

**EXAMINING LOWER LEG BIOMECHANICS DURING
TOE-IN AND TOE-OUT WALKING IN PEOPLE WITH MEDIAL
COMPARTMENT KNEE OSTEOARTHRITIS**

by

Jesse M Charlton

BPEC, Douglas College, 2014

A THESIS SUBMITTED IN PARTIAL FULFILLMENT OF THE
REQUIREMENTS FOR THE DEGREE OF

MASTER OF SCIENCE

in

THE FACULTY OF GRADUATE AND POSTDOCTORAL STUDIES

(Rehabilitation Sciences)

THE UNIVERSITY OF BRITISH COLUMBIA
(Vancouver)

May, 2017

© Jesse M Charlton, 2017

Abstract

Introduction:

Knee osteoarthritis is a common and painful disease, and is one of the leading causes of disability in Canada. It is thought that one of the primary causes of disease progression is excessive knee joint loading. Thus, conservative treatments have aimed to reduce knee joint load, predominantly targeting the knee adduction moment – a valid proxy of tibial joint load distribution. Toe-in and toe-out walking are two such strategies which have proven effective in the short term at reducing the knee adduction moment, but still require longer-term assessment and a more thorough understanding of the ancillary effects at joints other than the knee prior to clinical implementation. The ankle joint in particular may be subjected to altered biomechanics during toe-in and toe-out walking.

Purpose:

The purpose of this thesis was to examine ankle biomechanics during toe-in and toe-out foot rotations in those with medial compartment knee osteoarthritis.

Methods:

Fifteen individuals with medial compartment knee osteoarthritis were recruited. In a single session, participants were instructed to walk in four conditions guided by real-time biofeedback of performance: 1) toe-in (+10°), 2) neutral (0°), 3) toe-out (-10°) and 4) toe-out (-20°). Ankle kinematics, kinetics and muscle activity were examined during over-ground walking.

Results:

Toe-out walking exhibited an increase ($p=0.011$) in peak ankle eversion compared to toe-in walking, while toe-in walking exhibited an increase in ankle inversion at heel strike ($p<0.001$) and frontal plane ankle angle excursion ($p<0.01$) compared to toe-out walking. No differences in

ankle kinetics were observed. Toe-in walking exhibited a significant increase ($p=0.03$) in lateral gastrocnemius root mean square muscle activity compared to 20° toe-out. Lastly, toe-in walking was rated as most difficult and least preferred, while neutral walking was rated as least difficult and most preferred.

Conclusions:

Toe-in and toe-out walking are effective strategies for reducing knee joint load. However, altered ankle biomechanics may increase the risk of adverse events for some individuals. Longer-term studies are required to properly assess the relationship between lower extremity discomfort, ankle biomechanics and altered foot rotation in those with knee OA.

Lay Summary

Knee osteoarthritis is a painful and disabling disease often ending in joint replacement surgery. Conservative treatments (those not involving drugs or surgery) are being examined with the goal of slowing disease progression and improving symptoms. Toe-in and toe-out walking (turning the feet in or out) are potentially beneficial conservative treatments due to their ability to reduce the forces which pass through the inner side of the knee. However, the effects of these walking patterns on joints other than the knee are not known. Our findings indicate that, in addition to knee biomechanics, ankle biomechanics differ between toe-in and toe-out. Also, it was observed that discomfort did not differ between walking patterns, while toe-in walking was considered the most difficult and least preferred out of the four conditions examined. Longer-term studies are required to determine whether the observed changes to ankle biomechanics are associated with lower extremity discomfort.

Preface

This thesis contains the work of a research study conducted by Jesse Charlton under the supervision of Dr. Michael Hunt with the guidance of Dr. Gillian Hatfield and Dr. Jordan Guenette. The study design, data analysis, and writing of the manuscript were primarily the work of the candidate. Data collection was performed by the candidate with assistance from Natasha Krowchuk. A selection of work from this thesis will be submitted for publication in a relevant peer-reviewed journal.

Ethical approval for this proposed research study was provided by the University of British Columbia Clinical Research Ethics Board on February 15, 2016. The approval code is H16-00169.

Table of Contents

Abstract	ii
Lay Summary	iv
Preface	v
Table of Contents	vi
List of Tables	viii
List of Figures	ix
List of Abbreviations	x
Acknowledgments	xi
Chapter 1: Background	1
1.1 What is Knee Osteoarthritis?.....	1
1.2 Knee Joint Anatomy and Function.....	3
1.3 Epidemiology of Knee OA.....	4
1.4 Etiology of Knee OA.....	6
1.4.1 Risk Factors of Knee OA.....	6
1.5 The Biomechanics of Knee OA	9
1.5.1 The Implications of Joint Loading in Knee OA	10
1.5.2 The Knee Adduction Moment	11
1.5.3 The KAM and Disease Severity	13
1.5.4 The KAM and Disease Progression.....	15
1.5.5 The KAM and Pain.....	18
1.6 Treatment of Knee OA.....	19
1.6.1 Gait Modification	21
1.6.2 Ancillary Effects of Foot Rotation Modifications	26
1.7 Thesis Rationale, Objectives and Hypotheses.....	28
1.7.1 Thesis Rationale	28
1.7.2 Objectives	30
1.7.3 Hypotheses.....	30
Chapter 2: Introduction	32
Chapter 3: Methods	35
3.1 Study Design	35
3.2 Study Participants.....	35
3.2.1 Inclusion Criteria	36

3.2.2 Exclusion Criteria.....	36
3.2.3 Sample Size	37
3.3 Instrumentation.....	38
3.4 Data Collection.....	40
3.4.1 Initial Participant Preparation.....	41
3.4.2 Natural Over Ground Walking Trials.....	42
3.4.3 Gait Modification – Treadmill Training.....	42
3.4.4 Gait Modification – Over Ground Walking Trials	45
3.4.5 Self-Reported Assessment of Modified Gait.....	46
3.5 Data Analysis	46
3.5.1 Stride Selection.....	47
3.5.2 Kinematic Data	47
3.5.3 Kinetic Data	50
3.5.4 EMG Data.....	50
3.5.5 Statistical Analysis	52
Chapter 4: Results.....	54
4.1 Participant Demographics	54
4.2 Spatiotemporal Outcomes	56
4.3 Kinematic Outcomes	56
4.4 Kinetic Outcomes.....	60
4.5 EMG Outcomes.....	63
4.6 Patient Reported Outcomes.....	66
Chapter 5: Discussion.....	68
5.1 Interpretation of Findings.....	69
5.2 Limitations	77
5.3 Clinical Implications	80
5.4 Future Directions.....	82
Chapter 6: Conclusion.....	85
References.....	88

List of Tables

Table 3.1: List of outcome measures	52
Table 4.1: Demographic, questionnaire and radiographic data	55
Table 4.2: Spatiotemporal data	56
Table 4.3: Kinematic data	58
Table 4.4: Kinetic data	61
Table 4.5: Electromyographic data	64
Table 4.6: Patient reported data	67

List of Figures

Figure 1.1: Radiographic presentation of knee OA	2
Figure 1.2: The external knee adduction moment	12
Figure 1.3: Foot rotation	22
Figure 3.1: Marker placement.....	39
Figure 3.2: Wireless electrode placement.....	40
Figure 3.3: Foot placement on the protractor.....	44
Figure 3.4: Treadmill walking set up.....	45
Figure 3.5: Illustration of the segment coordinate systems	49
Figure 4.1: Sagittal and frontal plane ankle angle ensemble averages	59
Figure 4.2: Frontal plane ankle and knee moment ensemble averages.....	62
Figure 4.3: Muscle activation ensemble averages	65

List of Abbreviations

ANOVA	Analysis of variance
ASIS	Anterior superior iliac spine
EMG	Electromyography
GRF	Ground reaction force
Ht	Height
Hz	Hertz
KAM	Knee adduction moment
KFM	Knee flexion moment
KL	Kellgren and Lawrence
LG	Lateral gastrocnemius (m)
MG	Medial gastrocnemius (m)
MRI	Magnetic resonance image
MVIC	Maximum voluntary isometric contraction
Nm/kg	Newton metre per kilogram
NRS	Numeric rating scale
NT	Natural
OA	Osteoarthritis
OR	Odds ratio
PL	Peroneus longus (m)
RMS	Root mean square
SENIAM	Surface Electromyography for the Non-invasive Assessment of Muscles
SO	Soleus (m)
TA	Tibialis anterior (m)
TI	Toe-in
TKA	Total knee arthroplasty
TO	Toe-out
WOMAC	Western Ontario and McMaster University Osteoarthritis Index

Acknowledgments

First, I must thank Dr. Michael Hunt; you saw something in me I did not know I had and pushed me to achieve things I did not think I was capable of. You had great patience, but most of all, you always had my best interests in mind. For this I cannot thank you enough. Also, thank you to Jordan for taking me in and making me feel so welcome!

Second, I cannot go without thanking my colleagues in the MAB Lab. Natasha, you most certainly keep this ship afloat and are the rock of our lab. Gill, you have some impressive patience, thanks for being there whenever I needed some guidance. Judit, desk buddy, I could always trust your judgement and advice, thanks for sharing it so often. Chris, you taught me a great deal, but also pushed me to step out of my comfort zone. Connor, no question you helped keep me sane. Calvin, Angelo and JF, I am looking forward to the years ahead. I am proud to be able to call you all friends!

Lastly, I could not have made it to where I am today without the unconditional love and support from my parents. Thank you from the bottom of my heart for everything you do for me. I must also thank my wonderful partner Kylie. For all you do, all you put up with, and for being my biggest cheerleader. Thank you.

Chapter 1: Background

1.1 What is Knee Osteoarthritis?

Arthritic diseases are the most common cause of disability in Canada, most often manifesting as osteoarthritis (OA) (Bombardier et al., 2011). Osteoarthritis is a chronic and progressive synovial joint disease, where damage to articular cartilage goes unrepaired, ultimately leading to the degradation of the articular cartilage and subchondral bone within the joint (Brandt et al., 2008; Lane et al., 2011). This disease has the potential to lead to significant reductions in quality of life and limitations in daily function, while placing high demand on health care systems (Bombardier et al., 2011; Salaffi et al., 2005; White et al., 2015).

The knee joint is comprised of the patellofemoral and tibiofemoral joints – both of which can be further characterized into medial and lateral compartments. The knee is also the weight bearing joint most commonly affected with OA in the body (Lawrence et al., 2008). Within the tibiofemoral joint, the medial compartment is typically most affected (Dillon et al., 2006), usually resulting in localized pain, joint stiffness, swelling and muscle strength deficits (Bennell et al., 2008; Hunter et al., 2009; Hunter et al., 2006). The high prevalence of knee OA may be due to the fact the knee is a load bearing joint, which endures chronic mechanical stressors in daily living leading to the breakdown of cartilage and subchondral bone. In a healthy joint, these mechanical stressors and damage to the articulating surfaces are attenuated by constant biological repair mechanisms which maintain cartilage integrity. However, under specific circumstances, these stressors can overwhelm the cartilage repair process, causing net cartilage degradation, contributing to the eventual onset of OA.

Structurally, knee OA presents with articular cartilage loss, osteophytic bone growths on the perimeter of the joint space and subchondral bone maladaptation. Notably, common patient reported outcomes like pain are not necessarily indicative of an individual's structural disease state (Barker et al., 2004). That is, the relationship between structural changes and symptoms is still not clearly understood, demonstrating the complex nature of this disease. Due to this, knee OA is often diagnosed through the presence of both the aforementioned symptoms and structural severity (Figure 1.1), as graded using the Kellgren and Lawrence (KL) grading system (Kellgren & Lawrence, 1957).



Figure 1.1: Radiographic presentation of knee OA. A posteroanterior standing semi-flexed radiograph of knee joints, displaying bilateral structural signs of knee osteoarthritis. Note the significant joint space narrowing and prominent osteophytes on the margins of the joint.

Treatment strategies for knee OA have traditionally focused on pharmacological and surgical methods (Bombardier et al., 2011; Dieppe et al., 1999), which may be useful in managing symptoms or returning some function to the patient, but are also associated with significant potential side effects (Dieppe et al., 2004; Nilsson et al., 2009). Additionally, these treatments likely do not address a predominant cause of knee OA initiation or progression; that is, mechanical loading. As a preliminary strategy, conservative treatments (non-operative and non-pharmacological) are becoming more prevalent in the literature. This group of treatment strategies aims to improve pain and function, and slow disease progression all while reducing the economic burden placed on the individual and healthcare system (Reeves & Bowling, 2011).

1.2 Knee Joint Anatomy and Function

The knee joint is comprised of articulations between the femur, tibia and patella. The articulation between the distal femur and proximal tibia is composed of two compartments (medial and lateral), as is the articulation between the patella and distal anterior surface of the femur. For the purpose of this thesis, the knee joint will refer to the tibiofemoral joint only. The knee joint predominantly moves in the sagittal plane (flexion/extension), with significantly less motion in the frontal (abduction/adduction) and transverse planes (internal and external rotation).

The tibial plateau provides a relatively flat bony surface for the rounded femoral condyles to articulate. Atop the tibia, the menisci create a shallow cup of fibrocartilage with a rimmed perimeter. The menisci deepen the articulation in which the femoral condyles

move, assisting in joint stability and distribution of forces to reduce compressive stress on the tibia. Two centrally located cruciate ligaments, as well as a number of peripheral ligaments and tendons act to further increase joint stability by opposing unwanted secondary joint motions.

The articulating surfaces of the tibia and femur also have a thin layer of avascular hyaline cartilage consisting primarily of type II collagen matrix and proteoglycans arranged in distinct layers (Sophia Fox et al., 2009). These layers provide two major functions: to facilitate smooth joint motion and to attenuate force by distributing it over a greater surface area (Sophia Fox et al., 2009). The integrity of the most superficial layer of cartilage is vital to the conservation of the deeper matrix and the structures force attenuating properties (Sophia Fox et al., 2009). Chondrocytes are responsible for the upkeep of the matrix through the maintenance of equilibrate cartilage breakdown and synthesis. Though chondrocytes can repair the matrix to some degree, significant damage such as that associated with knee injuries will likely overwhelm this process. As mentioned above, damage of this nature that is left unrepaired will likely result in the beginning of osteoarthritic changes within the knee joint.

1.3 Epidemiology of Knee OA

Osteoarthritis is a highly prevalent disease within the North American adult population (Bombardier et al., 2011; Murphy & Helmick, 2012). A 2011 report by the Arthritis Alliance of Canada indicates that 13% of Canadian adults (>20 years of age) have OA, with a 30 year projection estimating an increase to more than 25.6% (Bombardier et al., 2011). Furthermore, it is estimated that 1 in 100 Canadian adults experience or have

experienced moderate to severe pain resulting in limitations of daily activities due to OA (Bombardier et al., 2011). As age-related factors are implicated in the disease process, it is expected that the number of individuals with OA will continue to rise as our population ages, placing further demand on the health care system. Currently, the Canadian annual economic burden due to OA is estimated to total \$27.5 billion with a cumulative total cost of \$1,455.5 billion over the next 30 years (Bombardier et al., 2011). These direct and indirect costs could be reduced if effective preventative and early stage disease management strategies aimed at slowing the progression of OA are implemented.

As previously mentioned, the knee is the most commonly affected weight bearing joint, which is reflected in the most recent epidemiological data. Between 2007 and 2008, estimates of knee OA prevalence within the US population were 6.9% (13.7 million); this estimate rose to 7.3% (15.1 million) during a subsequent assessment in 2011 and 2012 (Deshpande et al., 2016). Notably, these estimates are of symptomatic knee OA, and the numbers of individuals with radiographic signs but no reported symptoms are likely higher still. Expectedly, knee OA prevalence estimates increased with each age category, the highest percentage being in those 65 years or older (Deshpande et al., 2016). Furthermore, across all age groups and ethnicities, females consistently made up the majority of those affected (Deshpande et al., 2016). However, over half of those with symptomatic knee OA are under the age of 65, lending to the importance of identifying effective treatment strategies to manage pain and slow disease progression in younger individuals suffering from the disease. One could speculate that doing so would reduce the number of individuals needing costly treatment later in the disease. However, it is certainly a difficult task to develop such a treatment, as the causal factors associated with disease initiation and

progression are not completely understood, and likely interact in highly individual and complex ways.

1.4 Etiology of Knee OA

Osteoarthritis can present as a primary or secondary disease, the causes of which are typically multi-factorial in nature and involve local and systemic factors which combine, creating complex etiologies (Sharma et al., 2006). Knee OA initiation specifically, is suggested to be highly influenced by shifts in the load bearing regions within the knee onto regions which have not adapted to withstand such loading (Andriacchi et al., 2004). However, it has been proposed that cartilage degradation is not solely involved, as all tissues of the joint may be implicated in the initiation of OA (Brandt et al., 2006). That is, the ligaments, tendons, muscles, synovium and the nervous system, in addition to articular cartilage, may initiate mechanical changes within the knee triggering a cascade that may eventually result in joint degradation. Said another way, the initiation and progression of OA can be viewed as a system involving the interaction of biological/biochemical, biomechanical and structural factors (Andriacchi et al., 2015; Hunter et al., 2006).

1.4.1 Risk Factors of Knee OA

Proposed risk factors for the initiation and/or progression of the disease include, but are not limited to: previous menisci or anterior cruciate ligament injury (Lohmander et al., 2007), obesity (Lementowski & Zelicof, 2008), quadriceps strength deficiencies (Slemenda et al., 1998), joint malalignment (Brouwer et al., 2007; Sharma et al., 2010) and excessive, unbalanced knee joint loading (Miyazaki et al., 2002). As noted earlier, these factors

commonly act together and may influence the existence or relevance of another, thus furthering the complex and individual nature of the disease.

Previous knee joint injuries are a significant risk factor for the initiation of knee OA. A traumatic event resulting in injury to the knee joint has the potential to initiate biomechanical alterations leading to OA later in life. For example, cartilage or ligamentous injuries, such as the aptly named “Unhappy Triad”, can result in significant damage to the meniscus and surrounding joint tissues. Consequently alterations will likely occur within the knee over time (Lohmander et al., 2007), focalizing joint load on different, un-adapted or damaged regions; a suggested pathway for the initiation of knee OA (Andriacchi et al., 2004). This notion is supported with longitudinal data from a number of studies (Ajuied et al., 2014; Blagojevic et al., 2010; Felson, 1990; Gelber et al., 2000; Hootman et al., 2003)

It is well established that obesity is one of the main risk factors for developing knee OA (Lementowski & Zelicof, 2008). Mechanically, during gait the knee is subjected to large amounts of force, commonly equal to or greater than three times body weight (Taylor et al., 2004). Therefore, modest increases in body weight can result in significant increases in force across the knee joint. Furthermore, in the presence of other risk factors (for example, previous knee injury), obesity raises the odds ratio (OR) of knee OA by over 150% (Coggon et al., 2001). Overall, a number of investigations have supported the claim that obesity has a significant role in elevating the risk of knee OA initiation (Blagojevic et al., 2010; Felson, 1996; Felson et al., 1988; Reyes et al., 2016).

Muscle strength deficits have also been implicated in knee OA initiation. Knee injuries may be a causal factor of eventual muscle weakness as they often result in disuse, immobilization and pain which can lead to muscle atrophy, commonly of the quadriceps

(Suter & Herzog, 2000). Though little data currently exists, two studies did identify associations between peak knee extensor strength and knee OA (Slemenda et al., 1997; Slemenda et al., 1998). Specifically, lower knee extensor strength was observed in those with knee OA compared to asymptomatic individuals (Slemenda et al., 1997). Longitudinal analysis of this cohort observed that women with knee extensor strength deficits at baseline were at greater risk for incident knee OA, while in men, strength deficits did not predict incident knee OA at the 31.3 month follow-up (Slemenda et al., 1998). Muscle atrophy likely contributes to knee OA development as well (Ikeda et al., 2005), which may be due to the relationship between less muscle mass and the presence of strength deficits (Frontera et al., 1991). Like obesity, muscle strength is a modifiable factor, furthering the possibility that muscle strengthening could elicit a protective benefit in regards to preventing disease initiation, though it is suggested to be relatively less beneficial in prevention of disease progression (Bennell et al., 2008).

As the mechanical environment within the knee is a key factor in knee OA (Andriacchi et al., 2004), it stands to reason that alignment of the joint could contribute biomechanically to the initiation or progression of the disease. Deviation from a neutral hip-knee-ankle angle, a measurement of frontal plane alignment of the lower extremity (more varus or valgus), influences the relative position of the knee joint centre and the ground reaction force (GRF), thus altering load distribution across the knee joint (Andrews et al., 1996; Sharma et al., 2001). Longitudinal investigations have supported this mechanism, as more varus static knee alignment has been associated with disease initiation and progression (Brouwer et al., 2007; Sharma et al., 2010; Sharma et al., 2001). Additionally, as structural disease severity progresses in medial knee OA, the medial compartment begins to narrow,

resulting in a more varus alignment and the possibility for further accelerating this mechanism.

Dynamic joint load likely affords a more applicable measurement regarding the mechanical environment during every day activities such as walking, compared to static measures. Walking, being a primary locomotor activity, has received significant attention as a means of evaluating joint loading patterns related to knee OA. Numerous investigations have reported strong relationships between higher dynamic joint load and knee OA disease severity. Though many are cross-sectional in design (Astrophen et al., 2008b; Erhart-Hledik et al., 2015; Sharma et al., 1998), growing longitudinal evidence continues to support the hypothesis that dynamic load is related to knee OA progression (Bennell et al., 2011; Chehab et al., 2014; Miyazaki et al., 2002).

