GAIT MODIFICATION TO REDUCE PEAK KNEE ABDUCTION MOMENT

by

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A Dissertation
Submitted to the
Graduate Faculty
of
George Mason University
in Partial Fulfillment of
The Requirements for the Degree
of
Doctor of Philosophy
Education

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Date: _____ Spring Semester 2021
George Mason University
Fairfax, VA

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Dedication

I dedicate this dissertation and my education to my parents, without whom none of this would have been possible. Their unwavering support over the past 30 years is a testament to the kind of parents, and more importantly, the kind of people they are. I love you both.

Acknowledgements

I want to acknowledge all the hard work and extensive time my advisor, Dr. Nelson Cortes, put into mentoring me and making sure I was able to successfully navigate this process. More importantly than gaining a doctorate in my time at George Mason, I have gained a life-long friend.

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List of Abbreviations

KAM ..... First Peak Internal Knee Abduction Moment
KOA ..... Knee Osteoarthritis
IMU ..... Inertial Measurement Unit
RCT ..... Randomized Controlled Trial
OA ..... Osteoarthritis
RTB ..... Real-time Biofeedback
KEM ..... Peak Internal Knee Extension Moment
MCF ..... Medial Contact Force
GRF ..... Ground Reaction Force
MKT ..... Medial Knee Thrust
TL ..... Trunk Lean
FP ..... Reduced Foot Progression
WOMAC ..... Western Ontario and McMaster Universities Osteoarthritis Index

Abstract

GAIT MODIFICATION TO REDUCE PEAK KNEE ABDUCTION MOMENT

Bryndan W Lindsey, Ph.D.

George Mason University, 2021

Dissertation Director: Dr. Nelson Cortes

This dissertation evaluates the effects of various gait modification interventions on first peak knee abduction moment (KAM). As KAM is a commonly used surrogate measure for medial compartment knee osteoarthritis (KOA) severity and progression, the results of this dissertation may be used to provide evidence for the efficacy of gait modification as a clinical treatment for the disease. The contents of this dissertation covers four major areas: (1) The background and theoretical framework behind gait modification to reduce KAM and treat KOA, (2) A comparison of the acute effects of three gait modifications on KAM in healthy adults, (3) The feasibility of a wearable haptic biofeedback system to train gait modification outside of the laboratory environment, (4) A pilot study for a randomized-controlled trial investigating the effects of long-term gait modification intervention designed to reduce KAM in KOA patients. The results of the studies included in this dissertation have several implications for the future of this research area. The first study supports evidence from prior investigations that no one gait modification

is most effective to reduce KAM for all individuals. The wide range in individual response to both type and magnitude of gait modification on KAM suggests that future interventions should screen individuals for which modification is most appropriate. When an appropriate gait modification is found, the next concern is how to best train individuals in its adoption. Most studies have used complex systems (such as 3D motion capture software) to provide training feedback, which are only available in research settings. The results of the second study suggest that these feedback systems can be replaced by wearable inertial measurement units (IMU) which are advantageous in their portability and simplicity. Although more development is needed, there is potential for IMU systems to be worn outside of the laboratory environment while being controlled by patients through a smartphone application, allowing them to receive feedback based on gait during their activities of daily living. Lastly, as most prior literature on the topic has used quasi-experimental designs there is a pressing need for both gait modifications and feedback methods to be tested in the target population using study designs that provide the highest level of evidence. Preliminary results from a randomized-controlled trial (RCT) that employs both individual patient screening of gait modification response and use of a wearable real-time haptic biofeedback (RTB) system provide evidence that KAM reductions seen in healthy participants are replicable in KOA patients.

Chapter One: Introduction and Literature Review

Prevalence of Knee Osteoarthritis

Osteoarthritis (OA) is one of the leading causes of disability worldwide affecting over 300 million people globally in 2017, resulting in pain, stiffness, and functional instability.[1] Since 2007 the relative contribution of OA to overall musculoskeletal disease burden has increased by 31.4%[2] resulting in the disease being the second highest cause of years lived with disability,[3] and having a particularly large effect on the middle-aged and older.[2]

Knee osteoarthritis (KOA) is the predominant form of the disease, with the incidence of symptomatic KOA rising dramatically over the past twenty years.[4] This trend is particularly prominent in the U.S. In 2007-8, 13.7 million people older than 25 years (6.9% of total US population) had symptomatic knee OA, with 7.7 million of those (3.9%) having advanced knee OA (3 or greater on the Kellgren/Lawrence Scale).[5] By 2011-12 this had risen to 15.1 million (7.3%), with those having advanced knee OA increasing to 8.6 million (4.2%).[5] The increase in KOA has been attributed to greater obesity rates,[6] post-traumatic knee osteoarthritis due to joint injury,[7] and earlier clinical diagnosis of KOA compared prior decades.[5] The rise of KOA in the past decades is further supported by increasing rates of total knee replacement surgeries being performed, even in younger and middle-aged adults.[8]

The prevalence of KOA increases with every decade of life, however, the incidence is greatest in those between 55 and 64 years as there are nearly twice as many

individuals in the US between 45 and 64 compared to 65 and above.[5] Therefore, although the prevalence of KOA is higher in individuals older than 65, the overall amount of KOA is nearly equal between the two age groups.[5] The disease is not limited to those 45 and older, however, as 1.7 million individuals under the age of 45 had symptomatic KOA in 2011-12 with approximately 1/3 of those having advance KOA.[5] These data underline the impact KOA has on the individual and society and make a compelling argument for the development of an effective intervention.

Etiology of Knee Osteoarthritis

Knee osteoarthritis is thought to occur in two stages, an initiation phase, followed by a progression phase,[9] the mechanical loading environment of the joint being critical to both.[10] During the initiation phase, chronic or acute changes to healthy cartilage cause a mechanical shift of the load bearing contact location of the joint to a region not conditioned to frequent load bearing. Kinematic changes associated with aging (such as ligament stiffness, muscle weakness, and muscle activation), as well as traumatic joint injury (such as anterior cruciate ligament reconstructive surgery) can cause these shifts over time.[9] Lack of frequent loading over an area of cartilage can result in articular surface damage, increased fibrillation, and cause matrix consolidation at the site of reduced loading.[9] Degeneration of the articular cartilage causes morphological changes to the joint such as medial compartment joint space narrowing.[9,10] The progression phase is described by degenerative changes to the cartilage that leave it vulnerable to high loads. Therefore, once KOA is present, further degeneration is caused by increased compressive loads.[9]

Morphological changes occurring during the progression of KOA have been associated with kinetic variables such as the external knee adduction moment (KAM). It is important to note that although external joint moments (i.e., knee adduction moment) are most commonly reported in KOA literature, internal moments resist the action of external moments and can be thought of as equal but opposite in sign.[11] The studies conducted as part of this dissertation have computed internal joint moments, and therefore, the peak internal knee abduction will be reported as such but can be thought of as equal to KAM. As the cartilage thins and the joint space narrows, kinetic variables such as KAM increase, subsequently increasing the forces applied at the medial compartment of the knee joint.[12] The link between KAM and KOA progression is further supported by the fact that patients who progress towards more severe KOA show greater concomitant increases in KAM compared to those who do not.[12,13] Additional studies have found greater KAM magnitudes in individuals with symptomatic KOA compared to asymptomatic individuals[14] as well as a relation between higher KAM peaks and impulses with a greater risk of pain during a 6-min walking bout.[15] As clinical experience and laboratory studies have demonstrated that OA symptoms can be effectively treated by employing interventions that reduce load on osteoarthritic cartilage,[16,17] there has been much interest in developing a mechanical intervention to treat KOA by reducing KAM.

Current Treatments for Knee Osteoarthritis

Pharmacological

Multiple treatments are currently used to alleviate the symptoms of KOA. Paracetemol, a nonsteroidal anti-inflammatory drugs, and corticosteroid injections are all

prescribed to patients with OA for symptom alleviation.[18] Prior systematic reviews and meta-analyses, however, have showed only minimal improvements in pain and function with paracetamol,[19,20] and NSAIDs such as diclofenac have been associated with an increased risk of cardiovascular disease.[21] Additionally, corticosteroids are associated with greater cartilage loss after 2 years compared to intra-articular saline injections.[22] When the effects of corticosteroid injection were compared to non-injection on matched knees, the incidence of radiographic worsening was greater in knees receiving an injection.[23] Therefore, although pharmacological treatments can temporarily alleviate pain in KOA patients, the long-term consequences may outweigh any temporary benefits.

Therapeutic Exercise

Exercise has also been shown to have a beneficial effect on KOA including reduced pain and improved function,[24] although patients are often concerned that activity will worsen their joints.[25] These improvements, however, likely occur as a result of changes to non-biomechanical variables such as decreased body mass and increased muscular strength,[26] as a systematic review of exercise therapy for KOA patients showed that it had no effect on KAM.[27] While the potential benefits of exercise for KOA patients should not be discounted, long-term outcomes with this type of therapy only are also discouraging as evidence suggests that they are not sustained in the long-term.[28]

Mechanical

Both non-surgical and surgical interventions have been advocated to reduce KAM including the use of gait aids,[29] wedged insoles,[30-32], and high-tibial osteotomy.[33] Unfortunately, there are limitations to the effectiveness of these treatments for KOA.

Contralateral cane use can provide small reductions in KAM by offloading the weight borne through the affected lower extremity via the upper extremity.[34] Ipsilateral cane use can actually increase KAM[35] which may be detrimental as many individuals self-prescribe gait aids without receiving education on proper use.[36] Lateral wedge shoes are commonly prescribed as a treatment for KOA but have proven ineffective to improve symptoms or slow disease progression in clinical trials.[37-40] Additionally, insertion of a lateral wedge can compromise space within the shoe, leading to discomfort.[39] Lastly, although there is some evidence that high tibial osteotomy can improve knee function and reduce pain,[41] there is no clear evidence to suggest that osteotomy is more effective than conservative treatment, while any reported positive effects have deteriorated with time.[33]

Due to the limitations of these treatments and a desire to address the underlying dysfunctional mechanics associated with KOA, gait modification has recently been explored as it represents a simple and inexpensive treatment strategy that may be employed by a range of health professionals to reduce medial knee load.[42] The earliest review on the effectiveness of gait modifications to reduce KAM reported multiple types of modification including toe-out gait, increased step width, medial knee thrust, increased hip internal rotation and adduction, medial weight transfer of the foot, increased knee flexion and reduced acceleration, and lateral trunk lean.[42] Of these strategies medial knee thrust[43,44] and lateral trunk lean[45] demonstrated the greatest reductions in KAM. Most of the earlier studies investigating gait modification used verbal instructions or simple explicit guides to inform participants how to adopt the altered gait strategy. For example, internal and external foot rotation was guided by tape placed on the floor,[46] and medial

knee thrust and trunk sway were learned by patients who were provided verbal instructions to 'focus on rubbing the insides of the knees together', and move their trunk 'more from side to side'.[47]

More recent reviews, however, have investigated the effects of gait modification delivered with real-time biofeedback (RTB) to reduce KAM.[48,49] Real-time biofeedback has previously been used with positive effects in conditions such as stroke,[50-52] cerebral palsy,[53] Parkinson's disease,[54-56] and in the rehabilitation of amputees.[57,58] Both of these reviews found that various gait modifications including medial knee thrust,[59] medial weight shift,[60,61] trunk lean,[62,63] toe-in,[64-66] and toe-out[67] have had success using RTB to reduce KAM. The aforementioned gait modifications have used indirect feedback (feedback based on a kinematic parameter to reduce KAM), but other studies have explored the use of direct feedback[68,69] (feedback based on KAM) which has generally led to even greater KAM reductions.

Limitations of the Current Literature

Comparison of Gait Modifications

Despite these initial successes, there are still several concerns that need to be addressed before gait modification progresses to a clinical treatment for KOA patients. Effective comparison between gait modifications is currently limited due to a large amount of heterogeneity between study designs and methodologies.[48,49] The vast majority of prior literature has investigated the effects of a single modification on KAM, with comparison across studies being made difficult due to the confounding factors of modification size and RTB mode.[48,49] A small number of studies have attempted to

compare multiple modifications within the same sample, but once again, differences in the mode of feedback provided,[61] and varying amounts of kinematic change[47] means it is still unknown which modification is most effective to reduce KAM per unit of kinematic change.

Training Environment

Another significant limitation to the current literature is the use of laboratory-based RTB to implement gait modification interventions. Although these interventions have had success, future clinical implementation will still be limited if the technology to deliver the feedback is restricted to a lab setting requiring expensive equipment and significant technical expertise. Although direct feedback of KAM has produced the greatest reductions (likely due to elimination of kinematic redundancy),[48,49] kinetic feedback can currently only be achieved in a laboratory setting using force plates or instrumented treadmills. Conversely, other studies have successfully decreased KAM using indirect feedback based on kinematics such as frontal plane trunk,[62-64,70-73] and transverse plane foot angle.[64-66,72,74-76]

To enable future clinical use of gait modifications outside of the laboratory, an approach is needed that is portable and can be used during overground walking. A recent review by Shull et al.[77] noted that although much of the research with wearable sensors in the past has focused on healthy populations compared to pathological that trend is shifting.[77] Currently, most wearable sensors can measure kinematics, however, research in the field of gait modification has currently underutilized the ability of this technology to be implemented as part of gait modification interventions. These technologies are

particularly applicable for interventions requiring multiple training sessions spread out over weeks or months. An apt example of the use of wearable technology for an intervention purpose is that of weekly gait retraining sessions using wearables to train runners to run with less tibial shock, lowering the chance of tibial stress fracture.[78] Currently, wearable systems designed to reduce medial compartment loading are in early-stages of development with a majority being tested in proof-of-concept studies with healthy individuals and only a limited amount testing KOA patients.[77] Increased testing of these wearable sensors in both healthy, and more importantly KOA samples, is vital to developing feasible and practical long term gait modification interventions that can be performed outside of the lab setting.

Level of Research Evidence

Other significant limitations have been identified by systematic reviews on the topic and include a lack of high quality study designs employing a control group, lack of long-term studies testing retention of learned gait modifications, lack of control for confounding factors (with the exception of gait speed), and small sample sizes mainly consisting of healthy individuals.[48,49] Currently, there are only two studies that have used a randomized controlled trial study design to investigate the effects of gait modification on KAM in KOA patients.[79,80] Although both studies showed reduced KAM, and improved pain and function, methodological choices may limit the clinical implications of their findings. One study used direct feedback based on KAM and instructed participants to modify their gait any way within reason to achieve the desired reduction.[79] Although this form of feedback might be more powerful to reduce KAM as discussed

previously, its reliance on inverse dynamics to measure moments in real-time limits it usage to the laboratory setting. The other study employed a toe-out gait which, although it has been shown to reduce second peak knee adduction moment, is problematic as moderate to poor correlations seen between second peak knee adduction moment and medial tibiofemoral contact force means it may not be as effective to treat KOA as reduction of the first peak adduction moment is.

Summary

Knee osteoarthritis is one of the most prevalent musculoskeletal conditions worldwide, causing significant discomfort, pain, and functional disability. The results of these studies will assist to answer important questions in the development of a conservative, non-invasive treatment for KOA. Namely, which modification (or combination thereof) most effectively reduces KAM, how do we best implement at-home gait modification, and can the results of quasi-experimental studies with healthy participants be replicated with KOA patients in a randomized controlled trial design. Therefore, the purposes of these studies were to: (1) compare the relative reductions in KAM across three previously studied gait modifications within the same sample of healthy individuals, (3) investigate the feasibility of a novel wearable haptic biofeedback device to train gait modifications outside of the laboratory, and (3) pilot test the effects of a long-term gait modification intervention on KOA patients using a randomized controlled study design.

