EVALUATION OF INTERLIMB SYMMETRY IN INDIVIDUALS WITH KNEE OSTEOARTHRITIS DURING GAIT

by

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ABSTRACT

Knee osteoarthritis is a degenerative joint disease and is one of the leading causes of disability in the United States. While the etiology is not fully understood, mechanics have been implicated in the disease initiation and progression. Previous research has found that individuals with knee osteoarthritis exhibit abnormal kinematic and kinetic gait patterns. These studies, however, have focused on the symptomatic limb in comparison with healthy individuals leaving the mechanics of the contralateral limb largely unknown. Furthermore, there has been evidence suggesting that alterations on the symptomatic limb may result in an increased risk of osteoarthritis on the contralateral limb. The objective of this study was to investigate the mechanics of the contralateral limb and associated symmetry of individuals with knee osteoarthritis during gait.

Seventeen subjects with knee osteoarthritis were evaluated. Three-dimensional motion capture data was collected as each subject walked at self-selected speed on an instrumented split-belt treadmill. The symptomatic limb was selected as each subject’s self-described more painful knee and was verified radiographically to possess more severe osteoarthritis than the contralateral knee. Kinematic and kinetic analysis focused on sagittal plane knee motion during initial contact and early stance, peak vertical ground reaction force, and loading rate. In order to assess interlimb symmetry on a more global limb level, various total support moment parameters were investigated. Interlimb differences for all variables were assessed using paired t-tests.
The results revealed that the symptomatic knee contacted the ground with more flexion, exhibited less excursion during stance and displayed less total excursion than the contralateral limb. In comparison with the contralateral limb, the symptomatic limb also experienced a reduced peak vertical ground reaction force and vertical loading rate. Additionally, there were no interlimb differences for peak or angular impulse of total support moment; however the symptomatic limb displayed a decreased knee contribution and an increased ankle contribution to peak total support moment when compared with the contralateral limb.

The presence of interlimb asymmetries at the joint and limb levels suggests that individuals with knee osteoarthritis are using their symptomatic and contralateral limbs differently during gait. These asymmetries could represent compensation by the contralateral limb to decrease joint loading and limit knee motion for the more painful limb. Future research should focus on comparing the contralateral limb to limbs of healthy individuals in order to determine if clinical interventions should target one or both limbs to restore gait symmetry.
Chapter 1

INTRODUCTION

1.1 Osteoarthritis

Estimates show that approximately 27 million adults are affected by osteoarthritis (OA) in the United States alone (Lawrence et al. 2008) and that this number is expected to increase to over 67 million by the year 2030 (Hootman and Helmick 2006). The symptoms of the disease include pain, inflammation, and joint stiffness (Griffin and Guilak 2005; Jackson et al. 2004) which often result in decreased functionality and quality of life (Davis et al. 1991). The debilitating symptoms and high prevalence of OA subsequently lead to a large societal burden. In the US, the disease is one of the leading causes of disability (Gupta et al. 2005) and economic costs are approximately 60 billion dollars per year (Buckwalter et al. 2004). Currently there is no cure for knee OA, but several treatment modalities exist to diminish the symptoms. Conservative solutions such as weight loss and exercise have been frequently used to manage pain and maintain joint function (Fajardo and Cesare 2005). Other non-surgical options such as pharmacological treatments and intra-articular injections are also commonly utilized (Fajardo and Cesare 2005). However, total knee arthroplasty is the only way to completely relieve the symptoms (Hawker et al. 1998).

The etiology of the disease is not completely understood, but factors such as genetics (Spector et al. 1996), gender (Arden and Nevitt 2006), previous injury (Gelber et al. 2000), obesity (Felson et al. 2000), and age (Buckwalter et al. 2004) have all been linked to the disease. The risk factors of age and obesity present a
specific concern as both are on the rise in the US which will likely result in a significant increase in the prevalence of knee OA (CDC 2003; Ogden et al. 2012). Mechanics have also been largely implicated in the pathogenesis and progression of knee OA (Andriacchi et al. 2004; Buckwalter et al. 2004; Miyazaki et al. 2002; Sharma et al. 1998; Wu et al. 2000). In a healthy knee joint, the articular cartilage of the tibia, femur, and patella provides a low friction surface to allow for smooth transmission and distribution of loading (Lavangie and Norkin 2011). Knee OA is characterized by a deterioration of the articular cartilage due to a metabolic imbalance in chondrocyte activity (Griffin and Guilak 2005). It has been shown that considerable alterations in loading can initiate this breakdown of cartilage (Andriacchi et al. 2004; Arsever and Bole 1986; Suter et al. 1998; Wu et al. 2000). Abnormal kinematics are thought to dictate changes in loading and the subsequent breakdown of cartilage by altering the location of loading within the knee joint to regions not adapted to high loads (Andriacchi et al. 2004; Biswal et al. 2002). Several factors such as injury, increased joint laxity, neuromuscular changes, obesity and aging have been suggested to induce these abnormal kinematics and loading patterns (Andriacchi and Mündermann 2006). The subsequent progression of the disease, however, is associated with a repetition of high loads to damaged cartilage (Andriacchi et al. 2004). Consequently, the gait of individuals with knee OA is often studied due to the inherent repetition of substantial forces at the knee (Anderson and Pandy 2001; D’Lima et al. 2007; Schipplein and Andriacchi 1991).

1.2 Interlimb Symmetry

Traditionally, healthy individuals have been assumed to have symmetric gait, while asymmetries were thought to be indicative of a pathological condition. Various
definitions for ‘gait symmetry’ have been proposed, but the common qualifier of all is that both limbs behave identically (Sadeghi et al. 2000). Some studies have investigated healthy gait and concluded that it was symmetric with respect to various kinematic and kinetic parameters (Hannah et al. 1984; Menard et al. 1992). However, other studies came to a conflicting conclusion that healthy gait was asymmetric (Gundersen et al. 1989; Hamill et al. 1984). One primary reason for such contradictory results is that there is no consensus on the criteria for classifying gait as symmetric or asymmetric. Typically studies determine gait symmetry based on a unique set of a few variables, while other studies may investigate an entirely different set of parameters to decide if gait is symmetric. This emphasizes the idea that when analyzing gait symmetry of a specific pathological population, it is of upmost importance to select the most relevant parameters for that population.