1.5 The Biomechanics of Knee OA

The use of gait as a model to investigate knee OA is ubiquitous within current literature and Andriacchi and Mundermann have outlined a theoretical model of knee OA initiation and progression based on gait biomechanics. The model states that healthy cartilage will continually adapt to the demands placed on the joint, maintaining a homeostatic equilibrium between cartilage synthesis and degradation, so long as the loading occurs in familiar regions within the joint (Andriacchi & Mundermann, 2006). Recent data have supported this, as variations in regional knee loading correlate with variations in regional cartilage thickness (Erhart-Hledik et al., 2015). When kinematic changes occur, due to a surgical intervention (for example, meniscectomy) (Erhart-Hledik et al., 2016; Titchenal et al., 2016), load is shifted away from the previously adapted cartilage to un-adapted regions

which may not have the integrity to withstand the altered load, and subsequent degradation begins (Andriacchi & Mundermann, 2006). However, this is not universal, as procedures like high tibial osteotomies (HTO) do result in load shifts away from the medial compartment and may offer improvements in symptoms and function (Birmingham et al., 2009). Once knee OA is initiated, further loading of the diseased cartilage can drive progression. Moreover, data exists indicating the possible relationship between kinematic changes at the knee and symptomatic progression in those with knee OA (Maly et al., 2008). Therefore, a thorough understanding of how joint loading, joint motion, cartilage degradation and patient reported outcomes relate to knee OA is necessary to properly target conservative treatment strategies.

1.5.1 The Implications of Joint Loading in Knee OA

Early research into the role of joint loading in articular cartilage degradation utilized animal models to understand this relationship. Radin et al subjected rabbits to repetitive knee loading over six weeks with aims to determine the relative sequence of tissue degradation due to repetitive loading. The resulting evidence indicated that such repetitive loading initiated subchondral bone stiffening prior to articular cartilage damage, which was then followed by metabolic up regulation (Radin et al., 1984). The stiffening of subchondral bone may diminish the force attenuating properties those structures possess, resulting in the cartilage sustaining higher proportions of the applied load. A later study by Chen et al utilized cultured canine articular cartilage which was subjected *in vitro* to either rapid or slow applications of repetitive loading. Cartilage damage was found to increase with greater applications of load and frequency, resulting in early signs of osteoarthritic changes in the cultured cartilage (Chen et al., 1999). These investigations presented compelling evidence for the mechanically instigated structural damage that may precede OA initiation.

While these initial studies provided important information relating cartilage load and cartilage health, they are limited by their inability to equate loading *in vivo* with cartilage health outcomes. As a result, new methods of measuring joint loading, particularly in humans, needed development. The role of dynamic gait analysis to achieve this has received significant attention in the research literature.

1.5.2 The Knee Adduction Moment

The most common outcome quantifying dynamic loading within the tibiofemoral joint in those with knee OA is the external knee adduction moment (KAM), a valid (Zhao et al., 2007) and reliable (Birmingham et al., 2007) proxy for the distribution of load across the tibial plateau during walking. Specifically, this moment tends to adduct the tibia relative to the femur and must be counteracted by an internal knee abduction moment (Schipplein & Andriacchi, 1991) which is predominantly generated by medial compartment compression. The KAM is primarily the product of the frontal plane GRF and the perpendicular distance between this vector and the knee centre of rotation (i.e. moment arm) (Figure 1.2). A study in 2007 compared knee kinetics during walking via inverse kinematics and an implanted prosthesis in order to compare the internal (medial contact force) and external (KAM) loading environment of the knee (Zhao et al., 2007). In a single participant, the KAM was strongly correlated with medial contact force ($R^2=0.77$) and medial-to-total contact force ($R^2=0.69$) (Zhao et al., 2007). Therefore, we can be reasonably confident that increases in the KAM likely relate to increases in medial knee contact force, though other factors such as muscle forces are not accounted for. Nonetheless, the KAM is considered a useful outcome related to knee joint load, particularly in knee OA populations, and thus has been the focus of a number of investigations.

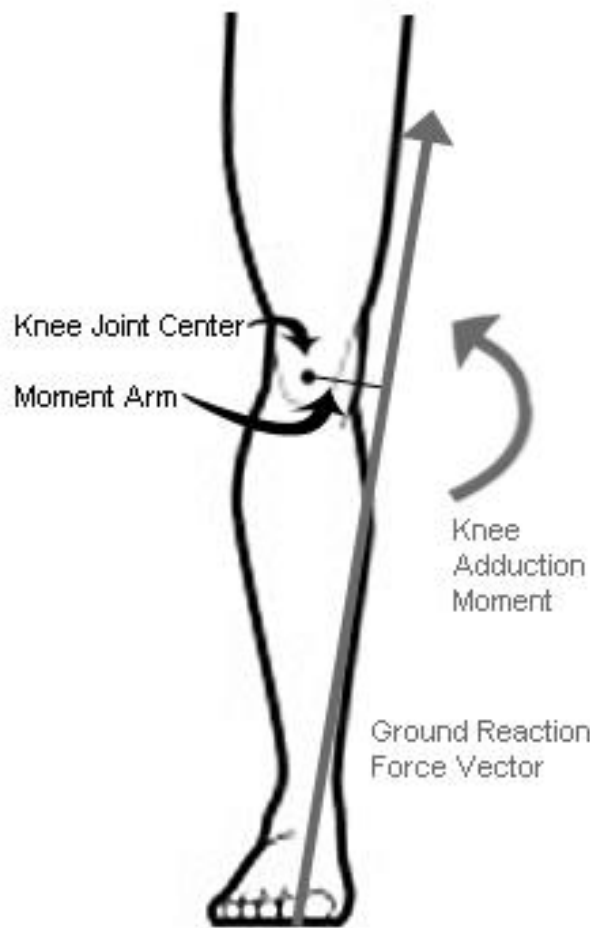


Figure 1.2: The external knee adduction moment. The GRF originates at the foot centre of pressure and is oriented approximately toward the total body centre of mass. It passes medially to the knee joint centre for most of the stance phase of gait, tending to adduct the tibia with respect to the femur in the frontal plane. The magnitude of the KAM is determined primarily by the length of the moment arm and the magnitude of the GRF.

In recent years, the external knee flexion moment (KFM) has received increasing attention as an important variable in disease progression in addition to the KAM. Multiple cross-sectional studies have reported significant associations between the peak KFM and disease progression. A study of 180 individuals with varying degrees of knee OA observed, through principle component analysis, that individuals with knee OA walked with a reduced

KFM compared to asymptomatic individuals (Aststephen et al., 2008a). This was replicated in a cohort of individuals with only moderate OA (Landry et al., 2007). A supporting investigation reported a more detailed description of this association (Erhart-Hledik et al., 2015). Individuals with less severe OA walked with a higher (2.18 %BW*ht) KFM compared to those with more severe OA (2.04 %BW*ht) (Erhart-Hledik et al., 2015). Additionally, regression analysis found lower peak KFM magnitudes, were correlated ($r=-0.151$) with posterior tibial cartilage thinning (Erhart-Hledik et al., 2015). It has been suggested, that abnormalities in the KFM have greater influence during early stages of the disease, while the KAM has greater influence in later disease states (Erhart-Hledik et al., 2015). This differentiation could assist in improving early detection of the disease, and assist in targeting interventions at different stages of the disease. However, as the focus of this thesis is on ankle biomechanics, further examination of the KFM is beyond the scope of this document.

1.5.3 The KAM and Disease Severity

The implication of the KAM in the disease process has largely been based on cross-sectional research over the past 30 years. Individuals with knee OA have been reported to exhibit a variety of distinct kinetic characteristics during gait. Though not universal, elevated KAM outcomes have been observed in those with symptomatic knee OA and include peak KAM (Baliunas et al., 2002), KAM impulse (Hall et al., 2017) and mid-stance KAM (Aststephen et al., 2008a; Landry et al., 2007).

A number of cross-sectional studies have been conducted with aims of determining how knee kinetics differs between individuals with and without knee OA. Sharma et al examined the relationship between the peak KAM and OA severity via structural and

metabolic markers in 54 individuals with symptomatic medial knee OA. Peak KAM magnitude was significantly higher in more severe (5.1 %BW*ht) compared to less severe knees (3.0 %BW*ht). After adjustment for age, sex and pain, peak KAM was found to strongly correlate with KL score ($r=0.61, 0.71$ for right and left knees, respectively) (Sharma et al., 1998). Specifically a strong negative correlation between joint space width (a marker of disease severity) and knee loading was observed; for every 1.0 %BW*ht of KAM increase (which equated to an approximate 29.4% increase in that cohort), joint space width was reduced 0.63mm (Sharma et al., 1998). Later, Baliunas et al. (2002) conducted gait analysis on 31 individuals with a range of disease severity and compared them to an equal number of age, weight and height matched controls. Though no discrete data were reported for the KAM, the authors indicated the presence of significantly higher peak KAM in those with knee OA compared to controls (Baliunas et al., 2002). Mundermann et al observed similar results when they evaluated lower extremity biomechanics in 42 patients with bilateral medial knee OA (Mundermann et al., 2005). The participants were grouped into asymptomatic, less severe (KL 1-2) and more severe (KL 3-4) knee OA. First peak KAM was reportedly 11.4% and 27.9% higher in more severe individuals compared to controls and those with less severe OA, respectively (Mundermann et al., 2005). More recently, using a similar stratification of severity, an investigation of 70 individuals indicated that the KAM was related to regional cartilage thinning within the knee joint. Peak KAM magnitude was 0.59 %BW*ht higher (equating to a 21.8% difference) in the more severe group compared to less severe, and was moderately ($R^2=0.26$) associated with medial-to-lateral cartilage thickness ratio, but only in the more severe group (Erhart-Hledik et al., 2015). These

investigations indicate that those in later stages of the disease present with elevated knee loading, which has the potential to further accelerate disease progression.

A pair of studies (Aststephen et al., 2008a; Aststephen et al., 2008b) also investigated the relationship between gait biomechanics and knee OA severity. Gait analysis was conducted on 121 individuals grouped into asymptomatic (n=61), moderate (n=60) and severe OA (n=60). One of the studies (Aststephen et al., 2008a) extracted discrete gait variables and observed that elevated mid-stance KAM was present in both OA groups compared to the asymptomatic group. The other study (Aststephen et al., 2008b) conducted multivariate analyses to attempt to discriminate between the three severities of knee OA. All principal components of the KAM were found not to contribute to discrimination of any combination of asymptomatic, moderate and severe OA (Aststephen et al., 2008b). The discrepancy between the studies may be due to the differing statistical methods utilized.

Taken together, these cross-sectional studies suggest a possible link between increased KAM magnitudes and more severe structural disease. However, in order to more thoroughly understand the role knee kinetics have in structural disease progression, longitudinal studies must be considered.

1.5.4 The KAM and Disease Progression

Multiple longitudinal studies have investigated the role of knee joint loading and disease progression over time. A highly-cited study by Miyazaki et al followed a cohort of 106 individuals with medial knee OA over six-years in which radiographic disease severity was evaluated at baseline and follow-up. It was observed that those with and without disease progression exhibited average baseline KAM values of 6.1 %BW*ht and 4.0 %BW*ht, respectively. On average, individuals experienced 1.4mm of joint space width loss, this

change was most strongly correlated ($r=0.62$) with baseline KAM magnitudes (Miyazaki et al., 2002), compared to knee alignment ($r=0.41$), pain ($r=-0.37$) and baseline joint space width ($r=-0.25$). Further regression analysis determined that for every 1.0 %BW*ht increase (approximately 25%) in KAM, the risk of disease progression was 6.46 times greater (Miyazaki et al., 2002). These results directly support the cross-sectional work which related both KAM and knee alignment to disease severity (Sharma et al., 1998; Sharma et al., 2001). Furthermore, in 16 individuals with medial knee OA, baseline peak KAM magnitudes were found to correlate with measures of cartilage thinning at a five-year follow-up assessment (Chehab et al., 2014). Specifically, baseline peak KAM magnitudes were associated with femoral ($R^2=0.40$) and tibial ($R^2=0.41$) medial-to-lateral cartilage thickness ratio, indicative of greater thinning of the medial compartment cartilage (Chehab et al., 2014).

Bennell et al investigated KAM impulse, the area under the KAM-time curve ($\text{Nm}\cdot\text{s}/\% \text{BW}\cdot\text{ht}$), as it related to disease progression measured via magnetic resonance imaging (MRI) in 144 participants. The measurement of KAM impulse is valuable as it takes into consideration the time under which a moment acts. Individuals with higher, compared to lower, KAM impulse at baseline exhibited greater cartilage volume loss at the 12-month follow-up (Bennell et al., 2011). Interestingly, peak KAM and KAM impulse were not associated with bone marrow lesion progression or cartilage defects (Bennell et al., 2011). After adjustment for a large number of confounders (age, gender and BMI among them), a regression analysis determined that for a 1.0% $\text{Nm}\cdot\text{s}/\% \text{BW}\cdot\text{ht}$ increase (approximately 76.9% in this cohort) in KAM impulse a 29.2 mm^3 loss of tibial cartilage volume was predicted (Bennell et al., 2011). Work by Chang et al reported similar findings in a cohort of 204 individuals with medial knee OA over two years. Disease progression was determined in the

same manner, and investigators assessed bone marrow lesions, cartilage damage and regional cartilage thickness loss. Among a number of significant correlations, peak KAM and KAM impulse at baseline were both associated with tibial and femoral cartilage thickness loss ($\geq 5\%$) in multiple sub regions (β range: 1.25-12.16) (Chang et al., 2015). KAM impulse alone was also associated with bone marrow lesion progression (OR range: 1.52-3.29) (Chang et al., 2015), a contrasting result compared to the earlier reported findings (Bennell et al., 2011).

In further support of the relationship between higher knee loading and disease progression, Hatfield et al examined biomechanical predictors of disease progression (those who progressed to total knee arthroplasty (TKA)) over a 5-8-year period in 54 individuals with medial knee OA. Using principal component analysis, the authors reported increased overall KAM magnitude and decreased difference between early and mid-stance KAM magnitude in those that progressed to TKA compared to those that did not (Hatfield et al., 2015). This is evidence that those with a greater risk of disease progression exhibit gait patterns indicative of increased overall medial knee loads and reduced mid-stance unloading, increasing the duration under which the knee experiences higher loads.

Overall, fairly compelling evidence exists implicating higher dynamic knee load in OA pathogenesis. Though, in comparison to previously mentioned factors associated with OA (knee injuries, obesity, and static alignment), the dynamic loading environment of the knee is readily modifiable. Therefore, conservative treatments which aim to reduce the KAM are an important research and clinical objective. Thus, if treatment strategies can favourably modify the KAM, attenuating disease progression may be possible, which could delay the need for surgical or pharmacological interventions and benefit both the individual as well as

the health care system. Therefore, conservative treatments which aim to reduce the KAM are an important research and clinical objective.

1.5.5 The KAM and Pain

It is important to consider the entire disease state when discussing the characteristics of knee OA, particularly patient reported outcomes like pain or discomfort. Knee pain is the most common and debilitating of all symptoms in knee OA and is suggested to predominantly be of mechanical origin (Felson, 2005; Maly et al., 2008). Some aspects of disease progression, such as worsening of bone marrow lesions, a mechanically induced disease characteristic, could also increase the risk of pain occurrence (Felson et al., 2001). Thus, the relationship between knee pain and joint loading may have implications in how clinicians approach treatment.

A 2010 study by Henriksen et al demonstrated that experimental knee pain, induced via hypotonic saline injection to the infrapatellar fat pad of healthy participants can incite biomechanical alterations that reduce both frontal and sagittal plane knee moments (Henriksen et al., 2010). The reductions in KAM within the pain-induced healthy group were similar to the natural KAM magnitudes of the less severe ($KL \leq 2$) knee OA group (Henriksen et al., 2010). A follow-up investigation (Henriksen et al., 2012) in 137 individuals with symptomatic knee OA supported these findings. Those with less severe knee OA exhibited a negative relationship ($\beta = -0.167$) between pain intensity and peak KAM, indicating that lower KAM magnitudes were associated with greater pain (Henriksen et al., 2012). However, those with more severe OA ($KL \geq 2$) exhibited a slight positive relationship ($\beta = 0.081$), though with KAM impulse (Henriksen et al., 2012). An investigation by Hurwitz *et al* corroborated these findings. It was observed that individuals with knee OA who reported an increase in pain

over a two-week period exhibited significant decreases in KAM, while those who reported decreases in pain exhibited a nonsignificant trend towards increases in KAM (Hurwitz et al., 2000). These findings suggest that for those with less severe knee OA, the presence of pain may result in a protective feedback loop by altering the gait biomechanics of the individual in such a way that the KAM is reduced. The fact this relationship does not exist in those with severe knee OA may contribute to the elevated KAM magnitudes found in more severe cohorts, possibly leading to accelerated disease progression. Overall, these investigations suggest pain may have a protective effect on joint load though one can only speculate with this level of evidence.

1.6 Treatment of Knee OA

Three key treatment options have traditionally been proposed for those with OA: surgical interventions, pharmacological pain management and obesity reduction (Bombardier et al., 2011). With the exception of obesity reduction, these interventions are costly (Bombardier et al., 2011) and carry significant risks of side effects. A variety of surgical options are available to those with knee OA, particularly those who have reached end stages of disease (Richmond, 2013). A detailed description of these procedures is beyond the scope of this thesis; however, a brief list of common procedures is provided. Arthroscopic surgery may be a less invasive option, though it is predominantly indicated for the removal of loose cartilage bodies or the repair of meniscal tears as a result of disease progression (Richmond, 2013). High tibial osteotomies have been indicated for more active individuals with medial knee OA, and involve the insertion of a bone wedge into the proximal tibia (Richmond, 2013). In effect, this procedure restores some level of normal alignment within the knee, thus

resulting in a beneficial redistribution of knee load away from the medial compartment. Typically reserved for end stage disease and older individuals (>70 years of age), TKA is a significant surgery involving the replacement of the tibial plateau, femoral condyles, or (more commonly) both, with a synthetic joint surface. Patient satisfaction varies with TKA and a concern for a revision of the implant is present in younger patients opting for TKA, as the maximum lifespan of the implant is approximately 20 years (Richmond, 2013). However, this procedure has been generally successful in the short and long term (Ethgen et al., 2004; Nilsson et al., 2009).

Pain management may be another treatment arm for those with knee OA. A large variety of drug types exist and are commonly prescribed for those with knee OA (Vaishya et al., 2016). Non-steroidal anti-inflammatory drugs (i.e. Ibuprofen), acetaminophen (Paracetamol) and even opioid drugs, among many others are used to manage the symptoms of osteoarthritis. However, side effects and complications are a risk when using these drugs and their use should be considered carefully (Dieppe et al., 2004; Vaishya et al., 2016). Furthermore, the possibility of increasing joint load may be another concern when using pain reducing medication (Schnitzer et al., 1993).

Non-pharmacological and non-surgical options exist as well. Among generalized physical therapy and exercise aimed at muscle strengthening and weight loss, gait modification offers an attractive conservative approach to treating knee OA progression, with the potential to alter both joint biomechanics as well as pain, and is the focus of this thesis. Gait modification can involve many different strategies (Simic et al., 2010) which take advantage of different mechanisms to achieve a similar goal. These strategies have garnered

significant attention, due to their relative ease of implementation, low cost and effectiveness (Simic et al., 2010).

1.6.1 Gait Modification

Several gait modification-based interventions have been examined for their ability to reduce KAM magnitudes in people with knee OA. Typically, such approaches centre on indirectly reducing KAM by changing one or both of its primary component parts (moment arm or GRF). Crucially, the KAM is more strongly associated with the frontal plane moment arm about the knee joint than the peak frontal plane GRF (Hunt et al., 2006). This would suggest that alterations which predominantly function to reduce the knee frontal plane moment arm are likely more optimal and may provide a better value in KAM change for a given amount of patient burden.

A variety of differing modifications have been investigated including trunk lean (Simic et al., 2012), medial knee thrust (Fregly et al., 2007), and foot rotation (Lynn et al., 2008; Shull et al., 2013a) with wide ranging reductions in KAM magnitudes reported (Simic et al., 2010). Though these modifications have demonstrated favourable reductions of the KAM, they may not be equivalently feasible due to differences in comfort and ease of performance, or even aesthetics. Indeed, within the literature, changes in foot rotation have been the predominant method of gait modification for KAM reductions in people with knee OA (Simic et al., 2010), likely due to greater feasibility.

Toe-in (TI) and toe-out (TO) foot rotation are measured as the angle of the long axis of the foot with respect to the global coordinate system of the lab (Simic et al., 2013), and when combined with the line of forward progression of the body, are sometimes used to calculate foot progression angle (Figure 1.3). Both TI and TO walking act by translating the

GRF vector closer to the centre of the knee joint via the lateralization of the centre of pressure of the foot (Chang et al., 2007), thus reducing the moment arm of the KAM (Reeves & Bowling, 2011). Typically, TO walking exhibits a reduction in late stance peak KAM, while TI walking can reduce early stance peak KAM (Reeves & Bowling, 2011). Though it is prudent to note that TO walking in particular, has the potential to increase early stance knee flexion moment magnitudes as well (Jenkyn et al., 2008), which should be considered when assessing the total loading environment about the knee joint.