Chapter Two: Reductions in Peak Knee Abduction Moment in Three Previously Studied Gait Modification Strategies

Title: Reductions in Peak Knee Abduction Moment in Three Previously Studied Gait Modification Strategies

Brief Running Head: Knee Abduction Moment During Gait Modification

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Abstract

Background: First peak internal knee abduction moment (KAM) has been associated with knee osteoarthritis progression. Gait modification using real-time biofeedback including lateral trunk lean, medial knee thrust, and toe-in gait have been shown to reduce KAM. Due to heterogeneity between limited study designs, however, it remains unclear which strategy is most effective. We compared the effects of these modifications in healthy individuals to determine which is most effective to reduce KAM as well as internal knee extension moment (KEM), and medial contact force (MCF). **Methods:** Twenty healthy individuals volunteered for this study (26.7±4.7 years, 1.75±0.1 m, 73.4±12.4 kg). Using visual real-time biofeedback, we collected 10 trials for each modification using individualized target gait parameters based on participants' baseline mean and standard deviation (SD). Two sizes of each modification were tested: 1-3 SD greater (toe-in and trunk lean) or lesser (knee adduction) than baseline for the first 5 trials and 3-5 SD greater or lesser than baseline for the last 5 trials. **Results:** A significant main effect was found for KAM and KEM ($p<.001$). All modifications reduced KAM from baseline by at least 5%, however, only medial knee thrust and small trunk lean modifications resulted in significant KAM reduction. Only medial knee thrust reduced KEM from baseline. No reductions in MCF were noted ($p>0.05$). **Conclusion:** Medial knee thrust was superior to trunk lean and toe-in modifications in reducing KAM. Subsequent increases in KEM and large variation in individual responses to gait modification suggests that future interventions should be

individualize by type and magnitude to optimize KAM reductions and avoid detrimental effects.

Introduction

Knee osteoarthritis (KOA) is one of the leading causes of disability worldwide, causing pain, stiffness, and functional instability.[1] Increased first peak internal knee abduction moment (KAM) due to altered gait mechanics has been associated with increased KOA severity.[81] Therefore, reducing KAM in individuals with KOA may reduce pain,[82] decrease severity,[83] and slow progression.[13] Gait modifications using real-time biofeedback such as medial knee thrust (MKT), lateral trunk lean (TL), and toe-in (FP) gait have shown relative effectiveness in reducing KAM.[48] Medial knee thrust and trunk lean modifications have demonstrated reductions in KAM of up to 38% [61] and 25%,[62] respectively. However, these modifications require substantial and complex adjustments that may limit clinical adoptability. In comparison, toe-in gait is easier to implement, requiring only a small change to normal walking, but has resulted in smaller reductions in KAM.[65,66] Comparison of the effects of such modifications on KAM are necessary to make informed clinical decisions in the future.

Effective comparison between gait modifications is currently limited. There is considerable heterogeneity between studies, including differences in sample characteristics, biofeedback type, and size of modification.[48] Several prior studies have compared multiple modifications, however, methodological limitations such as differences in mode of biofeedback provided,[61] and varying amounts of kinematic change due to participant self-selection of modification[47] make it difficult to compare their effectiveness

in reducing KAM per unit of kinematic change. This limitation also exists across studies, as various interventions using the same gait modification have commonly used different sizes of modification. Standardization of kinematic change during gait modification will assist in effectively comparing which modification best reduces KAM.

The ultimate goal of reducing KAM through gait modification is to decrease knee joint contact forces, reducing symptoms and slowing the rate of OA progression. In this effort, KAM is commonly used as a surrogate measure due to the difficulty of measuring *in vivo* joint forces.[84,85] To our knowledge only one prior study has attempted to directly measure the effect of a modification designed to reduce KAM on medial knee contact force (MCF).[86] Their results suggest that decreased KAM may not lead to corresponding reductions in MCF, particularly when internal knee extension moment (KEM) is subsequently increased; a phenomenon that has been observed during medial knee thrust[43,59,86] but not in other modifications such as toe-in[65,66] and trunk lean gait. This suggests that KEM should be considered along with KAM when evaluating the effectiveness of gait modification, as KAM alone may not reflect the overall loading environment.[12,87]

The primary purposes of this study were to i) compare the effects of medial knee thrust, lateral trunk lean, and toe-in gait on KAM and KEM in healthy individuals, and ii) investigate if decreased KAM significantly reduces MCF. We hypothesized that i) all gait modifications will significantly reduce KAM from baseline, subsequently reducing MCF ii) only medial knee thrust will significantly increase KEM.

Methods

Participants

Twenty healthy participants volunteered for this study after they gave informed consent approved by the Institution Review Board. A within-group repeated measures study design was used to compare joint kinematics and kinetics of participants' dominant limb across different gait conditions. Dominant limb was defined as the preferred leg in a kicking task.[88] Participants were only eligible if they were free from any knee, hip, or back pain that required treatment within the prior 6 months and no history of lower limb or back surgery. Participants were excluded if they had any neurological or musculoskeletal impairment that would affect gait or any cognitive impairment that would inhibit motor learning. Participant demographics are presented in Table 1.

Table 1. Participant Characteristics

Characteristic	Mean	(SD)
N	20	
Gender (M/F)	12/8	
Dominant Limb (R/L)	18/2	
Age (yrs)	26.7	(4.7)
Height (m)	1.75	(0.1)
Mass (kg)	73.4	(12.4)
BMI	23.9	(3.02)

Instrumentation

Fifty three retroreflective markers were attached to the trunk and lower extremities of participants (Figure 1). Six tracking clusters (31 markers) were placed bilaterally on the lower back, thigh, shank, and foot segments with an additional twelve tracking markers placed on various anatomical locations. Ten additional calibration markers were also attached during static and dynamic calibration trials. Eight high-speed motion analysis cameras (Vicon, Oxford, England) sampling at 200 Hz were used to track marker trajectories. Ground reaction force (GRF) was acquired using four floor embedded force plates sampling at 1000 Hz (Bertec, Columbus, OH) which were aligned in a 2.4 meter long row. A static calibration trial was collected by having participants stand on a force plate with both feet parallel to the anterior-posterior axis of the laboratory. Participants also performed a dynamic calibration to estimate hip joint center by completing three clockwise rotations of the pelvis.[89] Calibration markers were removed for walking trials. From the static trial, a kinematic model was created for each participant using Visual 3D software (C-Motion, Germantown, MD, USA) (C-Motion, Germantown MD, USA) which included the trunk, pelvis, and bilateral thigh, shank, and foot segments.

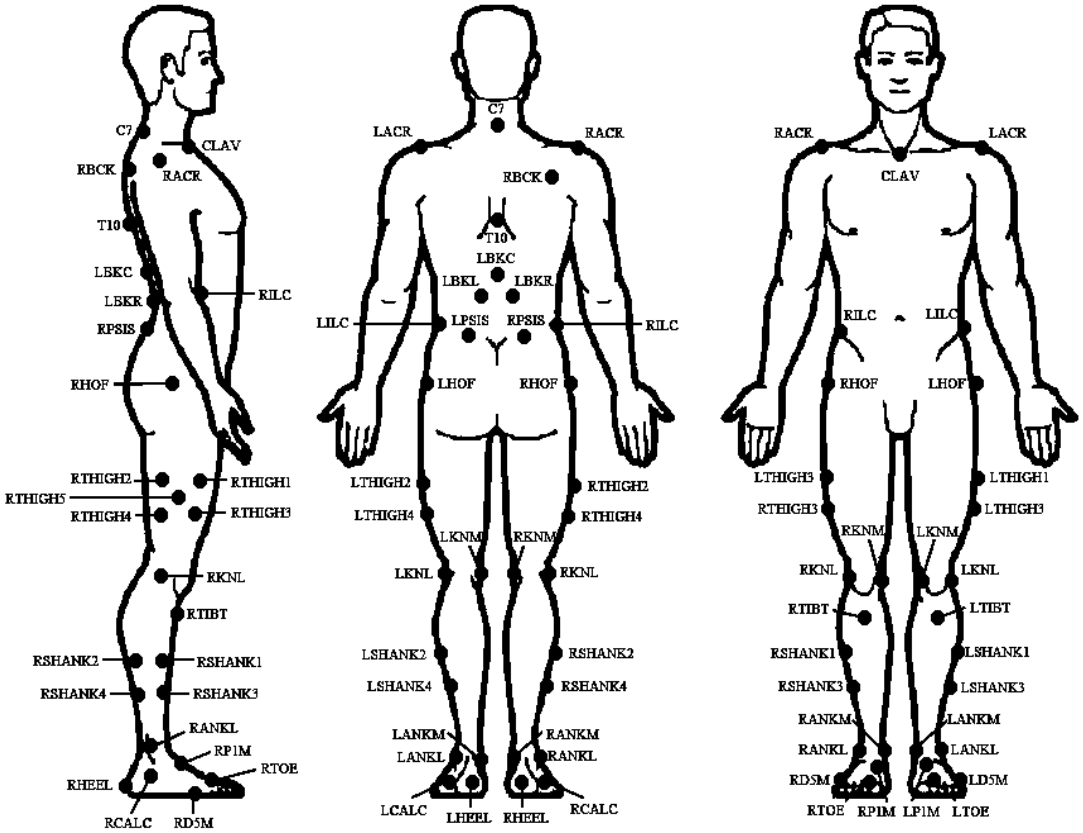

Figure 1. Experimental marker placement. Four tracking clusters (18 markers) were placed on the lateral aspect of each thigh and shank. Additional tracking markers (22 markers) were attached to the manubrium, 7th cervical vertebrae, right scapula, 10th thoracic vertebrae, and bilaterally to the following locations: posterior and lateral calcaneus, 5th distal metatarsal, 1st proximal metatarsal, 2nd metatarsophalangeal joint, tibial tuberosity, lateral iliac spine, posterior superior iliac spine, and acromion. Three tracking markers, arranged to form a triangular cluster, were attached to the lower back. Ten additional calibration markers were attached bilaterally to the following anatomical landmarks: lateral and medial malleoli, lateral and medial knee joint lines, and greater trochanters.

Baseline Trials

Participants were instructed to walk along a 6-meter long walkway in the laboratory at a self-selected speed. Timing gates (Brower Timing Systems, Draper UT, USA) positioned at each end of the force plates were used to record walking speed for 10 baseline walking trials. For a trial to be deemed successful, one full contact with the foot of the dominant limb on the force plates was required. Recorded data were exported to Visual 3D where the mean and standard deviation (SD) for three gait modification parameters were calculated: frontal plane trunk and knee angle, and transverse plane foot angle. Trunk angle was defined as the frontal plane deviation of the trunk segment represented by the right scapula, 10th thoracic, and left/right lower back markers from the vertical laboratory axis.[62] Knee angle was defined as the frontal plane knee angle created between the thigh and shank segments.[59] Foot progression angle was found as the offset between the lines formed by the posterior calcaneus and 2nd metatarsophalangeal joint markers, and the anterior-posterior laboratory axis.[65] Increased trunk angle lean to the dominant limb was quantified as positive, increased knee abduction as negative and reduced foot progression angle as positive.

Individualization of Gait Modification

Gait modifications were individualized using participants' mean and SD from baseline trials. Target ranges were created for each participant so that gait modification parameters fell within a range of 1-3 SD greater (toe-in and trunk lean) or lesser (knee

adduction) than baseline for the first 5 trials and 3-5 SD greater or lesser than baseline for the last 5 trials. The 1-3 SD range was considered small modification, whereas the 3-5 SD range was considered large modification. Therefore, six target ranges were calculated for each participant: small and large TL, small and large MKT, and small and large FP.

Gait Modification Trials

Ten trials were completed for each gait modification strategy using visual real-time biofeedback, which was delivered in the form of a line graph projected on a wall in front of the walkway. The graph displayed the angle of the current gait modification parameter over stance and was updated during each step of the dominant limb. A bandwidth representing the range between the lower and upper limits of the gait modification parameter (1-3 or 3-5 SD) was displayed on the graph. Participants were instructed to walk so that the line representing the gait modification parameter fell within the bandwidth. During each trial the line representing the gait modification parameter was updated in real-time. Participants were instructed to observe where the line fell and adjust their gait on the subsequent trial if necessary.

Gait modification trials were completed in the following order: TL, MKT, and FP. Participants were provided standardized verbal instructions before implementing each modification. Participants completed as many practice trials as needed to become familiar with each gait modification. Additional verbal feedback was provided during practice trials as needed. Successful trials required one full foot contact of the dominant limb within a force plate and average gait speed of ±5% relative to baseline. Only successful trials counted towards the 10 required for each modification.

Data Processing

The kinematic model created in Visual 3D was used to quantify the motion at the hip, knee, and ankle joints with rotations being expressed relative to the static trial. A Cardan angle sequence (X-Y-Z) was used to calculate joint angles[90] and a standard inverse dynamics analysis was conducted to synthesize the trajectory and vertical ground reaction force (vGRF) data for internal joint moment estimation. Although external joint moments are most commonly reported in KOA literature, internal moments resist the action of external moments and can be thought of as equal but opposite in sign.[11] Joint kinematics and kinetics were smoothed using a low-pass Butterwoth filter with a cut off frequency of 8 Hz to reduce the effects of artifacts based on results from residual analysis. Joint angles were measured in degrees, and all internal joint moments were normalized to mass and height Nm/(kg*m). Ground reaction force data were normalized to body weight and all gait trials were normalized to 100 percent of stance. Mean values were computed and used for all statistical analyses.

Gait modification parameters were calculated as the average across the entire stance phase. First peak for KAM and KEM was defined as the peak minimum and maximum value respectively between heel strike and midstance (50% between heel contact and toe-off). The second peak of the internal knee abduction moment (second peak KAM) and the knee abduction moment impulse (KAM impulse) were also calculated to more better understand the cumulative effects of modifications on the entire stance phase. Second peak KAM was defined as the peak minimum between midstance and toe-off, while KAM impulse was calculated as the integrated signal for knee abduction moment between heel

strike and toe-off. Kinematic data in the frontal plane were analyzed at the time of first peak KAM while sagittal plane kinematic data were analyzed at KEM. Values for absolute KAM and KEM were used to estimate MCF using a previously derived linear regression.[86]

Medial Concact Force $\approx (0.31*KAM_{rectified}) + (0.09*KEM) + 0.82$

Data Analysis

Analyses were performed using SPSS (Version 24, IBM Corp, Armonk, NY) with alpha level set *a priori* at 0.05. Descriptive information was obtained using means and standard deviations, as well as 95% confidence intervals. Repeated measures analysis of variance (ANOVA) was used to determine if differences existed between dependent variables among gait conditions (baseline and gait modifications). Where results were significant, pairwise comparisons were used to evaluate which conditions exhibited differences from baseline.

Results

Mean changes in gait modification parameters are shown in Table 2. Participants increased foot angle by 5.38º and 8.02º, decreased knee angle by 0.73º and 1.15º, and increased trunk angle by 2.98º and 3.94º during small and large modifications respectively. The percentage of trials that participants' modification parameters fell within the prescribed bandwidth ranged from only 17%-28% (Table 2, "% Between"). However, the majority of trials were equal to or above the lower boundary of the target bandwidth ranging from 66% during small MKT to 95% during large FP (Table 2). This meant that although it was difficult for participants land within the lower and upper boundaries of the bandwidth for each trial, they consistently exceeded the lower limit of prescribed

modification (Table 2, "% Above"). Participants walked with similar gait speed and stride length across conditions, however, stride width was significantly increased during small FP and both sizes of TL (Table 3).