While the lack of an agreed upon classifying criteria for overall gait symmetry is a limitation, interlimb analysis can still provide useful insight. Identifying gait asymmetries in the knee OA population is particularly important as abnormal kinematic or kinetic patterns can lead to an increased risk for initiation and progression of the disease (Andriacchi et al. 2004; Arsever and Bole 1986; Miyazaki et al. 2002; Sharma et al. 1998; Wu et al. 2000). In knee OA research, a vast majority of studies have only evaluated the symptomatic limb and compared it to healthy control limbs. Although this approach is important for understanding biomechanical differences in the symptomatic limb, it leaves the mechanics of the contralateral limb entirely unknown. This is of concern as specific risks to the contralateral limb have been identified. Studies investigating pathological gait of other conditions such as hip OA (White and Lifeso 2005), total knee replacement (Mizner and Snyder-Mackler
2005), anterior cruciate ligament injury (Roewer et al. 2011), and amputees (Skinner and Effeney 1985) have shown there to be significant interlimb asymmetries during gait. Asymmetric alterations to decrease loading in the symptomatic limb have been shown to lead to increased loading in the contralateral limb in individuals with hip OA (McCrory et al. 2001). Similarly, a study by Shakoor and colleagues (2002) showed that after total knee replacement the altered loading in the operated limb lead to a non-random progression of OA to the joints of the contralateral limb, especially the contralateral knee joint (Shakoor et al. 2002). Additionally, the contralateral knee exhibits equivalent proprioceptive deficits as the symptomatic knee (Sharma et al. 1997). These studies strongly suggest that that the contralateral knee is at an elevated risk of OA initiation and progression.

Despite the apparent risks, knee OA research has rarely investigated both limbs during gait. A few studies analyzed both the right and left limbs of individuals with knee OA compared with healthy controls and found differences between the limbs of the OA subjects for a limited number of parameters (Gök et al. 2002; Liikavainio et al. 2007; Sharma et al. 1998). While these three studies examining both the left and right limbs consider laterality, they are not able to offer insight on the influence of knee OA on the observed interlimb asymmetries due to the failure to account for changes in mechanics based on pathological condition. Distinction between the more OA symptomatic limb and less symptomatic limb is necessary to elucidate asymmetries induced by the disease. Some studies have separately analyzed the symptomatic and the contralateral limbs during other activities of daily living. One study of weight-bearing asymmetries in knee OA subjects during sit to stand tasks found the contralateral limb had a higher ground reaction force (Christiansen and Stevens-
Lapsley 2010). Another study found reduced peak knee flexion moments on the symptomatic limb during stair climbing (Asay et al. 2009). These two studies, however, did not investigate gait. Messier et al. (1992) studied both OA limbs during level walking and found a few kinematic and kinetic asymmetries (Messier et al. 1992). While this study did address interlimb differences, interlimb symmetry was not a primary focus of the research. A recent study evaluated the gait symmetry of subjects with knee OA and found several significant interlimb differences (Creaby et al. 2012). However, this study only investigated a few parameters such as trunk lean and knee adduction moment and did not concentrate on sagittal plane measures.

A common limitation of many gait symmetry studies is that only single joint, single plane parameters are used to assess symmetry. Although this type of analysis is suitable for obtaining a localized joint level depiction of symmetry, it is unable to give a more global limb level description. The two major goals of ambulation are to provide support against gravity and forward propulsion (Anderson and Pandy 2003; Kepple et al. 1997; Perry 1992a) and classifying gait symmetry based on these primary functions has been proposed as a way of assessing symmetry on a larger, limb level scale (Sadeghi 1997). Rather than investigating a variety of joint level parameters, this method focuses only on parameters that elucidate the role of each limb to the progression and support tasks during ambulation in order to assess functional gait symmetry. Studies have found evidence of functional asymmetry in healthy gait, meaning one limb is used more for support while the other is predominantly used for propulsion (Hirasawa 1981; Hirasawa 1979; Sadeghi 1997). These studies, however, focused on joint power generation and absorption and did not investigate kinematics or joint moments. Other research assessing the presence of
functional asymmetry found no evidence to support this theory (Rice and Seeley 2010; Seeley et al. 2008). While there is disagreement whether healthy individuals exhibit functional asymmetry, no studies have assessed the interlimb symmetry of global limb level parameters for individuals with knee OA.

Based on the apparent risks to the contralateral limb, it is clear that there is need for more research dedicated to the evaluation of the contralateral limb mechanics and associated symmetry at both the local joint and global limb levels to further understand the degree of risk of OA initiation and progression.

1.3 Aim 1: Kinematic Gait Alterations

Decreased total knee excursion during gait has been associated with knee OA (Al-Zahrani and Bakheit 2002; Astephen et al. 2008; Brinkmann and Perry 1985; Messier et al. 1992). This behavior, however, is more frequently observed in individuals with more advanced OA (Astephen et al. 2008). Decreased total knee excursion has traditionally been thought of as a response to knee pain (Radin et al. 1991; Robon et al. 2000; Stauffer et al. 1977), but diminished joint proprioception has also been suggested as a contributor (Pai et al. 1997; Sharma et al. 1997). Both explanations are supported by the fact that individuals with moderate OA generally have less severe symptoms and also have a greater knee joint range of motion compared persons with more severe OA. Compensatory alterations at the hip and ankle during gait can be adopted as a result of kinematic changes at the knee. Very few studies have investigated total excursion of the hip and ankle during gait in the knee OA population. One gait study did report decreased total joint excursion at the hip and ankle along with the decreased total joint excursion at the knee, but only for subjects with severe knee OA (Astephen et al. 2008). Messier et al. (1992) found that
while there was no difference in ankle motion between OA subjects and healthy controls, the patient group displayed an increase in total hip excursion (Messier et al. 1992). This study suggested that OA subjects utilized an increased hip range of motion to compensate for the decreased knee motion in order to maintain more normal spatio-temporal gait parameters. The varying findings at the hip and ankle between studies could be explained by differences in OA severity and walking speed as subjects with more advanced knee OA exhibit slower walking speeds which can alter lower extremity joint kinematics (Astephen et al. 2008; Mündermann et al. 2004; Robon et al. 2000; Zeni and Higginson 2009). Asymmetries in total joint excursions at the hip, knee, and ankle could provide a simple indicator of potentially detrimental gait strategies.

