimum 1(kg/N)	-0.037 (0.023)	-0.040 (0.025)	9.8	0.045
ML GRF Minimum 2 (kg/N)	-0.006 (0.009)	-0.008 (0.009)	39.8	0.007
APGRF Maximum 1 (kg/N)	0.036 (0.018)	0.036 (0.019)	-0.2	0.903
APGRF Maximum 2 (kg/N)	0.165 (0.035)	0.172 (0.034)	4.2	0.005
APGRF Minimum 1 (kg/N)	-0.166 (0.038)	-0.176 (0.039)	6.6	0.002
APGRF Minimum 2 (kg/N)	-0.014 (0.010)	-0.014 (0.010)	2.3	0.732
Mean (SD)				
VAS=visual analog scale; WOMAC=Western Ontario and McMaster Universities Arthritis Index; ML=mediolateral; 1=first 50% of stance phase; 2=second 50% of stance phase				

The changes in gait function following a 4 week intervention are displayed in Table 2. Maximum gait speed, represented by the 20 meter walk test, improved significantly following intervention ($p<0.001$). COP sway velocity and L displacement both significantly increased with intervention, while there was a trend for higher COP sway path ($p=0.055$). GRFs were measured as the vertical (V), mediolateral (ML), and anteroposterior (AP) forces. Significant increases in minimum MLGRF during the first and second 50% of stance were found. Significant changes

were also found in APGRF with the minimum during the first 50% of stance time and the maximum during the second 50% increasing following intervention.

To determine the relationship between gait speed and stability in KOA patients (research question 1), correlation coefficients were computed between 20 meter walk test score and COP variables using baseline values. This analysis showed that maximum gait speed was correlated with sway velocity ($r(53)=-0.318$, $p=0.02$). No significant correlations were found between maximum gait speed and ML COP position at baseline.

Although initial baseline analysis results did not show meaningful significance, the relationship was further explored by computing correlation coefficients comparing change scores of maximum gait speed, COP variables, and GRF variables (Table 3). No significant correlations were found between the 20 meter walk test and any COP variables, data is not reported. Stance time was significantly correlated with four and approached significance with one of ten GRF variables. When controlling for baseline maximum gait speed, the correlation between the change in the 20 meter walk test and AP GRF maximum during the first 50% of gait becomes significant ($r(53)=0.289$, $p=0.037$), while the other values remained significant.

Table 3. Change score Pearson's correlations between COP and GRF variables

	Stance Time (s)	Ellipse Area (cm ²)	Sway Path (cm)	Sway Velocity (cm/s)
V GRF Maximum 1	-0.25	0.20	0.25	0.27
V GRF Maximum 2	-0.05	0.26	0.04	0.06
ML GRF Maximum 1	-0.27+	0.20	0.12	0.17
ML GRF Maximum 2	-0.35*	0.21	0.19	0.25
ML GRF Minimum 1	0.05	0.03	-0.00	-0.02
ML GRF Minimum 2	-0.14	0.09	0.27	0.28*
AP GRF Maximum 1	0.12	-0.11	-0.13	-0.14
AP GRF Maximum 2	-0.44*	0.42*	0.38*	0.44*
AP GRF Minimum 1	0.34*	-0.15	-0.21	-0.26
AP GRF Minimum 2	0.38*	-0.05	-0.06	-0.16

*indicates P<0.05

COP=center of pressure; GRF=ground reaction force; WOMAC= Western Ontario and McMaster Universities Arthritis Index; 1=first 50% of stance phase; 2=second 50% of stance phase; V=vertical; ML=mediolateral; AP=anteroposterior

In order to fully answer research question 2 and determine the relationship between the participant characteristics and gait cycle, correlation coefficients between baseline COP variables and subject characteristics were computed (Table 4). No relationships between any of the variables were observed.