Main effects of kinetic and temporospatial variables are presented in Table 3. Mean KAM across gait conditions across the entire stance phase is shown in Figure 2, with a significant main effect found between conditions. Both sizes of medial knee thrust resulted insignificantly lower KAM compared to other modifications, with large medial knee thrust showing the greatest effect. Compared to baseline, KAM was significantly reduced with both sizes of medial knee thrust, and with small trunk lean. This resulted in reductions in KAM of 41% and 28% during large and small medial knee thrust respectively, and 9% during small trunk lean (Figure 3). Although the remaining gait modifications did not result in significant changes to KAM from baseline, reductions of 7% during both sizes of toe-in, and 5% during large trunk lean were observed. There were no significant differences in KAM between either size of trunk lean and toe-in gait.

Table 2. Mean (SD) changes in gait parameters during gait modifications.

Gait Modification		Baseline	Low	Target	High	Achieved Value	Difference	% Between	% Above
Toe-in	Small	-4.12 (4.40)	-2.86 (4.37)	-1.60 (4.27)	-0.34 (4.42)	1.26 (4.92)	2.86 (2.96)	22 (21)	92 (14)
	Large		-0.34 (4.42)	0.92 (4.37)	2.18 (4.58)	3.90 (5.31)	2.98 (3.21)	28 (27)	95 (11)
Medial Knee Thrust	Small	3.01(2.53)	2.80 (2.51)	2.58 (2.44)	2.37 (2.50)	2.28 (2.53)	0.30 (1.13)	17 (24)	66 (41)
	Large		2.37 (2.50)	2.15 (2.43)	1.94 (2.50)	1.83 (2.52)	0.32 (1.49)	23 (28)	74 (36)
Trunk Lean	Small	2.03 (2.26)	2.76 (1.98)	3.22 (1.93)	3.69 (2.00)	5.01 (2.22)	1.79 (2.23)	26 (28)	87 (23)
	Large		3.69 (2.00)	4.15 (1.98)	4.61 (2.06	5.97 (1.98)	1.82 (2.32)	17 (25)	88 (28)

Mean foot progression, knee, and trunk angle (º) are provided for their corresponding gait modification (i.e., toe-in and foot progression angle, medial knee thrust and knee adduction angle, trunk lean and trunk angle). Target bandwidths were created for each participant so that gait modification parameters fell within a range of 1-3 SD greater (toe-in or trunk lean) or lesser (knee adduction) than baseline for the first 5 trials and 3-5 SD greater or lesser than baseline for the last 5 trials. The 1-3 SD range was considered small modification, whereas the 3-5 SD range was considered large modification. “Low” and “High” are the lower and upper boundaries of the target bandwidth for each modification with target representing the middle of the bandwidth. “Achieved Value” is how participants actually performed on average during modification trials. “Difference” is the error between achieved value and target. A positive difference indicates that the gait modification parameter was changed more than the target, while a negative difference indicates that the parameter did not reach the target. “% Between” is the percentage of trials where participants were within their target bandwidth, while “% Above” is the percentage of trials where participants were at least above the lower boundary of their target bandwidth.

Table 3. Descriptive and inferential statistics for temporospatial and kinetic variables across gait modifications.

	Group Main Effect			Gait Modification						
					Foot Progression		Medial Knee Thrust		Trunk Lean	
	F-val	*P-val*	Partial Eta^2	Baseline	Small	Large	Small	Large	Small	Large
Temporospatial										
Speed (m/s)	1.410	0.217	0.069	1.35 (0.18)	1.37 (0.19)	1.36 (0.19)	1.35 (0.19)	1.36 (0.19)	1.36 (0.19)	1.36 (0.20)
Stride Length (m)	0.523	0.737	0.027	1.44 (0.18)	1.44 (0.19)	1.42 (0.18)	1.44 (0.20)	1.45 (0.17)	1.43 (0.19)	1.43 (0.16)
Stride Width (m)	2.481	0.027	0.116	0.13^{b,d,f,g} (0.03)	0.14^{a} (0.03)	0.14 (0.03)	0.14^{a} (0.03)	0.14 (0.04)	0.15^{a} (0.04)	0.15^{a} (0.04)
Knee Kinetics										
KAM1 Nm/(kg*m)	14.459	<0.001	0.432	-0.28^{d,e,f} (0.09)	-0.26^{d,e} (0.08)	-0.26^{d,e} (0.07)	-0.20^{a,b,c,e,f,g} (0.07)	-0.17^{a,b,c,d,f,g} (0.09)	-0.25^{a,d,e} (0.08)	-0.26^{d,e} (0.10)
KAM2 Nm/(kg*m)	5.748	0.002	0.232	-0.24^{c} (0.11)	-0.26^{e,g} (0.12)	-0.27^{a,d,g} (0.13)	-0.22^{c} (0.11)	-0.20^{b} (0.10)	-0.24 (0.12)	-0.22^{b,c} (0.14)
KEM Nm/(kg*m)	18.703	<0.001	0.496	0.20^{d,e} (0.14)	0.21^{d,e} (0.16)	0.21^{d,e} (0.16)	0.41^{a,b,c,f,g} (0.25)	0.45^{a,b,c,f,g} (0.24)	0.20^{d,e} (0.17)	0.23^{d,e} (0.19)
KAM Impulse Nm/(kg*m/s)	13.161	<0.001	0.409	-0.10^{d,e} (0.05)	-0.10^{d,e} (0.05)	-0.10^{d,e} (0.05)	-0.07^{a,b,c,e} (0.05)	-0.06^{a,b,c,e} (0.05)	-0.09^{d,e} (0.05)	-0.08^{d,e} (0.06)
MCF	0.557	0.663	0.028	0.79 (0.03)	0.79 (0.03)	0.79 (0.03)	0.79 (0.04)	0.79 (0.05)	0.78 (0.03)	0.79 (0.05)

Mean (SD) values are provided for each gait modification. Internal knee abduction moment (KAM) and knee extension moment (KEM) are reported as peak magnitudes during the first half of stance. Medial knee contact force (MCF) is estimated using a previously derived regression that incorporates KAM and absolute KEM. Superscript letter indicates significant difference from gait modification: Baseline (a), small FP (b), large FP (c), small MKT (d), large MKT (e), small TL (f), and large TL (g).

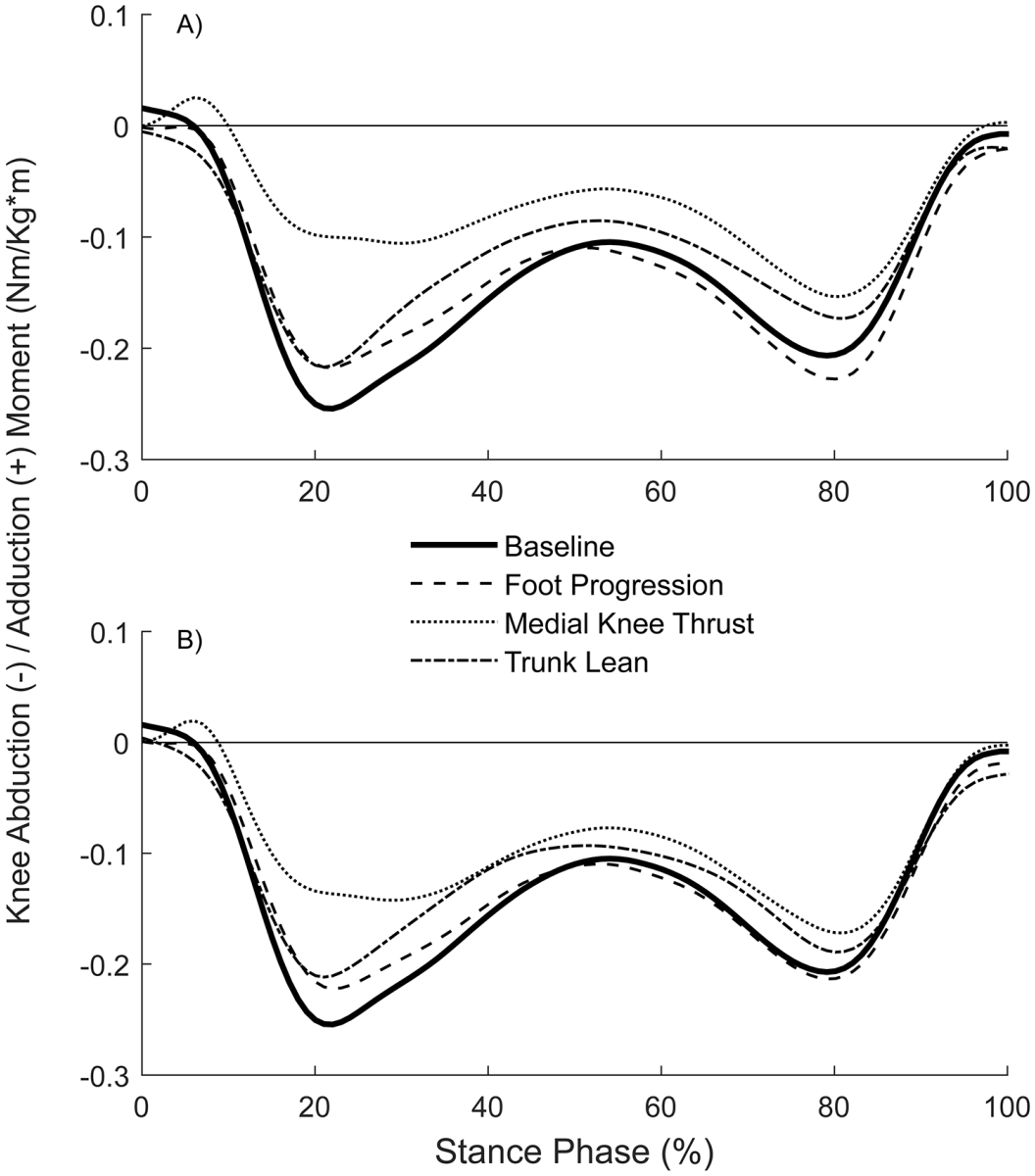

Figure 2. Time series of mean KAM and KEM across gait conditions. (A) KAM across large modification (B) KAM across small modification (C) KEM across large modification (D) KEM across small modification.

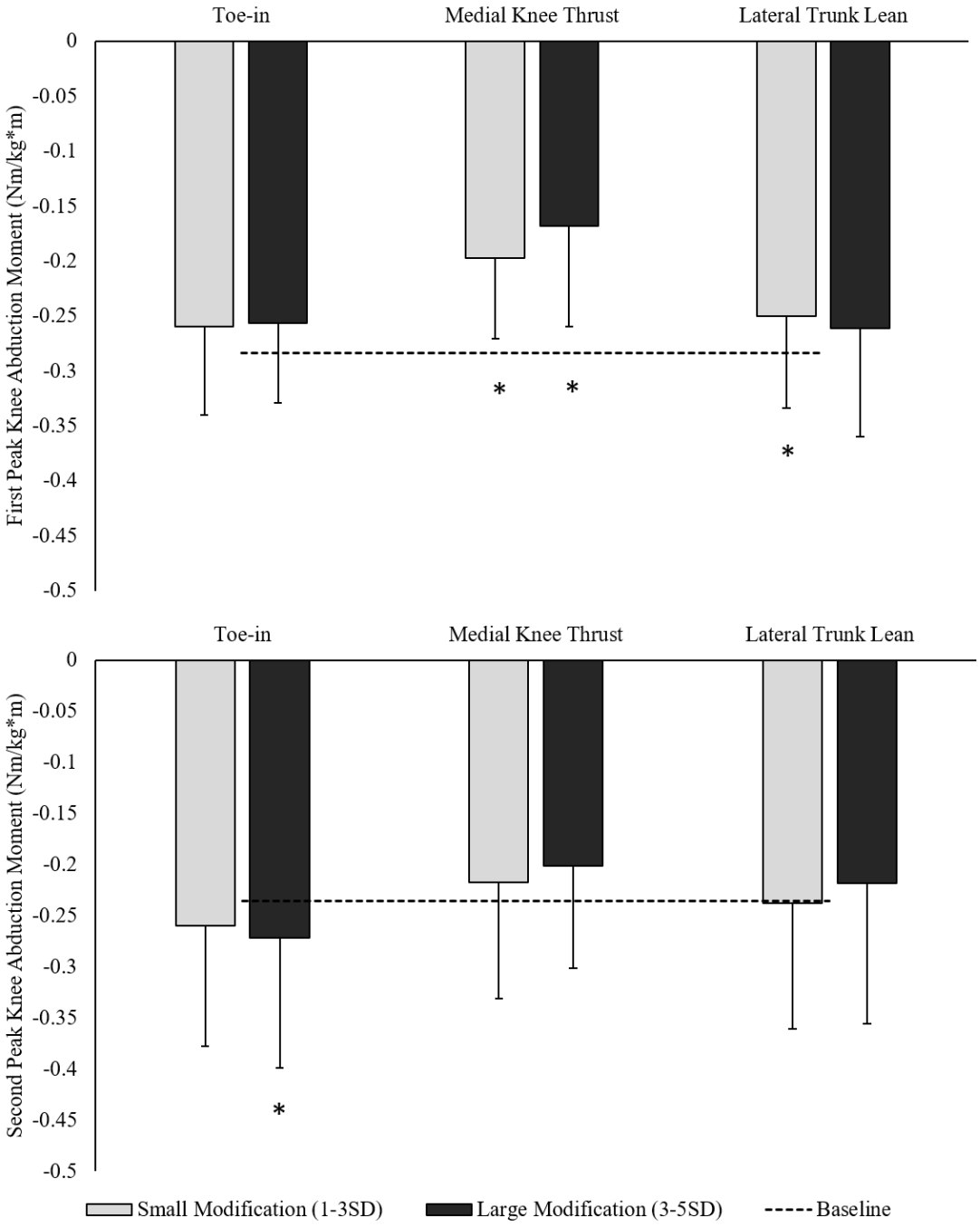

Figure 3. Mean first and second peak KAM across gait modifications. Dashed horizontal line represents mean peak KAM at baseline. The asterisks below the bars indicate significant difference from baseline ($p<0.05$).

Similar to KAM, a statistically significant main effect was found for KEM. Both sizes of medial knee thrust resulted in significantly greater KEM compared to other modifications, but were not significantly different from each other. There was no significant difference in KEM between either size of trunk lean and toe-in gait. Compared to baseline, only medial knee thrust significantly increased KEM. A significant main effect was found for both second peak KAM and KAM impulse. The mean difference between modifications demonstrates a pattern of second peak KAM reduction that was greatest during medial knee thrust, followed by trunk lean, with toe-in gait showing an increase from baseline. However, only large toe-in modification was statistically significantly increased from baseline (Figure 3). KAM impulse was significantly smaller in both sizes of medial knee thrust compared to all other conditions, and was the only modification to significantly reduce impulse from baseline. No significant main effect was found for MCF.