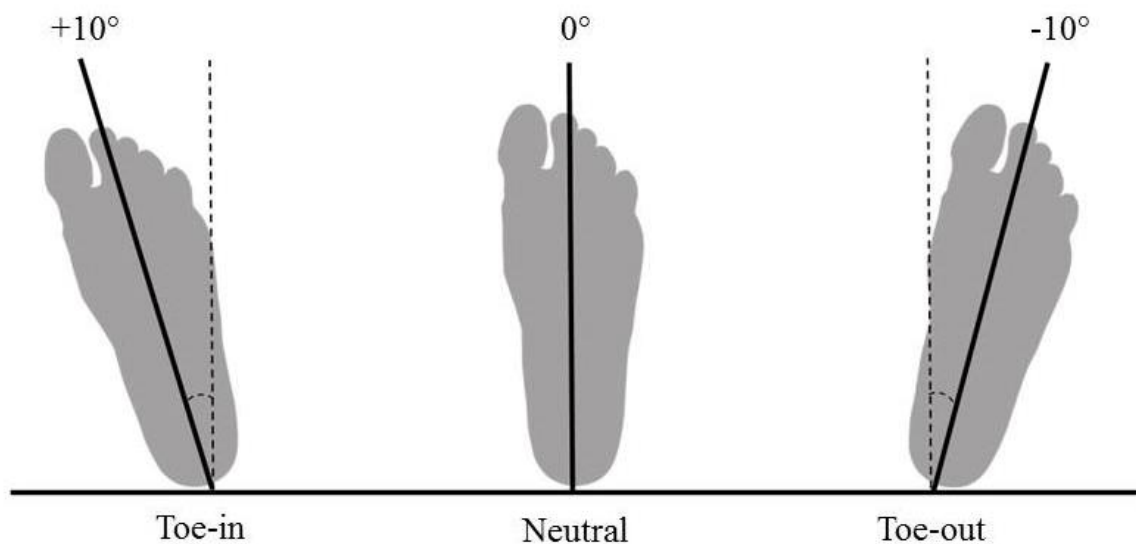


Figure 1.3: Foot rotation. An illustration of three foot rotations relative to the direction of walking. Toe-out foot rotation values are generally presented as negative, while Toe-in foot rotation values are typically presented as positive.

Cross-sectional data from healthy participants has demonstrated a significant inverse correlation between KAM magnitudes and TO angles (Andrews et al., 1996). Specifically, Andrews et al observed a low, but significant, inverse correlation ($r=-0.44$), wherein those with greater TO angles exhibited lower KAM values during late stance (Andrews et al., 1996). Another investigation in a healthy population observed significant decreases in late stance KAM and mediolateral shear force during TO walking (Lynn et al., 2008).

Specifically, during TO (mean foot rotation value of -40.2° , representing 40.2° in the direction of toe-out/external foot rotation) compared to normal (mean value of -18.5°) walking, group mean late stance KAM magnitudes were significantly reduced by 0.33 Nm/kg, a very large 94% reduction (Lynn et al., 2008), though likely due to the large TO angle performed. This is likely not a feasible change in a disease population. Additionally, no difference was observed in early stance KAM during TI (mean foot rotation value of $+9.1^\circ$, representing 9.1° in the direction of toe-in/internal foot rotation) or TO walking, while TI walking resulted in an increase in late stance KAM of 0.13 Nm/kg (31% in this cohort) compared to normal walking (Lynn et al., 2008).

Subsequent studies on the effect of single-session gait modification showed more modest reductions in KAM magnitudes due to foot rotation changes. Guo et al investigated a pain free population, observing a 0.9 %BW*ht reduction (39% in this cohort) in the group mean second peak KAM while walking with increased TO (mean value of -18.6°) compared to natural (mean value of -2.0°) walking (Guo et al., 2007). In follow-up to their study in healthy individuals, Lynn and Costigan examined the effect of TI, natural and TO foot rotation on knee loading during walking in individuals with medial knee OA. Toe-out walking (mean of -17.1°) resulted in group mean late stance KAM reductions in this cohort of 0.09 Nm/kg (22.5%) and 0.08 Nm/kg (20.5%) compared to natural foot rotation (mean value of -7.5°) and TI walking (mean value of 4.4°) respectively (Lynn & Costigan, 2008). No reductions, particularly during early stance KAM were observed while TI walking, with respect to natural walking (Lynn & Costigan, 2008). Therefore, in both healthy individuals as well as those with medial knee OA, TO walking can reduce the KAM, while the benefit of TI walking remains unclear.

A study by Simic et al followed previous research with a more expansive assessment of five different foot rotation angles during walking. Twenty-two individuals with symptomatic medial knee OA were instructed to walk with +10° TI, neutral, -10°, -20° and -30° TO, though participants reported difficulty reaching -30° (Simic et al., 2013). During TI walking (mean of +9.7°) compared to natural gait (mean of -4.5°) a 0.26 %BW*ht reduction (6.9% in this cohort) in group mean early stance KAM was observed, while late stance KAM and KAM impulse increased (22% and 5.7% respectively in this cohort) (Simic et al., 2013). Conversely, TO walking (mean value of -12.6° and -20.8°) compared to natural gait elicited a group mean increase (4.8% and 9.4% respectively) in early stance KAM while reducing late stance KAM by 0.33 %BW*ht (15.6%) and 0.75 %BW*ht (35.5%) respectively, in this cohort. Furthermore, the authors observed larger TO angles reduced the KAM impulse with a dose response effect (Simic et al., 2013). Another 2013 study supported the findings regarding TI walking, wherein modest TI walking (5° from natural) reduced early stance KAM by 13% in this cohort (Shull et al., 2013a). These data suggest that TI and TO walking result in favourably altered frontal plane loading patterns within the knee. However, these modifications must be investigated over extended periods of time to better determine their feasibility, in addition to the effects on patient reported outcomes.

Based on these previous investigations, initial research examining the implementation of multi-session gait modification programs provided the necessary confirmation that foot rotation was a viable conservative treatment for medial knee OA (Hunt & Takacs, 2014; Shull et al., 2013b). First, Shull et al performed a six-week TI gait retraining program in ten symptomatic individuals with knee OA. The authors utilized real-time haptic-feedback and a fading feedback design to guide the TI modification resulting in favourable alterations to

knee joint loading. From natural walking at baseline (mean value of -2.1°) participants achieved TI walking (mean value of $+5.1^{\circ}$) after the six-weeks of training (Shull et al., 2013b). At follow-up, the group mean early stance KAM was significantly reduced by 0.5 %BW*ht (16.1% in this cohort) compared to baseline. Furthermore, at the one-month retention visit, group mean early stance KAM maintained a reduction of 0.4 %BW*ht (14% in this cohort) compared to baseline. Measures of pain and function were also all reduced at both time points compared to baseline. Therefore, TI walking has the potential to be an effective form of gait modification, though anecdotal evidence suggests it may be more difficult to perform, compared to TO walking.

More recently, Hunt and Takacs conducted a ten-week TO gait modification program in 15 individuals with symptomatic medial knee OA. Real-time biofeedback in the form of a foot rotation trace projected on a screen was used to guide the TO modification. Participants were instructed to increase their TO by -10° (i.e. more TO), though on average an increase of only -6.7° was achieved by follow-up (Hunt & Takacs, 2014). A group mean reduction in late stance peak KAM of 0.30 %BW*ht (10.5% in this cohort) at follow-up was reported. Additionally, significant reductions in pain as measured by Western Ontario and McMaster University Osteoarthritis Index (WOMAC) (28.4% in this cohort) and numerical rating scale (NRS) (42.2% in this cohort) as well as function were exhibited after the ten-week program (Hunt & Takacs, 2014). Importantly, this study demonstrated that individuals with knee OA could feasibly perform this modification with relatively high confidence and reports of only moderate difficulty (Hunt & Takacs, 2014). These preliminary studies demonstrate evidence that TI and TO gait modification may be effective conservative treatment strategies for medial knee OA. However, these studies are limited by the fact they did not investigate

muscle activation patterns during their respective interventions. This is important as it does not take into consideration the influence muscle has on internal knee joint kinetics or the presence of elevated muscle activation which may indicate high demands placed on a given muscle due to the intervention. Furthermore, the effects of foot rotation alterations on joints other than the knee were not investigated. In particular, ankle joint biomechanics may be different due to a change in how the foot contacts the ground when walking.

1.6.2 Ancillary Effects of Foot Rotation Modifications

Foot rotation alterations have been associated with changes in activation patterns of some lower extremity muscles in both healthy populations and those with knee OA (Lynn & Costigan, 2008). Due to the implications muscle activation patterns likely have on knee joint loading (Schipplein & Andriacchi, 1991; Shelburne et al., 2006; Winby et al., 2009), it is logical that these patterns are also considered in joints other than the knee. Previous investigations of muscle activation patterns during foot rotation-based gait modifications are limited, and have only focused on the thigh and gastrocnemii muscles.

The aforementioned study by Lynn and Costigan examined the difference in medial versus lateral hamstring activation while performing TO, natural and TI walking patterns (-17.1° , -7.5° , and $+4.4^\circ$ respectively). Group mean medial to lateral hamstring activation ratio was observed to significantly decrease with TO (0.51) compared to normal walking (0.66) in this cohort, indicating a preferential activation of the lateral hamstrings (Lynn & Costigan, 2008). More recently, Rutherford et al investigated the effects of instructing individuals to increase their natural TO by -10° (more TO) on muscle activation patterns of the upper and lower leg (Rutherford et al., 2010). Seventeen individuals with symptomatic knee OA and 20 asymptomatic controls were compared. Those with knee OA increased their group mean TO

angle (-21.7°) from natural (-6.6°) while asymptomatic controls similarly increased to -21.6° from natural (-4.9°). Both groups within this cohort exhibited a shift of the gastrocnemius activation burst later into stance (Rutherford et al., 2010). Additionally, those with knee OA exhibited an increase in overall quadriceps activation as well as prolonged duration of activation (Rutherford et al., 2010). Consequently, modifications to foot rotation during walking may have significant effects on muscle activation requirements of the lower legs in those with knee OA. Apart from these investigations, little is known regarding muscle activation patterns of the lower leg, particularly the muscles which control the ankle and foot, and are therefore likely sensitive to changes in ankle and foot kinematics.

Alterations to foot rotation during the stance phase of walking likely influence ankle kinematics, though little is known in this regard. When the foot is rotated away from neutral during the stance phase of walking, the ankle is subsequently rotated and therein will undergo changes in joint motion as the foot contacts the ground differently. Frontal plane ankle motion in particular is likely influenced by TI and TO walking, as the frontal plane ground reaction force component is significantly different than during natural walking (Simpson & Jiang, 1999). Possible frontal plane ankle kinematic changes, particularly excessive eversion, may also cause foot or ankle discomfort. This was supported, though due to lateral wedges, wherein greater eversion (mean of -4.3°) of the ankle due to the lateral wedge was associated with more foot discomfort compared to (-3.3°) frontal plane ankle motion while walking without a wedge (Hatfield et al., 2016). Furthermore, a recent investigation observed that the presence of foot or ankle pain (particularly of the contralateral extremity), in those at risk of developing knee OA, was associated with an increased risk of developing knee symptoms and symptomatic knee OA (Paterson et al., 2016). Therefore,

possible foot or ankle pain brought on by foot rotation alterations may place individuals at risk of developing more knee symptoms in the contralateral limb. However, to the author's knowledge, there is no research to date specifically examining ankle biomechanics during TI or TO walking.

1.7 Thesis Rationale, Objectives and Hypotheses

1.7.1 Thesis Rationale

Gait modifications, specifically TI and TO walking, have elicited favourable knee joint load alterations for those with medial knee OA. However, considering the literature to date regarding this treatment strategy, a more thorough understanding of the biomechanical alterations that may occur at joints other than the knee is still needed. This is particularly important in order to identify possible adverse effects that could influence the successful implementation of TI and TO walking as a conservative treatment approach for medial knee OA.

Specifically, given that foot rotation is inherently linked to foot and ankle movement, a better understanding of foot and ankle kinematics during foot rotation modifications will provide relevant information on any potential negative consequences of this gait modification, despite known mechanical benefits at the knee. Further, with little data regarding loading at the ankle, it is imperative that ankle joint loading characteristics are investigated during TI and TO walking, considering that there likely are kinematic differences. Lastly, knowledge of muscle activation requirements to perform these movements will assist in the development of supplementary exercise programs to enable patients to perform these movements successfully.

No known research exists regarding ankle joint kinetics during TI and TO walking. This is problematic as alterations of foot position during walking will likely affect the relative position of the GRF and the ankle joint centre, albeit to a lesser degree than the knee. It has been suggested that TO walking could alter the frontal plane ankle moment (Wang et al., 1990). However, the consequences of alterations in ankle joint loading, beneficial or otherwise, are largely unknown. Accordingly, investigating ankle joint loading during TI and TO walking is warranted to illuminate possible areas of interest in longer duration clinical investigations.

Muscle activation of the lower leg has not been substantially investigated, specifically during foot rotation modifications. The sparse data that has been reported does indicate that differences in the gastrocnemii muscles may exist (Rutherford et al., 2010). With expected alterations in both lower leg kinematics and kinetics, it follows that activation patterns of other lower leg muscles will likely differ when TI or TO walking.

The present study is the first to investigate lower leg biomechanics during a variety of foot rotation walking patterns specific to conservative treatment of medial compartment knee OA. It provides relevant data that has the potential to meaningfully inform the clinical implementation of these walking patterns. Moreover, the following results may assist in identifying supplementary treatment modalities such as targeted lower leg muscle strengthening, that have the potential to improve TI and TO walking performance while minimising adverse effects.

1.7.2 Objectives

The primary objective of this investigation was to examine lower leg kinematics, kinetics and EMG during TI and TO walking patterns in those with symptomatic medial knee OA. Specifically, we sought to:

- i. Compare ankle kinematics during +10° toe-in, 0°, -10° and -20° toe-out walking in those with medial knee OA
- ii. Compare knee and ankle kinetics during +10° toe-in, 0°, -10° and -20° toe-out walking in those with medial knee OA
- iii. Compare lower leg muscle activation during +10° toe-in, 0°, -10° and -20° toe-out walking in those with medial knee OA

1.7.3 Hypotheses

The hypotheses of the present study were based on the limited data in existence regarding ankle biomechanics during walking with altered foot rotations and general biomechanical rationale. Specifically, we hypothesized:

- i. While walking with increased TO angles, participants will exhibit altered ankle kinematics compared to 0° and +10° TI.
 - a. Increased peak ankle eversion angle
 - b. Increased ankle eversion angle excursion
- ii. While walking with increased TO angles, participants will exhibit altered knee and ankle kinetics compared to 0° and +10° TI.
 - a. Decreased peak KAM and KAM impulse during the second half of stance (late stance); TI walking will elicit decreased peak KAM and KAM impulse during the first half of stance (early stance)

- b. Increased ankle eversion moment
- iii. While walking with increased TO angles, participants will exhibit altered lower leg root mean square (RMS) and peak muscle activity compared to 0° and +10°
TI.
 - a. Increased RMS and peak peroneus longus (PL) and lateral gastrocnemius (LG) muscle activity; TI walking will elicit increased RMS and peak tibialis anterior (TA), medial gastrocnemius (MG) and soleus (SO) muscle activity

Chapter 2: Introduction

OA is a painful, disabling disease and can result in significant reductions in quality of life (Salaffi et al., 2005). In Canada specifically, OA is a leading cause of long-term physical disability and the cause of significant economic impact (Bombardier et al., 2011). Nationally, more than 10% of adults are afflicted by OA with cumulative costs exceeding \$28 billion annually (Bombardier et al., 2011). Osteoarthritis commonly occurs in the patellofemoral and tibiofemoral joints, though within the tibiofemoral joint the medial compartment is typically more affected (Hinman et al., 2014). Given the expected dramatic rise in the prevalence of OA in the coming years, there is an urgent need for treatments that can effectively manage symptoms and slow disease progression, all while minimizing economic costs and side effects.

It is generally accepted that knee OA progression is influenced by excessive joint load (Andriacchi & Mundermann, 2006). The external knee adduction moment (KAM) in particular, is acknowledged as a surrogate of knee joint load distribution during walking (Zhao et al., 2007) and has received significant attention over the years, as its relationship with disease progression specific to medial compartment knee OA is well established (Bennell et al., 2011; Chang et al., 2015; Chehab et al., 2014; Hatfield et al., 2015). Notably, a 25% increase in KAM during walking has been associated with a 6.46 times greater risk of disease progression over six years (Miyazaki et al., 2002), while the area under the KAM curve (KAM impulse) has been associated with significant increases in tibial cartilage volume loss over a one year period (Bennell et al., 2011). Therefore, identification of load-normalizing treatments may have the potential to slow disease progression

One approach involves the altering of foot rotation during walking. External (TO) and internal (TI) rotation of the foot has been shown to influence KAM magnitudes during single-session gait modification sessions (Simic et al., 2013). Longer-term studies with multiple training sessions have advanced these findings. Shull et al conducted a six-week TI gait modification program resulting in a group mean reduction of the early stance KAM by 20% (based on mean TI increases of 7°), and clinically significant reductions in knee pain (Shull et al., 2013b). Hunt and Takacs conducted a ten-week TO gait modification program and reported a group mean reduction in late stance KAM of 10.5% with reductions in WOMAC pain and total scores (Hunt & Takacs, 2014). These studies provide initial evidence of the efficacy of TI and TO gait modification as a conservative treatment for knee OA that may provide beneficial biomechanical and clinical outcomes. However, altering foot rotation during walking, despite its positive influence on the knee joint, may have potentially deleterious effects on more distal joints of the lower leg, such as the ankle, which may detract from the overall benefits or require supplementary treatment approaches.

Foot rotation changes during walking are likely to be associated with ankle joint biomechanics. However, to our knowledge, no data currently exists examining biomechanical changes at the ankle joint during TI and TO walking in people with knee OA. If gait modification strategies such as foot rotation changes are to be implemented clinically, it is important to more thoroughly understand how these modifications affect areas of the lower limb apart from the knee. Furthermore, if overall lower limb biomechanics, including muscle activation requirements, are altered in comparison to natural walking, targeted muscle strengthening exercises may be useful as a supplementary treatment and as a means of improving performance.

Therefore, the purpose of the present study was to provide a comparison of ankle joint biomechanics and lower leg muscle activation patterns while performing TI and TO walking patterns by people with medial compartment knee OA. We examined four different foot rotation conditions known to produce changes in the KAM in people with knee OA; +10° TI, 0°, -10° and -20° TO. Our specific objectives were to measure ankle joint kinematics, kinetics and EMG of the periarticular ankle muscles while walking in the four conditions. It was hypothesized that walking with a TO pattern will exhibit greater peak ankle eversion angles, eversion excursion, eversion moments, and peroneus longus and lateral gastrocnemius RMS muscles activation; when compared to 0° and +10° TI walking. Meanwhile, TI walking would exhibit increases in peak and RMS muscle activity of the TA, MG and SO, compared to TO walking.

Chapter 3: Methods

3.1 Study Design

This was a within-subject, repeated measures study examining lower leg biomechanics during 10° TI (TI10), neutral 0° (ZR), 10° TO (TO10) and 20° TO (TO20) walking in individuals with medial compartment knee OA. All participants were screened for the study by the candidate as per inclusion and exclusion criteria listed below in sections 3.2.1 and 3.2.2, respectively. All eligible participants were issued a consent form prior to any data collection. The testing sessions occurred in a single testing session at the Motion Analysis and Biofeedback Laboratory, located within the University of British Columbia Hospital. Testing consisted of established biomechanical data measurement techniques capturing kinematics, kinetics and EMG during level over ground walking in four different foot rotation conditions in addition to natural (NT) self-selected walking. Data analysis was completed by the candidate.

3.2 Study Participants

All participants were initially screened via phone or email conversation by the candidate to determine their preliminary eligibility for the study. In-person, physical screening was then conducted to determine a prospective participant's eligibility for the study, namely natural foot rotation angle (section 3.2.2-2) and any balance or coordination issues that could affect their performance of the foot rotation conditions or walking on a treadmill. Participants were then required to undergo radiographic imaging of the knee (if a radiograph in the last 18 months was not available) to confirm medial knee OA. Study limb

selection was based on the knee which presented with predominantly medial knee OA. However, in the event that an eligible participant had bilateral knee OA on radiograph, the most symptomatic knee was chosen.