Table 4. Baseline COP correlations with subject characteristics

	Maximum Gait Speed (s)	Stance Time (s)	Ellipse Area (cm ²)	Sway Path (cm)	Sway Velocity (cm/s)
Pain (VAS, cm)	-0.09	-0.15	0.16	-0.02	-0.03
WOMAC	-0.24	-0.03	0.2	-0.11	-0.14
CAR	-0.12	0.10	-0.14	0.07	-0.06
KL Score	0.20	-0.7	0.01	0.00	-0.14
Height (m)	-0.17	-0.02	-0.21	0.21	0.08
Weight (kg)	0.04	0.05	-0.08	0.19	-0.04

*indicates P<0.05

COP = center of pressure; WOMAC=Western Ontario and McMaster Universities Arthritis Index; CAR = central activation ratio; KL=Kellgren-Lawrence; VAS=visual analog scale

In the subpopulation that completed DEXA scans (n=7), both total body lean mass and lean mass in the legs showed a significant correlation to M and L COP displacement (Table 5). A

positive correlation with M displacement shows that the COP has greater movement medially, while L displacement shows that the COP has less movement laterally. An increase in ML excursion would result from an increase in M displacement and a decrease in L displacement.

Table 5. Baseline DEXA correlation coefficients with COP displacement

	ML Excursion (cm)	L Displacement (cm)	M Displacement (cm)
Total Mass (kg)	0.85*	0.27	0.89*
Total Body Fat Percent	-0.08	-0.85*	-0.46
Total Fat Mass (kg)	0.59	-0.75	0.18
Total Lean Mass† (kg)	0.87	0.92*	0.95*
Total Mass Legs† (kg)	0.71	0.78	0.78
Fat Mass Legs† (kg)	-0.68	-0.78	-0.77
Lean Mass Legs† (kg)	0.84	0.95*	0.94*

*indicates P<0.05; †indicates n=5

BMI = body mass index; CAR = central activation ratio; COP = center of pressure; ML = mediolateral

CHAPTER 5: DISCUSSION

The aim of this study was to assess the change in gait speed and COP characteristics following a 4 week intervention and determine their association with participant characteristics. Following intervention, subjects had a significant improvement in pain and WOMAC score, as well as maximum gait speed, assessed using the 20 meter walk test score. Improved GRF scores following intervention included increased maximum and minimum AP GRFs during the second and first half of the gait cycle, respectively. Change score correlations indicated that only maximum gait speed was inversely related to COP sway velocity. These results contribute to the literature on KOA and the impact of common treatment methods, showing that not only can maximum gait speed improve following intervention, but the health of the effected leg improves since they are able to have higher propulsive and braking forces.

To compare the relationship between gait speed and gait stability, several correlation coefficients were calculated. These were done using the baseline values and change score values with maximum gait speed, stance time, COP sway path, COP sway velocity being the variables of primary interest. Maximum gait speed increased following the intervention, as expected based on another study which included a slightly longer intervention of 6 weeks and showed an increase in gait speed of nearly the same magnitude⁷⁰. Maximum walking speed has been shown to be a reliable measure in gait testing, specifically in KOA patients⁷¹.

Baseline and change score values of gait speed were negatively correlated with baseline and change score values of COP sway velocity. Increased COP sway velocity has been used in previous studies to measure decreased stability^{10 69}. These inverse relationships support other research showing that a slower walking speed is not more stable^{41 72}. The loss of stability indicated with higher COP velocity may be the result of increased ML COP velocity. However, we were unable to differentiate between ML and AP COP velocity in our current study, allowing this to remain speculative and an area for further study.

Although stance time and gait speed changed as expected with stance time decreasing as speed increased, they were not significantly correlated to each other. Both variables were compared to GRF variables to further explore gait changes that occurred. APGRF minimum during the first and second 50% of stance phase were positively correlated with gait speed, supporting previous literature⁷³, and indicating an increased braking force upon initial contact and as weight shifts to the forefoot. As suggested by Peterson et al., an increase in posterior GRF indicates a healthier gait cycle since it is a mechanism by which gait is controlled⁷³. The maximum MLGRF, which is negatively correlated with stance time, indicates there is a greater medial force. The negative correlation may not be due to an increase in overall GRF, but rather a greater posterior force in the first and second half of stance phase. If the posterior force is a higher relative proportion of the total force, the medial force would consequently decrease.

The secondary research question addressed by the study explored the relationship between subject characteristics such as pain, WOMAC score, CAR, and body composition to gait speed. In this study, no significant baseline correlations with these variables and maximum gait speed were found.