During gait, initial contact occurs when the foot first strikes the ground. This event marks the beginning of a gait cycle. The kinematics at this early phase of gait are extremely informative with respect to shock absorption of the ground reaction force throughout the lower limb joints. Shock is defined as a sudden impact force such as initial contact during gait; shock absorption is the dissipation of the kinetic energy created by an impact force. In particular, knee flexion angle at initial contact and during loading response is of great interest as the knee is extremely important for shock absorption (Perry 1992b). Rapid impact forces have been implicated in cartilage deterioration and thus knee angle at initial contact could help explain this aspect of disease progression (Ewers et al. 2001; Ewers et al. 2002; Kerin et al. 2003). Increased knee flexion at initial contact could decrease the lower limb stiffness which would allow for decreased peak force and loading rate (Butler 2003). Additionally, increased knee flexion during early stance requires greater quadriceps action to
decelerate the rate of knee flexion induced by gravity; thus increased quadriceps activity can act to attenuate the rate of vertical loading on the lower limb (Perry 1992b). From a purely mechanical standpoint, knee angle at initial contact can also influence the type of loading at the knee joint caused by the ground reaction force. Furthermore, differences in knee flexion at initial contact could alter the location of contact loading within the knee joint, which has been suggested as mechanism of OA disease initiation (Andriacchi et al. 2004; Biswal et al. 2002). While increased knee flexion during initial contact could be a mechanism to improve shock absorption, it may lead to potentially detrimental changes in type of loading and location of loading within the knee joint. Previous knee OA literature investigating knee flexion angle at initial contact have found conflicting results. Three studies (Baliunas et al. 2002; Childs et al. 2004; Weidow et al. 2006) reported that subjects with knee OA contacted the ground with a more flexed knee than healthy controls, while a study by Mündermann et al. (2005) found that knee OA subjects landed in a more extended position (Mündermann et al. 2005). However, due to differences in protocols between studies (walking speed, drug wash-out period, and classification of OA groups), a characteristic knee angle at initial contact has not been conclusively determined for individuals with knee OA.

Since the main objective of the loading response phase of gait is shock absorption, knee motion during weight acceptance may be an important kinematic factor influencing the initiation and progression of OA. Less knee motion during weight acceptance is associated with higher limb stiffness due to the decreased vertical displacement of the center of mass (Butler 2003). The result is higher loading rates and increased peak forces on the knee which are both risk factors for cartilage damage.
Knee kinematics during the first 10% of the gait cycle are especially influential in determining how the knee joint absorbs the loading. Knee excursion during stance is defined as the range of sagittal plane knee flexion from initial foot contact to peak knee flexion during stance. Several studies have found that subjects with knee OA exhibit decreased knee excursion during stance (Childs et al. 2004; Gök et al. 2002; Ramsey et al. 2007; Zeni and Higginson 2009). Decreased knee excursion during stance may be a gait alteration driven by persistent quadriceps weakness (Ramsey et al. 2007). This behavior could also represent an effort to increase joint stability through decreased mobility. Regardless, reduced knee flexion during weight acceptance may inhibit the lower limb’s capability to properly absorb loading which would subsequently elevate the risk of cartilage degeneration (Ewers et al. 2001). Interlimb symmetry of kinematic parameters during initial contact and loading response is important to understand as it may elucidate a compensatory strategy designed to decrease loading on the symptomatic limb which may then increase loading on the contralateral side.

A vast amount of research has investigated sagittal plane kinematics of subjects with knee OA and found evidence of abnormal gait mechanics on the symptomatic limb; however, the previous studies have largely overlooked the implications of primary knee OA on the contralateral limb. The potential increased risk for OA initiation and progression to the contralateral knee caused by abnormal kinematics on the symptomatic limb has provided motivation for Specific Aim 1:

*To assess the interlimb symmetry of sagittal plane kinematics within the OA population during gait.*
\textbf{Hypothesis 1.1}: The OA symptomatic limb will exhibit significantly decreased total knee excursion than the contralateral limb. There will be no interlimb differences in total joint excursions at the hip or ankle.

\textbf{Hypothesis 1.2}: The OA symptomatic limb will display greater knee flexion at initial contact than the contralateral limb.

\textbf{Hypothesis 1.3}: The OA symptomatic limb will demonstrate reduced knee excursion during stance than the contralateral limb.

1.4 \hspace{1em} \textbf{Aim 2: Kinetic Gait Alterations}

Higher joint contact forces likely influence disease pathomechanics, however these forces are extremely difficult to directly measure (Jackson et al. 2004). As an alternative, external joint moments are frequently studied in knee OA gait analysis as a surrogate measure for joint contact force (Baliunas et al. 2002; Boyer et al. 2008). A clear relationship between knee adduction moment and disease progression has already been established (Miyazaki et al. 2002; Mündermann et al. 2005; Sharma et al. 1998). In the sagittal plane, the peak external knee flexion moment has been studied in knee OA with mixed results. While some studies have found no difference between OA and healthy subjects (Baliunas et al. 2002; Mündermann et al. 2005), results of many other studies show that individuals with knee OA exhibit decreased peak knee flexion moment (Astephen et al. 2008; Gök et al. 2002; Kaufman et al. 2001; Landry et al. 2007; Weidow et al. 2006; Zeni and Higginson 2009). The quadriceps muscles, which counteract external knee flexion moment, are major contributors to joint contact forces at the knee (Sasaki and Neptune 2010). Decreased peak knee flexion moment is likely achieved by maintaining a more extended knee during loading response and mid-stance, which would reduce the need for quadriceps activation, thus diminishing
the joint contact force. Although many knee OA studies have examined knee flexion moment, very few have analyzed it for both the symptomatic and contralateral limbs.

Vertical ground reaction force is a parameter frequently investigated in gait studies as it plays a large role in determining joint forces and moments. With higher vertical ground reaction forces, joints will typically experience higher loading. In knee OA research, peak vertical ground reaction force during gait is often investigated as both magnitude (Jeffrey et al. 1995) and repetition (Kerin et al. 2003) of loading is a risk factor for cartilage deterioration. It commonly thought that subjects with knee OA aim to reduce peak vertical ground reaction force in an effort to limit painful joint contact forces. While there are studies that have found no difference (Messier et al. 1992; Mündermann et al. 2005; Radin et al. 1991), other authors have found that individuals with knee OA do decrease their peak vertical ground reaction force when compared with healthy controls (Childs et al. 2004; Gök et al. 2002; Zeni and Higginson 2009). Differences in speed could very well explain the difference as knee OA subjects typically walk at a slower self-selected speed. One study looked at the interlimb symmetry of peak vertical ground reaction force in knee OA subjects and found no significant asymmetries between the right and left limbs during level walking (Liikavainio et al. 2007). Examining interlimb symmetry between the symptomatic and contralateral limbs could provide insight to whether reducing peak vertical ground reaction force is a compensatory mechanism for subjects with knee OA.