3.2.1 Inclusion Criteria

Participants were deemed eligible if they met the following criteria:

1. 50 years of age or greater
2. Radiographic evidence of medial knee OA with a KL grade ≥ 2 (graded by Dr. Michael Hunt and Natasha Krowchuk)
3. Knee pain on most days of the previous month
4. Comfortable with walking on a treadmill
5. Able to walk intermittently for 40 minutes

3.2.2 Exclusion Criteria

Exclusion criteria were predominantly aimed at ensuring participants did not have any comorbidities that could affect their walking performance. Criteria two below was aimed at excluding individuals who had a significant natural, self-selected TI or TO angle which could result in excessive difficulty or discomfort when attempting the foot rotation conditions at the other end of the foot rotation spectrum. Criteria seven was intended to reduce the risk of adverse effects during performance of the walking patterns being examined. Specifically, the exclusion criteria included:

1. Greater radiographic KL grade in the lateral compartment compared to the medial compartment
2. Foot rotation (TI or TO) during natural walking greater than $\pm 15^\circ$
3. Diagnosis of an inflammatory arthritic condition

4. History of TKA at any time, or arthroscopic knee surgery within the past six months
5. Recent use of corticosteroids
6. Requiring the use of a gait aid during walking
7. Self-reported foot pain
8. Cardiovascular disease that would prevent participation in a moderate intensity bout of exercise.
9. Non-English speaking

3.2.3 Sample Size

No previous investigations to the candidate's knowledge have directly compared ankle biomechanics across different foot rotations during walking. Therefore, studies which examined KAM differences during TI and TO walking of similar amounts to those used in the present study were utilized to inform a sample size calculation.

Previous research has reported variable effect sizes regarding the effect of TI and TO walking on peak KAM. Specifically, effect sizes based on early and late stance KAM decreases during foot rotation alterations from natural walking range from 0.23 to 1.55 (Guo et al., 2007; Shull et al., 2013a; Simic et al., 2013). Due to the widely varying effect sizes reported in the literature, and the aim of the present study to investigate ankle, as opposed to knee biomechanics, a conservative effect size was most optimal. Therefore, the average of the lowest two effect sizes was calculated (0.35); which was utilized in the sample size estimation for use in the repeated measures analyses of variance (ANOVA) tests. With an effect size of 0.35 ($\alpha = 0.05$, power = 0.80), it was determined that a minimum of 13 participants was necessary (G*Power 3.1.9.2) (Faul et al., 2007).

3.3 Instrumentation

Lower leg kinematic, kinetic and EMG data were collected synchronously from participants as they walked across a 10m level wooden walkway. Three-dimensional kinematic data were sampled at 100 Hertz (Hz) using a 14-camera motion capture system (Motion Analysis Corporation, Santa Rosa, CA). Forty-seven passive retroreflective markers (Figure 3.1) were initially affixed to the skin over various anatomical landmarks similar to a previously published marker set intended to measure similar outcomes (Hatfield et al., 2016). Bilaterally, markers were affixed to the anterior superior iliac spines (ASIS), anterior aspects of both thighs and shanks, lateral femoral epicondyles, lateral malleoli and the second metatarsal heads. A single marker was placed over the sacrum. Four rigid plastic plates with four markers each were affixed bilaterally over the lateral aspects of the thighs and shanks. A four-marker cluster was affixed bilaterally over the medial, lateral and posterior aspects of the calcanei (Figure 3.1, inset). Additionally, ten extra markers affixed bilaterally over the greater trochanters, medial femoral epicondyles, medial malleoli, and the first and fifth metatarsal heads were utilized during static calibration trials to estimate joint centres and establish marker orientations.

One floor mounted force platform (Advanced Medical Technology Inc., Watertown, MA) sampling at 2000Hz, collected GRF data for a single foot strike during each walking trial. Additionally, two photoelectric timers were placed at fixed locations along the walkway and were utilized to track walking velocity during walking trials.



Figure 3.1: Marker placement. Forty-seven markers were affixed to the skin where possible to reduce movement artifact. The inset depicts a close up of the marker cluster placed on the calcanei. Ten markers were removed prior to walking trials.

Lower leg muscle activity was measured using five wireless bipolar surface EMG electrodes (Delsys Inc., Natick, MA) sampling at 2000Hz. Electrodes were placed parallel to the muscle fibres over the midpoint of the muscle bellies of the medial gastrocnemius, lateral gastrocnemius, soleus, tibialis anterior and peroneus longus (Figure 3.2) in accordance with international guidelines (SENIAM) (Hermens et al., 2000). Electrode placement was validated via palpation and targeted isometric contractions. Prior to placement, each muscle site was marked, lightly shaved and cleaned using a 70% alcohol wipe.



Figure 3.2: Wireless electrode placement. Five wireless electrodes were affixed to the skin over the muscle bellies of five lower leg muscles. Tape was then utilized to secure the electrodes in place (not shown, for clarity).

3.4 Data Collection

Participants first completed a general medical history questionnaire to rule out any previously withheld exclusion criteria. Next, participants completed a four-question NRS to assess knee pain and restrictions to daily activity during the week prior to testing (0 = “no pain or restriction”, and 10 = “The most pain or restriction possible”). Thereafter, the WOMAC questionnaire (Likert version; 0 = none to 4 = severe) was administered in order to characterize each participant’s pain (score range: 0-20), stiffness (0-8) and physical function

(0-68) during common activities (total score: 0-96). The WOMAC was developed in part for, and validated in, knee OA populations (Bellamy et al., 1988). Higher scores are indicative of more pain and stiffness, and physical dysfunction. It is often utilized for the characterization of a sample population in knee OA studies, but also as a marker of change.

3.4.1 Initial Participant Preparation

Preparation began with the placement of the five EMG electrodes on the study limb as outlined previously (section 3.3). In order to both verify the location of the sensors, as well as provide a measure of relative muscle activation, participants completed four maximum voluntary isometric contraction (MVIC) motions, manually resisted by the candidate and according to established guidelines (Hermens et al., 2000). The motions utilized for the MVIC data collection included; 1) ankle eversion, 2) ankle dorsiflexion, 3) seated ankle plantarflexion and 4) standing single leg ankle plantarflexion. The first three MVIC motions were performed in high sitting with the knee joint at 90°; the fourth MVIC motion was performed while standing on one leg (study leg) and the hands resting on an adjacent table for balance with the study knee at approximately 0°. Each MVIC motion was performed first as a practice, followed by two recorded trials at maximal effort that lasted three seconds each. Ten to thirty seconds of rest were provided between MVIC trials to ensure the participant was recovered and prepared to provide maximal effort again. After each MVIC motion was completed, a single resting trial was conducted in which the participant was asked to lay supine and completely relax. Data from this trial provided a measure of ambient muscle activity (resting bias), theoretically in the absence of any voluntary activation.

Next, participants were fitted with 47 retro-reflective markers affixed according to the details provided previously (section 3.3). The heel marker group was further secured to the skin with tape in order to minimize the chance that these markers would fall off during the succeeding walking trials. Participant height and foot width were also recorded for use in 3D modeling. An initial static trial while standing on the force platform was conducted to determine joint centres and marker orientations, as well as to measure body mass. After the static trial, the ten extra markers (outlined above) were removed and a template trial was completed. The template trial permitted the display of segment kinematics in real-time. Thereafter, participants were directed to practice walking on the walkway in order to establish optimal start positioning and their starting step leg to ensure foot strikes would occur on the force platform (this intention was not revealed to the participant). All walking was performed barefoot.

3.4.2 Natural Over Ground Walking Trials

Participants were asked to walk across the platform in their natural walking pattern, and at a self-selected speed, until a minimum of five foot strikes were recorded. The average time to pass between the photoelectric timers among the five trials was calculated. All subsequent over ground walking trials were kept to within $\pm 5\%$ of this average time. Trials that were performed outside of this acceptable range were not analyzed.

3.4.3 Gait Modification – Treadmill Training

Thereafter, the treadmill was placed in the centre of the room and participants were provided with approximately 2-3 minutes to become accustomed to walking on the treadmill, while also determining the speed at which they felt most comfortable walking (speed was held constant across conditions). A custom-made protractor was then placed under the study

limb foot and aligned with the direction of the treadmill belt (Figure 3.3). The foot was aligned with the specific foot rotation angle required by the given condition and the motion capture-derived foot rotation angle magnitude in this static position was used as the target guideline during the treadmill training (Hunt et al., 2014). The guideline consisted of a single vertical line (Figure 3.4b) at the specific foot rotation magnitude required for the condition. Foot rotation angle was defined as the angle of the long axis of the foot (distal calcaneal marker to the second metatarsal head marker) in reference to the horizontal plane of the global coordinate system (the lab). Participants were familiarized with what the foot rotation angle signal looked like (Figure 3.4a) and the specific aspect of the signal corresponding with foot flat (Figure 3.4c) that they were to match with the guideline. Importantly, participants were instructed on how to manipulate the foot rotation angle signal in order to achieve the required target.



Figure 3.3: Foot placement on the protractor. The foot was placed on the protractor in line with the given condition's required foot rotation angle. The foot rotation angle magnitude while the foot was in this position was then used to determine the guideline position on screen to direct treadmill training.

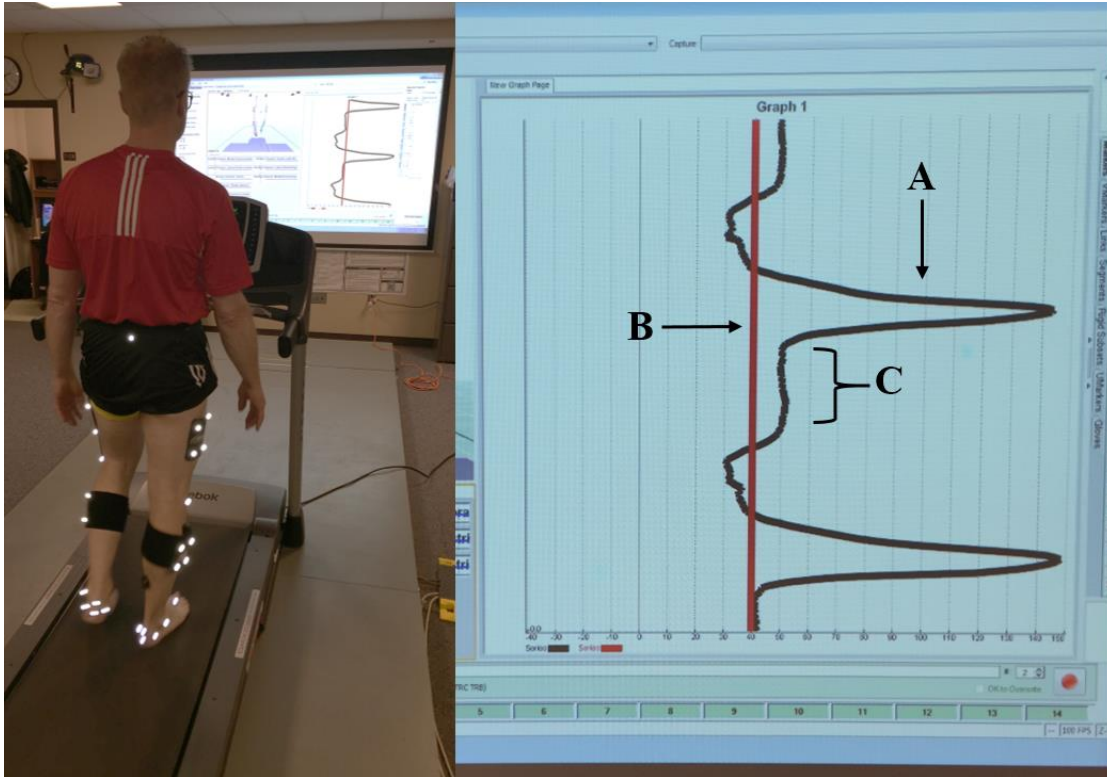


Figure 3.4: Treadmill walking set up. A participant walking on the treadmill with the foot rotation angle projected (a) on the screen in real time, the guideline (b) used to direct gait modification for each condition, and (c) the component of the signal during foot flat.

Each training condition consisted of five minutes of treadmill walking to practice with the biofeedback followed by walking trials on the walkway in which participants were asked to reproduce the practiced foot rotation (see section 3.4.4). The four conditions consisted of $+10^\circ$ TI, 0° , -10° and -20° TO, and were performed in a randomized order. The order was determined by random number generation, used to sort the order of the four conditions for each participant in ascending order based on the random numbers. The randomization was performed for all participants prior to the first data collection.

3.4.4 Gait Modification – Over Ground Walking Trials

Following treadmill training for each condition, participants walked in both directions along the level walkway and trials were recorded until a minimum of five walking passes

satisfied all of the following requirements: 1) clean strike on the platform with the study limb; 2) walking velocity within $\pm 5\%$ of their natural velocity; and 3) the foot rotation angle was deemed accurate by the candidate. In regard to the third condition, the candidate utilized the real-time biofeedback signal and guideline (defined above) as well as visual assessment of the marker trajectories of the foot segment to approximate the accuracy of the participant's foot rotation for a given condition. Verbal feedback was provided between walking trials to encourage a subsequent successful walking pass.

3.4.5 Self-Reported Assessment of Modified Gait

After each condition, participants were asked a series of questions on an 11 point NRS. Firstly, participants were asked to individually rate their ankle, knee and hip joint discomfort (0 = “no discomfort”, 10 = “most discomfort possible/imaginable”). Next, participants were asked to rate their overall self-perceived difficulty in achieving the given target angle for the condition (0 = “no difficulty”, 10 = “most difficulty possible/imaginable”). Upon conclusion of all conditions, participants were asked to select their “most preferred” and “least preferred” walking condition.

3.5 Data Analysis

All kinematic and kinetic data were normalized to a percent of the stance phase of gait, and EMG data were normalized to a percent of the total gait cycle to best illustrate the ensemble average. Stance phase was defined as the period between heel strike and toe-off of the study limb, while a gait cycle was defined as the period between a heel strike and the subsequent heel strike of the study limb.

3.5.1 Stride Selection

All successful walking trials (including natural walking trials) were analyzed as part of standard post-processing. After data were filtered and modeled (see section 3.5.2 and 3.5.3), the foot rotation angles during the period of foot flat were calculated for each trial. Foot flat was defined as the period between 15%-50% of the stance phase of a given stride, as previously suggested (Simic et al., 2013). All the trials were then sorted in ascending order according to each stride's difference from the four target condition values, regardless of when the trial was performed. For example, a trial with -12° of foot rotation would be sorted higher (less difference, therefore more accurate) than -15° , when determining trials to include for analysis of the TO10 condition. All trials were considered for all conditions, as the primary goal of the present study was to examine ankle biomechanics during specific foot rotations, not to evaluate a participant's ability to perform a given foot rotation immediately after training. After sorting, the five trials closest to a given condition's requirement were selected for further analysis and ensemble averaging. A cut off of $\pm 5^{\circ}$ of difference was utilized, and a given trial was only utilized for one condition; thus, not all conditions had five trials for analysis for all participants.

3.5.2 Kinematic Data

Marker trajectories were filtered using a fourth order low-pass Butterworth filter (cut-off frequency = 6 Hz) in Cortex (Motion Analysis Corp, Santa Rosa, CA). Data were then exported into Visual 3D (C-Motion Inc., Rockville, MD) for modeling of the foot, shank, thigh, and pelvis segments according to the joint coordinate system (Grood & Suntay, 1983). The rear-foot segment was defined by the lateral and medial calcaneal markers and the first and fifth metatarsal head. The shank segment was defined proximally by the medial and

lateral femoral epicondyles and distally by the medial and lateral malleoli. The thigh segment was defined by the medial and lateral femoral epicondyles, the ASIS and the hip joint centre (Bell et al., 1989). The pelvis segment was defined by the ASIS markers and the sacral marker. The orientation of the heel marker group, shank and thigh plate markers with respect to the segment definition markers were utilized to track motion of the specific segment during walking trials.

Segment coordinate systems are illustrated in figure 3.5. The origin of the rear-foot coordinate system was located at the midpoint between the medial and lateral calcaneal markers. The anterior-posterior axis was oriented to the midpoint of the first and fifth metatarsal markers, the medial-lateral axis was oriented from the medial to lateral calcaneal markers, and the vertical axis was orthogonal to the other two axes. The origin for the shank coordinate system was located at the midpoint between the femoral epicondyle markers. The vertical axis was oriented to the midpoint of the lateral and medial malleoli, the anterior-posterior axis was oriented orthogonal to the plane formed by the four segment definition markers, and the medial-lateral axis was oriented orthogonal to the other two axes. The origin for the thigh coordinate system was located at the hip centre. The vertical axis was oriented to the midpoint of the lateral and medial femoral condyles, the anterior-posterior axis was oriented orthogonal to the plane formed by the four segment definition markers, and the medial-lateral axis was oriented orthogonal to the other two axes. The origin of the pelvis segment was located at the midpoint between the two ASIS markers. The medial-lateral axis was oriented to the right ASIS marker, the vertical axis was oriented orthogonal to the medial-lateral axis, and the anterior-posterior axis was orthogonal to the medial-lateral and vertical axes.

All joint angles were computed as the distal segment relative to the proximal segment, with the exception of foot rotation. As previously outlined, foot rotation was calculated with respect to the horizontal plane of the global coordinate system. A Cardan XYZ sequence of rotations and six degrees of freedom were used for all biomechanical calculations (Grood & Suntay, 1983).

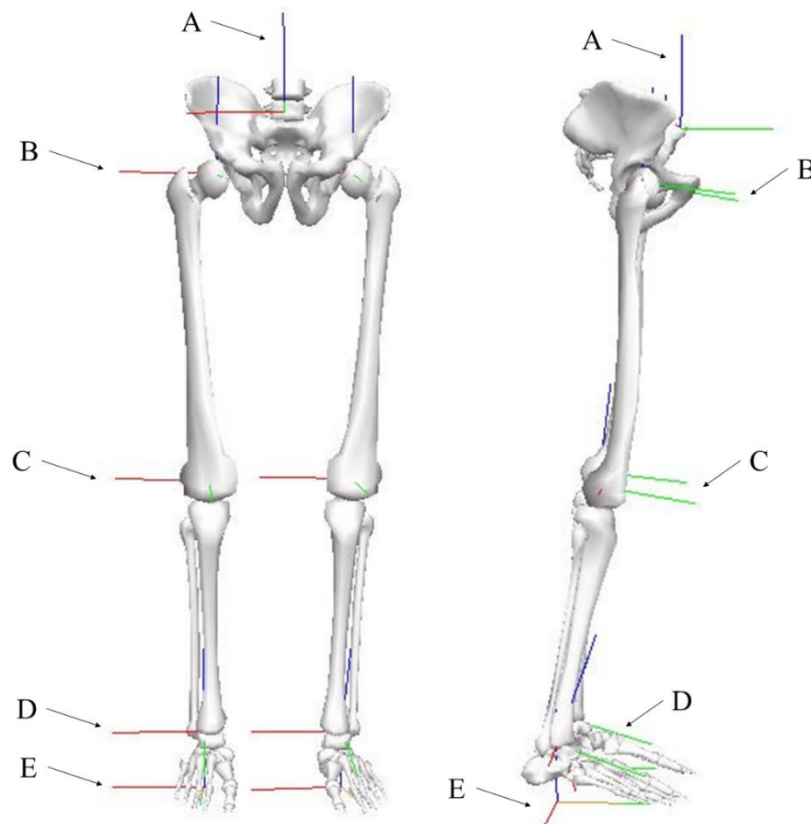


Figure 3.5: Illustration of the segment coordinate systems. a) pelvis, b) thigh, c) shank, d) foot segment coordinate system as represented in Visual 3D. e) represents the kinematic foot segment coordinate system which was projected onto the horizontal plane of the lab to normalize ankle joint angles during the static calibration trial.

Discrete outcome measures were extracted from the walking trials for each condition. Kinematic outcome measures included: ankle joint angles in the sagittal and frontal planes, and excursion in the frontal plane (defined as the difference between the frontal plane angle

at heel strike and the peak frontal plane angle during stance). Ensemble averages for the ankle sagittal and frontal plane angles were generated by averaging all time-normalized data from participants' trials for each condition.

Additionally, spatiotemporal outcomes were extracted including: gait velocity, stride length, and stride width. Gait velocity (m/s) was defined as stride length divided by stride time. Stride length (m) was defined as the distance between the proximal end position of the foot segment at ipsilateral consecutive heel strikes. Stride width (m) was defined as the mediolateral distance between the proximal end position of the foot at ipsilateral heel strike to the proximal end position of the foot at the next contralateral heel strike.

3.5.3 Kinetic Data

Raw GRF data were filtered with a fourth order low-pass Butterworth filter (cut-off frequency = 50Hz). External joint moments were computed within Visual 3D using inverse dynamics and were normalized to body mass (Nm/kg). External joint moments about the ankle and knee in the frontal plane were computed. Ensemble averages for ankle and knee moments were generated using the same methods utilized for kinematic data described above.

3.5.4 EMG Data

Processing of EMG data primarily occurred using a custom MATLAB script (Mathworks Inc., Natick, MA). Prior to determining peak MVIC magnitudes and computing outcome measures from the walking trials, all EMG data were filtered and quality checked. First, resting muscle activity was subtracted from all MVIC and walking trials. All EMG data were then converted from arbitrary units to volts, and the known 48 millisecond time delay between the sensors and the motion capture software was removed. Next, the signals were

bandpass filtered with a second order Butterworth filter from 20-500Hz. Thereafter, a frequency spectrum was plotted to quality check for noise in the signals. If noise was present in an EMG signal for a given muscle during a trial, that muscle's data for that trial were excluded. Finally, the signals were full wave rectified and again filtered with a fourth order low-pass Butterworth filter at 25Hz. This process resulted in rectified and filtered EMG data which were then time and amplitude normalized.