Discussion

This study compared the effects of three previously studied gait modifications on KAM in healthy individuals. The primary purpose of this study was to compare the effects of medial knee thrust, lateral trunk lean, and toe-in gait on KAM in healthy individuals. Our first hypothesis was only partially supported by our results. All modifications showed a mean reduction in KAM compared to baseline, however, significant reductions were only found during both sizes of medial knee thrust and small trunk lean gait. Medial knee thrust was most effective in decreasing KAM with reductions comparable to those seen in prior

studies of between 20% and 38%.[47,59,61] Additionally, medial knee thrust was the only modification that demonstrated a significant difference in KAM between sizes, suggesting a greater dose-response relationship with KAM compared to trunk lean and toe-in gait. These results disagree with prior literature showing that trunk lean is more effective than medial knee thrust in the same sample of KOA patients.[47] This can be explained by differences in changes to the gait modification parameters between studies, as in the prior study, participants modified trunk angle by 12.6° and knee angle by only 3.9° (compared to 3.94° and 1.15° for trunk and knee angle respectively in the current study) when instructed to modify their gait as much as possible within comfort.[47] This suggests that participants' comfort with a gait modification strategy is an important consideration in terms of its effectiveness. Preferences to certain modifications based on comfort have been demonstrated in other studies where participants given the option of multiple modification strategies have most often chose to use toe-in gait.[66,69] Therefore, although our results demonstrate that medial knee thrust may be more effective in reducing KAM, when given the choice participants may prefer to modify their trunk or foot, making trunk lean and toe-in gait more clinically viable interventions.

Reductions in KAM during trunk lean and toe-in gait were slightly lower than those reported in prior studies using trunk lean[47,62,63,71] and toe-in[65,66,75] Smaller KAM reductions during these modifications may be partially explained by the fact that two participants demonstrated large increases in KAM during trunk lean and toe-in gait (Figure 2). The negative responses experienced by these two participants reflect a noteworthy finding of this study; despite an overall mean reduction in KAM there was a large variation in

individual response, with some participants increasing KAM during modifications (Figure 4). This effect was seen across all modifications when analyzing individual change in KAM. Negative effects have been observed during a study investigating toe-out modification, where 5 out of 15 patients increased second peak KAM, and one patient reported an increase in knee pain.[67] Similarly, a recent study comparing the effects of subject-specific toe-in gait modification to a uniform toe-in gait modification demonstrated that participants reduced KAM more when using the subject-specific modification.[75] This demonstrates the importance of assessing individual kinematics and kinetics to identify the most appropriate intervention. This is supported by recent evidence reporting that allowing participants to determine their own kinematic strategy is more beneficial in reducing KAM than imposing a singular gait strategy.[48,49] This likely requires providing feedback directly based on KAM as opposed to a single kinematic parameter. Although direct kinetic feedback has been shown to be more effective in reducing KAM compared to kinematic feedback,[48,49] it requires participants to train only in a laboratory setting limiting future clinical applicability.

We also aimed to compare the effects of gait modification on KEM. Our results supported our second hypothesis, as although medial knee thrust was most effective in reducing KAM, it also was the only modification that significantly increased KEM compared to baseline. Internal knee extension moment has been previously associated with changes in cartilage thickness[12] and is suggested to attenuate reductions in joint load by increasing joint compression.[12,86] Prior studies investigating medial knee thrust have shown similar increases in KEM.[43,59,86] Some authors have suggested that an emphasis on

increased internal hip rotation without a corresponding increase in knee flexion may mitigate increases in KEM.[59,86] We did not provide participants instructions regarding knee flexion during medial knee thrust in our study, suggesting that subsequent increases in KEM may occur naturally without additional cueing. Therefore, despite large reductions in KAM seen during medial knee thrust, it may be less effective in reducing overall knee joint load compared to trunk lean and toe-in gait if increased knee flexion cannot be controlled.

In addition to KAM and KEM, we reported second peak KAM and KAM impulse to better understand the effects of the modifications on frontal plane moment throughout the entire stance phase. Although first peak KAM has received the most attention in the literature, second peak KAM has been found to be significantly lower in patients with less severe KOA compared to patients with more severe KOA and matched controls.[91] Additionally, KAM impulse has been shown to be greater the more severe the KOA.[92] It is plausible, therefore, that any benefits from KAM reduction in the first half of stance may be negated if KAM in the second half of stance and KAM impulse are subsequently increased.

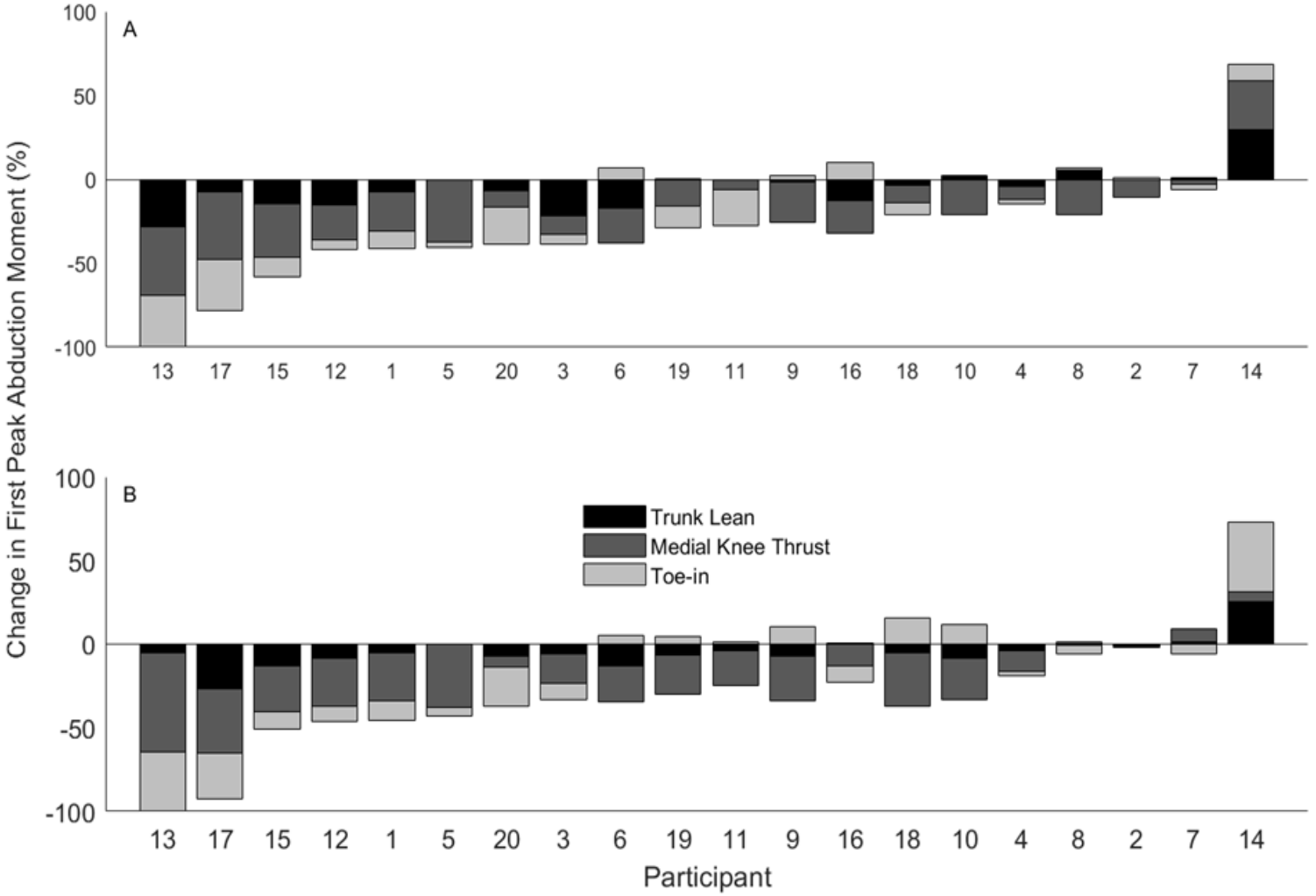

Figure 4. Individual percent change in KAM for all gait modifications during small (A) and large (B) modification. Participant number is ranked ascending across the horizontal axis according to the average percent KAM reduction in all gait modifications. Negative percent reduction indicates reduced KAM and a positive response to modification, while positive percent reduction indicated increased KAM and a negative response to modification. The reduction in KAM is not cumulative, meaning that the height of the bar for a single modification indicates how much it reduced KAM in that participant.

In the current study, medial knee thrust and trunk lean did not significantly change second peak KAM, in contrast to large toe-in gait which increased second peak KAM compared to baseline. This supports prior studies in terms of medial knee thrust[47,61] and trunk lean[47,62,63] which have all shown reductions in second peak KAM. Toe-out gait has previously been shown to reduce second peak KAM,[67] however, the evidence in regards to toe-in gait on second peak KAM is less clear. Two prior studies reported no change in second peak KAM with toe-in gait, however, mean difference in second peak KAM between toe-in gait and normal walking were in opposite directions,[65,67] therefore, more research is needed to understand the effects of toe-in gait on second peak KAM.

Medial knee thrust was the only modification to reduce KAM impulse from baseline. This is consistent with the literature in terms of medial knee thrust,[47] however, conflicts with prior evidence which has showed a significant reduction in KAM impulse with lateral trunk lean.[47,63] This is likely due to the much larger magnitudes of trunk lean achieved in the prior studies. Although a mean reduction in KAM impulse was observed during both sizes of trunk lean, we would hypothesize that with similar magnitudes of trunk lean achieved in prior studies, the individuals in our sample would achieve significant reductions in KAM impulse. Toe-in gait resulted in neither a significant nor mean reduction in KAM impulse. When combined with the effect of toe-in gait on second peak KAM, our results suggest that toe-in gait may only be effective in reducing the abduction moment in the first half of stance.

Our second purpose was to investigate if decreasing KAM significantly reduced MCF. Our results did not support our third hypothesis, as no change in MCF was found

across gait conditions. This is consistent with prior studies using a force-measuring knee implant[86] and regression equation from the implant data[75] which have suggested that reducing KAM does not guarantee a decrease in MCF. This is further supported by musculoskeletal modeling data which showed that although gait modification reduced the ratio of medial to total knee contact force, it did not reduce the MCF itself.[93] The concomitant increases in KEM noticeable during medial knee thrust partially supports these findings.[86] In contrast, trunk lean and toe-in gait did not significantly increase KEM, suggesting that there are additional factors related to MCF than solely KEM. Knee extension moment has been related to quadriceps activity which can increase knee loads.[94] Additionally, co-contraction of the quadriceps-hamstring muscles has been related to cartilage volume loss.[95] Electromyography and musculoskeletal modeling may be required in future research to investigate the neuromuscular contributions to MCF.

There were several limitations to our study. Firstly, our sample was composed of healthy individuals limiting the generalizability of our results in terms of KOA patients. Medial contact force was estimated during the first half of stance using coefficients from a prior study.[86] These coefficients were based on contact force measurements from an instrumented knee implant in a single participant. Therefore, caution must be used when interpreting MCF results. We did not randomize the order of modifications introducing the possibility of order effects. However, motor learning and retention were not objectives of this study, and as such we did not attempt to draw conclusions about the long-term effectiveness of the modifications or mode of real-time biofeedback. Due to our healthy sample, we did not record measures of pain or discomfort during modification; anecdotally,

medially knee thrust was subjectively the most difficult modification to adopt across participants while toe-in gait was the easiest.

We used a novel method to select individual modification magnitudes, where participants were prescribed individualized target ranges calculated using their baseline gait data. This method attempted to standardize the amount of kinematic change across participants to more effectively investigate which modification best reduces KAM per unit of kinematic change. The limitation of this method, however, was that it was greatly affected by participants' baseline gait. Individuals with smaller baseline SD had smaller prescribed gait modification parameters and narrower target ranges. Smaller amounts of modification may have limited KAM reductions, and narrower ranges were more difficult to successfully target. Participants in this study were not required to land within the target range for a trial to be considered successful. This was due to the fact that the bandwidths created using 2 SD from each participant's baseline gat modification parameters were quite narrow, making it difficult for many participants to land successfully within the target bandwidths. Therefore, we encouraged participants to use fall above the lowest boundary of the target bandwidth, which they were largely successful in doing. Future studies, however, should consider using larger target ranges if real-time biofeedback requires participants to land successfully within a specified range. In the current study, most participants modified gait modifications parameters greater than their target range during trunk lean and toe-in gait, and lesser than their target range during medial knee thrust. These results suggest that we were not fully successful in standardizing the amount of kinematic change across modifications. However, it provides evidence that trunk lean and

toe-in gait are easier to implement, as participants could easily modify the gait modification parameter above their target range. In comparison, participants struggled to reach their target range during medial knee thrust, suggesting that knee angle was more difficult to modify.

Conclusion

This study demonstrated that medial knee thrust, lateral trunk lean, and toe-in gait modifications all resulted in mean reductions in KAM, however, their effectiveness is varied when considering factors such as KEM, second peak KAM and KAM impulse, MCF, and individual dose-response. Medial knee thrust was most effective in reducing KAM, second peak KAM and KAM impulse, but concurrently increased KEM; this may negate any potential reduction in joint load. Trunk lean and toe-in gait showed smaller reductions in KAM without subsequently increasing KEM, potentially making them a more suitable intervention for patients with KOA, however, toe-in gait may only be effective to reduce abduction moment in the first half of stance. Additionally, estimates of MCF suggest that reductions in KAM may not correspond to subsequent reductions in MCF. This study also provides evidence that not all gait modifications are appropriate for every individual and that some can even be detrimental. Future studies should implement true experimental designs investigating the effects of long-term modifications that are individualized to each KOA patient.

Chapter Three: Feasibility of Wearable Haptic Biofeedback Training for Reducing the Knee Abduction Moment During Overground Walking

Title: Feasibility of Wearable Haptic Biofeedback Training for Reducing the Knee Abduction Moment During Overground Walking

Brief Running Head: Wearable Haptic Biofeedback to Reduce KAM

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Abstract

Gait modifications are effective in reducing the first peak knee abduction moment (KAM), a commonly used surrogate for knee loading. Reliance on 3D motion capture currently restricts these modifications to the laboratory. Therefore, our purpose was to test the feasibility of a novel wearable biofeedback system to train 1) toe-in and trunk lean modifications and 2) combined toe-in and trunk lean modifications to reduce KAM during overground walking outside of the laboratory. Twelve healthy participants practiced modifications in a university hallway directly after performing five normal walking trials. The wearable feedback system provided real-time haptic biofeedback during training trials to inform participants if they were within prescribed modification range (7°-12° greater than baseline). Participants were instructed to move to the next modification only once they felt comfortable and could perform it with minimal errors. Following training, five trials of each modification were immediately performed in the gait laboratory without feedback. All participants successfully modified their foot progression and trunk angle using the wearable feedback system. At posttest, KAM decreased from baseline by 62%, 55%, and 28% during combined, trunk lean and toe-in gait, respectively. The wearable feedback system was effective to modify participants' foot and trunk angle by the prescribed amount, resulting in reduced KAM during all modifications at posttest. Participants were also able to perform a combined modification, although it took longer to report feeling comfortable doing so. This study demonstrates

that a wearable feedback system is feasible to modify kinematic parameters and train gait modifications outside the laboratory.