FM in women and LM in men have previously been linked to the presence of KOA^{22 23}. In an exploratory analysis of body composition measure via DEXA (N=7), both total body lean mass and lower extremity lean mass were significantly correlated with an increased L and M COP displacement. A greater M COP displacement value indicates that the COP is further medially, whereas a greater L COP displacement indicates that the COP travels laterally to a lesser extent. Greater medial movement of the COP may not necessarily indicate a decline in COP trajectory. Instead, the increased displacement may suggest that as the lean tissue increases, force production also increases⁵², and the COP moves to a greater extent because there is now a greater ability to control movement laterally without a loss of balance. Improved balance will consequently result in better physical function and increase quality of life. However, due to a small sample size that completed DEXA scans, we are unable to fully address this question at this time. However, this question should be reevaluated with a larger sample and subjects ranging from healthy controls to severe KOA patients.

The study was limited due to its reliance on the subject walking at a maximum gait speed at each visit. The gait speed selected may be influenced by factors other than the intervention such as fatigue and pain from activities other than TE. Subjects were also asked to self-report for pain and WOMAC scores. Each individual's interpretation of "mild", "moderate", or "severe" may differ on these questionnaires, but the WOMAC has been established as a valid assessment of dysfunction for KOA patients. The implications from the change in COP velocity were also limited because we could not differentiate between ML and AP COP velocity through the Matlab code used.

In summary, this study further explored the effects of common treatments used for KOA rehabilitation. Treatments are proven to be effective since following intervention, the maximum

gait speed increases and pain, and WOMAC scores decrease. Other meaningful implications come from the increased maximum AP GRF and the decreased minimum AP GRF, which indicate that the involved limb can withstand higher propulsive and braking forces after treatment. Further exploration is warranted to determine the implications of FM and LM on the gait cycle in KOA patients. However, this study contributes to the existing literature by expanding upon the treatment effects of TE and TENS in KOA, specifically that improvements in gait speed following treatment are concurrent with improvements in dynamic stability and allow KOA patients to complete activities of daily living while minimizing the fall risk.

APPENDIX A

University of North Carolina at Chapel Hill

Consent to Participate in a Research Study

Adult Participants

Consent Form Version Date: 7-05-2016

IRB Study # 15-1150

Title of Study: The KNEEhabilitation Study: Improving Disability in Individuals with Knee Osteoarthritis

Principal Investigator: Brian Pietrosimone

Principal Investigator Department: Exercise and Sport Science

Principal Investigator Phone number: 919-962-3617

Principal Investigator Email Address: brian@unc.edu

Co-Investigators: Todd Schwartz, Leigh Callahan, Troy Blackburn, Jeffrey Spang, Yvonne Golightly, Daniel Nissman, David Berkoff, Joanne Jordan, Robert Creighton, Daniel Del Gaizo, Ganesh Kamath, Darin Padua, Harry Stafford, Lauren Porras

Funding Source and/or Sponsor: NATIONAL INSTITUTE OF ARTHRITIS AND MUSCULOSKELETAL AND SKIN DISEASES (NIAMS)

Study Contact Telephone Number: 843-2014

Study Contact Email: bluc@live.unc.edu

What are some general things you should know about research studies?

You are being asked to take part in a research study. To join the study is voluntary.

You may refuse to join, or you may withdraw your consent to be in the study, for any reason, without penalty.

Research studies are designed to obtain new knowledge. This new information may help people in the future. You may not receive any direct benefit from being in the research study. There also may be risks to being in research studies. Deciding not to be in the study or leaving the study before it is done will not affect your relationship with the researcher, your health care provider, or the University of North Carolina-Chapel Hill (UNC). If you are a patient with an illness, you do not have to be in the research study in order to receive health care.

Details about this study are discussed below. It is important that you understand this information so that you can make an informed choice about being in this research study. You will be given a copy of this consent form. You should ask the researchers named above, or staff members who may assist them, any questions you have about this study at any time.

What is the purpose of this study?