All walking trial EMG data were time normalized to a percentage of the gait cycle. In order to relate EMG data across participants, data from each muscle during each walking condition was calculated as a percentage of the respective muscle's peak MVIC magnitude (%MVIC). To perform this normalization, EMG data from each MVIC trial were averaged using a 100ms moving window, from which the maximum average magnitude within a given 100 millisecond window, for a given muscle, was taken as the peak MVIC for that muscle. This represented the maximum electrical activity detected under the electrode during the MVIC trials. Candidate inspection confirmed that the peak was due to muscle activity and not noise. Each walking trial was then amplitude normalized to the specific muscle's peak MVIC magnitude previously calculated.

The RMS and peak EMG magnitude for each muscle during each of the walking trials in a condition were averaged and exported. RMS was calculated by taking the sum of the squared individual amplitude points and dividing it by the time constant, followed by the square root of the sum. Peak EMG was then identified as the maximum signal magnitude of a muscle in a single trial. Ensemble averages were generated for each muscle in each condition.

A list of all outcome measures used in this study are summarized in Table 3.1.

Table 3.1: List of outcome measures. Biomechanical and patient reported outcome measures assessed during over ground walking trials.

Category	Outcome (units)
Spatiotemporal	Gait velocity (m/s) Stride length (m) Stride width (m)
Kinematics	Foot rotation angle during foot flat (°) Ankle Joint Sagittal plane angle at heel strike (°) Frontal plane angle at heel strike (°) Peak frontal plane angle during stance (°) Frontal plane angle excursion (°)
Kinetics	Ankle Joint Peak frontal plane moment (Nm/kg) Knee Joint Early stance peak KAM (Nm/kg) Late stance peak KAM (Nm/kg) Total KAM impulse (Nm/kg*s) Early stance KAM impulse (Nm/kg*s) Late stance KAM impulse (Nm/kg*s)
Electromyography	RMS LG, MG, SO, TA, PL muscles (%MVIC) Peak LG, MG, SO, TA, PL muscles (%MVIC)
Patient Reported Outcomes	Discomfort Ankle/foot, knee and hip (0-10) Difficulty Difficulty of performing foot rotation (0-10)

3.5.5 Statistical Analysis

Descriptive statistics were reported as means (standard deviation (SD)) across participants. All data were screened for normality and sphericity using Shapiro-Wilk tests (Ghasemi & Zahediasl, 2012) and Mauchley's test, respectively. If Mauchley's test was violated, a Greenhouse-Geisser adjustment was performed. To examine the within-subject differences in outcomes (see Table 3.1) across the walking conditions, repeated measures

ANOVAs were conducted with an alpha level set at 0.05. Pairwise comparisons were conducted utilizing a post-hoc Bonferroni correction across the four conditions ($k=6$). Statistical analyses were performed using the Statistical Package for the Social Sciences software (SPSS V. 22; IBM Corp., Armonk, NY).

Chapter 4: Results

4.1 Participant Demographics

Participant demographic data are reported in Table 4.1. Fifteen individuals were recruited for the study between September 2016 and April 2017. All participants had bilateral (73.3%) or unilateral (26.7%) medial compartment knee OA as determined by radiographic assessment. A total of 46.7% of participants exhibited radiographic signs of knee OA severity indicative of a KL score of 2 and 53.3% had a KL score of 3; no participant had a KL score of 4. During NT walking participants exhibited a mean (SD) of -7.7° (8.1°) TO foot rotation.

Table 4.1: Demographic, questionnaire and radiographic data. Mean (SD) data for all participants included in the study.

Outcome		(n=15)
Sex (M:F)		6:9
Age (years)		67.9 (9.4)
Height (m)		1.67 (10.7)
Body Mass (kg)		75.6 (15.0)
BMI (kg/m ²)		26.7 (3.7)
Laterality (bilateral:unilateral)		11:4
KL Score (n)	2	7
	3	8
	4	0
NRS (0-10)		2.3 (1.5)
WOMAC	Pain (0-20)	4.4 (2.2)
	Stiffness (0-8)	3.0 (1.3)
	Function (0-68)	15.4 (8.0)
	Total (0-96)	22.8 (10.1)
Natural foot rotation angle (°)		-7.7 (8.1)

BMI, body mass index; KL, Kellgren and Lawrence grading scale of osteoarthritis severity; NRS, numeric rating scale of pain during walking in the last week; WOMAC, Western Ontario and McMaster University Osteoarthritis Index (higher scores = worse pain, stiffness or function)

4.2 Spatiotemporal Outcomes

Spatiotemporal outcomes were examined for main effects across all conditions and are reported in Table 4.2. No significant main effects were observed between conditions for gait velocity ($p=0.985$) and stride length ($p=0.738$). However, a significant main effect ($p=0.022$) was observed for stride width. Pairwise comparisons revealed significantly increased stride width ($p=0.020$) in the TI10 condition compared to ZR.

Table 4.2: Spatiotemporal data. Mean (SD) for spatiotemporal data for all conditions.

Outcome	Condition			
	TI10	ZR	TO10	TO20
Gait Velocity (m/s)	1.22 (0.11)	1.22 (0.11)	1.23 (0.11)	1.22 (0.11)
Stride Length (m)	1.31 (0.14)	1.31 (0.14)	1.31 (0.15)	1.31 (0.14)
Stride Width (m)	0.15 (0.03)*	0.12 (0.03)	0.12 (0.03)	0.12 (0.03)

*significantly different than ZR condition. Results are considered significant if $p<0.05$.

4.3 Kinematic Outcomes

Kinematic outcomes were examined for main effects across all conditions and are reported in Table 4.3. A significant main effect ($p<0.001$) was observed for foot rotation angles and pairwise comparisons indicated all the conditions were significantly different from each other ($p<0.001$). A significant main effect ($p<0.001$) for sagittal plane ankle angles at heel strike was observed. Pairwise comparisons revealed the TI10 condition exhibited significantly increased dorsiflexion angles at heel strike compared to both the ZR ($p=0.004$) and TO10 ($p=0.014$) conditions. The TO20 condition also exhibited increased

dorsiflexion angles at heel strike compared to both the ZR ($p=0.003$) and TO10 ($p<0.001$) conditions.

A significant main effect ($p<0.001$) for frontal plane ankle angles at heel strike was also observed. Pairwise comparisons revealed the TI10 condition exhibited significantly increased inversion ankle angles compared to the ZR ($p=0.004$), TO10 ($p<0.001$) and TO20 ($p<0.001$) conditions. The TO20 condition also resulted in significantly decreased inversion angles compared to the ZR ($p=0.003$) and TO10 ($p=0.014$) conditions; while the ZR and TO10 conditions did not differ from each other. A significant main effect ($p<0.001$) was observed for peak frontal plane ankle angles during stance. Pairwise comparisons revealed the TI10 condition exhibited significantly decreased ankle eversion compared to the TO10 ($p=0.011$) and TO20 ($p=0.011$) conditions.

Lastly, a significant main effect ($p<0.001$) for frontal plane ankle angle excursion was observed. Pairwise comparison revealed the TI10 condition exhibited significantly increased frontal plane ankle excursion compared to the TO10 ($p=0.005$) and TO20 ($p<0.001$) conditions. Additionally, the ZR condition resulted in significantly increased frontal plane ankle angle excursion compared to TO20 ($p=0.004$), but not TO10. Ensemble average curves for sagittal and frontal plane ankle angles are presented in Figure 4.1.

Table 4.3: Kinematic data. Mean (SD) for foot rotation (°) and ankle kinematic (°) data for all conditions.

Outcome	Condition			
	TI10	ZR	TO10	TO20
Foot rotation angle (°)	+10.1 (1.6)*†‡	-0.1 (2.1)§†‡	-10.3 (1.3)§*†	-20.0 (0.9)§*†
Sagittal plane ankle angle				
At heel strike (°)	0.7 (2.9)*†	-1.4 (2.8)§†	-1.8 (3.4)§†	0.8 (3.0)*†
Frontal plane ankle angle				
At heel strike (°)	7.1 (4.1)*†‡	4.2 (4.7)§†	2.8 (3.7)§†	1.6 (3.5) §*†
Peak during stance (°)	-1.5 (3.1)†‡	-2.9 (3.7)	-3.5 (3.0)§	-3.9 (3.1)§
Excursion (°)	8.6 (2.3)†‡	7.1 (3.1)‡	6.3 (2.9)§	5.4 (5.6)§*

§significantly different than TI10; *significantly different than ZR; †significantly different than TO10; ‡significantly different than TO20; (+) values indicate toe-in, dorsiflexion and inversion, (-) values indicate toe-out, plantarflexion and eversion; Results are considered significant if $p < 0.05$.

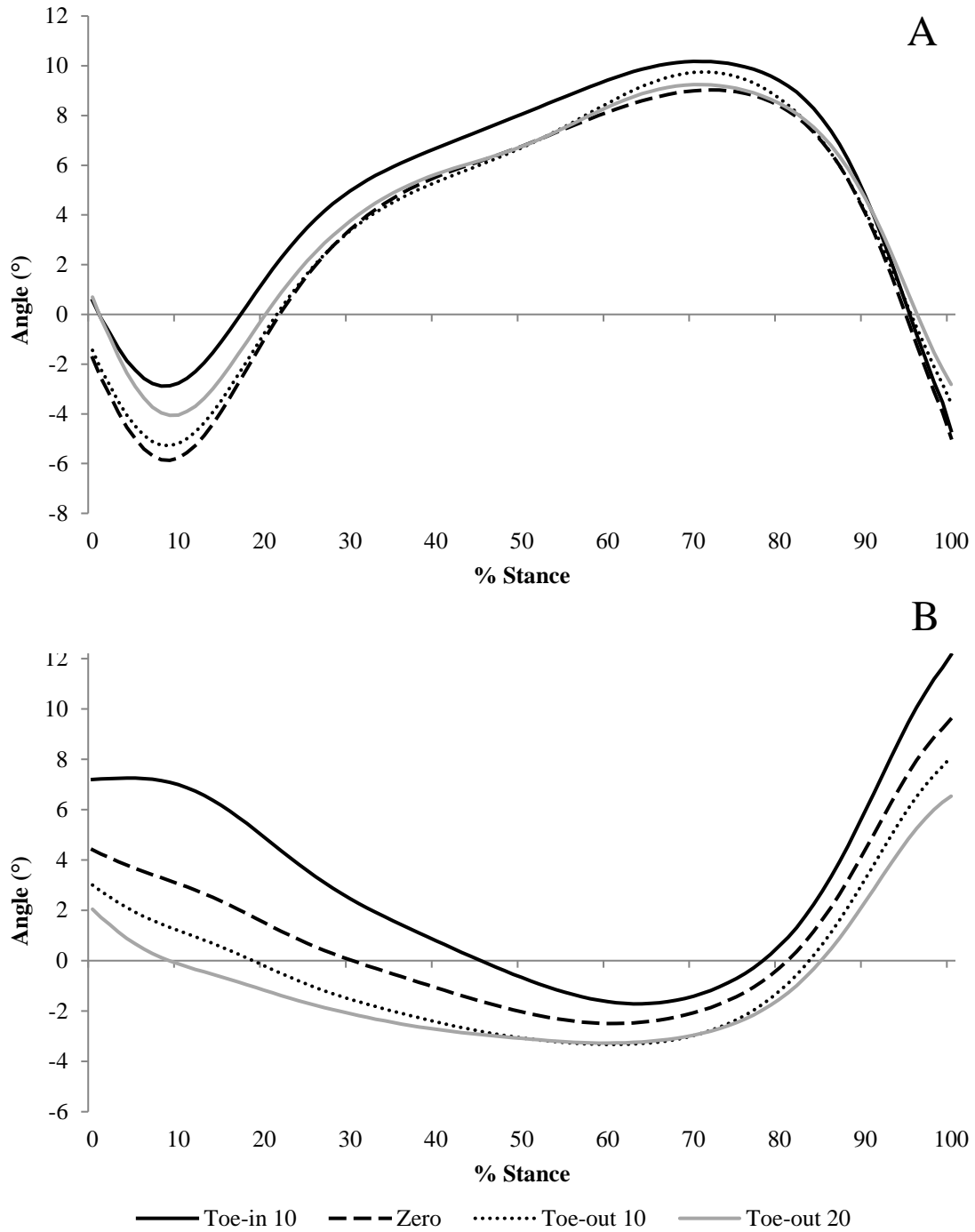


Figure 4.1: Sagittal and frontal plane ankle angle ensemble averages. The (a) sagittal and (b) frontal plane ankle angle curves are presented as a percent of stance. Positive values indicate dorsiflexion and inversion while negative values indicate plantarflexion and eversion.

4.4 Kinetic Outcomes

Kinetic outcomes were examined for main effects across all conditions and are reported in Table 4.4. A main effect ($p=0.641$) was not observed for peak frontal plane ankle moments. However, significant main effects for early ($p<0.001$) and late stance KAM ($p<0.001$) magnitudes were observed. Pairwise comparison revealed peak early stance KAM magnitudes were significantly different (highest: $p=0.037$, lowest: $p<0.001$) among all conditions; TI exhibited the lowest magnitude while TO20 exhibited the highest magnitude. Additionally, pairwise comparison revealed peak late stance KAM magnitudes were significantly different (highest: $p=0.021$, lowest: $p<0.001$) among all conditions; TI exhibited the highest magnitude while TO20 exhibited the lowest magnitude.

No main effect ($p=0.065$) was observed for total KAM impulse, however early ($p<0.001$) and late stance ($p<0.001$) KAM impulse did elicit significant main effects. Pairwise comparisons revealed early stance KAM impulse was significantly different (highest: $p=0.014$, lowest: $p<0.001$) among all conditions; TI exhibited the lowest impulse while TO20 exhibited the highest impulse. Additionally, pairwise comparisons revealed that late stance KAM impulse was significantly different (highest: $p=0.002$, lowest: $p<0.001$) among all conditions except between TI and ZR ($p=0.051$); TI exhibited the highest mean impulse while TO20 exhibited the lowest mean impulse. Ensemble average curves for ankle and knee frontal plane moments are presented in Figure 4.2.

Table 4.4: Kinetic data. Mean (SD) for frontal plane ankle and knee moments (Nm/kg) and moment impulses (Nm/kg*s) for all conditions.

Outcome	Condition			
	TI10	ZR	TO10	TO20
Ankle Joint				
Peak frontal plane moment (Nm/kg)	-0.13 (0.07)	-0.13 (0.07)	-0.14 (0.06)	-0.14 (0.06)
Knee Joint				
Early stance peak KAM (Nm/kg)	0.41 (0.13)*†‡	0.46 (0.15)§†‡	0.49 (0.16)§*†‡	0.53 (0.16)§*†
Late stance peak KAM (Nm/kg)	0.50 (0.14)*†‡	0.45 (0.14)§†‡	0.39 (0.13)§*†‡	0.34 (0.13)§*†
Total KAM impulse (Nm/kg*s)	0.20 (0.07)	0.20 (0.07)	0.20 (0.07)	0.19 (0.07)
Early stance KAM impulse (Nm/kg*s)	0.08 (0.03)*†‡	0.10 (0.04)§†‡	0.11 (0.04)§*†‡	0.11 (0.04)§*†
Late stance KAM impulse (Nm/kg*s)	0.11 (0.04)†‡	0.10 (0.04)†‡	0.08 (0.04)§*†‡	0.07 (0.04)§*†

KAM, knee adduction moment. §significantly different than TI10; *significantly different than ZR; †significantly different than TO10; ‡significantly different than TO20; (+) values indicate adduction and inversion moments, (-) values indicate abduction and eversion moments; Results are considered significant if $p < 0.05$.

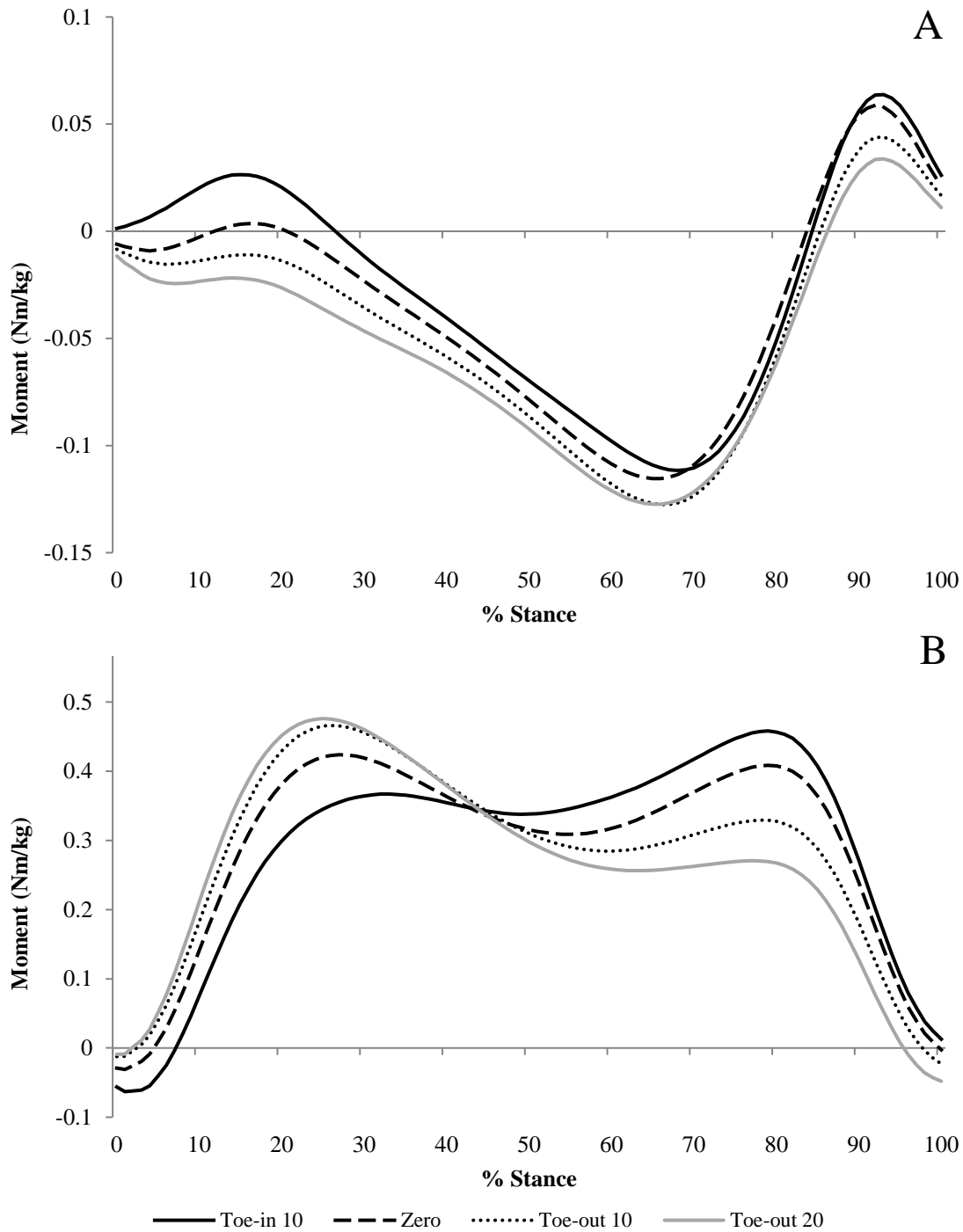


Figure 4.2: Frontal plane ankle and knee moment ensemble averages. The ankle (a) and knee (b) moment curves are presented as a percentage of the stance phase of gait. Positive values represent external inversion and adduction moments, while negative values represent external eversion and abduction moments.

4.5 EMG Outcomes

Electromyographic outcomes were examined for main effects across all conditions and are reported in Table 4.5. A significant main effect was observed for LG ($p=0.004$) and MG RMS ($p=0.008$) muscle activity. Pairwise comparison revealed TI10 exhibited significantly increased ($p=0.03$) LG RMS muscle activity compared to TO20, however no significant pairwise comparisons were revealed for MG RMS. A significant main effect ($p=0.001$) was observed for peak MG muscle activity, however pairwise comparison did not reveal any significant differences between conditions. Ensemble average curves for the muscle activity of all five muscles are presented in Figure 4.3.

Table 4.5: Electromyographic data. Mean (SD) for the RMS (%MVIC) and peak (%MVIC) muscle activity of the MG, LG, SO, TA and PL muscles for all conditions.

Outcome	Condition			
	TI10	ZR	TO10	TO20
RMS muscle activity				
Medial Gastrocnemius (%MVIC)	10.08 (3.69)	11.59 (4.49)	12.11 (4.75)	12.43 (5.17)
Lateral Gastrocnemius (%MVIC)	13.79 (5.89)‡	12.32 (6.07)	10.84 (5.23)	10.11 (5.02)§
Soleus (%MVIC)	16.11 (4.85)	15.49 (4.72)	14.80 (6.32)	15.74 (6.15)
Tibialis Anterior (%MVIC)	15.22 (5.11)	14.40 (5.69)	14.16 (3.22)	14.95 (5.65)
Peroneus Longus (%MVIC)	14.41 (5.34)	13.46 (2.81)	13.25 (3.31)	13.48 (4.04)
Peak muscle activity				
Medial Gastrocnemius (%MVIC)	31.47 (11.44)	34.02 (13.69)	39.26 (15.27)	39.55 (15.98)
Lateral Gastrocnemius (%MVIC)	41.86 (17.10)	40.18 (19.32)	36.75 (15.85)	35.21 (16.71)
Soleus (%MVIC)	50.39 (23.57)	42.90 (12.04)	43.71 (18.34)	48.63 (16.77)
Tibialis Anterior (%MVIC)	40.05 (11.71)	38.84 (13.52)	39.01 (8.44)	41.12 (16.39)
Peroneus Longus (%MVIC)	43.04 (13.42)	39.20 (8.13)	37.73 (8.48)	39.94 (11.05)

RMS, root mean square. §significantly different than TI10; ‡significantly different than TO20; Results are considered significant if $p < 0.05$.