Vertical loading rate describes how rapidly the vertical ground reaction force develops. It is defined as the average slope of the vertical ground reaction force curve during the first 10% of the gait cycle. Increased loading rates have shown to result in
more frequent surface fissuring of articular cartilage (Ewers et al. 2002) as well as propagation of existing fissures (Kerin et al. 2003). Consequently, vertical loading rate is of great interest, as this breakdown of cartilage is a primary concern in initiation and progression of OA. Previous studies have reported conflicting results with higher (Mündermann et al. 2005) and lower (Childs et al. 2004) vertical loading rates in OA groups when compared with healthy controls. Zeni et al. (2009) found that while differences existed between groups, the results were highly dependent on walking speed (Zeni and Higginson 2009). One other major factor that influences vertical loading rate is the amount of shock absorption in the lower limb at initial contact and loading response. Messier et al. (1992) found that the unaffected limb had higher vertical loading rates than the symptomatic limb and suggested that this behavior was an attempt to reduce pain in the symptomatic limb by rapidly shifting weight to the contralateral limb (Messier et al. 1992). Knee angle at initial contact and knee excursion are kinematic variables that reflect how the lower limb absorbs shock; this adaptive asymmetry could be a major risk factor for OA initiation and progression in the contralateral limb.

The kinetics of OA gait have been frequently evaluated. The vast majority of these studies have only investigated the more symptomatic limb. Consequently, the kinetics of the contralateral limb remain largely unknown. Knee OA research on the contralateral limb is important as there has been evidence that the contralateral limb could have an elevated risk of OA (Shakoor et al. 2002). The lack of research on the contralateral limb combined with the potential increased risk for OA initiation and progression to the contralateral knee has led to the development of Specific Aim 2:
To assess the interlimb symmetry of sagittal plane kinetics within the OA population during gait.

**Hypothesis 2.1:** The OA symptomatic limb will exhibit a significantly decreased peak knee flexion moment than the contralateral limb.

**Hypothesis 2.2:** The OA symptomatic limb will demonstrate reduced peak vertical ground reaction force and vertical loading rate than then contralateral limb.

1.5 Aim 3: Total Support Moment

The lower limb segments and joints are inherently dependent on one another and act synergistically during functional tasks such as ambulation. While individual joint moments provide valuable insight, they can only offer information about a single joint. In order to obtain a more robust understanding of the contralateral limb and associated symmetry, it may be beneficial to analyze a measure that captures information at the limb level in order to assess a more global limb function. The total support moment is defined as the sum of the internal hip, knee, and ankle extensor moments and was first proposed as a measure of lower limb coordination and function (Winter 1980). These internal extensor moments prevent the lower limb from collapsing under body weight. The total support moment has been evaluated and shown to be a reliable parameter (Flanagan and Salem 2005) and less variable than analyzing individual joint moments (Winter 1980). A recent study found that while there was no difference in peak total support moment between subjects with knee OA and healthy individuals at controlled and self-selected speeds, the OA group showed a diminished peak total support moment at their freely chosen fast walking speed (Zeni and Higginson 2011). The peak total support moment can offer limb level insight that
cannot be obtained by individual joint moments in order to estimate if the peak sagittal plane torque is similar between the symptomatic and contralateral limbs.

In addition to quantifying the lower limb as a whole, the peak total support moment can be decomposed in order to investigate hip, knee, and ankle contributions. Examining the percent contribution of the individual joints to the total support moment allows for a more refined method of evaluating lower limb function while still accounting for coordination between joints. Zeni et al. (2011) found that when compared with controls, subjects with knee OA significantly decreased their knee contribution and increased their ankle contribution to peak total support moment at self-selected speed (Zeni and Higginson 2011). By decomposing the total support moment into individual joint contributions and observing how the load is distributed across the hip, knee and ankle, it is possible to gain insight about the strategy utilized by each limb to achieve body weight support.

While useful, peak total support moment only represents an instant of a gait cycle and does not account for duration of loading. In order to obtain information about limb loading over a longer time period, the total support moment curve can be integrated to attain the angular impulse of total support moment. The single support phase of gait represents the period of the gait cycle when only one limb is in contact with the ground and is solely responsible for supporting the body. By selecting to integrate total support moment over the single support phase of gait, the study limb is isolated and direct compensation by the opposite limb is prevented. Knee OA research utilizing angular impulse of knee adduction moment found that the OA group displayed greater values than the healthy control group, suggesting that individuals with OA experience more knee loading which could lead to an increased rate of
disease progression (Thorp et al. 2006). The angular impulse of total support moment during single support can further elucidate the limb level gait mechanics of the OA symptomatic and contralateral limbs.

The synergistic nature of the lower limb segments and joints during gait are well acknowledged. However, very few studies have utilized parameters such as the total support moment to quantify lower limb coordination and function. An understanding of the OA symptomatic and contralateral limb mechanics on a limb level will offer insight that joint level parameters cannot provide. No healthy or knee OA research has used total support moment to analyze interlimb differences of how the lower limb is coordinating support. These factors provided the motivation for Specific Aim 3:

*To assess the interlimb symmetry on a global limb level by using total support moment parameters within the OA population during gait.*

**Hypothesis 3.1:** The OA symptomatic and contralateral limbs will demonstrate similar peak total support moments.

**Hypothesis 3.2:** The OA symptomatic limb will possess a reduced knee contribution and an increased ankle contribution to peak total support moment when compared with the contralateral limb.