Thigh muscle strength is important for improving function in individuals with knee osteoarthritis. There is evidence that stronger thigh muscles allow people with knee osteoarthritis to be more physically active and to do more activities without pain. One cause of muscle weakness in individuals with knee osteoarthritis stems from the inability of nerves to “turn on” the muscles in the leg. Physical therapy is one method for changing how those leg muscles “turn on”. "There is some evidence that using transcutaneous electrical nerve stimulation (TENS), which is a commonly used form of electrical stimulation that can be put on your knee, may also help to “turn on” muscles in people who have muscle weakness. The purpose of this research study is to test how TENS used with physical therapy and during

daily activities changes your ability to “turn on” your thigh muscles as well as how TENS and physical therapy may improve your thigh muscle strength, ability walk and perform activities of daily living, and potentially changes feelings about your knee function. We are evaluating the effect of TENS and physical therapy in people with knee osteoarthritis, who feel some disability related to knee function and have difficulty turning “their muscles on”. You are being asked to be in the study because you have been diagnosed with knee osteoarthritis, you feel some limitations in performing activities because of you have been diagnosed with knee osteoarthritis.

Are there any reasons you should not be in this study?

You should not be in this study if you have: 1) been diagnosed with a cardiovascular condition restricting you from participating in exercise; 2) had a corticosteroid or hyaluronic acid injection in your knee in the past 2-weeks; 3) a pacemaker; 4) a neurodegenerative condition; 5) rheumatoid arthritis; 6) cancer; 7) neural sensory dysfunction over the knee 8) a BMI over 35; 9) history of lower extremity orthopaedic surgery in the past year; 10) a history of a traumatic knee injury in the past 6 months; 11) any history of a total knee arthroplasty (or joint replacement) in either extremity; or 12) a diagnosed, non-reconstructed knee ligament tear. Also you should not be in this study if you need an assistive device, such as a cane or walker, to walk. You should not be in this study if you are currently pregnant or plan to become pregnant during this study.

How many people will take part in this study?

A total of approximately 177 people may be screened to participate in this study while 90 people with knee osteoarthritis from this institution will be enrolled in the intervention portion of the study.

How long will your part in this study last?

The study will consist of a screening/ baseline session, 10 visits of physical therapy over 4-weeks, as well as two follow-up tests at 4 and 8 weeks after beginning your first physical therapy visit. The screening session will last approximately 1 hour. If you qualify for the study and still would like to participate, we will conduct a few extra measurements over an additional 1-hour as part of the baseline session. Each of the 10 physical therapy sessions will last 45-60 minutes. Each of the two follow up testing session will consist of two 1.5 hour sessions at time points occurring at 4 and 8-weeks after your first physical therapy session.

What will happen if you take part in the study?

If you decide to take part in this study, you will be assigned to receive a study group that is provided a TENS unit and physical therapy or a group that only receives physical therapy.

Once included, you will be asked to report to the Sports Medicine Research Laboratory (SMRL) Laboratory in Fetzer Hall at the University of North Carolina at Chapel Hill for 3 separate testing sessions and to the UNC Meadowmont Physical Therapy Clinic for 10 supervised physical therapy sessions.

Testing Session 1 (will last approximately 2 hours) will consist of a screening and eligibility session where you will first complete the **Western Ontario and McMaster Universities Osteoarthritis index (WOMAC) questionnaire** as well as a **Thigh Muscle Function Assessment**. If your outcomes from these two measurements meet the inclusion criteria we will ask you to sign a HIPPA form, which will allow our study team to determine the severity of your knee osteoarthritis based on the last knee x-ray in your UNC Medical Records. If you are not eligible for the study at this point you will be excluded.

If you are eligible for the study at this point we will conduct a few additional tests during session one that include knee pain and physical activity surveys, a thigh muscle function assessment, knee range of motion assessment, gait biomechanics assessment and a physical performance assessment.

Testing Sessions 2 and 3 (will last approximately 1.5 hours each) will consist of questionnaires and surveys about your knee function, pain and physical activity as well as the thigh muscle function assessment, knee range of motion assessment, gait biomechanics assessment and a physical performance assessment. Testing sessions 2 and 3 will take place 4 and 8-weeks after your first physical therapy session.

Body Composition Assessment

During each lab visit, you will have a DEXA full body scan which will measure your fat free mass, fat mass, and bone mineral content. A DEXA uses minimal amounts of radiation, the test lasts 6 minutes and requires you to lie on the table and remain still.