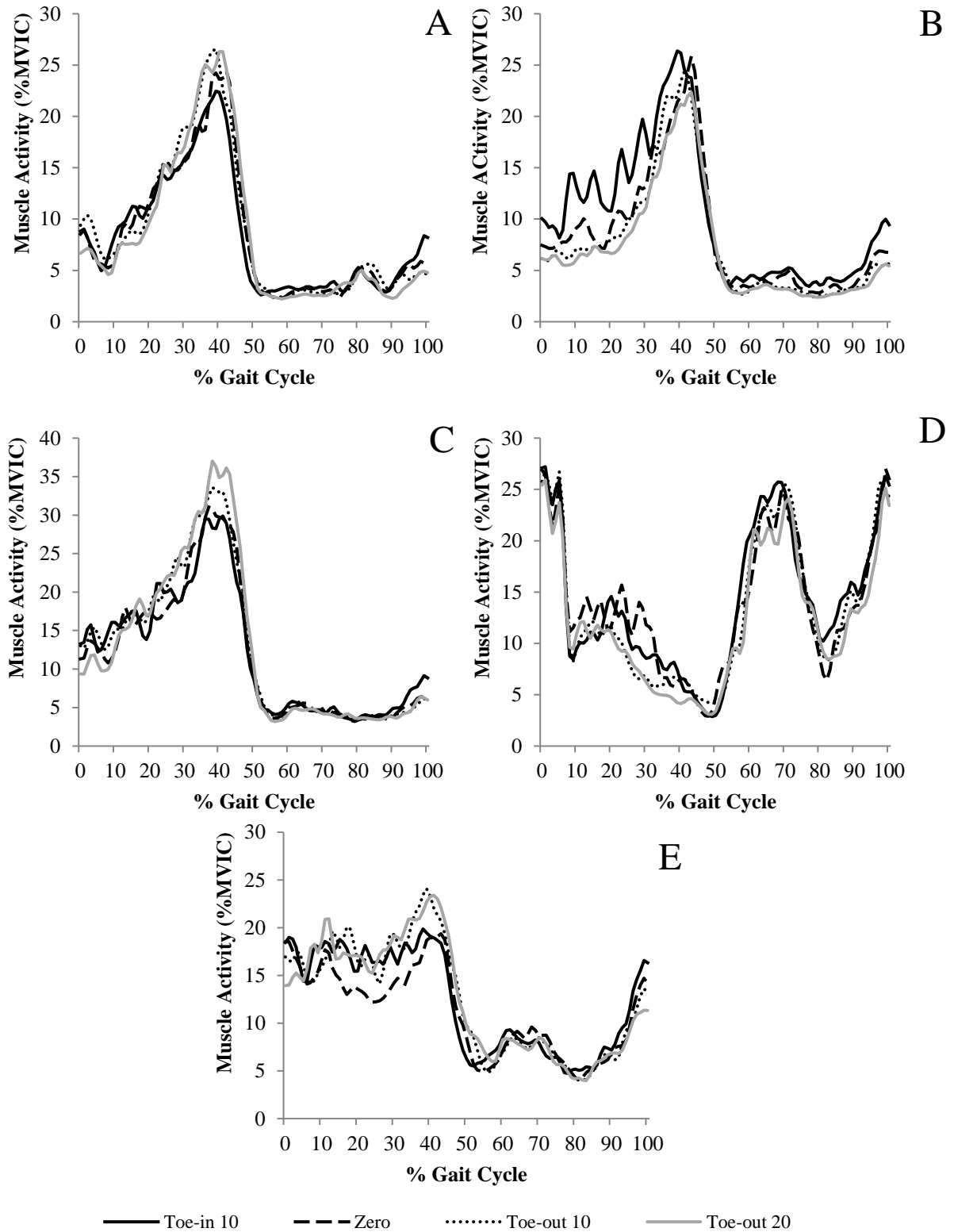


Figure 4.3: Muscle activation ensemble averages. The (a) MG, (b) LG, (c) SO, (d) TA and (e) PL muscle activation waveforms are presented as a percentage of the gait cycle for all conditions.

4.6 Patient Reported Outcomes

Difficulty of performance, walking condition preference and discomfort were examined for main effects across all conditions and are reported in Table 4.6. A significant main effect ($p=0.001$) for the rating of difficulty performing the condition was observed. Pairwise comparison revealed participants rated TI10 as more difficult ($p=0.006$) compared to ZR; however, TI10 was not significantly more difficult than TO10 or TO20. The TI10 condition was most frequently indicated as “least preferred” while TO20 was second most frequently indicated. The ZR condition was rated as the “most preferred” condition while TO10 was second most frequently indicated. No main effects ($p>0.05$) were observed for ankle/foot, knee or hip discomfort during walking.

Table 4.6: Patient reported data. Mean (SD) for patient reported outcomes for all conditions, except for preference which is the number of participants who indicated the condition as most or least preferred.

Outcomes	Conditions			
	TI10	ZR	TO10	TO20
Difficulty (0-10)	3.6 (2.3)*	1.2 (1.4)	1.9 (1.6)	2.8 (2.0)
Preference (participants)				
Least	8	1	0	6
Most	1	8	4	2
Discomfort (0-10)				
Ankle/Foot	0.7 (1.3)	0.5 (1.3)	0.5 (1.0)	0.6 (1.1)
Knee	0.8 (1.5)	0.8 (1.0)	1.1 (1.4)	1.3 (1.1)
Hip	0.3 (0.5)	0.2 (0.4)	0.3 (0.6)	0.1 (0.4)

*significantly different compared to the ZR condition. Results are considered significant if $p < 0.05$.

Chapter 5: Discussion

The purpose of the present study was to examine ankle biomechanics during single session TI and TO gait modification in those with medial compartment knee OA. The present study demonstrated that while walking with TI and TO foot rotation, the biomechanics of the ankle are indeed altered. Specifically, our first hypothesis was partially supported as group mean ankle eversion angles were increased (more everted) during TO10 and TO20 compared to TI10, but not compared to ZR. Additionally, frontal plane ankle excursion was significantly increased in TI10 compared to TO10 and TO20. Furthermore, we observed a significant increase in ankle inversion angle at heel strike in the TI10 compared to all other conditions, while TO20 was significantly decreased compared to all other conditions, while ZR and TO10 did not differ. The second hypothesis was also partially supported as group means for early stance KAM and KAM impulse were decreased during TI10 compared to all other conditions. Furthermore, group means for late stance KAM and KAM impulse were decreased during the TO10 and TO20 conditions compared to all other conditions. However, peak frontal plane ankle moments were not significantly different across all conditions. Finally, the third hypothesis was not supported as the few results were in direct opposition to our initial hypothesis. Specifically, TI10 exhibited significantly increased LG RMS compared to TO20.

Overall, participants rated the difficulty of TI10 as significantly higher than ZR, however the other conditions were not significantly more or less difficult compared to one another. There were no differences in pain in any location across conditions. The preceding results would suggest that ankle biomechanics are altered during single session TI and TO

gait modification, however, there does not appear to be a consistent trend for a given condition, and the relevance of these alterations to possible adverse events are unclear.

5.1 Interpretation of Findings

Our findings partially support our primary hypothesis that during TO walking compared to TI walking, greater peak ankle eversion angles during stance would be exhibited. In opposition to our primary hypothesis, TI walking exhibited increased frontal plane ankle excursion compared to TO10 and TO20. This is the first study, to our knowledge, that has examined frontal plane ankle kinematics during TI and TO walking. Therefore, it is difficult to determine the implications in the small, but significant, observed differences between conditions. However, ankle eversion has been positively correlated ($r=0.59$) with decreases in KAM magnitudes (Levinger et al., 2013), therefore any hypothetically detrimental effects of increased eversion must be considered in this light. Our cohort exhibited a 33% and 39% increase in peak ankle eversion angle during TO10 and TO20 respectively, relative to ZR.

The observed differences in eversion may be due to the specific lower extremity kinematics associated with TO walking. That is, when TO walking, the ankle joint is externally rotated along with the foot which likely results in the lateral aspect of the heel contacting the ground. Therefore, instead of the heel rocker action occurring primarily in the sagittal plane, a portion of the heel rocker action is transferred to the frontal plane of the ankle as the stance phase of gait progresses from heel strike to foot flat. The present study partially supports this through the decrease in the ankle inversion angle exhibited at heel strike during TO10 and TO20. Conversely, TI walking requires the internal rotation of the

ankle joint, likely resulting in a more medial contact point between the foot and ground. Therein a similarly altered heel rocker action likely occurs, but in the direction of inversion, instead of eversion. These speculations are likely further supported by the pattern of frontal plane ankle joint loading during loading response. Though we did not directly conduct a statistical analysis on such an outcome, Figure 4.2a shows a consistent trend towards more eversion with greater TO angles, while TI10 exhibits a clear increase in inversion moment at this point in stance. As such, during TO walking, the moment would tend to evert the ankle joint and during TI walking the moment would tend to invert the ankle. However, the clinical implications of alterations to frontal plane ankle kinematics are not yet clear.

The connection between increased ankle eversion angles and clinically relevant implications such as discomfort are not clear, despite a connection being commonly suggested in the literature. Two systematic reviews and meta-analyses identified generally limited evidence supporting the link between static (Neal et al., 2014) and dynamic (Dowling et al., 2014) everted foot posture and the risk of lower extremity injuries, though the included studies typically consisted of younger healthy individuals. Those with knee OA often exhibit a more everted and less mobile rear-foot compared to their asymptomatic counterparts (Levinger et al., 2012) and the presence of flat foot postures conferred a 1.3 and 1.4 times greater risk of also having knee pain and knee cartilage damage, respectively, compared to more neutral or cavus foot postures (Gross et al., 2011). Lateral wedge insole use in those with knee OA may provide indirect support for the connection between greater ankle eversion angles and discomfort. Lateral wedge insoles have the potential to reduce KAM (Arnold et al., 2016), but also increase peak ankle eversion angles (mean difference 1.07°, 0.77° respectively) and discomfort compared to a medially supported wedge condition

(Hatfield et al., 2016; Jones et al., 2013). The addition of a medial arch support to the lateral wedge insole, which reduced ankle eversion angles, also decreased discomfort (Hatfield et al., 2016; Jones et al., 2013). It has been suggested that the increased ankle eversion angles due to lateral wedge insoles are driving discomfort via increased medial ankle and longitudinal arch stress (Jones et al., 2013). In support, a cadaver study demonstrated that inversion and eversion of the ankle can decrease the contact area and increase the average pressure per unit area of the articulations between the talus and the distal tibiofibular surfaces (Calhoun et al., 1994), a possible mechanism for discomfort.

The present study did not observe any significant differences in discomfort between walking conditions for any joint despite differences in ankle eversion angles of similar magnitudes (largest mean difference 1.4°) compared to the lateral wedge insole studies mentioned previously. This may be explained by the fact participants were walking in each condition for no more than 15 minutes, which was likely not a long enough time period to elicit detectable changes in discomfort, if any were present. As such, further investigation is required to determine whether increased peak ankle eversion angles associated with TO walking have the potential to cause ankle joint discomfort over the longer-term. However, in the interim, the prescription of TO walking to individuals already exhibiting ankle eversion should be done with care.

Ankle inversion at heel strike was significantly increased during TI10 compared to ZR, TO10 and TO20 with mean differences ranging from 2.9° to 5.5° . Ankle inversion may be exhibited as a means of maintaining the required TI foot rotation position as the foot comes into contact with the ground. Though, it is not known whether increased ankle inversion is a consequence or product of TI walking. Furthermore, the implications of such

an increase in inversion during heel strike are not known. The observed increase in ankle inversion at heel strike likely drove the increase in frontal plane ankle excursion in the TI10 condition compared to TO10 and TO20. However, this increase may not have significant implications, as the range of motion exhibited in the TI10 condition was within the physiological frontal plane range of motion of the ankle (Brockett & Chapman, 2016; Perry, 1992).

Though we did not offer a hypothesis regarding sagittal plane ankle kinematics, we did examine ankle flexion at heel strike. We observed that during TI10 and TO20, participants contacted the ground with less plantarflexion (slightly dorsiflexed) at heel strike. With no data that we know of that corroborates this finding; we may only offer a tentative explanation. Due to TI10 and TO20 being the furthest foot rotation conditions from our cohort's natural foot rotation, the dorsiflexed ankle position may have been a result of trying to maintain a relatively foreign foot rotation position during heel strike and delay foot flat to ensure the foot was placed correctly. However, the differences in ankle angles are small (within 2°) and thus are likely not clinically relevant.

Contrary to our secondary hypothesis, peak ankle joint moments did not significantly differ across conditions. Changes to mediolateral GRF properties can occur during TO walking (Simpson & Jiang, 1999), however the direct impact of altered GRF properties on ankle moments are not known. Although a shift in the centre of pressure of the foot is likely occurring during TI and TO walking (Jenkyn et al., 2008; Shull et al., 2013a), the ankle joint centre is in close proximity to the centre of pressure in early stance, thus the potential for a change in the ankle joint moment arm is quite small. Despite this, it has been reported that an increase in ankle eversion moments when walking with a lateral wedge insole can occur

(Chapman et al., 2015; Hatfield et al., 2016; Jones et al., 2013). However, the mediolateral centre of pressure changes due to lateral wedge insoles are lower (Maly et al., 2002) compared to TI and TO walking. Thus, difference in ankle eversion moments are likely due to another factor, such as medial displacement of the ankle joint centre. Of course, the centre of pressure was not measured in the present study and therefore we may only speculate. Nonetheless, a lack of change in ankle eversion moments across conditions is a positive result in regard to the use of TI and TO walking considering the role increased joint moments can play in joint diseases, such as knee OA.

Our results provide continued support for the load altering effects of TI and TO walking at the knee joint. Similar to previous work (Guo et al., 2007; Lynn & Costigan, 2008; Shull et al., 2013a; Simic et al., 2013), TI walking decreased the early stance peak KAM (group mean difference of 0.05 Nm/kg) while TO walking decreased the late stance peak KAM (group mean difference of 0.11 Nm/kg). Simultaneously, TI walking increased late stance peak KAM while TO walking increased early stance peak KAM, which is in agreement with previous reports (Simic et al., 2013). The TO10 condition elicited greater reductions in knee kinetic outcomes (16.7% reduction in late stance peak KAM in this cohort) compared to TI10 (10.9% reduction in early stance peak KAM in this cohort) relative to ZR. Expectedly, the TO20 condition elicited an even larger decrease in late stance peak KAM (24.4% reduction in this cohort) compared to ZR. These values are similar, though generally smaller, compared to previously reported decreases in KAM outcomes due to foot rotation angle changes of similar magnitudes (Lynn & Costigan, 2008; Shull et al., 2013a; Simic et al., 2013). While Simic et al observed significant differences in total KAM impulse between TI and TO walking, we only observed a trend toward a main effect ($p=0.065$). We

did however observe a significant reduction in KAM impulse during early and late stance for TI and TO walking, respectively. As KAM impulse accounts for the duration of loading in addition to the magnitude of load, and is associated with disease progression (Bennell et al., 2011), it is an equally important variable to target for reduction. Our study suggests that TI and TO walking both exhibit reductions in KAM impulse of similar magnitudes (0.02 and 0.03 Nm/kg*s respectively).

The mechanism driving KAM magnitude decreases has been hypothesized to be, in part, a result of shifting the centre of pressure at different time points during stance (Jenkyn et al., 2008). That is, TI walking likely reduces early stance KAM by shifting the heel laterally, displacing the centre of pressure laterally at heel strike (Shull et al., 2013a). This is supported by our observation, as well as previous observations (Simic et al., 2013), that stance width during TI walking was significantly increased. TO walking likely achieves similar reductions in late stance due to the lateral shift of the forefoot, displacing the centre of pressure laterally during mid- and terminal stance (Jenkyn et al., 2008). Overall, despite no differences in ankle joint kinetics, our results corroborate previous work regarding changes to knee joint kinetics due to TI and TO walking.

As with ankle kinematics and kinetics, little data exists regarding muscle activation patterns of the lower leg in those with knee OA. Our tertiary hypothesis was not supported, as only a significant increase in LG RMS during TI10 compared to TO20 was observed. The difference in LG RMS during TI10 compared to TO20 constituted a 3.7% MVIC average increase. This increase may have been a response to the significantly increased inversion angles that occur at heel strike during TI walking compared to all other conditions. Since the LG has a significant inversion moment arm when the ankle is inverted (Lee & Piazza, 2008),

elevated activity may result; first to facilitate an inverted ankle position at heel strike and second to eccentrically decelerate ankle eversion as one progresses toward foot flat.

However, it is not likely that such an increase is clinically significant.

Our lack of EMG results overall may be due to the nature of a single session study. That is, without significant time for participants to adopt the walking pattern and develop a preferred method of performance, there may be a large degree of variation in muscle activation patterns each participant utilized to achieve the given foot rotation. Although unique muscle activation patterns have been associated with TI and TO walking, such as preferential activation of lateral thigh musculature (Lynn & Costigan, 2008) and a shift of the gastrocnemii activation later into stance (Rutherford et al., 2010), our data cannot corroborate these findings. A post hoc analysis of peak EMG location (as a percent of the gait cycle) revealed a main effect for MG ($p=0.022$), however pairwise comparison did not reveal any significant differences between conditions. Therefore, despite small differences, muscle activity patterns seem to be relatively similar between conditions. Though, as mentioned, the lack of observed differences may be a product of between-subject variation in muscle activity patterns due to the minimal time participants had to practice the walking patterns.

No differences were observed between conditions with respect to discomfort in any joint. This is in support of previously reported single session TI and TO gait modification (Simic et al., 2013). Low ratings of discomfort during natural walking have been cited as a limitation in observing differences between conditions (Simic et al., 2013). Our cohort had even lower natural walking discomfort ratings (mean ankle/foot = 0.13, knee = 0.73, hip = 0.00) thus presenting further difficulty in detecting differences. A cohort of individuals with

higher pain ratings may elicit detectable differences in discomfort between TI and TO walking. However, it is likely that the experience of discomfort is individual and may be driven by a number of factors, in addition to increased ankle eversion angles. Thus, it is difficult to speculate based on our results alone.

Differences in difficulty are likely a clinically relevant outcome, particularly in relation to the successful implementation of TI and TO walking. To the candidate's knowledge, this was the first investigation to directly quantify difficulty between TI and TO walking. Participants rated TI10 as more difficult than ZR but not TO10 or TO20. Additionally, TO20 trended toward being rated as more difficult compared to ZR ($p=0.069$). These results are likely explained by a mean NT foot rotation angle of -7.7° , therefore the ZR and TO10 conditions were likely similar enough to not require significant difficulty to perform. Difficulty ratings were low overall however, which was expected as the cohort recruited for the present study was relatively high functioning, as evidenced by WOMAC function scores which were 3.6 points lower than a cohort recruited for a similar study (Simic et al., 2013).

This study has three key strengths. First, all trials with successful foot strikes, regardless of which condition they were produced in, were considered in the data analysis. Specifically, all trials were filtered according to foot rotation magnitude relative to each condition. Therein, we were able to examine biomechanical differences due to specific alterations (approximately 10° intervals) in foot rotation. This provides an advantage over the methods previously performed (Simic et al., 2013) which relied upon participants producing accurate foot rotations during each specific condition. This is a difficult task, as is supported by the differences in reported foot rotation data compared to the target foot rotation –

especially at larger TO magnitudes (Simic et al., 2013) – and anecdotal evidence. Second, this investigation evaluated lower leg kinematics, kinetics and EMG during TI and TO walking. Therein a more comprehensive dataset is provided to inform future investigations. Previous literature has focused primarily on knee biomechanics for obvious reasons, however extending the biomechanical understanding beyond the knee is an important step to inform the development and implementation of foot rotation based gait modifications. Third, the present study utilized real-time biofeedback to drive the foot rotation modifications during treadmill walking. As previously reported, real-time biofeedback for TO gait modification resulted in the lowest mean performance error (3.81° in that cohort) which was 28.4% and 35.0% lower when compared to video and mirror based feedback respectively (Hunt et al., 2014). As such, we were able to reduce the amount of time needed to alter gait during treadmill walking, while minimizing performance error. Additionally, during each over-ground walking trial, a subjective analysis of foot rotation error could be determined and help guide the participant in performance, reducing the time walking with each condition even further. This may have been helpful in decreasing the cumulative discomfort or fatigue during the participant's data collection session and therefore reducing the possibility of altered gait mechanics due to unnecessary increases in pain or fatigue.