**Hypothesis 3.3:** The OA symptomatic limb will exhibit a greater angular impulse of total support over single support than the contralateral limb.
Chapter 2

KINEMATIC AND KINETIC INTERLIMB GAIT ASYMMETRY IN INDIVIDUALS WITH KNEE OSTEOARTHRITIS

2.1 Introduction

Knee osteoarthritis (OA) is a degenerative joint disease affecting over 27 million adults in the US (Lawrence et al. 2008). Clinical symptoms of knee OA include joint pain and stiffness, which often result in decreased physical function and quality of life (Davis et al. 1991; Jackson et al. 2004). While the etiology of the disease is not completely understood, abnormal gait mechanics have been linked to the initiation and progression of knee OA (Andriacchi et al. 2004; Buckwalter and Martin 2006; Miyazaki et al. 2002; Sharma et al. 1998; Wu et al. 2000). Specifically, the mechanics of gait are frequently studied due to the inherent repetition of substantial forces experienced at the knee during walking (Anderson and Pandy 2001; D’Lima et al. 2007; Schippelein and Andriacchi 1991).

Kinematic gait alterations are commonly utilized by individuals with knee OA and include decreases in total knee excursion (Al-Zahrani and Bakheit 2002; Astephen et al. 2008; Brinkmann and Perry 1985; Messier et al. 1992) and knee excursion during stance (Childs et al. 2004; Gök et al. 2002; Ramsey et al. 2007; Zeni and Higginson 2009), as well as increases in knee flexion at initial contact (Baliunas et al. 2002; Childs et al. 2004; Weidow et al. 2006) compared to healthy gait. These gait alterations are suggested to be a mechanism to alleviate pain (Hurwitz et al. 2000; Schnitzer et al. 1993; Stauffer et al. 1977), particularly during the loading response.
phase of gait. Some kinetic analyses reported diminished peak vertical ground reaction forces in OA subjects (Childs et al. 2004; Gök et al. 2002; Zeni and Higginson 2009). There have been conflicting results as to whether individuals with knee OA exhibit increased (Mündermann et al. 2005) or decreased (Childs et al. 2004; Messier et al. 1992; Zeni and Higginson 2009) vertical loading rates, although both the magnitude (Jeffrey et al. 1995) and rate (Ewers et al. 2002; Ewers et al. 2001; Kerin et al. 2003) of loading are known risk factors for articular cartilage deterioration; this makes it important to further elucidate changes in loading rate in this population. Additionally, external knee flexion moments are frequently studied due to their association with joint loading, which has been linked to disease progression (Miyazaki et al. 2002; Zhao et al. 2007). Many studies have reported a reduction in peak external knee flexion moment in subjects with knee OA (Astephen et al. 2008; Gök et al. 2002; Kaufman et al. 2001; Landry et al. 2007; Weidow et al. 2006), while others found no change (Baliunas et al. 2002; Mündermann et al. 2005). While greater external knee adduction moment is perhaps the measure most commonly associated with individuals with knee OA (Baliunas et al. 2002; Gök et al. 2002; Hurwitz et al. 2002; Mündermann et al. 2005), interlimb analysis has previously been conducted and found no significant interlimb asymmetry (Creaby et al. 2012). Understanding the altered gait mechanics of individuals with knee OA can reveal factors that may increase or adversely shift joint loading.

Although there are many known gait alterations with knee OA, nearly all previous studies have focused only on the OA symptomatic limb in comparison with limbs of healthy individuals, while the impact on the contralateral limb remains unknown. One study involving patients with unilateral total knee arthroplasty found
that the contralateral knee is significantly more likely to require replacement than other contralateral or ipsilateral joints (Shakoor et al. 2002). These findings suggest that changes on a more symptomatic limb could lead to altered and increased loading on the contralateral limb. Given the possible risk of OA development in the contralateral limb, analyses should not be restricted to the more symptomatic limb; it is also necessary to study the mechanics of the contralateral limb and the associated gait symmetry.

Traditionally, healthy individuals have been assumed to have symmetric gait, whereas asymmetries were thought to be indicative of a pathological condition. While there have been conflicting findings on the symmetry of healthy gait (Gundersen et al. 1989; Hamill et al. 1984; Hannah et al. 1984; Menard et al. 1992), several lower extremity conditions such as hip OA (White and Lifeso 2005), total knee replacement (Mizner and Snyder-Mackler 2005), ACL injury (Roewer et al. 2011), and trans-tibial amputation (Skinner and Effeney 1985) have shown there can be significant interlimb asymmetries during gait. Two previous studies have investigated the OA symptomatic and contralateral limbs during gait (Creaby et al. 2012; Messier et al. 1992), but only one focused on interlimb comparisons (Creaby et al. 2012). Although Creaby et al. (2012) found interlimb differences in average knee varus angle, peak knee flexion, peak knee flexion moment, and average trunk lean, their study did not address early stance sagittal plane kinematics or magnitude and rate of loading, which are of interest for the knee OA population.

This study examined kinematic and kinetic parameters in the OA symptomatic and contralateral limbs in order to evaluate interlimb symmetry of individuals with knee OA during gait. We hypothesized that the OA symptomatic limb would exhibit
increased knee flexion at heel strike and decreased knee excursion during stance and total knee excursion when compared with the contralateral limb. Additionally, we hypothesized that there would be significant reductions in vertical loading rate, peak vertical ground reaction force, and peak external knee flexion moment on the OA symptomatic limb compared to the contralateral limb. Knowledge of kinematic and kinetic interlimb differences during gait will aid in assessing the potentially elevated risk of OA initiation and progression on the contralateral limb.

2.2 Methods

Subjects with probable knee OA were recruited from the local community and excluded from this study if they had a history of cardiopulmonary or neurological conditions, had any lower limb condition other than knee OA, had any lower limb surgery, or had intra-articular injections within 6 months prior to testing. The presence and severity of tibiofemoral OA was assessed from bilateral, anterior-posterior, 30 degree flexed knee radiographs using the Kellgren Lawrence (K-L) grading scale (Kellgren & Lawrence 1957). Subjects included in this study (n=17) were confirmed to have moderate (K-L grade 2 - 3) and medially dominant OA on one or both knees. The OA symptomatic limb was selected as the subject’s self-described more painful knee and was confirmed to have a greater K-L grade than the contralateral limb. Data collected for the first nine subjects was used to conduct a power analysis with 80% power and an alpha level of 0.05 for several key parameters (total knee excursion, knee flexion angle at initial contact, knee excursion during stance, peak vertical ground reaction force, and vertical loading rate). Based on the results, it was concluded that a total of 17 subjects would provide sufficient power for the study. Demographic information for all subjects is presented in Table 2.1.
Table 2.1. Demographic data for all subjects (n=17) as mean (SD).