Thigh Muscle Function Assessment

Similar to the screening measurement, you will be asked to perform maximal contractions of the quadriceps muscle on the front of your thigh. You will be seated and asked to kick out your leg as hard as you can against a device that measures how much force you can produce. During the contraction, a very brief (less than 1/1,000th of a second) pulse of electricity will be sent to your quadriceps muscle. This pulse of electricity will allow us to measure muscle function and is similar to a strong “carpet shock”. You will be allowed to perform at least 2 practice trials to become comfortable and familiar with the electrical stimulus, after which 3 trials will be recorded. You will similarly be asked to push your heel into the pad without an electric pulse as you sit in the chair and side lie on a table.

Range of Motion Testing

We will test how far you are able to bend and straighten your knee as you lie down on a table.

Gait Biomechanics Assessment

You be asked to walk forward along a 20 foot walkway at a comfortable, self-selected speed over a device called a force plate that is embedded in the walkway. You will perform at least 5 practice trials to ensure that you are comfortable walking over the force plate with a natural stride and without “aiming” for the force plate. We will put small reflective markers on different parts of your legs which will allow cameras in the SMRL to track how your knees move while you walk.

Performance Testing

You will be asked to do three different performance tests.

The first is a chair stand test, in which you will start seated in a chair and we will count how many times you can stand up and sit down in a 30 second period. Next, we will determine how fast you can comfortable walk forty-meters. We will time you 3 times (with at least a 1-minute rest period in between each trial). Finally we will test how fast you can climb 10 stairs at a fast but comfortable pace and you will be timed with a stopwatch. We will time 3 trials with at least a 1-minute rest period in between each trial.

Physical Therapy Intervention at the UNC Meadowmont Clinic

The physical therapy intervention will consist of 10 sessions supervised by a Licensed Physical Therapist at the UNC Meadowmont Clinic. Additionally, you may be randomized into a group that receives a Transcutaneous Electrical Stimulation (TENS) unit in combination to the 10 physical therapy sessions (over four weeks) of physical therapy. Being randomized into a group that receives a TENS stimulator means that you will be assigned by chance, like flipping a coin. This is a blinded trial which means we

will ask that you do not tell the investigator that will be collecting data from you in the SMRL what intervention you received. You can always contact the study coordinator Brittney Luc, or the Principal Investigator Brian Pietrosimone about the TENS unit.

Physical Therapy

All groups will complete a standardized rehabilitation program. You will receive therapeutic exercise 2 to 3 times per week for a total of 10 sessions over a 4 week period. Ten physical therapy sessions over a 4-week period is the current standard of care for patients with knee osteoarthritis at our facility. A lower extremity physical assessment will be conducted bilaterally for each participant to identify deficits and establish clinical baseline measures prior to beginning rehabilitation and following the 4 -week intervention. *The goals of the therapeutic exercise program are to increase thigh muscle strength and your ability to do activities of daily living.*

Being Randomized to a TENS group with Physical Therapy

If you are randomized into a TENS group, you will receive a *Select System TENS unit*, self-adhesive electrodes and batteries. A licensed health care professional will assist you in applying the electrodes on the knee joint and will educate you on how to operate the TENS unit. An instruction manual will be provided to you for reference purposes explaining operation of the device. The sensation of the electrical stimulation may vary among people. The strength of the perceived stimulation will vary among subjects from little or nothing to modest tingling, depending on the dosing you are randomized to receive. You will also complete the standardized physical therapy program under the supervision of your physical therapist at the UNC Meadowmont Clinic. The TENS unit will be worn during all therapeutic exercise sessions and at least 8 hours per day when you are the most active. We will ask you to keep a log that will indicate how long you wore the TENS unit each day. We will collect the log from you at the end of each week as well as ask you how well you are tolerating the intervention each week (you will indicate this on a questionnaire form).

Not Being Randomized to a TENS group with Physical Therapy

If assigned, you will still receive the standard of care of therapeutic strengthening exercises for the 10 sessions over the 4-week period. You will not be provided with any TENS unit.

What are the possible benefits from being in this study?

Research is designed to benefit society by gaining new knowledge. The benefits to you from being in this study may be that you may increase the strength of your leg muscles, which may result in less knee pain and less disability compared to what you may have experienced before you started the study.

What are the possible risks or discomforts involved from being in this study?