5.2 Limitations

These results must be interpreted in the light of the limitations of this study. First, participants were exposed to each walking condition for only a short period of time. This likely did not allow each participant to become proficient with the walking pattern and develop a consistent, repeatable technique for achieving the given foot rotation. To counter

this limitation, we selected the five closest trials to the given condition for analysis, regardless of when they were produced. In effect, we were able to examine the differences between very specific foot rotation angles without concern for the significant acquisition time associated with gait modification and the inaccuracy of participants in a single session study setting. Indeed, the accurate performance was further assisted by the fact that our cohort was high functioning, as evidenced by the relatively low WOMAC physical function and total scores reported in the present study. However, this also constitutes a second limitation. Our participants were high functioning and also reported low knee pain ratings the week prior to and during the testing session. Therefore, we likely cannot extrapolate these results to lower functioning/higher pain cohorts due to the gait modifying effects of pain (Henriksen et al., 2012; Henriksen et al., 2010).

A third limitation of the present study is that foot posture was not comprehensively assessed. Foot posture may confound the symptomatic response to foot rotation, especially since flat foot postures alone have been associated with knee pain (Gross et al., 2011). During the present study, we visually assessed the static alignment of the rear-foot during standing and found 53% of participants presented with everted rear-foot alignment, 27% with neutral alignment and 20% with inverted alignment. However, due to the small subgroup sample sizes, we cannot draw any significant interpretations from any subgroup analysis.

A fourth limitation is that we controlled gait speed between conditions. As kinetic differences, namely increases in joint moments (Landry et al., 2007), occur with faster gait speeds, maintaining consistent speed is necessary for kinetic comparisons. However, it is not unreasonable to hypothesize that natural gait speed may differ between TI and TO walking patterns, particularly if an individual finds the pattern difficult or unnatural. A change in gait

speed could alter joint kinematics, kinetics, or muscle activity patterns in addition to that which occurs due to the foot rotation itself.

A fifth limitation is that participants were asked to walk barefoot on a wooden walkway. Walking barefoot is known to alter lower extremity biomechanics (Shakoor & Block, 2006). In addition to this, the environment associated with in-lab gait analysis is typically foreign to the participant and most certainly different than their everyday walking environments. Although this provides control over study variables, it lacks external validity. An improvement, as technology allows, would be to measure similar biomechanical measures outside of the lab during daily activities.

A sixth limitation is that electrode placement may have altered the observed EMG magnitudes. Small variations in individual muscle architecture could have resulted in the electrodes not being placed in the centre of the muscle belly. As such, the electrodes may have been subject to crosstalk from adjacent muscles. We attempted to minimize this via placement of the electrodes using standardized guidelines established by SENIAM.org (outlined in section 3.3) in addition to visual assessment of EMG waveforms during targeted exercise maneuvers.

Lastly, the present study was cross-sectional in design and therefore we cannot make any judgement regarding cause and effect. Specifically, the cause and effect relationship between discomfort, ankle biomechanics and foot rotation modifications cannot be determined via the present study. Though, the observed differences do provide support for longitudinal investigations which can shed light on the relationships between these variables.

5.3 Clinical Implications

Previous single session studies (Guo et al., 2007; Shull et al., 2013a; Simic et al., 2013) have demonstrated the load modifying effects of TI and TO walking on the KAM. Additionally TI and TO gait modification in knee OA populations have been examined over short-term clinical trials and have resulted in clinically relevant improvements in pain and function (Hunt & Takacs, 2014; Shull et al., 2013b). The present study supports these findings, but builds upon the current literature in a small but meaningful way.

We have demonstrated that ankle eversion angles increase with TO walking while ankle inversion at heel strike and frontal plane excursion increase with TI walking. Despite commonly suggested links between excessive ankle eversion and injury or pain, little data exists to support this. However, reports of those with knee OA exhibiting greater ankle eversion (Levinger et al., 2012) and/or flat feet (Levinger et al., 2010) may suggest that a further increase in ankle eversion is not ideal in regards to adverse events. However, due to the known association between increased ankle eversion and decreased KAM (a beneficial association); this statement is made with reservation. Therefore, a longitudinal assessment of the possible (if any) incidence of discomfort associated with TI or TO gait modification is needed. However, the adaptive capacity of soft-tissue to biomechanical changes which occur in a progressive and long-term manner cannot be dismissed. Therefore, it could be speculated that the small differences observed in the present study could be adapted to, if foot rotation modifications are applied progressively. However, as it is known that individuals with knee OA often present with immobile ankle joints, this population may not adapt as favourably to increases in frontal plan ankle motion.

Despite ankle kinematic differences, frontal plane ankle joint moments did not differ between conditions. This may suggest that TI and TO walking have less potential to alter joint load at the ankle comparatively to treatment strategies like lateral wedge insoles. Importantly, it is still unknown as to what (joint kinematics, kinetics or otherwise) may cause ankle joint discomfort, if any, making it difficult to definitively speculate. Therefore, TI and TO walking may be a treatment strategy with a lower chance of inciting ankle joint load alterations and the possible joint deterioration that can be associated with such load alterations, as is seen in knee OA.

Increases in muscle activity patterns associated with gait modifications may indicate a greater demand placed on a given muscle. However, the present study only observed a small increase in the LG during TI walking, suggesting that lower leg muscle activity demands between TI and TO walking are generally not significantly different. However, examining muscle activity change over multi-month gait modification programs is warranted before a recommendation can be made. This is especially important as the present study may not have allowed adequate time for participants to integrate each walking pattern and practice their individual manner of achieving the specific foot rotation. Over time, as an individual becomes more practiced at TI or TO walking, muscle activity pattern changes may become more apparent. Generally, the present study would suggest that alternate or adjunct treatments to TI and TO walking (e.g. targeted muscle strengthening or stretching) are not necessary on the basis of altered muscle activity patterns. Though, more data are required.

The method of delivery of a gait modification intervention is an important consideration when assessing the feasibility of implementation in the clinical setting. Despite real-time biofeedback being a strength in the present study, it is also a limitation in regard to

clinical applicability due to the exuberant associated costs and limited accessibility. Real-time biofeedback does provide an advantage by minimizing the foot rotation error during teaching sessions compared to mirror or video based feedback, as mentioned previously. However, a difference of approximately 2° compared to mirror or video based methods is likely not meaningfully different, and clinicians should feel comfortable delivering gait modification via mirror based feedback. The present study utilized real-time biofeedback as the goal was to capture walking trials with very specific parameters for the purposes of comparing between different walking patterns. This level of accuracy is of course not necessary when providing treatment in a clinical setting. The small difference compared to mirror based feedback, and the specific parameters needed to successfully complete this study required real-time biofeedback, however the candidate believes this does not limit the clinical applicability of our results.

In summary, TI and TO walking are an effective treatment strategy for decreasing knee joint loading and improving pain and function in those with medial knee OA. However, due to the observed differences in ankle joint kinematics, it may be important to assess foot/ankle function and baseline ankle kinematics prior to prescribing TO gait modification. However, a longitudinal examination of ankle eversion increases and the incidence of discomfort during TI or TO gait modification is necessary before definitive recommendations can be made.

5.4 Future Directions

The present study has provided initial data suggesting that ankle biomechanics may be altered during TI and TO walking, however more work is needed to determine the

implications of such alterations and whether they exist over long-term gait modification programs. Future investigations should aim to track discomfort longitudinally in the ankle/foot in addition to the knee. The present study was likely not long enough to elicit significant differences in discomfort. However, discomfort could very well exist after multiple weeks of walking with TI or TO foot rotations as an individual's tissues and gait patterns are adapting to the new walking kinematics. If discomfort does result, determining whether it is typically transient or sustained will be an important outcome to examine. The ultimate goal is to provide a comprehensive gait modification strategy to clinicians with as many caveats and contraindications as possible to guide individual implementation, with hopes of maximizing success rates. Determining the nature of discomfort, if any, associated with TI and TO walking over time is an important step in achieving this goal.

Foot posture may be an important variable to consider when prescribing TI or TO walking. A comprehensive examination of foot posture as it relates to the changes in ankle eversion angle during TO walking are likely warranted. Although, it was reported that static measurements of ankle alignment (everted or inverted) do not elicit differences in peak ankle eversion during walking (Cornwall & McPoil, 1994). However, this investigation was done in healthy individuals and may not apply to individuals with knee OA. A similar investigation should be done in a knee OA population to confirm this finding and inform whether or not foot posture is an important outcome in relation to TI or TO gait modifications.

Reports of muscle activity changes due to TI and TO walking are limited and the present study observed a small increase in only the LG during TI walking. The lack of differences between conditions may be predominantly due to the single session nature of the

investigation which did not provide adequate time for participants to develop consistent and coordinated walking patterns. A longitudinal investigation examining muscle activity changes after weeks and/or months of TI or TO walking will likely provide more definitive information in this regard.

Overall, gait modification seems to be a feasible and effective conservative treatment strategy for those with knee OA. However, a large barrier still exists in the delivery methodology currently reported in the literature. Despite mirror based feedback systems being a viable option, this method still places high demand on the clinician and does not provide a method of feedback or retention assessment outside of the specific training session. The delivery of gait modifications, especially TI or TO walking, via wearable sensor systems would likely solve both of these issues and open up the possibility to examine the walking habits of those with knee OA outside of the lab or clinic. This will be important to examine how TI and TO walking are integrated into daily living activities, but could also provide a means of delivering gait modification to patients while reducing clinician burden and possibly shortening the time that is required for an individual to assimilate the new walking pattern into their walking habits. The candidate believes that gait modification examined and delivered via wearable sensor systems is an important next step in advancing our conservative treatment approaches for individuals with knee OA.

Chapter 6: Conclusion

Knee OA is a disabling and painful disease and traditional treatment methods do not directly address joint loading, which is a key factor in disease progression. Gait modification, specifically TI and TO walking, have exhibited favourable reductions in knee joint load compared to natural walking in those with knee OA and may offer a conservative treatment strategy to slow disease progression and improve symptoms and function. However, it is important that TI and TO walking are examined more closely to better understand possible ancillary biomechanical alterations that occur at joints other than the knee. To our knowledge, this was the first study which examined ankle kinematics, kinetics and EMG during TI and TO walking in those with knee OA.

The present study demonstrated that TI and TO walking do indeed alter ankle joint kinematics. Specifically, TO walking increases peak ankle joint eversion angle during stance while TI walking increases ankle inversion angle at heel strike and frontal plane angle excursion. The implications of these changes are not known. However, the observed differences are small and individuals may be able to adapt to these changes if the gait modification is applied in a progressive manner. But this conclusion is speculative, as the relationship between increased ankle eversion and discomfort, pain or lower extremity injury is not yet clear. The present study did not observe any differences in discomfort between conditions, though this may be due to the limited time participants spent walking in a given condition and the relatively low pain ratings overall. A longitudinal study is warranted to determine if long-term increases in ankle eversion are associated with any discomfort.

No differences were observed in peak ankle joint eversion moments while the observed differences in KAM magnitudes agree with previous findings. Therefore, TI and

TO walking may not place the ankle joint under elevated risk due to joint moment differences when compared to neutral walking; but still exhibit load modifying affects at the knee joint. Notably, decreases in early stance peak KAM were accompanied by increases in the late stance peak KAM, and vice versa. As it is likely that overall reductions in KAM are ideal, determining the foot rotation pattern which maximizes KAM reductions for an individual while minimizing the risks of adverse effects should be prioritized.

Average muscle activation of the LG was significantly increased during TI walking. However, the change was likely not clinically significant. It is possible that the limited time each participant spent walking in a given condition resulted in, on average, less coordinated and more variable muscle activation patterns. Therefore, longitudinal assessment of muscle activation after TI or TO gait modification is warranted.

Generally, participants did not experience significant differences in lower extremity discomfort across conditions. Due to the cohort being relatively high functioning with low overall pain ratings, we may have been limited in detecting discomfort differences. Participants did rate TI10 as significantly more difficult than ZR, but not compared to TO10 or TO20. The overall low ratings of difficulty were again likely due to a high functioning cohort, with the potential to be higher in a cohort with more severe disease, higher pain or lower function. Notably, TI10 was most frequently rated as least preferred, though with our small sample size it is difficult to extrapolate this to the knee OA population at large.

Overall, the results of the present investigation demonstrate that TI and TO walking alter ankle kinematics but not ankle kinetics. Additionally, increased average muscle activity in the LG during TI walking was observed but is likely not clinically significant. Our results support TI and TO walking as a viable conservative treatment strategy for medial knee OA

with generally low difficulty and perceived discomfort. However, the implications of increased ankle eversion angles during TO walking over longer periods of time are not clear and further investigations are needed. Moreover, lower extremity discomfort should be examined longitudinally during TI and TO gait modification programs to better inform whether lower extremity discomfort is transient or not, and what specific joints may be at risk. The present study suggests the ankle may be of interest in that regard.

References

- Ajuied, A., Wong, F., Smith, C., Norris, M., Earnshaw, P., Back, D., et al. (2014). Anterior Cruciate Ligament Injury and Radiologic Progression of Knee Osteoarthritis. *American Journal of Sports Medicine*, 42(9), 2242-2252.
- Andrews, M., Noyes, F. R., Hewett, T. E., & Andriacchi, T. P. (1996). Lower limb alignment and foot angle are related to stance phase knee adduction in normal subjects: a critical analysis of the reliability of gait analysis data. *Journal of Orthopaedic Research*, 14(2), 289-295.
- Andriacchi, T. P., Favre, J., Erhart-Hledik, J. C., & Chu, C. R. (2015). A systems view of risk factors for knee osteoarthritis reveals insights into the pathogenesis of the disease. *Annals of Biomedical Engineering*, 43(2), 376-387.
- Andriacchi, T. P., & Mundermann, A. (2006). The role of ambulatory mechanics in the initiation and progression of knee osteoarthritis. *Current Opinion in Rheumatology*, 18(5), 514-518.
- Andriacchi, T. P., Mundermann, A., Smith, R. L., Alexander, E. J., Dyrby, C. O., & Koo, S. (2004). A framework for the in vivo pathomechanics of osteoarthritis at the knee. *Annals of Biomedical Engineering*, 32(3), 447-457.
- Arnold, J. B., Wong, D. X., Jones, R. K., Hill, C. L., & Thewlis, D. (2016). Lateral Wedge Insoles for Reducing Biomechanical Risk Factors for Medial Knee Osteoarthritis Progression: A Systematic Review and Meta-Analysis. *Arthritis Care & Research*, 68(7), 936-951.
- Astephen, J. L., Deluzio, K. J., Caldwell, G. E., & Dunbar, M. J. (2008a). Biomechanical changes at the hip, knee, and ankle joints during gait are associated with knee osteoarthritis severity. *Journal of Orthopaedic Research*, 26(3), 332-341.
- Astephen, J. L., Deluzio, K. J., Caldwell, G. E., Dunbar, M. J., & Hubble-Kozey, C. L. (2008b). Gait and neuromuscular pattern changes are associated with differences in knee osteoarthritis severity levels. *Journal of Biomechanics*, 41(4), 868-876.
- Baliunas, A. J., Hurwitz, D. E., Ryals, A. B., Karrar, A., Case, J. P., Block, J. A., et al. (2002). Increased knee joint loads during walking are present in subjects with knee osteoarthritis. *Osteoarthritis and Cartilage*, 10(7), 573-579.
- Barker, K., Lamb, S. E., Toye, F., Jackson, S., & Barrington, S. (2004). Association between radiographic joint space narrowing, function, pain and muscle power in severe osteoarthritis of the knee. *Clinical Rehabilitation*, 18(7), 793-800.
- Bell, A. L., Pedersen, D. R., & Brand, R. A. (1989). Prediction of hip joint center location from external landmarks. *Human Movement Science*, 3-16.

- Bellamy, N., Buchanan, W. W., Goldsmith, C. H., Campbell, J., & Stitt, L. W. (1988). Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. *Journal of Rheumatology*, *15*(12), 1833-1840.
- Bennell, K. L., Bowles, K. A., Wang, Y., Cicuttini, F., Davies-Tuck, M., & Hinman, R. S. (2011). Higher dynamic medial knee load predicts greater cartilage loss over 12 months in medial knee osteoarthritis. *Annals of the Rheumatic Diseases*, *70*(10), 1770-1774.
- Bennell, K. L., Hunt, M. A., Wrigley, T. V., Lim, B. W., & Hinman, R. S. (2008). Role of muscle in genesis and management of knee osteoarthritis. *Rheumatic Disease Clinics of North America*, *34*, 731-754.
- Birmingham, T., Hunt, M., Jones, I., Jenkyn, T., & Giffin, J. (2007). Test-retest reliability of the peak knee adduction moment during walking in patients with medial compartment knee osteoarthritis. *Arthritis Care & Research*, *57*(6), 1012-1017.
- Birmingham, T. B., Giffin, J. R., Chesworth, B. M., Bryant, D. M., Litchfield, R. B., Willits, K., et al. (2009). Medial opening wedge high tibial osteotomy: a prospective cohort study of gait, radiographic, and patient-reported outcomes. *Arthritis & Rheumatism*, *61*(5), 648-657.
- Blagojevic, M., Jinks, C., Jeffery, A., & Jordan, K. P. (2010). Risk factors for onset of osteoarthritis of the knee in older adults: a systematic review and meta-analysis. *Osteoarthritis and Cartilage*, *18*(1), 24-33.
- Bombardier, C., Hawker, G., & Mosher, D. (2011). The impact of arthritis in Canada: Today and over the next 30 years. (pp. 52). Ottawa, ON: Arthritis Alliance of Canada
- Brandt, K. D., Dieppe, P., & Radin, E. L. (2008). Etiopathogenesis of osteoarthritis. *Rheumatic Disease Clinics of North America*, *34*(3), 531-559.
- Brandt, K. D., Radin, E. L., Dieppe, P. A., & van de Putte, L. (2006). Yet more evidence that osteoarthritis is not a cartilage disease. *Annals of the Rheumatic Diseases*, *65*(10), 1261-1264.
- Brockett, C. L., & Chapman, G. J. (2016). Biomechanics of the ankle. *Orthopaedics and Trauma*, *30*(3), 232-238.
- Brouwer, G. M., van Tol, A. W., Bergink, A. P., Belo, J. N., Bernsen, R. M., Reijman, M., et al. (2007). Association between valgus and varus alignment and the development and progression of radiographic osteoarthritis of the knee. *Arthritis & Rheumatism*, *56*(4), 1204-1211.
- Calhoun, J. H., Li, F., Ledbetter, B. R., & Viegas, S. F. (1994). A comprehensive study of pressure distribution in the ankle joint with inversion and eversion. *Foot & Ankle International*, *15*(3), 125-133.

- Chang, A., Hurwitz, D., Dunlop, D., Song, J., Cahue, S., Hayes, K., et al. (2007). The relationship between toe-out angle during gait and progression of medial tibiofemoral osteoarthritis. *Annals of the Rheumatic Diseases*, 66(10), 1271-1275.
- Chang, A. H., Moio, K. C., Chmiel, J. S., Eckstein, F., Guermazi, A., Prasad, P. V., et al. (2015). External knee adduction and flexion moments during gait and medial tibiofemoral disease progression in knee osteoarthritis. *Osteoarthritis and Cartilage*, 23(7), 1099-1106.
- Chapman, G. J., Parkes, M. J., Forsythe, L., Felson, D. T., & Jones, R. K. (2015). Ankle motion influences the external knee adduction moment and may predict who will respond to lateral wedge insoles?: an ancillary analysis from the SILK trial. *Osteoarthritis and Cartilage*, 23(8), 1316-1322.
- Chehab, E. F., Favre, J., Erhart-Hledik, J. C., & Andriacchi, T. P. (2014). Baseline knee adduction and flexion moments during walking are both associated with 5 year cartilage changes in patients with medial knee osteoarthritis. *Osteoarthritis and Cartilage*, 22(11), 1833-1839.
- Chen, C. T., Burton-Wurster, N., Lust, G., Bank, R. A., & Tekoppele, J. M. (1999). Compositional and metabolic changes in damaged cartilage are peak-stress, stress-rate, and loading-duration dependent. *Journal of Orthopaedic Research*, 17(6), 870-879.
- Coggon, D., Reading, I., Croft, P., McLaren, M., Barrett, D., & Cooper, C. (2001). Knee osteoarthritis and obesity. *International Journal of Obesity and Related Metabolic Disorders*, 25(5), 622-627.
- Cornwall, M. W., & McPoil, T. G. (1994). The influence of tibialis anterior muscle activity on rearfoot motion during walking. *Foot & Ankle International*, 15(2), 75-79.
- Deshpande, B. R., Katz, J. N., Solomon, D. H., Yelin, E. H., Hunter, D. J., Messier, S. P., et al. (2016). Number of Persons With Symptomatic Knee Osteoarthritis in the US: Impact of Race and Ethnicity, Age, Sex, and Obesity. *Arthritis Care & Research*, 68(12), 1743-1750.
- Dieppe, P., Bartlett, C., Davey, P., Doyal, L., & Ebrahim, S. (2004). Balancing benefits and harms: the example of non-steroidal anti-inflammatory drugs. *BMJ*, 329(7456), 31-34.
- Dieppe, P., Basler, H. D., Chard, J., Croft, P., Dixon, J., Hurley, M., et al. (1999). Knee replacement surgery for osteoarthritis: effectiveness, practice variations, indications and possible determinants of utilization. *Rheumatology*, 38(1), 73-83.
- Dillon, C. F., Rasch, E. K., Gu, Q., & Hirsch, R. (2006). Prevalence of knee osteoarthritis in the United States: arthritis data from the Third National Health and Nutrition Examination Survey 1991-94. *Journal of Rheumatology*, 33(11), 2271-2279.