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>62.3  (9.2)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>85.6 (12.0)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>30.2  (4.9)</td>
</tr>
<tr>
<td>Gender</td>
<td>10F/7M</td>
</tr>
</tbody>
</table>

All subjects walked at their self-selected speed on an instrumented split-belt treadmill (Bertec Corp., Columbus, OH). Individual self-selected walking speeds were determined by a timed 10 m overground walk. After familiarization with treadmill walking (Zeni and Higginson 2010), subjects continued to walk while data was recorded for 30 s. Ground reaction force and center of pressure data was collected at 1080 Hz. Three-dimensional kinematics were recorded by an eight camera motion capture system (Motion Analysis, Santa Rosa, CA) at 60 Hz from 23 retroreflective markers.

Coordinate marker data was smoothed using a 4th order, phase-corrected, Butterworth filter with a cutoff frequency of 6 Hz (Cortex 1.3, Motion Analysis). Joint angles and moments were calculated using inverse dynamics (Orthotrak 6.3.4, Motion Analysis). All joint moments were normalized to body mass. Data for each trial was divided into individual gait cycles which, were then averaged and normalized to 101 points by a custom program in LabView 8.2 (National Instruments, Austin TX). Each subject’s averaged and normalized gait cycle was used for comparisons.

Sagittal plane total joint excursion for the hip, knee, and ankle as well as knee flexion at initial contact and knee excursion during stance were examined. Knee excursion during stance was defined as the range of knee flexion from initial contact
to peak flexion during stance. Kinetic measures included peak external knee flexion moment, peak vertical ground reaction force, and vertical loading rate. Vertical loading rate was computed as the average slope of the vertical ground reaction force over the first 10\% of the gait cycle (Mündermann et al. 2005). Interlimb differences were assessed using paired t-tests for all variables. Statistical differences were defined as significant for $p \leq 0.05$. All statistical analyses were performed using SPSS v.18 (Chicago, IL).

2.3 Results

Subjects walked at an average self-selected speed of $1.14 \pm 0.13$ m/s. There were no significant interlimb differences for stride length ($p = 0.113$), cadence ($p = 0.276$), or percent stance ($p = 0.096$).

There were no significant interlimb differences in total joint excursion at the hip ($p = 0.190$) or ankle ($p = 0.279$) (Table 2.2). However, the OA symptomatic limb displayed significantly reduced total knee excursion compared with the contralateral side ($p < 0.001$) (Fig. 2.1; Table 2.2). The OA symptomatic limb exhibited diminished knee excursion during stance in comparison with the contralateral limb ($p < 0.001$) (Fig. 2.1; Fig. 2.2A; Table 2.2). Subjects also showed significantly increased knee flexion angle at initial contact on the OA symptomatic limb versus the contralateral limb ($p = 0.015$) (Fig. 2.1; Table 2.2).
Table 2.2. Symptomatic and contralateral limb values for all kinematic and kinetic gait parameters. Interlimb difference values of all subjects (contralateral – symptomatic). All data presented as mean (SD). All significant interlimb differences denoted with (*).

<table>
<thead>
<tr>
<th>Kinematics</th>
<th>Symptomatic</th>
<th>Contralateral</th>
<th>Interlimb Difference (Contra. – Sympt.)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Hip Excursion (°)</td>
<td>43.9 (4.0)</td>
<td>44.9 (5.1)</td>
<td>1.0 (3.1)</td>
<td>0.190</td>
</tr>
<tr>
<td>Total Knee Excursion (°)</td>
<td>58.7 (5.1)</td>
<td>63.5 (4.3)</td>
<td>4.7 (4.1)</td>
<td>&lt; 0.001 *</td>
</tr>
<tr>
<td>Total Ankle Excursion (°)</td>
<td>29.3 (7.2)</td>
<td>27.8 (4.1)</td>
<td>-1.5 (5.6)</td>
<td>0.279</td>
</tr>
<tr>
<td>Knee Excursion during Stance (°)</td>
<td>12.7 (4.6)</td>
<td>15.9 (4.5)</td>
<td>3.2 (3.2)</td>
<td>&lt; 0.001 *</td>
</tr>
<tr>
<td>Knee Flexion Angle at Initial Contact (°)</td>
<td>5.0 (7.7)</td>
<td>1.9 (8.6)</td>
<td>-3.4 (5.1)</td>
<td>0.015 *</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Kinetics</th>
<th>Symptomatic</th>
<th>Contralateral</th>
<th>Interlimb Difference (Contra. – Sympt.)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peak Vertical Ground Reaction Force (BW)</td>
<td>1.08 (0.07)</td>
<td>1.11 (0.07)</td>
<td>0.03 (0.03)</td>
<td>0.002 *</td>
</tr>
<tr>
<td>Loading Rate (BW/s)</td>
<td>8.19 (1.03)</td>
<td>8.71 (1.01)</td>
<td>0.51 (0.63)</td>
<td>0.004 *</td>
</tr>
<tr>
<td>Peak Knee Flexion Moment (Nm/kg)</td>
<td>0.36 (0.26)</td>
<td>0.48 (0.27)</td>
<td>0.12 (0.34)</td>
<td>0.179</td>
</tr>
</tbody>
</table>
Figure 2.1. Average symptomatic and contralateral knee flexion angles throughout gait cycle with the average and standard deviation of the interlimb difference of all subjects (contralateral – symptomatic). Total knee excursion and knee excursion during stance were both significantly reduced on the OA symptomatic limb in comparison with the contralateral limb. Knee flexion angle at initial contact was significantly lower on the OA symptomatic limb when compared with the contralateral limb.

Peak vertical ground reaction force was significantly reduced in the OA symptomatic limb (Table 2.2). Additionally, subjects exhibited a reduced vertical loading rate on the OA symptomatic limb when compared with the contralateral limb.
(Fig. 2.2B; Table 2.2). No interlimb differences were present for peak external knee flexion moment (Table 2.2).