Introduction

Knee osteoarthritis (KOA) is one of the leading causes of disability worldwide, causing pain, stiffness, and functional instability.[1] First peak knee abduction moment (KAM) is regarded as a valid surrogate for *in vitro* measurement of knee load during gait as it has been associated with the severity,[83] symptoms,[82] and progression,[13] of the disease. Therefore, there is interest in developing conservative interventions that reduce KAM.[42] Gait modifications have shown to be effective in reducing KAM in both healthy and knee OA samples with reductions varying based on type of modification used and feedback provided. Direct feedback of KAM has produced greater reductions in KAM, likely due to elimination of kinematic redundancy.[48,49] However, kinetic feedback can currently only be achieved in a laboratory setting using force plates or instrumented treadmills, limiting their clinical utility. Conversely, other studies have successfully decreased KAM using indirect feedback based on kinematics such as frontal plane trunk,[62-64,70-73] and transverse plane foot angle.[64-66,72,74-76]

Toe-in gait is performed by increasing foot progression angle (FP), in turn decreasing KAM through a combination of lateralization of the vertical ground reaction force[96,97] as well as medialization of the knee joint center due to a necessary amount of knee abduction required to toe-in successfully.[98] Increased ipsilateral trunk lean (TL) gait has shown similar success in reducing KAM by lateralizing the vertical ground reaction force vector.[62] Limited studies have also combined multiple gait modifications

simultaneously, showing greater reductions in KAM compared to single parameter modifications.[64,99] Research into the implementation of multi-parameter modifications, however, suggests that despite larger effects on KAM, poor perception of multiple, simultaneous feedbacks during training can overwhelm the user.[100] Therefore, although multi-parameter modifications may reduce KAM by a greater amount, their complexity may discourage patient compliance, limiting clinical efficacy. This effect can potentially be diminished if using different feedback schemes designed to facilitate the implementation of multiple parameter modifications.[100]

Previous studies investigating these modifications have been limited to laboratory testing and training (i.e., treadmills). To enable future clinical use of gait modifications outside of the laboratory, an approach is needed that is portable and can be used during overground walking. A novel wearable biofeedback system using inertial measurement units has recently been developed to measure joint kinematics and provide haptic RTB to patients.[101] Using this system, healthy older adults improved their static posture and alter foot progression angle during gait.[101] The configurable nature of the system, along with its portability and extended battery of life makes it an appealing option for implementation of gait modification outside the laboratory setting. However, prior evidence comes from a proof-of-concept study utilizing treadmill walking.[101] More research is needed to assess the system's ability to train multiple gait modification strategies (both single and multi-parameter) during overground walking outside of the laboratory, and the subsequent effects on KAM. Therefore, the purpose of this study was to test the feasibility of a wearable haptic biofeedback system during overground walking

outside of the laboratory to train (1) toe-in and trunk lean gait (single parameter) and (2) combined toe-in and trunk lean gait (multi-parameter) to reduce KAM. We hypothesized that 1) participants would be able to significantly alter their foot and trunk angle as prescribed during gait modifications using RTB from wearable feedback system and (2) that participants would be able to accurately replicate practiced modifications at posttest, resulting in significant reductions in KAM.

Methods

Participants

Twelve healthy participants (age = 25.9±2.4 years, mass = 68.0±7.4 kg, height = 1.8±0.1 meters) with no known history of lower limb and neurological disorders that could affect gait volunteered for this study. A within-group repeated measures study design was used to compare joint kinematics and kinetics of participants' dominant limb across gait conditions (baseline and three gait modifications). Dominant limb was defined as the preferred leg in a kicking task.[88]

Instrumentation

Fifty three retroreflective markers were attached to the trunk and lower extremities of participants in a similar manner to our prior studies.[72,102,103] Six tracking clusters (31 markers) were placed bilaterally on the lower back, thigh, shank, and foot segments with an additional twelve tracking markers placed on various anatomical locations. Ten additional calibration markers were also attached during static and dynamic calibration trials.

A wearable biofeedback system (SageMotion, Kalispell, MT) that has been previously described[101] was used to provide real-time haptic feedback to train single- and multi-parameter gait modifications during overground walking trials (Fig. 1). The system consists of eight wearable wireless nodes, that can either be configured for real-time sensing (up to 50 Hz), or real-time haptic feedback (167 Hz). For the current study, one sensing node was placed on the dorsal side of the foot of the dominant limb, with another placed at the spine at approximately the L4/L5 level. Two feedback nodes were also placed at the medial and lateral sides of the mid shank of the dominant limb, and two more were placed on the left and right sides of the torso, also at approximately the L4/L5 level.[101]

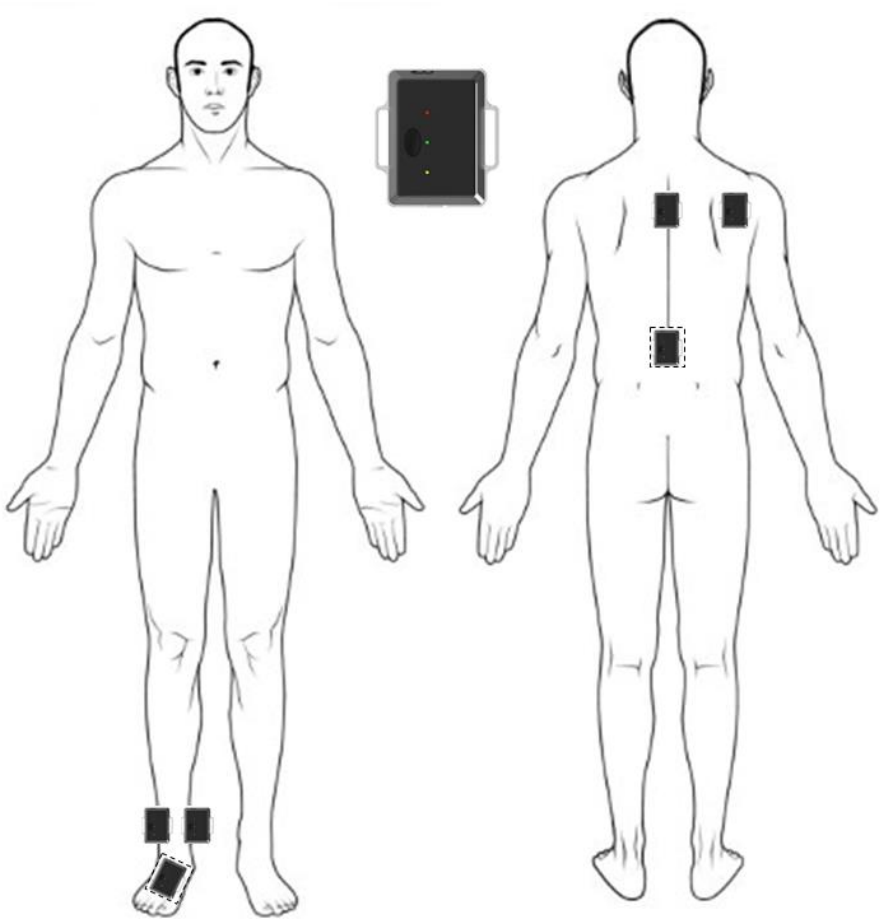

Figure 5. Experimental set-up of wearable feedback system. Sensing nodes (outlined with dashed box) for foot progression and trunk lean angle were placed on the dorsal side of the dominant foot and at the spine (L4/L5 level), respectively. Feedback nodes were strapped to the dominant ankle (just above the lateral and medial malleoli) and taped to the upper back (central and lateral in line with the supraspinous fossa). A larger image of an example node is placed in the center of the figure.

Fourteen high-speed motion analysis cameras (Vicon, Oxford, England) sampling at 200 Hz were used to track marker trajectory and three floor embedded force plates sampling at 1000 Hz (AMTI, Watertown, MA) were used to measure ground reaction force (GRF) during baseline and posttest trials. Force plates were aligned in a 1.8 meter long row placed 3.2 meters from the beginning of the 6.9 meter walkway. A static calibration trial was collected by having participants stand on a force plate with both feet parallel to the anterior-posterior axis of the laboratory. Participants also performed a dynamic calibration to estimate hip joint center by completing three clockwise rotations of the pelvis.[89] Calibration makers were removed for walking trials. From the static trial, a kinematic model was created for each participant using Visual 3D software (C-Motion, Germantown, MD) which included the trunk, pelvis, and bilateral thigh, shank, and foot segments.

Baseline Trials

Participants were instructed to walk normally along the 6.9 meter walkway at a self-selected speed. Ten normal walking trials were collected, with successful trials consisting of at least one full contact of the dominant limb on the force plates. Kinematic data collected by the wearable feedback system (foot angle, trunk angle, and stride time) were downloaded and exported into Miscrosoft Excel (Microsoft, Redmond, WA) where the mean for each modification parameter (transverse plane foot and frontal plane trunk angle) and stride time across normal walking trials were calculated.

Individualization of Gait Modification

Gait modifications were individualized using participants' means from baseline walking trials. Target ranges for each modification were created for each participant so that the wearable feedback system would provide feedback if their respective modification parameters (transverse plane foot angle with toe-in gait and frontal plane trunk angle with trunk lean gait) fell outside a range of 7° to 12° greater than baseline. This magnitude of modification was chosen to best reflect the amount seen in prior studies investigating the effects of these two kinematic changes on KAM and to be both feasible and relatively comfortable to adopt. Modifications have ranged between 4.7°-14.2° for toe-in gait[64-66,74,75] and 8.1°-12.7° for trunk lean gait.[47,62,63,70,71] If the gait parameter fell below the target range, haptic feedback was provided using a "pull" stimulus (i.e. stimulus was provided in the direction of the desired correction) as opposed to a "push" stimulus (stimulus provided in the opposite direction of the desired correction). Participants have performed faster and reported a more natural response to pulling stimulus in prior studies.[100] Haptic stimulus using separate nodes on either side of the modified segment and a single pulse pattern to indicate an increase or decrease needed in the target parameter was used. Participants have had difficulty perceiving the difference between haptic cues with saltation and patterns that use the same location for both motions.[100]

Gait Modification Training with Wearable Feedback System Outside of the Laboratory

Participants performed all three gait modifications in a single session directly following the calculation of individual target ranges. Toe-in and trunk lean modification

order was randomly assigned for each participant. The combined modification was always performed last, as participants had to learn the two single-parameter modifications to properly execute the combined strategy. Training was performed in a long hallway just outside the laboratory. Before each modification, participants were provided standardized instructions on how to properly perform the modification and how to respond to feedback.

For toe-in modification trials, participants were instructed to "*rotate the foot of your dominant limb more inward relative to your opposite limb immediately after your foot makes contact with the ground. Haptic feedback will be provided to help you rotate your foot the appropriate amount. If the node on the inside of your dominant limb vibrates, you have not rotated your foot inward enough, so please attempt to rotate your foot inwards more on the next step. If the node on the outside of your dominant limb vibrates, you have rotated your foot inward too much, so please attempt to rotate your foot inward less on the next step. Your goal is to walk so that you receive no feedback."*

For trunk lean modification trials, participants were instructed to "*attempt to lean your torso over your dominant limb immediately after your foot makes contact with ground. It is important to perform this lean as soon as possible after initial ground contact. When performing this modification, imagine bringing your whole upper body over the dominant limb, rather than simply laterally flexing your torso. Haptic feedback will be provided to help you lean your torso the appropriate amount. If the node on the outside of your torso vibrates, you have not leaned enough, so please attempt to lean more on the next step. If the node in the middle of your torse vibrates you have leaned too*

much, so please attempt to lean less on the next step. Your goal is to walk so that you receive no feedback."

Lastly, during combined gait modification trials, participants were instructed to "*rotate the foot of your dominant limb more inward relative to your opposite limb, and lean your torso over your dominant limb immediately after your foot makes contact with the ground. Haptic feedback will be provided in a priority scheme, where if both the foot and trunk are outside of the target range, you will only be provided feedback on trunk angle, in the same manner as TL trials. If your trunk angle is within the target range, but your foot angle is outside the target range, you will be provided feedback at the foot in the same manner as FP trials. If both your trunk and foot angle are within their respective target ranges, you will receive no feedback. Your goal is to walk so that you receive no feedback."* A priority scheme was chosen as prior studies have shown it to be the most suitable for training multi-parameter motions [100]. Trunk angle was given the priority as we hypothesized that trunk lean gait would be more difficult to master compared to toe-in gait.

Participants were told to perform as many training trials as necessary with the current modification until they felt comfortable that they could execute it with minimal feedback and could replicate it without feedback if asked. Participants could only move to the next modification after they reported that this was the case. Rest was provided as needed between trials and modifications.

Post-test Trials

Immediately after participants completed all gait modifications (self-reporting that they could execute the modifications successfully and replicate upon demand), posttest trials without feedback were performed in the laboratory using the motion capture system previously described. Ten trials for each modification were captured, the order of which was randomly assigned for each participant. Similar to baseline trials, successful trials consisted of at least one full contact of the dominant limb on the force plates. Participants rested for 5 minutes between each modification to reduce the likelihood of carryover effects.

Data Processing

Motion Capture

For baseline and posttest trials, a kinematic model created in Visual 3D was used to quantify the motion at the hip, knee, and ankle joints with rotations being expressed relative to the static trial. A cardan angle sequence was used to calculate joint angles[90] and a standard inverse dynamics analysis was conducted to synthesize the trajectory and vertical ground reaction force data for internal joint moment estimation. Although external joint moments are most commonly reported in KOA literature, internal moments resist the action of external moments and can be thought of as equal but opposite in sign.[11] Joint kinematics and kinetics were smoothed using a fourth order low-pass Butterwoth filter with a cut off frequency of 8 Hz to reduce the effects of artifacts based on results from residual analysis.[104] Joint angles were measured in degrees, and all internal joint moments were normalized to mass and height (N.m/Kg.m). Ground reaction force data were normalized

to bodyweight and all gait trials were normalized to 100 percent of stance. Gait modification parameters were calculated as the average across the entire stance phase. First peak of the knee abduction moment was defined as the peak minimum and maximum value respectively between heel strike and midstance (50% between heel contact and toe-off).

Wearable Feedback System

For baseline and posttest trials, average foot and trunk angles were calculated from the step of the dominant limb on the force plate, matching the step analyzed in Visual 3D. During training trials, average foot and trunk angles across all steps of the dominant limb per trial were calculated. Additional measures captured by the wearable feedback system include number of steps taken per trial, and if feedback was or was not provided during each step. From this data the percentage of steps that participants fell within their prescribed range for each modification condition was calculated (percent accuracy).

Statistical Analysis

Statistical analyses were conducted using R[105] (R Core Team; Vienna, Austria) with alpha level set *a priori* at 0.05. Normality of data was confirmed using a Shapiro-Wilk's test ($p<0.05$), skewness and kurtosis values, and visual investigation of histograms, normal Q-Q plots, and box plots and descriptive data were calculated. Repeated measures analysis of variance were conducted to determine significant differences between gait conditions for kinematic variables as well as percent accuracy. A second repeated measures ANOVA was performed to determine significant differences in KAM across baseline and posttest conditions. Where results were significant, pairwise comparisons with Bonferroni

corrections were conducted. Effect sizes (Cohen's D) for KAM were calculated between baseline and gait modifications.

Results

Descriptive statistics (mean and standard deviation) of kinematic parameters and KAM across conditions are presented in Table 1. All participants were able to successfully modify their foot progression and trunk angle from baseline during hallway training using the wearable feedback system, and were able to replicate the learned changes at posttest. Foot progression angle was reduced by an average of 10.3° and 12.5° with toe-in gait, while average trunk angle was increased by 7.9° and 7.5° with trunk lean gait during training and posttest respectively. Similar kinematic changes were seen during the combined modification, where on average foot progression angle was reduced by 12.0° and 11.8° and trunk lean angle increased by 7.4° and 7.6°during training and posttest.

The average percentage of steps participants fell within their target range for respective gait parameters (foot progression and trunk lean angle) across modifications is shown in Fig. 2. Mean accuracy was greater during trunk lean compared to toe-in gait ($p<0.05$); however, no other significant differences were found for mean accuracy across modifications. A significant difference was found for the number of steps required for participants to report feeling comfortable performing modifications between both toe-in (71±35) and trunk lean gait (51±14) and the combined modification (105±55) ($p<0.05$). No significant difference was found for steps between toe-in and trunk lean gait. Achieved kinematic changes during all gait modifications significantly reduced KAM

from baseline during posttest. The combined modification showed the greatest average reduction in KAM of 62%, followed by reductions of 55%, and 28% during trunk lean and toe-in gait respectively (Fig. 3). Effect sizes for KAM reduction from baseline were 1.57, 3.22, and 3.64 for toe-in, trunk lean, and combined gait modifications, respectively.