- Dowling, G. J., Murley, G. S., Munteanu, S. E., Smith, M. M., Neal, B. S., Griffiths, I. B., et al. (2014). Dynamic foot function as a risk factor for lower limb overuse injury: a systematic review. *Journal of Foot and Ankle Research*, 7(1), 53.
- Erhart-Hledik, J. C., Chu, C. R., Asay, J. L., & Andriacchi, T. P. (2016). Gait mechanics 2 years after anterior cruciate ligament reconstruction are associated with longer-term changes in patient-reported outcomes. *Journal of Orthopaedic Research*, 634-640.
- Erhart-Hledik, J. C., Favre, J., & Andriacchi, T. P. (2015). New insight in the relationship between regional patterns of knee cartilage thickness, osteoarthritis disease severity, and gait mechanics. *Journal of Biomechanics*, 48(14), 3868-3875.
- Ethgen, O., Bruyere, O., Richey, F., Dardennes, C., & Reginster, J. Y. (2004). Health-related quality of life in total hip and total knee arthroplasty. A qualitative and systematic review of the literature. *Journal of Bone and Joint Surgery. American Volume*, 86-A(5), 963-974.
- Faul, F., Erdfelder, E., Lang, A. G., & Buchner, A. (2007). G*Power 3: a flexible statistical power analysis program for the social, behavioral, and biomedical sciences. *Behavior Research Methods*, 39(2), 175-191.
- Felson, D. T. (1990). The epidemiology of knee osteoarthritis: results from the Framingham Osteoarthritis Study. *Seminars in Arthritis and Rheumatism*, 20(3 Suppl 1), 42-50.
- Felson, D. T. (1996). Weight and osteoarthritis. *American Journal of Clinical Nutrition*, 63(3 Suppl), 430-432.
- Felson, D. T. (2005). The sources of pain in knee osteoarthritis. *Current Opinion in Rheumatology*, 17(5), 624-628.
- Felson, D. T., Anderson, J. J., Naimark, A., Walker, A. M., & Meenan, R. F. (1988). Obesity and knee osteoarthritis. The Framingham Study. *Annals of Internal Medicine*, 109(1), 18-24.
- Felson, D. T., Chaisson, C. E., Hill, C. L., Totterman, S. M., Gale, M. E., Skinner, K. M., et al. (2001). The association of bone marrow lesions with pain in knee osteoarthritis. *Annals of Internal Medicine*, 134(7), 541-549.
- Fregly, B. J., Reinbolt, J. A., Rooney, K. L., Mitchell, K. H., & Chmielewski, T. L. (2007). Design of patient-specific gait modifications for knee osteoarthritis rehabilitation. *IEEE Transactions on Biomedical Engineering*, 54(9), 1687-1695.
- Frontera, W. R., Hughes, V. A., Lutz, K. J., & Evans, W. J. (1991). A cross-sectional study of muscle strength and mass in 45- to 78-yr-old men and women. *Journal of Applied Physiology*, 71(2), 644-650.

- Gelber, A. C., Hochberg, M. C., Mead, L. A., Wang, N. Y., Wigley, F. M., & Klag, M. J. (2000). Joint injury in young adults and risk for subsequent knee and hip osteoarthritis. *Annals of Internal Medicine*, 133(5), 321-328.
- Ghasemi, A., & Zahediasl, S. (2012). Normality tests for statistical analysis: a guide for non-statisticians. *International Journal of Endocrinology & Metabolism*, 10(2), 486-489.
- Grood, E. S., & Suntay, W. J. (1983). A joint coordinate system for the clinical description of three-dimensional motions: application to the knee. *Journal of Biomechanical Engineering*, 105(2), 136-144.
- Gross, K. D., Felson, D. T., Niu, J., Hunter, D. J., Guermazi, A., Roemer, F. W., et al. (2011). Association of flat feet with knee pain and cartilage damage in older adults. *Arthritis Care & Research*, 63(7), 937-944.
- Guo, M., Axe, M. J., & Manal, K. (2007). The influence of foot progression angle on the knee adduction moment during walking and stair climbing in pain free individuals with knee osteoarthritis. *Gait & Posture*, 26(3), 436-441.
- Hall, M., Bennell, K. L., Wrigley, T. V., Metcalf, B. R., Campbell, P. K., Kasza, J., et al. (2017). The knee adduction moment and knee osteoarthritis symptoms: relationships according to radiographic disease severity. *Osteoarthritis and Cartilage*, 25(1), 34-41.
- Hatfield, G. L., Cochrane, C. K., Takacs, J., Krowchuk, N. M., Chang, R., Hinman, R. S., et al. (2016). Knee and ankle biomechanics with lateral wedges with and without a custom arch support in those with medial knee osteoarthritis and flat feet. *Journal of Orthopaedic Research*, 1597-1605.
- Hatfield, G. L., Stanish, W. D., & Hubble-Kozey, C. L. (2015). Three-dimensional biomechanical gait characteristics at baseline are associated with progression to total knee arthroplasty. *Arthritis Care & Research*, 67(7), 1004-1014.
- Henriksen, M., Aaboe, J., & Bliddal, H. (2012). The relationship between pain and dynamic knee joint loading in knee osteoarthritis varies with radiographic disease severity. A cross sectional study. *Knee*, 19(4), 392-398.
- Henriksen, M., Graven-Nielsen, T., Aaboe, J., Andriacchi, T. P., & Bliddal, H. (2010). Gait changes in patients with knee osteoarthritis are replicated by experimental knee pain. *Arthritis Care & Research*, 62(4), 501-509.
- Hermens, H. J., Freriks, B., Disselhorst-Klug, C., & Rau, G. (2000). Development of recommendations for SEMG sensors and sensor placement procedures. *Journal of Electromyography and Kinesiology*, 10(5), 361-374.
- Hinman, R. S., Lentzos, J., Vicenzino, B., & Crossley, K. M. (2014). Is patellofemoral osteoarthritis common in middle-aged people with chronic patellofemoral pain? *Arthritis Care & Research*, 66(8), 1252-1257.

- Hootman, J. M., Macera, C. A., Helmick, C. G., & Blair, S. N. (2003). Influence of physical activity-related joint stress on the risk of self-reported hip/knee osteoarthritis: a new method to quantify physical activity. *Preventive Medicine, 36*(5), 636-644.
- Hunt, M. A., Birmingham, T. B., Giffin, J. R., & Jenkyn, T. R. (2006). Associations among knee adduction moment, frontal plane ground reaction force, and lever arm during walking in patients with knee osteoarthritis. *Journal of Biomechanics, 39*(12), 2213-2220.
- Hunt, M. A., & Takacs, J. (2014). Effects of a 10-week toe-out gait modification intervention in people with medial knee osteoarthritis: a pilot, feasibility study. *Osteoarthritis and Cartilage, 22*(7), 904-911.
- Hunt, M. A., Takacs, J., Hart, K., Massong, E., Fuchko, K., & Biegler, J. (2014). Comparison of mirror, raw video, and real-time visual biofeedback for training toe-out gait in individuals with knee osteoarthritis. *Archives of Physical Medicine and Rehabilitation, 95*(10), 1912-1917.
- Hunter, D. J., McDougall, J. J., & Keefe, F. J. (2009). The symptoms of osteoarthritis and the genesis of pain. *Medical Clinics of North America, 93*(1), 83-100.
- Hunter, D. J., Zhang, Y. Q., Niu, J. B., Tu, X., Amin, S., Clancy, M., et al. (2006). The association of meniscal pathologic changes with cartilage loss in symptomatic knee osteoarthritis. *Arthritis & Rheumatism, 54*(3), 795-801.
- Hurwitz, D. E., Ryals, A. R., Block, J. A., Sharma, L., Schnitzer, T. J., & Andriacchi, T. P. (2000). Knee pain and joint loading in subjects with osteoarthritis of the knee. *Journal of Orthopaedic Research, 18*(4), 572-579.
- Ikeda, S., Tsumura, H., & Torisu, T. (2005). Age-related quadriceps-dominant muscle atrophy and incident radiographic knee osteoarthritis. *Journal of Orthopaedic Science, 10*(2), 121-126.
- Jenkyn, T. R., Hunt, M. A., Jones, I. C., Giffin, J. R., & Birmingham, T. B. (2008). Toe-out gait in patients with knee osteoarthritis partially transforms external knee adduction moment into flexion moment during early stance phase of gait: a tri-planar kinetic mechanism. *Journal of Biomechanics, 41*(2), 276-283.
- Jones, R. K., Zhang, M., Laxton, P., Findlow, A. H., & Liu, A. (2013). The biomechanical effects of a new design of lateral wedge insole on the knee and ankle during walking. *Human Movement Science, 32*(4), 596-604.
- Kellgren, J. H., & Lawrence, J. S. (1957). Radiological assessment of rheumatoid arthritis. *Annals of the Rheumatic Diseases, 16*(4), 485-493.
- Landry, S. C., McKean, K. A., Hubble-Kozey, C. L., Stanish, W. D., & Deluzio, K. J. (2007). Knee biomechanics of moderate OA patients measured during gait at a self-selected and fast walking speed. *Journal of Biomechanics, 40*(8), 1754-1761.

- Lane, N. E., Brandt, K., Hawker, G., Peeva, E., Schreyer, E., Tsuji, W., et al. (2011). OARSI-FDA initiative: defining the disease state of osteoarthritis. *Osteoarthritis and Cartilage*, 19(5), 478-482.
- Lawrence, R. C., Felson, D. T., Helmick, C. G., Arnold, L. M., Choi, H., Deyo, R. A., et al. (2008). Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part II. *Arthritis & Rheumatism*, 58(1), 26-35.
- Lee, S. S., & Piazza, S. J. (2008). Inversion-eversion moment arms of gastrocnemius and tibialis anterior measured in vivo. *Journal of Biomechanics*, 41(16), 3366-3370.
- Lementowski, P. W., & Zelicof, S. B. (2008). Obesity and osteoarthritis. *American Journal of Orthopedics*, 37(3), 148-151.
- Levinger, P., Menz, H. B., Fotoohabadi, M. R., Feller, J. A., Bartlett, J. R., & Bergman, N. R. (2010). Foot posture in people with medial compartment knee osteoarthritis. *Journal of Foot and Ankle Research*, 3(29), 1-8.
- Levinger, P., Menz, H. B., Morrow, A. D., Bartlett, J. R., Feller, J. A., & Bergman, N. R. (2013). Relationship between foot function and medial knee joint loading in people with medial compartment knee osteoarthritis. *Journal of Foot and Ankle Research*, 6(1), 33.
- Levinger, P., Menz, H. B., Morrow, A. D., Feller, J. A., Bartlett, J. R., & Bergman, N. R. (2012). Foot kinematics in people with medial compartment knee osteoarthritis. *Rheumatology*, 51(12), 2191-2198.
- Lohmander, L. S., Englund, P. M., Dahl, L. L., & Roos, E. M. (2007). The long-term consequence of anterior cruciate ligament and meniscus injuries: osteoarthritis. *American Journal of Sports Medicine*, 35(10), 1756-1769.
- Lynn, S. K., & Costigan, P. A. (2008). Effect of foot rotation on knee kinetics and hamstring activation in older adults with and without signs of knee osteoarthritis. *Clinical Biomechanics*, 23(6), 779-786.
- Lynn, S. K., Kajaks, T., & Costigan, P. A. (2008). The effect of internal and external foot rotation on the adduction moment and lateral-medial shear force at the knee during gait. *Journal of Science and Medicine in Sport*, 11(5), 444-451.
- Maly, M. R., Costigan, P. A., & Olney, S. J. (2008). Mechanical factors relate to pain in knee osteoarthritis. *Clinical Biomechanics*, 23(6), 796-805.
- Maly, M. R., Culham, E. G., & Costigan, P. A. (2002). Static and dynamic biomechanics of foot orthoses in people with medial compartment knee osteoarthritis. *Clinical Biomechanics*, 17(8), 603-610.

- Miyazaki, T., Wada, M., Kawahara, H., Sato, M., Baba, H., & Shimada, S. (2002). Dynamic load at baseline can predict radiographic disease progression in medial compartment knee osteoarthritis. *Annals of the Rheumatic Diseases*, *61*, 617-622.
- Mundermann, A., Dyrby, C. O., & Andriacchi, T. P. (2005). Secondary gait changes in patients with medial compartment knee osteoarthritis: increased load at the ankle, knee, and hip during walking. *Arthritis & Rheumatism*, *52*(9), 2835-2844.
- Murphy, L., & Helmick, C. G. (2012). The impact of osteoarthritis in the United States: a population-health perspective. *American Journal of Nursing*, *112*(3 Suppl 1), 13-19.
- Neal, B. S., Griffiths, I. B., Dowling, G. J., Murley, G. S., Munteanu, S. E., Franettovich Smith, M. M., et al. (2014). Foot posture as a risk factor for lower limb overuse injury: a systematic review and meta-analysis. *Journal of Foot and Ankle Research*, *7*(1), 55.
- Nilsson, A. K., Toksvig-Larsen, S., & Roos, E. M. (2009). A 5 year prospective study of patient-relevant outcomes after total knee replacement. *Osteoarthritis and Cartilage*, *17*(5), 601-606.
- Paterson, K. L., Kasza, J., Hunter, D. J., Hinman, R. S., Menz, H. B., Peat, G., et al. (2016). The relationship between foot and ankle symptoms and risk of developing knee osteoarthritis: data from the osteoarthritis initiative. *Osteoarthritis and Cartilage*.
- Perry, J. (1992). *Gait analysis : normal and pathological function*. Thorofare, N.J.: SLACK inc.
- Radin, E. L., Martin, R. B., Burr, D. B., Caterson, B., Boyd, R. D., & Goodwin, C. (1984). Effects of mechanical loading on the tissues of the rabbit knee. *Journal of Orthopaedic Research*, *2*(3), 221-234.
- Reeves, N. D., & Bowling, F. L. (2011). Conservative biomechanical strategies for knee osteoarthritis. *Nature Reviews Rheumatology*, *7*(2), 113-122.
- Reyes, C., Leyland, K. M., Peat, G., Cooper, C., Arden, N. K., & Prieto-Alhambra, D. (2016). Association Between Overweight and Obesity and Risk of Clinically Diagnosed Knee, Hip, and Hand Osteoarthritis: A Population-Based Cohort Study. *Arthritis & Rheumatology*, *68*(8), 1869-1875.
- Richmond, J. C. (2013). Surgery for osteoarthritis of the knee. *Rheumatic Disease Clinics of North America*, *39*(1), 203-211.
- Rutherford, D. J., Hubley-Kozey, C. L., & Stanish, W. D. (2010). The neuromuscular demands of altering foot progression angle during gait in asymptomatic individuals and those with knee osteoarthritis. *Osteoarthritis and Cartilage*, *18*(5), 654-661.
- Salaffi, F., Carotti, M., Stancati, A., & Grassi, W. (2005). Health-related quality of life in older adults with symptomatic hip and knee osteoarthritis: a comparison with

- matched healthy controls. *Aging Clinical and Experimental Research*, 17(4), 255-263.
- Schipplein, O. D., & Andriacchi, T. P. (1991). Interaction between active and passive knee stabilizers during level walking. *Journal of Orthopaedic Research*, 9(1), 113-119.
- Schnitzer, T. J., Popovich, J. M., Andersson, G. B., & Andriacchi, T. P. (1993). Effect of piroxicam on gait in patients with osteoarthritis of the knee. *Arthritis & Rheumatology*, 36(9), 1207-1213.
- Shakoor, N., & Block, J. A. (2006). Walking barefoot decreases loading on the lower extremity joints in knee osteoarthritis. *Arthritis & Rheumatism*, 54(9), 2923-2927.
- Sharma, L., Hurwitz, D. E., Thonar, E. J., Sum, J. A., Lenz, M. E., Dunlop, D. D., et al. (1998). Knee adduction moment, serum hyaluronan level, and disease severity in medial tibiofemoral osteoarthritis. *Arthritis & Rheumatism*, 41(7), 1233-1240.
- Sharma, L., Kapoor, D., & Issa, S. (2006). Epidemiology of osteoarthritis: an update. *Current Opinion in Rheumatology*, 18, 147-156.
- Sharma, L., Song, J., Dunlop, D., Felson, D., Lewis, C. E., Segal, N., et al. (2010). Varus and valgus alignment and incident and progressive knee osteoarthritis. *Annals of the Rheumatic Diseases*, 69(11), 1940-1945.
- Sharma, L., Song, J., Felson, D. T., Cahue, S., Shamiyeh, E., & Dunlop, D. D. (2001). The role of knee alignment in disease progression and functional decline in knee osteoarthritis. *Journal of the American Medical Association*, 286(2), 188-195.
- Shelburne, K. B., Torry, M. R., & Pandy, M. G. (2006). Muscle, ligament, and joint-contact forces at the knee during walking. *Medicine and Science in Sports and Exercise*, 37(11), 1948-1956.
- Shull, P. B., Shultz, R., Silder, A., Dragoo, J. L., Besier, T. F., Cutkosky, M. R., et al. (2013a). Toe-in gait reduces the first peak knee adduction moment in patients with medial compartment knee osteoarthritis. *Journal of Biomechanics*, 46(1), 122-128.
- Shull, P. B., Silder, A., Shultz, R., Dragoo, J. L., Besier, T. F., Delp, S. L., et al. (2013b). Six-week gait retraining program reduces knee adduction moment, reduces pain, and improves function for individuals with medial compartment knee osteoarthritis. *Journal of Orthopaedic Research*, 31(7), 1020-1025.
- Simic, M., Hinman, R. S., Wrigley, T. V., Bennell, K. L., & Hunt, M. A. (2010). Gait modification strategies for altering medial knee joint load: A systematic review. *Arthritis Care & Research*, 405-426.
- Simic, M., Hunt, M. A., Bennell, K. L., Hinman, R. S., & Wrigley, T. V. (2012). Trunk lean gait modification and knee joint load in people with medial knee osteoarthritis: the effect of varying trunk lean angles. *Arthritis Care & Research*, 64(10), 1545-1553.

- Simic, M., Wrigley, T. V., Hinman, R. S., Hunt, M. A., & Bennell, K. L. (2013). Altering foot progression angle in people with medial knee osteoarthritis: the effects of varying toe-in and toe-out angles are mediated by pain and malalignment. *Osteoarthritis and Cartilage*, *21*(9), 1272-1280.
- Simpson, K. J., & Jiang, P. (1999). Foot landing position during gait influences ground reaction forces. *Clinical Biomechanics*, *14*(6), 396-402.
- Slemenda, C., Brandt, K. D., Heilman, D. K., Mazzuca, S., Braunstein, E. M., Katz, B. P., et al. (1997). Quadriceps weakness and osteoarthritis of the knee. *Annals of Internal Medicine*, *127*(2), 97-104.
- Slemenda, C., Heilman, D. K., Brandt, K. D., Katz, B. P., Mazzuca, S. A., Braunstein, E. M., et al. (1998). Reduced quadriceps strength relative to body weight: a risk factor for knee osteoarthritis in women? *Arthritis & Rheumatism*, *41*(11), 1951-1959.
- Sophia Fox, A. J., Bedi, A., & Rodeo, S. A. (2009). The basic science of articular cartilage: structure, composition, and function. *Sports Health*, *1*(6), 461-468.
- Suter, E., & Herzog, W. (2000). Does Muscle Inhibition after Knee Injury Increase the Risk of Osteoarthritis? *Exercise and Sport Sciences Reviews*, *28*(1), 15-18.
- Taylor, W. R., Heller, M. O., Bergmann, G., & Duda, G. N. (2004). Tibio-femoral loading during human gait and stair climbing. *Journal of Orthopaedic Research*, *22*(3), 625-632.
- Titchenal, M. R., Chu, C. R., Erhart-Hledik, J. C., & Andriacchi, T. P. (2016). Early Changes in Knee Center of Rotation During Walking After Anterior Cruciate Ligament Reconstruction Correlate With Later Changes in Patient-Reported Outcomes. *American Journal of Sports Medicine*, *45*(4), 915-921.
- Vaishya, R., Pariyo, G. B., Agarwal, A. K., & Vijay, V. (2016). Non-operative management of osteoarthritis of the knee joint. *Journal of Clinical Orthopaedics and Trauma*, *7*(3), 170-176.
- Wang, J. W., Kuo, K. N., Andriacchi, T. P., & Galante, J. O. (1990). The influence of walking mechanics and time on the results of proximal tibial osteotomy. *Journal of Bone and Joint Surgery. American Volume*, *72*(6), 905-909.
- White, D. K., Neogi, T., Nguyen, U.-S. D. T., Niu, J., & Zhang, Y. (2015). Trajectories of functional decline in knee osteoarthritis: the Osteoarthritis Initiative. *Rheumatology*, *55*(5), 801-808.
- Winby, C. R., Lloyd, D. G., Besier, T. F., & Kirk, T. B. (2009). Muscle and external load contribution to knee joint contact loads during normal gait. *Journal of Biomechanics*, *42*(14), 2294-2300.

Zhao, D., Banks, S. A., Mitchell, K. H., D'Lima, D. D., Colwell, C. W., Jr., & Fregly, B. J. (2007). Correlation between the knee adduction torque and medial contact force for a variety of gait patterns. *Journal of Orthopaedic Research*, 25(6), 789-797.