**Figure 2.2.** A: Average symptomatic and contralateral knee excursions during stance with the average and standard deviation of the interlimb difference of all subjects (contralateral – symptomatic). Knee excursion during stance was significantly reduced on the OA symptomatic limb in comparison with the contralateral side. B: Average symptomatic and contralateral vertical loading rates with the average and standard deviation of the interlimb difference of subjects (contralateral – symptomatic). Vertical loading rate on the OA symptomatic limb was significantly lower than the contralateral limb.

### 2.4 Discussion

Many studies have examined the biomechanics of gait in individuals with knee OA (Al-Zahrani and Bakheit 2002; Astephen et al. 2008; Baliunas et al. 2002; Brinkmann and Perry 1985; Childs et al. 2004; Gök et al. 2002; Hurwitz et al. 2000; Kaufman et al. 2001; Landry et al. 2007; Messier et al. 1992; Mündermann et al. 2005; Ramsey et al. 2007; Schnitzer et al. 1993; Stauffer et al. 1977; Weidow et al. 2006;
Zeni and Higginson 2009; Zhao et al. 2007), however nearly all previous research has focused only on the OA symptomatic limb. In this study, we aimed to investigate differences in gait mechanics between the OA symptomatic limb and the contralateral limb, which may help to assess the risk of disease initiation and progression on the contralateral limb. The results of the present study indicate that individuals with knee OA demonstrate significant interlimb asymmetries for several key kinematic and kinetic gait parameters.

Previous research revealed that individuals with knee OA contact the ground with a more flexed knee (Baliunas et al. 2002; Childs et al. 2004; Weidow et al. 2006) and have reduced knee flexion excursion (Childs et al. 2004; Gök et al. 2002; Ramsey et al. 2007; Zeni and Higginson 2009) than healthy individuals. In the current study, the OA symptomatic limb displayed approximately 3-4° more knee flexion at initial contact and about 3° less knee excursion than the contralateral limb. The diminished knee excursion on the OA symptomatic limb is likely a result of the ipsilateral increased knee flexion at initial contact. Our values for both measures on the OA symptomatic limb agree closely with those reported for individuals with knee OA in other studies (Childs et al. 2004; Ramsey et al. 2007; Zeni and Higginson 2009). In general, the contralateral limb data for knee flexion at initial contact and knee excursion in the current study appear to be more consistent with the data for healthy individuals reported previously (Childs et al. 2004; Ramsey et al. 2007; Zeni and Higginson 2009). This suggests that while the OA symptomatic limb exhibits altered knee kinematics during weight acceptance, the contralateral limb seems to remain similar to healthy individuals for these parameters.
Both the initial position and excursion of the knee during the loading response may play an important role in shock absorption. The results of the present study showed that the OA symptomatic limb had a decreased vertical loading rate and peak vertical ground reaction force when compared with the contralateral side. One explanation may be that maintaining a more flexed knee during this period provides a more compliant limb, which would allow for dissipation of the loading over a greater interval of time, thus reducing the rate of loading and peak vertical ground reaction force. However, many OA studies report higher levels of muscle co-contraction in the quadriceps and hamstrings, which should lead to a less compliant knee joint (Hubley-Kozey et al. 2008; Schmitt and Rudolph 2007; Zeni et al. 2010). In fact, the observed interlimb difference may be due to greater peak vertical ground reaction forces and loading rates on the contralateral limb. Messier et al. (1992) reported a trend for the contralateral limb to have a higher loading rate than the OA symptomatic limb and suggested that this behavior may be an attempt to rapidly shift loading off the more painful limb. A more rapid shift to the contralateral limb may be contributing to the interlimb differences reported in our results. Comparison between our values for peak vertical ground reaction force and vertical loading rate and those of previous OA literature shows that the contralateral limb values are generally between those of OA subjects and healthy subjects. However, these comparisons are limited due to differences in walking speed and protocols between studies. Based on the known risk posed by magnitude and rate of loading to cartilage deterioration, future research is warranted to determine if contralateral limb values for these parameters are above normal.
During walking, the OA symptomatic limb displayed a significantly lower total knee excursion. This difference seems to be due to the minimum knee flexion angle which occurs during terminal stance or initial contact, as the maximum knee flexion angle during swing appears to be similar between limbs (Fig. 2.1). The reduction in total excursion on the symptomatic knee may be caused by an effort to avoid pain associated with joint motion. It has been suggested that a loss of motion at the knee joint could be compensated by increased motion at the ipsilateral hip and ankle joints (Nordin and Frankel 2001). However, based on our statistical results there does not appear to be any compensation by the ipsilateral hip and ankle for the reduced knee motion on the symptomatic limb.

Previous research has predominantly reported that knee OA subjects exhibit lower peak knee flexion moments than healthy individuals (Astephen et al. 2008; Gök et al. 2002; Kaufman et al. 2001; Landry et al. 2007; Weidow et al. 2006). Interlimb differences in this measure have only recently been investigated in those with knee OA, and these studies found significant asymmetry between limbs (Creaby et al. 2012). In the current study the OA symptomatic limb demonstrated a trend for lower peak knee flexion moments than the contralateral limb; however, no significant interlimb differences existed for peak knee flexion moment in this study. A primary reason for lack of statistically significant interlimb differences is likely a result of the high variability of this parameter. The observed interlimb symmetry could also be attributed to the similar knee flexion angles between limbs during the time of peak knee flexion moment (Fig. 2.1).

Although this study has identified several kinematic and kinetic interlimb differences, it is unclear as to whether these asymmetries are due to changes on one or
both limbs. This distinction is critical towards assessing the risk of disease initiation and progression in the contralateral limb. Future research involving control subjects would be necessary to definitively determine if the contralateral limb maintains healthy gait mechanics or displays abnormal patterns that may increase the risk of OA initiation or progression. We classified the OA symptomatic limb based on the subject’s self-described more painful knee and imposed the constraint that the more painful limb must also have more radiographically severe OA. While this method provides valuable insight to the role of pain in the reported gait alterations, a more robust pain scale would allow for a more complete understanding. Additionally, five of the seventeen subjects possessed bilateral OA (K-L Grade ≥ 2 on the contralateral knee). Another limitation of this study was sample size. A larger sample size would provide an improved representation of the OA population given the relatively high variability in gait parameters.

We found no significant interlimb differences for stride length, cadence or percent stance, thus the observed interlimb asymmetries cannot be attributed to differences in spatiotemporal parameters. This demonstrates that the gait asymmetry in individuals with knee OA is not so severe as to necessitate spending less time on their OA symptomatic limb, which would be an indication of antalgic gait.