Exercise in general, including therapeutic exercise performed in physical therapy, carries the risk of pain and soreness/discomfort. As such, you may experience soreness in your leg muscles from the physical therapy or the thigh muscle assessment/ performance testing. It is also possible, though highly unlikely, that you could injure a muscle or your knee during these contractions. The tasks you will be asked to perform in this study are common to activities of daily living, rehabilitative exercises, and strength training exercises, and do not place you at greater risk of injury compared to these same tasks when you perform them during daily activity and your regular exercise routine. You may also experience mild discomfort for a brief period of time (less than 1 second) during the electrical stimulation used during the thigh muscle function assessment. You will be familiarized with the electrical stimulation to ensure you

are comfortable with it before the testing procedures begin. There is also a possibility of acquiring some mild, transient skin irritation from the sticky TENS electrodes if you are randomized to the TENS group. There may be uncommon or previously unknown risks. You should report any problems to the principal investigator, Brian Pietrosimone.

What if we learn about new findings or information during the study?

You will be given any new information gained during the course of the study that might affect your willingness to continue your participation.

How will information about you be protected?

Any information obtained in connection with this research study that can be linked to you will remain confidential. You will be identified only by a subject identification number. A code list that associates your name and information with a specific subject identification number will be kept under lock-and-key on a password-protected computer in the Neuromuscular Research Laboratory. Only the research team will have access to this information. Participants will not be identified in any report or publication about this study. Although every effort will be made to keep research records private, there may be times when federal or state law requires the disclosure of such records, including personal information. This is very unlikely, but if disclosure is ever required, UNC-Chapel Hill will take steps allowable by law to protect the privacy of personal information. In some cases, your information in this research study could be reviewed by representatives of the University, research sponsors, or government agencies (for example, the FDA) for purposes such as quality control or safety.

What will happen if you are injured by this research?

All research involves a chance that something bad might happen to you. This may include the risk of personal injury. In spite of all safety measures, you might develop a reaction or injury from being in this study. If such problems occur, the researchers will help you get medical care, but any costs for the medical care will be billed to you and/or your insurance company. The University of North Carolina at Chapel Hill has not set aside funds to pay you for any such reactions or injuries, or for the related medical care. You do not give up any of your legal rights by signing this form.

What if you want to stop before your part in the study is complete?

You can withdraw from this study at any time, without penalty. The investigators also have the right to stop your participation at any time. This could be because you have had an unexpected reaction, or have failed to follow instructions, or because the entire study has been stopped.

Will you receive anything for being in this study?

You will receive all physical therapy associated with this study free of charge. You will be compensated a total of \$100 for attending all three outcomes assessments. You will not be compensated for the screening portion of the study. After screening into the study, you will be compensated \$20 for baseline measurements and \$40 for the 4-week and 8-week post-baseline testing sessions. You will be compensated after your last completed outcome session study. Compensation will be in the form of a \$100 Visa gift card.

Will it cost you anything to be in this study?

It will not cost you anything to be in this study. All physical therapy sessions will be fully reimbursed by the grant supported by the National Institutes of Health (NIAMS).

Who is sponsoring this study?

This research is funded by the National Institutes of Health. This means that the research team is being paid by the sponsor for doing the study. The researchers do not, however, have a direct financial interest with the sponsor or in the final results of the study.

What if you have questions about this study?

You have the right to ask, and have answered, any questions you may have about this research. If you have questions, complaints, or concerns about the study; or if a research-related injury occurs, you should contact the researchers listed on the first page of this form.

A description of this clinical trial will be available on www.clinicaltrials.gov, as required by U.S. Law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

What if you are a UNC employee?

Taking part in this research is not a part of your University duties, and refusing will not affect your job. You will not be offered or receive any special job-related consideration if you take part in this research

What if you have questions about your rights as a research participant?

All research on human volunteers is reviewed by a committee that works to protect your rights and welfare. If you have questions or concerns about your rights as a research subject, or if you would like to obtain information or offer input, you may contact the Institutional Review Board at 919-966-3113 or by email to IRB_subjects@unc.edu.

Participant's Agreement:

I have read the information provided above. I have asked all the questions I have at this time. I voluntarily agree to participate in this research study.

Signature of Research Participant

Date

Printed Name of Research Participant

Signature of Research Team Member Obtaining Consent

Date

Printed Name of Research Team Member Obtaining Consent

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