Table 4. Descriptive and inferential statistics for gait modification parameters and first peak knee abduction moment (KAM) across all conditions.

			Gait Condition						
				Training			Posttest		
	F-val	P-val	Baseline	Toe-in	Trunk Lean	Combined	Toe-in	Trunk Lean	Combined
Foot Progression Angle (°)	95.47	<0.001	-5.0[b,d,e,f,g] (4.4)	5.3[a,c,f] (3.6)	-4.4[b,d,e,g] (5.9)	7.0[a,c,f] (4.0)	7.5[a,c,f] (6.8)	-2.3[a,b,d,e,g] (6.7)	6.8[a,c,f] (7.5)
Trunk Angle (°)	52.08	<0.001	0.7[c,d,f,g] (1.1)	1.2[c,d,f,g] (1.6)	8.6[a,b,e] (2.6)	8.1[a,b,e] (2.5)	2.3[c,d,f,g] (2.2)	8.2[a,b,e] (4.7)	8.3[a,b,e] (4.4)
KAM (Nm/kgm)	311.28	<0.001	-0.29[e,g,f] (0.07)	-	-	-	-0.21[a,g,f] (0.07)	-0.13[a,e,g] (0.06)	-0.11[a,e,f] (0.06)

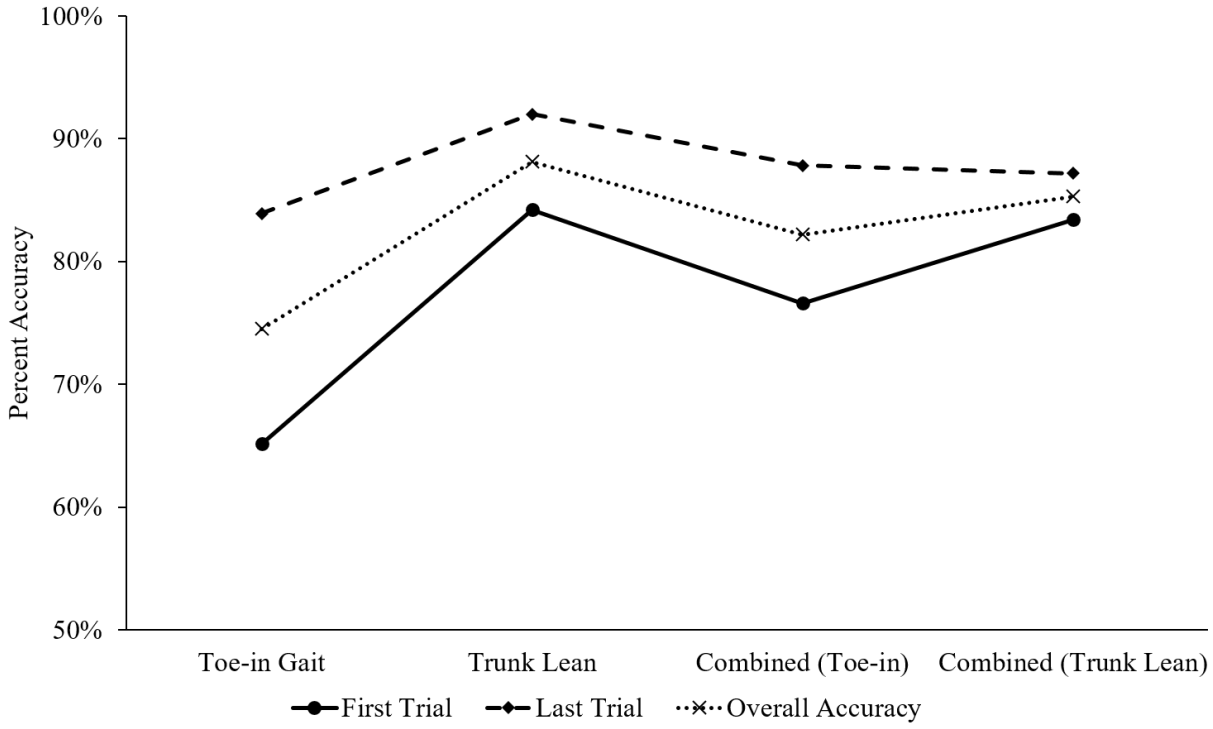

Figure 6. Percentage of steps participants fell within target range for respective gait parameters across modifications. Participants were defined as having successfully landed within their target range if they were within 7°-12° greater than baseline value. During toe-in and trunk lean gait, accuracy was based only on foot progression and trunk lean angle respectively. Although combined gait was only one modification, percent accuracy was assessed for the two separate components: foot progression angle for toe-in gait, and trunk lean angle for trunk lean gait.

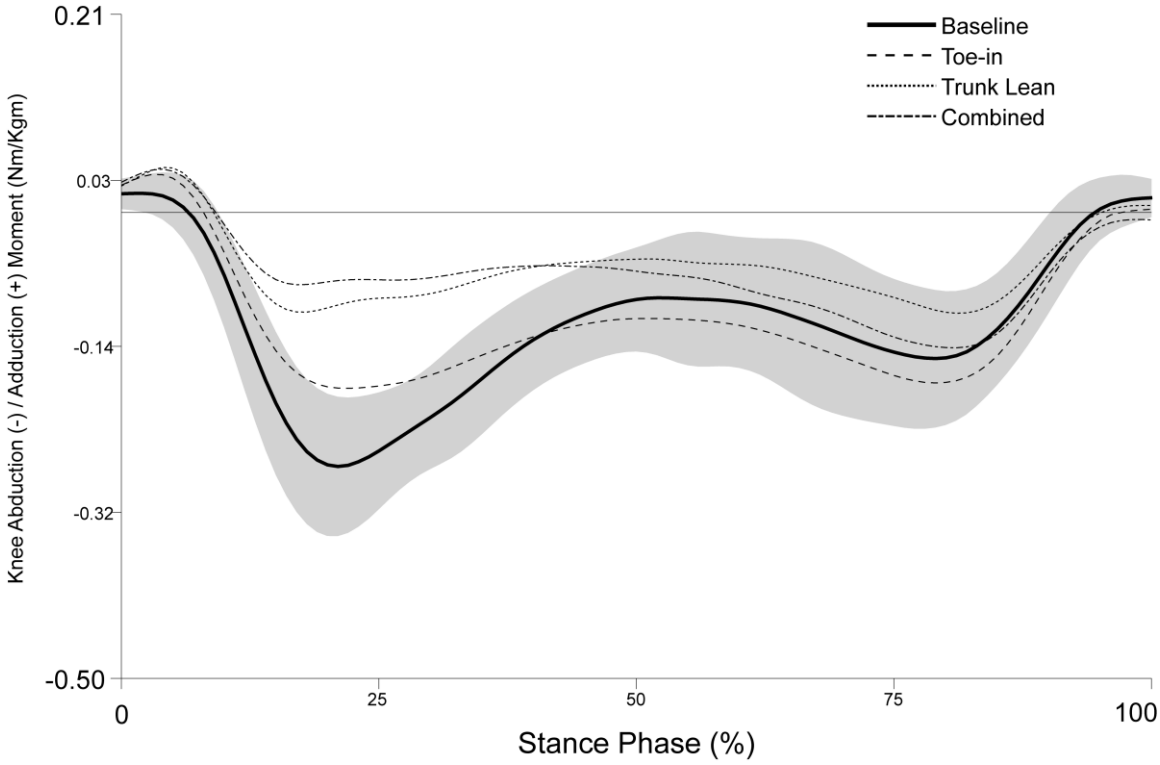

Figure 7. Average knee abduction moment (Nm/Kgm) during stance across gait conditions. All gait modifications were significantly different from baseline at the first peak of the adduction moment ($p<0.05$).

Discussion

Our primary purpose was to assess the feasibility of a novel wearable feedback system to train single and multi-parameter gait modifications (toe-in, trunk lean, and combined toe-in and trunk lean gait) during overground walking outside the laboratory. Our first hypothesis was confirmed, as all participants were able to significantly alter their target kinematic parameters in the intended direction and magnitude during training trials using the wearable feedback system, and were able to accurately replicate those changes at posttest. This demonstrates the system's ability to train participants to modify their gait by the targeted 7-12° reduction from baseline. Notably, participants were able to modify kinematic parameters equally accurately during the combined modification compared to toe-in and trunk lean gait in the single session.

On average, participants reported feeling comfortable performing toe-in gait the quickest, followed by trunk lean, with the combined modification taking the longest to feel comfortable performing. Interestingly, the percentage of steps in which participants were within their target range was greater on average when performing trunk lean gait, compared to toe-in. This may suggest that, although trunk lean gait was most easily modifiable by the prescribed amount, it is a more awkward modification, meaning it may take longer before participants are comfortable using it. This is supported by evidence from prior studies investigating trunk lean gait, where participants consistently reported some amount of difficulty while performing the prescribed amount of lean.[62]Additionally, in studies where participants were given the option of multiple modification strategies to reduce PKAM, most have chosen toe-in gait.[66,69] Although participants consistently took

longer to comfortably perform the combined modification, the average percent of steps within the target range did not significantly change. It is plausible that similar to trunk lean gait, the combined modification may feel more awkward, and therefore, take longer to comfortably perform. However, it appears that participants can successfully perform it given enough time, to an equivalent level of accuracy compared to the single parameter toe-in and trunk lean gait modifications.

Our second hypothesis was also confirmed as participants were able to accurately replicate these changes at posttest resulting in significant reductions in KAM. The kinematic changes achieved during training described above are comparable to those seen for toe-in[65,66,74,75] and trunk lean[45,62,63] modifications in prior literature. At posttest, toe-in gait reduced KAM by an average of 28%, which slightly greater than reductions seen in a prior study where participants reduced foot progression angle from baseline by an average of 7.0°.[66] In comparison, trunk lean gait resulted in a much greater average reduction in KAM of 55%. This reduction is also much greater than up to the 20% reduction in KAM seen in the majority of prior literature with comparable magnitudes of trunk lean.[62,63] A potential explanation for the greater reductions in KAM seen in this study during trunk lean gait, is discrepancy in relative timing of peak trunk lean. Prior studies have provided participants visual RTB showing trunk angle over the entire stance phase, with the instructions to lean their trunk so that the line represents real-time trunk angle reaches a vertical line denoting the target range.[62,63] The system was designed to provide feedback only during the range of stance where KAM typically occurs (20-50%).[42,106] It is possible that providing RTB only during early stance trained participants

to achieve peak trunk lean earlier during stance, thereby having a greater effect on KAM. Despite these discrepancies, KAM reductions in this study are similar to those found during a bilateral trunk sway modification which reduced KAM by 65% in a sample of healthy individuals. Overall, these results suggest that the wearable feedback system is capable of significantly reducing KAM as a result of training changes to kinematic parameters such as foot progression and trunk lean angle.

A secondary purpose of this study was the combination of two single-parameter gait modifications (toe-in and trunk lean gait) in order to investigate the relative effectiveness of implementing a multi-parameter gait modification to reduce KAM. Prior studies implementing multi-parameter modifications have shown large reductions in KAM of between 39%[64] and 49%.[99] Additionally, unintended secondary changes naturally occur when implementing single-parameter modifications suggesting that combining multiple modifications may feel more natural and beneficial.[70,99] Evidence from this study suggests that combining toe-in and trunk lean modifications results in greater KAM reductions than either single modification (62% during the combined modification compared to 55% and 28% in trunk lean and toe-in gait, respectively). However, despite the large reduction in PKAM during the combined modification, participants took longer to feel comfortable performing it, and subjectively, reported it as the most awkward to adopt. It is likely that only certain combinations of modifications are natural (i.e. toe-in gait and speed, and trunk lean gait and step width).[99] Based on prior literature, reducing foot progression angle does not naturally concomitantly increase trunk lean and vice versa.[99] While in the present study combining toe-in and trunk lean

gait could be performed successfully, the reductions in KAM were relatively comparable to the single parameter trunk lean modification meaning the complexity and awkwardness of implementing the strategy may not be justified. It is also unclear if these findings would be replicable in individuals with KOA. Despite the KAM reductions seen with the combined modification, the complexity and 'awkwardness' of the modification may limit patients' willingness to adopt it. Additionally, the ease of adoption seen with toe-in gait may encourage patient compliance to the point where it is clinically more efficacious than trunk lean gait. Future studies should investigate ratings of comfort and awkwardness, as well as compliance and retention over time for these modifications with a clinical sample.

There are several limitations to the current study. Our sample size was relatively small, however, reported effect sizes suggest that KAM reductions were approximately 1.5 to 3.5 times greater than baseline standard deviation suggesting that results were not due to chance. Our sample was composed of healthy individuals, therefore although both kinematic and kinetic changes were consistent with prior literature, it is unclear if our results would be replicable with KOA patients. For example, performing the combined modification was a demanding task for even our young, healthy participants. It is possible that it may be too complex of a task for an older individual with KOA that may have additional comorbidities. We attempted to test the wearable feedback system in a "real-world environment". We believe we found a suitable facsimile for it in the form of a university hallway. Although this was not the laboratory setting per se, it had less distractions, and environmental challenges compared to what would be expected at a

patient's home or on the street. Future studies should attempt to assess the feasibility of this system to modify gait on KOA patients in their natural environments.

Conclusion

This study demonstrates that a novel wearable feedback system can be used to effectively implement toe-in, trunk lean, and combined toe-in and trunk lean gait modifications in healthy individuals outside of the laboratory setting. These modifications could all be learned in a single session, and were replicable at posttest upon request, leading to significant reductions in KAM. Overall, the results of this study suggest that such a wearable feedback system may be a valid tool to implement gait modifications in patients with KOA to reduce KAM, without the need for laboratory based training. Future studies should investigate if these results translate to KOA patients in their natural environment.

Chapter Four: Eight-Week Gait Modification Intervention to Reduce Knee Adduction Moment: Pilot Study

Title: Eight-Week Gait Modification Intervention to Reduce Knee Adduction Moment: Pilot Study

Brief Running Head: Eight-week Intervention to Reduce KAM

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Abstract

Background: Increased first peak internal knee abduction moment (KAM) due to altered gait mechanics has been associated with increased knee osteoarthritis (KOA) severity. Gait modifications using real-time biofeedback have shown to be effective in reducing KAM. Prior studies, however, have largely relied on single-session designs with healthy participants, limiting generalizability of their findings. Therefore, the purpose of this study was to evaluate the preliminary data from a randomized controlled trial investigating the effect on KAM of an 8-week gait modification intervention compared to a control intervention of normal walking. **Methods:** Eight individuals with medial compartment KOA have currently completed the intervention. Participants were randomized into either performing 8-weeks of gait modification training using trunk lean gait (n=3), or a control protocol of 8-weeks normal walking (n=5). A mixed effects linear regression model was developed to assess changes in mean KAM across sessions and treatment groups. **Results:** Estimated effects showed that, during the final posttest, the intervention group exhibited a significant reduction in KAM from baseline ($p<0.05$) while the control group did not. **Conclusion:** The preliminary results of this randomized controlled trial (RCT) provide strong support for prior quasi-experimental studies showing that gait modification strategies are effective to reduce KAM in both healthy and KOA samples. Upon the completion of the current RCT, we believe it will provide a valuable addition to the current literature. Future studies should aim to investigate the

long-term effects of KAM reduction via gait modification on pain function, and quality of life in individuals with medial KOA.

Introduction

Increased first peak internal knee abduction moment (KAM) during gait has been identified as both a determinant and surrogate for medial compartment knee joint loading in patients with medial compartment knee osteoarthritis (KOA).[10,107] As increased medial compartment loading has been associated with increased KOA severity,[108] interventions that reduce KAM may reduce pain, and increase function in patients with early-stage KOA.[66,79,80]

Recent studies have experimented with gait modification interventions, using real-time biofeedback (RTB) to retrain patients to offset the load from the medial compartment using a variety of altered gait strategies.[48] Although results have been promising, the majority of prior studies have largely relied on single-session designs with healthy participants, limiting generalizability of their findings.[48] To our knowledge, only two studies have investigated the effects of a gait modification intervention on KAM using a randomized controlled study design.[79,80] Although both interventions showed reduced KAM, pain and improved function within their samples, limitations for clinical adoption persist. One study employed a toe-out gait modification[80] (an alteration designed to reduce second peak KAM) which may be problematic as moderate to poor correlations seen between late stance KAM and medial tibiofemoral contact force may reduce potential efficacy of the intervention.[109] The other study provided direct RTB based on KAM, which although it has previously shown greater reductions in KAM

compared to indirect[48] (RTB based on a kinematic parameter i.e. trunk angle), also reduces potential clinical efficacy as it requires technology only available in a laboratory environment.

Therefore, the purpose of this study was to evaluate the preliminary data from a randomized controlled trial investigating the effect an 8-week gait modification intervention on KAM compared to a control intervention of normal walking. The difference between this intervention and those prior is (1) participants were screened at baseline for which modification (trunk lean or toe-in gait; both of which are designed to reduce first peak KAM) most reduced KAM and had a random chance of being assigned to only either the control group or the modification that most reduced KAM, and (2) gait retraining was performed using indirect RTB from an inertial measurement unit (IMU) system designed to operate outside of the laboratory environment. We hypothesized that KAM would be reduced at all posttests compared to baseline in the intervention group, but would not change from baseline in the control group.

Methods

Participants

A non-blinded randomized controlled design was used to determine the effects of an 8-week gait modification intervention compared to control on KAM. Eight individuals with self-reported clinical diagnosis of medial compartment knee osteoarthritis[110] (female = 6, age = 52.75 ± 12.6 years, BMI = 27.91 ± 3.32 kg/m^2, left knee symptomatic limb = 6) have currently completed the intervention. In the case of bilateral KOA, the limb with

the greatest score on the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) questionnaire[111,112] was studied.

To be eligible for inclusion, individuals were required to be between the ages of 18 and 80, diagnosed with medial compartment knee osteoarthritis, self-reported knee pain at least once per week during the prior month before recruitment, and able to walk unaided for a minimum of one hour. Recruited individuals were excluded if they had a history of lower back, hip, or knee surgery in the past two years, knee arthroscopy or pharmacological injection in the past 6 months, or used a gait aid such as an orthotic shoe insert or hinged knee brace. This registered randomized controlled trial (NCT03663790) was conducted according to the Declaration of Helsinki guidelines and all procedures were approved by the University's Institutional Review Board for use of human subjects in research. Informed consent was obtained for all participants before starting the trial.

Baseline Testing

Three-dimensional motion capture was performed in the same manner as prior studies.[113-115] Briefly, motion capture was performed using 8 high-speed video cameras sampling at 200 Hz (VICON, Oxford, England) with ground reaction forces captured using four floor embedded force plates sampling at 1000 Hz (Bertec, Columbus, OH). Fifty-three retro-reflective markers were placed on specific anatomical landmarks, with 10 being calibration markers.[72,102,116] A static calibration trial was collected by having participants stand on a force plate with both feet parallel to the anterior-posterior axis of the laboratory. Participants also performed a dynamic calibration to estimate hip joint center by completing three clockwise rotations of the pelvis.[89] Calibration markers were

removed for walking trials. From the static trial, a kinematic model was created for each participant using Visual 3D software (C-Motion, Germantown MD, USA) which included the trunk, pelvis, and bilateral thigh, shank, and foot segments.

Participants first performed five normal walking trials. From these trials, mean for kinematic variables (trunk angle and foot angle), and walking speed were calculated. Foot angle was defined as the offset between the lines formed by the posterior calcaneus and 2nd metatarsophalangeal joint markers, and the anterior-posterior laboratory axis,[65] while trunk angle was defined as the frontal plane deviation of the trunk segment represented by the right scapula, 10th thoracic, and left/right lower back markers from the vertical laboratory axis.[62] Based on participant's baseline kinematics, four modification conditions were calculated: (1) small foot progression (2) large foot progression (3) small trunk lean (4) large trunk lean. Small modification was calculated as a range 3°-7° greater than baseline values in the target kinematic parameter. Large modification was calculated as a range 7°-12° greater than baseline values in the target kinematic parameter.

Participants then performed five walking trials of each modification condition, with the order randomly assigned per participant. Real-time visual feedback was provided to the participants during trials in the form of a line graph with the target range represented as a horizontal green band. Participants were told to modify their gait as instructed so that the line representing the current target kinematic parameter fell within the green band. A trial was only successful if the line fell within the green band and participants walk ± 5% of baseline gait speed. After completion of the baseline session, mean KAM for each modification was calculated. The participants then had a random

chance of being assigned into the control group or the intervention group (using the modification that most reduced KAM). Do I really need to go into detail of how we randomized here? – simple vs stratified

Gait Retraining

Participants then completed one session per week of either gait retraining or normal walking for eight consecutive weeks. During gait retraining sessions, participants in the intervention group were provided with real-time haptic feedback (with the same acceptable modification range as what most reduced KAM during baseline) using a Bluetooth tactor device (Engineering Acoustics, Casselberry FL, USA). As participants in the intervention group walked while adopting their respective modification, small vibration motors on the skin provided feedback if they were modifying the target kinematic parameter too little or too much. For those performing trunk lean, vibration motors were places on the scapula of the symptomatic side and just lateral to the spine at the same vertical level. If the participant did not lean enough to be within the prescribed range, the vibration motor on the scapula would vibrate prompting them to lean more on the subsequent step. If they leaned too far and were outside the range, the motor just lateral to the spine would vibrate prompting them to lean less on the next step. For those performing toe-in gait, vibration motors were placed on both malleoli of the foot of the affected limb. If the participant did not totate their foot inward enough to be within the prescribed range, the vibration motor on the medial malleolus would vibrate prompting them to rotate inward more on the subsequent step. If they rotated too far inward, the motor on the lateral malleolus would vibrate prompting them to rotate less inward on the

next step. Participants were instructed to walk using their assigned modification with minimum feedback provided. Participants in the control group were instructed to walk normally and were not provided any feedback. Each session consisted of 20 minutes of training on the treadmill. Those in the intervention group were encouraged to practice walking with their modified gait as much as possible outside of the training sessions but were not instructed a mandatory amount of time to do so.

Post-testing

Post-tests were performed immediately before the 5th session, and one-week after the 8th training session. Participants in the intervention group were instructed to perform five trials of normal walking followed by five trials of their assigned modification without feedback. Participants in the control group were instructed to perform five normal walking trials. Just as during modification trials in the baseline assessment, trials were only successful if participants walked ± 5% of baseline gait speed.

Data Processing

The kinematic model created in Visual 3D was used to quantify the motion at the hip, knee, and ankle joints with rotations being expressed relative to the static trial. A Cardan angle sequence (X-Y-Z) was used to calculate joint angles[90] and a standard inverse dynamics analysis was conducted to synthesize the trajectory and vertical ground reaction force (vGRF) data for internal joint moment estimation. Although external joint moments are most commonly reported in KOA literature, internal moments resist the action of external moments and can be thought of as equal but opposite in sign.[11] Joint kinematics and kinetics were smoothed using a low-pass Butterwoth filter with a cut off

frequency of 8 Hz to reduce the effects of artifacts based on results from residual analysis.[104] Joint angles were measured in degrees, and first peak knee abduction moment was normalized to mass and height Nm/(kg*m). Ground reaction force data were normalized to body weight and all gait trials were normalized to 100 percent of stance. Mean values were computed and used for all statistical analyses.

Statistical Analysis

Analyses were performed using R (R Core Team; Vienna, Austria) with the level of significance set a priori to 0.05. In order to provide an appropriate estimate of the treatment effect that properly accounts for different sources of variation, we developed a mixed effects linear regression model. This model was used to assess changes in mean KAM across sessions and treatment groups via fixed effects while also accounting for variability across participants in baseline KAM values and change in KAM from baseline to posttests via random effects. Taken together, these random effects and fixed effects for sessions and treatment allowed for proper estimation of the treatment effect while accounting for variability across both sessions and participants. This model is as follows:

$$y_{ijk} = \beta_0 + u_{0j} + \beta_g group_{ijk} + (\beta_1 + u_{1j}) posttest1_{ijk} + (\beta_2 + u_{2j}) posttest2_{ijk} + (\beta_3 + u_{3j}) posttest3_{ijk} + \beta_{I1} group_{ijk} posttest1_{ijk} + \beta_{I2} group_{ijk} posttest2_{ijk} + \beta_{I3} group_{ijk} posttest3_{ijk} + \epsilon_{ijk}$$

where y_{ijk} is the observed KAM value for participant *j* on the *i*th trial of the *k*th session, $group_{ijk}$ is an indicator variable for treatment group such that $group_{ijk} = 1$ if the jth participant is in intervention group and $group_{ijk} = 0$ if the *j*th participant is in control group, $posttest1_{ijk}$ is an indicator variable for posttest 1 such that $posttest1_{ijk} = 1$ if the *i*th trial of *j*th participant corresponds to posttest 1 and $posttest1_{ijk} = 0$ otherwise, $posttest2_{ijk}$ and $posttest3_{ijk}$ are similarly defined for posttests 2 and 3, β_0 is a fixed global intercept term, β_g is the fixed treatment effect at baseline, β_1 , β_2 and β_3 are fixed coefficients representing the estimated change in mean KAM values from baseline to posttests 1, 2, and 3 respectively for the control group, β_{I1} , β_{I2} and β_{I3} are fixed coefficients representing the additional change in mean KAM values from baseline for the intervention group for posttests 1, 2, and 3 respectively, u_{0j} is the random intercept term for participant j and u_{1j}, u_{2j} and u_{3j} are random effects for changes in mean KAM values from baseline to posttests 1, 2, and 3 respectively for participant *j*. The random effects follow a zero mean multivariate normal distribution $N(0, \Sigma)$ where Σ is a four by four covariance matrix, and $e_{ij} \sim N(0, \sigma_e^2)$ is the error term which is normally distributed with zero mean and variance σ_e^2.

Additionally, we also tested for the average treatment effect across all posttests by constructing a confidence interval for the mean of β_1 , β_2 and β_3 for the control group and the mean of $\beta_1 + \beta_{I1}$, $\beta_2 + \beta_{I2}$ and $\beta_3 + \beta_{I3}$ for the intervention group.

Results

All participants in the intervention group (n=3) most reduced KAM with the 'large' trunk lean modification, therefore, that was the modification used as their intervention. The estimated effects from the mixed effects linear regression model are presented in Table 1. The estimated change in KAM values from baseline to all posttests for the intervention group were positive (0.057 to 0.111). There was significant variability across participants, which resulted in a lack of significance at posttests 1 and 2 (p-values 0.212 and 0.184 respectively). During the final posttest, however, the intervention group exhibited a significant reduction in KAM from baseline (p-value 0.005) with a 95% confidence interval indicating an estimated reduction in mean KAM of 0.054 to 0.189 units.

Table 5. Mixed effect modeling for first peak knee abduction moment (KAM)

Fixed effects			
Parameter	Estimate (SE)	P-Value	95% Confidence Interval
Intercept	-0.232 (0.066)	0.013	(-0.393, -0.070)
Posttest 1	-0.013(0.055)	0.820	(-0.147, 0.121)
Posttest 2	-0.002(0.024)	0.950	(-0.061, 0.057)
Posttest 3	-0.035(0.017)	0.081	(-0.077, 0.006)
Intervention Group	0.023(0.108)	0.837	(-0.240, 0.287)
Posttest 1* Intervention Group	0.124(0.089)	0.212	(-0.094, 0.343)
Posttest 2* Intervention Group	0.059(0.039)	0.184	(-0.037, 0.155)
Posttest 3* Intervention Group	0.121(0.027)**	0.005	(0.054, 0.189)
Random effects			
Parameter	Standard Deviation		95% Confidence Interval
Intercept	0.146		(0.082, 0.228)
Posttest 1	0.120		(0.066, 0.188)
Posttest 2	0.049		(0.021, 0.081)
Posttest 3	0.031		(0.004, 0.055)

Point estimates, P-value, 95% confidence intervals are provided for the effect of changes in groups and sessions on the KAM values. Asterisks indicate statistically significant difference (*** = <0.001, ** = <0.01, * = <0.05).

To further illustrate these findings, 95% confidence intervals for mean KAM values across sessions and groups are shown in Figure 1A. While the estimated KAM values at baseline were similar for the two groups, the intervention group exhibited smaller estimated KAM across posttests while estimated KAM values in the control group were relatively unchanged. While the difference in mean KAM values between

groups for each posttest are similar, there was more variability in KAM values across participants for the first two posttests (Figure 1B), resulting in wider confidence intervals for these sessions compared to the final posttest. This helps to explain why the last posttest was the only session to show a statistically significant treatment effect.

In order to estimate average treatment effect across all posttests, we constructed a 95% confidence interval for the average change in KAM values from baseline across all posttests for the intervention and control groups separately. The average change in KAM from baseline was estimated to be between –0.069 and 0.036 for the control group and between 0.017 and 0.153 for the intervention group. The average change in KAM from baseline for the intervention group was significantly different from zero, indicating a significant treatment effect, while the average change from baseline for the control group was not significantly different from zero. Therefore, we can conclude that these preliminary results indicate a meaningful effect of the treatment compared to the control group, with an estimated reduction in mean KAM between 0.017 and 0.153 units.

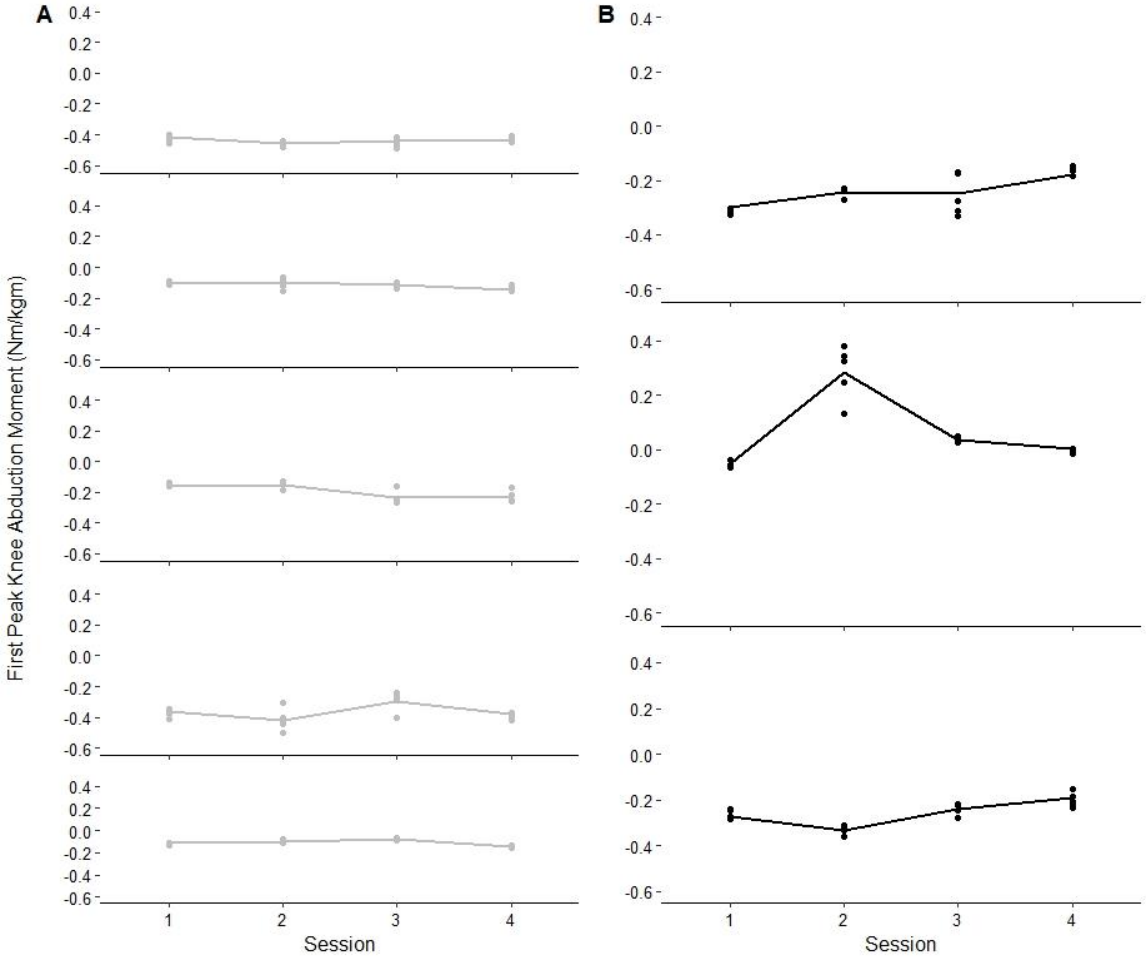

Figure 8. Peak knee abduction moment across session and condition**.** A) 95% confidence intervals for change in mean first peak knee abduction moment (KAM) from baseline to posttests by treatment group B) Trial-by-trial KAM values across sessions for control (left column) and intervention (right column) groups.

Discussion

The purpose of this study was to investigate the difference in KAM reduction between an 8-week gait modification intervention compared to a control of normal walking on individuals with KOA. The preliminary results support our hypothesis as mean KAM was significantly lower in the intervention group by the final posttest, whereas in the control group KAM remained unchanged. Our findings build on prior quasi-experimental studies showing that various gait modification strategies are effective to reduce KAM in both healthy and KOA samples.[48,49]

To our knowledge, only two other randomized controlled trials have also investigated the effects of gait modification on frontal plane knee moment.[79,80]. The results of this pilot study . It remains unknown if reduction in frontal plane knee moment translates to improved pain and function scores and reduced likelihood of total knee replacement (TKR) years after the intervention. However, the data from the current study supports that by Hunt et al. suggesting that gait modification is an effective method to reduce KAM greater than normal or progressive walking. Future studies should aim to investigate the long-term effects of KAM reduction via gait modification on pain function, and quality of life in individuals with medial KOA.

Chapter Five: Conclusions

The overall goal of this dissertation was to investigate some of the important questions that remain unanswered within the gait modification literature, with the aim of advancing knowledge in the field and providing recommendations for future research and clinical applications. Specifically, the primary purposes of these studies were to identify which gait modification(s) most effectively reduce KAM, to test the feasibility of a wearable device to train patients to modify their gait using haptic RTB, and to gather high quality evidence investigating if gait modification reduces KAM in the target population (KOA patients) greater than a control treatment of normal walking.

The results from the first study suggest that there is likely no one gait modification that is universally most effective to reduce KAM in all patients. Although our data suggest that on average MKT was the most effective modification to reduce KAM, the few other studies that have compared the effects of multiple gait modifications within the same sample have presented conflicting findings.[47,70] While this discrepancy can be partially ascribed to differences in mean kinematic modifications between studies, it raises a larger point regarding individual response to modification as well as patient comfort in adopting a new gait strategy. Secondary analysis of the data showed a large variation in individual KAM response to both type and magnitude of gait modification.[47,70,99] Additionally, other studies have reported consistent preferences amongst participants for certain modifications above others[66,69] with toe-in gait largerly being preferred due to the smaller kinematic change required. In comparison, MKT has

been described as the most challenging to adopt.[70] These findings were supported, at least anecdotally, by participants in the first study who consistently reported FP and TL gait as preferable to use compared to MKT. Patient comfort is vital, as even if a certain gait modification is found to be most effective to reduce KAM for an individual patient, they must be willing to adopt it to see any long-term benefits.

The impact of gait modification on KEM must also be taken into account as increases in this moment have been previously associated with changes in cartilage thickness[12] and is suggested to attenuate reductions in joint load by increasing joint compression.[12,86] While MKT most reduced KAM in our sample, it was the only modification that significantly increased KEM, potentially limiting its effectiveness as an intervention for KOA. The observations from the first study, therefore, suggest there is no 'one-size-fits-all' modification that best reduces KAM. Although it appears that TL and MKT gait most consistently reduce KAM by the greatest magnitudes, not all patients will respond positively to them both in terms of KAM reduction, KEM increase, and patient comfort. It is important that future studies and clinical interventions screen patients for their response to several gait modifications to determine which one will be most effective for them.

The second study assessed the feasibility of a novel wearable haptic device to train patients attempting to modify their gait. The ultimate goal of gait modification interventions should be to permanently alter how KOA patients walk, thereby reducing KAM and theoretically reducing medial compartment joint load. In a laboratory or clinic setting, patients are provided temporary factors like motivation, feedback, and attention

which increases motor performance. When these factors are removed, however, the patients performance is likely to dissipate.[117] Therefore, an essential step towards an effective clinical gait modification intervention is the ability for patients to receive feedback outside of the laboratory or clinic environment in order to obtain relative permanence of their newly modified gait. The results from the second study suggest that a novel, wearable haptic IMU system has potential to provide patients haptic RTB based on gait kinematics outside of the laboratory setting. Although our sample consisted of young, healthy volunteers, the simple 'pull' feedback scheme was effective in training them to change both their foot progression and trunk lean angle by the targeted 7-12° from baseline, resulting in significant KAM reductions. Although more development is needed before a similar system is useable by older adults with KOA in the home setting, these results demonstrate that continued at-home gait retraining is feasible with RTB provided through the use of a wearable IMU system.

The results of the third study provide pilot data to support other recent RCTs[79,80] which have demonstrated that gait modifications are effective to reduce KAM above and beyond the effects of normal or progressive walking programs matched for time. One of the largest gaps in the current literature is the lack of high-quality evidence, limiting the generalizability of promising results from quasi-experimental studies performed on healthy participants.[48,49] Although two other RCTs have been completed that investigate the effects of gait modification on KAM,[79,80] methodological differences including type of feedback provided (direct vs indirect), feedback mode (visual vs haptic) and modification tested (reduced/increased foot progression vs trunk lean) means that more

evidence is necessary to confirm the effectiveness of various gait modifications and feedback deliveries. The design of this pilot study differed from the other two RCTs mentioned in that it screened patients at baseline for which modification best reduced KAM when randomizing patients into intervention or control groups, and also employs a wearable haptic RTB for gait retraining. However, the results lend support to their prior findings that gait modifications are effective to reduce KAM within the target population of KOA patients. It is important to note that this is a pilot study, and therefore, caution must be taken when interpreting the results as the full study is currently underway.

The challenge of developing a non-invasive intervention to treat KOA is a complex one with many remaining questions, however, the findings from this dissertation provide evidence for some of the answers. The range of individual response seen as a result of different modifications suggests that no 'one-size fits all' when it comes to modifying gait to reduce KAM. As such, future research studies and clinical interventions should screen KOA patients for which modification is most effective, with effectiveness defined as a combination of KAM reduction without KEM increase as well as patient comfort and compliance. Initial testing of a novel wearable IMU device suggests that gait retraining with haptic RTB is feasible outside of the laboratory environment. Future interventions designed to change gait as a means for long-term KAM reduction should implement such devices to facilitate relative permanence through at-home gait retraining. One of the most of important questions remaining in the literature is the replicability of KAM reductions seen in lower level of evidence studies. Results from the final pilot study supports evidence from recently completed RCTs in that gait modification

significantly reduces KAM in KOA patients above and beyond normal walking, and therefore gait modification is a valid treatment option appropriate for further exploration.

Based on these findings, future research should attempt to construct individualized gait modification interventions where patients can continue to train at-home with the use of wearable haptic feedback system. Particular notice should be given to the motor learning process and how long is needed for patients to acquire relative permanence of learned gait and its long-term effects on outcomes that not only include KAM, such as pain, function, and diagnostic measures of cartilage health.

Appendix

IRB Approval Letter: Osteoarthritis in the ACL reconstructed knee: A Multifactorial Approach

Office of Research Development, Integrity, andAssurance

Research Hall, 4400 University Drive, MS 6D5, Fairfax, Virginia 22030 Phone: 703-993-5445; Fax: 703-993-9590

DATE:	August 1, 2019
TO:	Nelson Cortes
FROM:	George Mason University IRB
Project Title:	[477645-9] Osteoarthritis in the ACL reconstructed knee: A multifactorialapproach
Reference:	8095
SUBMISSION TYPE:	Continuing Review/Progress Report
ACTION:	APP
ROVED APPROVAL DATE:	Aug ust 1, 2019
EXPIRATION DATE:	July 31, 2020
REVIEW TYPE:	Expedited Review
REVIEW TYPE:	Expedited review categories 4, 7

Thank you for your submission of Continuing Review/Progress Report materials for this project. The George Mason University IRB has APPROVED your submission. This submission has received Expedited Review based on applicable federal regulations.

Please remember that all research must be conducted as described in the submitted materials.

Please remember that informed consent is a process beginning with a description of the project and insurance of participant understanding followed by a signed consent form unless the IRB has waived the requirement for a signature on the consent form or has waived the requirement for a consent process.
Informed consent must continue throughout the project via a dialogue between the researcher and research participant. Federal regulations require that each participant receives a copy of the consentdocument.

Please note that any revision to previously approved materials must be approved by the IRB prior to initiation. Please use the appropriate revision forms for this procedure.

All UNANTICIPATED PROBLEMS involving risks to subjects or others and SERIOUS and UNEXPECTEDadverse events must be reported promptly to the IRB office. Please use the appropriate reporting forms for this procedure. All FDA and sponsor reporting requirements should also be followed (if applicable).

All NON-COMPLIANCE issues or COMPLAINTS regarding this project must be reported promptly to the IRB.

The anniversary date of this study is July 31, 2020. This project requires continuing review by this committee on an annual basis. You may not collect data beyond this date without prior IRB approval.

A continuing review form must be completed and submitted to the IRB at least 30 days prior to the anniversary date or upon completion of this project. Prior to the anniversary date, IRBNet will send you a reminder regarding continuing review procedures.

Please note that all research records must be retained for a minimum of five years, or as described inyour submission, after the completion of the project.

Please note that department or other approvals may be required to conduct your research in addition toIRB approval.

If you have any questions, please contact Bess Dieffenbach at 703-993-5593 or edieffen@gmu.edu. Please include your project title and reference number in all correspondence with this committee.

GMU IRB Standard Operating Procedures can be found here: https://rdia.gmu.edu/topics-of-interest/human-or-animal-subjects/human-subjects/human-subjects-sops/

This letter has been electronically signed in accordance with all applicable regulations, and a copy is retained within George Mason University IRB's records.

IRB Approval Letter: Comparison of the Effects of Gait Modification Strategies on Knee Adduction Moment in Patients with Medial Knee Osteoarthritis:Randomized Controlled Trial

Office of Research Integrity and Assurance

Research Hall, 4400 University Drive, MS 6D5, Fairfax, Virginia 22030 Phone: 703-993-5445; Fax: 703-993-9590

DATE:	June 22, 2020
TO:	Nelson Cortes
FROM:	George Mason University IRB
Project Title:	[1315238-8] Comparison of the Effects of Gait Modification Strategies on Knee Adduction Moment in Patients with Medial Knee Osteoarthritis:Randomized Controlled Trial
SUBMISSION TYPE:	Continuing
Review/Progress ReportACTION:	APPROVED
APPROVAL DATE:	June 22, 2020
EXPIRATION DATE:	June 21, 2021
REVIEW TYPE:	Expedited Review
REVIEW TYPE:	Expedited review categories #4 & 7

Thank you for your submission of Continuing Review/Progress Report materials for this project. The George Mason University IRB has APPROVED your submission. This submission has received Expedited Review based on applicable federal regulations.

You are required to follow the George Mason University Covid-19 research continuity of operations guidance. You may not begin or resume any face-to-face interactions with human subjects until (i) Mason has generally authorized the types of activities you will conduct, or (ii) you have received advance written authorization to do so from Mason's Research Review Committee. In all cases, all safeguards for face-to-face contact that are required by Mason's COVID policies and procedures must be followed.

Please remember that all research must be conducted as described in the submitted materials.

Please remember that informed consent is a process beginning with a description of the project and insurance of participant understanding followed by a signed consent form unless the IRB has waived the requirement for a signature on the consent form or has waived the requirement for a consent process.
Informed consent must continue throughout the project via a dialogue between the researcher and research participant. Federal regulations require that each participant receives a copy of the consentdocument.

Please note that any revision to previously approved materials must be approved by the IRB prior to initiation. Please use the appropriate revision forms for this procedure.

All UNANTICIPATED PROBLEMS involving risks to subjects or others and SERIOUS and UNEXPECTEDadverse events must be reported promptly to the IRB office. Please use the appropriate reporting forms for this procedure. All FDA and sponsor reporting requirements should also be followed (if applicable).

All NON-COMPLIANCE issues or COMPLAINTS regarding this project must be reported promptly to the IRB.

The anniversary date of this study is June 21, 2021. This project requires continuing review by this committee on an annual basis. You may not collect data beyond this date without prior IRB approval.
A continuing review form must be completed and submitted to the IRB at least 30 days prior to the anniversary date or upon completion of this project. Prior to the anniversary date, IRBNet will send you a reminder regarding continuing review procedures.

Please note that all research records must be retained for a minimum of five years, or as described inyour submission, after the completion of the project.

Please note that department or other approvals may be required to conduct your research in addition toIRB approval.

If you have any questions, please contact Katie Brooks at (703) 993-4121 or kbrook14@gmu.edu. Pleaseinclude your project title and reference number in all correspondence with this committee.

GMU IRB Standard Operating Procedures can be found here: https://rdia.gmu.edu/topics-of-interest/human-or-animal-subjects/human-subjects/human-subjects-sops/

This letter has been electronically signed in accordance with all applicable regulations, and a copy is retained within George Mason University IRB's records.

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Biography

Bryndan Lindsey was born in Los Angeles, California, but grew up in the U.K., graduating from Leeds Grammar School in North Yorkshire in 2009. He initially studied Communications at San Jose State University before transferring to George Mason in 2011 and changing major to Athletic Training. He received his Bachelor of Science in 2014, and at the same time passed his Board of Certification examination to become a certified Athletic Trainer. He received his Master of Science from George Mason University in 2017 after two years of focusing on concussion epidemiology research and also branching out to study the effects of gait on joint load in knee osteoarthritis. Now, he is a PhD candidate in Education Specializing in Kinesiology at George Mason University. His primary focus has been to continue the research line he started during his Master degree to understand the effects of gait modification on knee abduction moment in patients with knee osteoarthritis, to which this dissertation is dedicated. He has also branched out into other areas of research in the past few years including assessing the accuracy of commonly used physiological measures in exercise science and the effects of the COVID-19 pandemic on physical activity.