The current results provide evidence of asymmetry in OA gait. This knowledge may be clinically relevant when designing therapeutic interventions to target both the symptomatic and contralateral limbs and to minimize the risk of OA initiation and progression. If the interlimb differences observed for vertical loading rate and vertical ground reaction force were due to abnormal increases on the contralateral limb, a gait retraining regimen targeted at restoring normal values for
vertical loading rate and peak vertical ground reaction force would be beneficial, as both parameters are linked to cartilage degeneration (Ewers et al. 2002; Ewers et al. 2001; Jeffrey et al. 1995; Kerin et al. 2003). Additionally, abnormal knee motion during stance observed in our study may cause a shift in the location of contact within the knee joint to areas of cartilage that are not adequately adapted to withstand the loading, thus increasing the risk of OA (Andriacchi et al. 2004). A targeted intervention to one or both limbs could help reestablish normal knee kinematics during stance.

This study establishes that significant kinematic and kinetic interlimb asymmetries exist between the OA symptomatic and contralateral limbs. Specifically, the OA symptomatic limb displayed decreased knee motion during weight acceptance while experiencing lower vertical loading rates and peak vertical ground reaction forces than the contralateral limb. These asymmetries may reflect compensation by the contralateral limb to alleviate loading and minimize knee motion for the more painful limb. Future work is warranted to further understand how these interlimb differences may affect OA initiation and progression.
Chapter 3

KNEE OSTEOARTHRITIS RESULTS IN ASYMMETRIC JOINT MOMENT DISTRIBUTION DURING GAIT

3.1 Introduction

Kinematic and kinetic alterations during ambulation are commonly observed in individuals with knee osteoarthritis (OA) (Al-Zahrani and Bakheit 2002; Astephen et al. 2008; Baliunas et al. 2002; Childs et al. 2004; Gök et al. 2002; Kaufman et al. 2001; Mündermann et al. 2005; Zeni and Higginson 2009). Although the mechanics of gait have been frequently implicated in the initiation and progression of the disease (Andriacchi et al. 2004; Buckwalter and Martin 2006; Wu et al. 2000), nearly all knee OA research focuses only on the more symptomatic limb in comparison with limbs of healthy individuals, leaving the impact on the contralateral limb largely unknown. Research on unilateral total knee arthroplasty found that the contralateral knee is far more likely to require replacement than any other contralateral or ipsilateral joints (Shakoor et al. 2002). This would suggest that alterations to diminish loading and minimize knee motion on the more painful limb could lead to altered and increased loading on the contralateral limb. With the joints of the contralateral limb at risk for development of OA, it is important not to limit analysis to the symptomatic limb, but to investigate the mechanics of the contralateral limb and implications for symmetry as well.

During gait, the sagittal plane hip, knee, and ankle internal extensor moments are responsible for the two principle goals of ambulation - providing vertical support
and forward propulsion of the center of mass (Anderson and Pandy 2003; Kepple et al. 1997; Perry 1992a). Combining these moments together yields a measure called the total support moment, which has been shown to be a reliable parameter (Flanagan and Salem 2005) and less variable than analyzing individual joint moments (Winter 1980). The total support moment is defined as the summation of the hip, knee, and ankle internal extensor moments and is a measure of lower limb coordination and function (Winter 1980). Previous research indicates that while individuals with knee OA have similar peak total support moments as healthy individuals, they exhibit decreased knee contributions and increased ankle contributions to peak total support on the symptomatic limb (Zeni and Higginson 2011). There is little research assessing bilateral differences between the OA symptomatic and contralateral limbs during gait despite individuals with knee OA demonstrating altered gait mechanics (Creaby et al. 2012; Messier et al. 1992). Given the synergistic nature of the lower limbs during gait, it could be beneficial to use the total support moment to analyze loading at the limb level as opposed to the individual joint level and include the contralateral side.

Although the redistribution of joint loading suggests that persons with knee OA adopt an altered coordination strategy to reduce knee loading at the instant of peak total support on the more painful side, it is unknown whether this behavior continues over the entire single stance phase of gait. Angular impulse, or the integral of moment over time, provides insight to both the magnitude and duration of joint loading (Stefanyshyn et al. 2006; Thorp et al. 2006). One study comparing subjects with mild (K-L grade 2) and moderate (K-L grade 3) knee OA found an increased angular impulse of adduction moment in the moderate group, despite there being no differences in the peak adduction moment (Thorp et al. 2006). Using angular impulse
may offer a more complete description of joint loading than analyzing peak moments, considering that individuals with knee OA walk at slower speeds (Kaufman et al. 2001) and utilize longer stance phases than healthy individuals (Al-Zahrani and Bakheit 2002; Gök et al. 2002).

The objectives of this study were to investigate interlimb differences in total support moment and individual joint contributions to peak total support moment within the knee OA population. We hypothesized that while there would be no interlimb difference in peak total support moment, there would be a reduced knee contribution and an increased ankle contribution on the symptomatic limb. Further, we hypothesized that the symptomatic limb would exhibit a larger angular impulse of total support moment than the contralateral limb during single stance. A better understanding of interlimb differences in loading during gait would provide valuable insight to the potential risks of OA initiation and progression on the contralateral limb.

3.2 Methods

A total of 17 subjects with previously diagnosed knee OA were recruited from the local community. Kellgren-Lawrence (K-L) grades of medial and lateral compartments of both knees were determined from a 30 degree bilateral flexed knee radiograph (Kellgren & Lawrence 1957). All subjects demonstrated medially dominant OA and K-L grades of 2 - 3 on at least one knee. The symptomatic limb was determined as the subject’s self-described more painful knee which was verified to have a greater K-L grade than the contralateral limb. Demographics for all subjects are presented in Table 3.1. Each subject signed an informed consent form approved by the Human Subjects Review Board at the University of Delaware.
### Table 3.1. Demographic data for all subjects (n=17) presented as mean (SD).

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>62.3±9.2</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>85.6±12.0</td>
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<tr>
<td>BMI (kg/m²)</td>
<td>30.2±4.9</td>
</tr>
<tr>
<td>Gender</td>
<td>10F/7M</td>
</tr>
</tbody>
</table>

Three-dimensional kinematics and kinetics were collected while each subject walked on an instrumented, split-belt treadmill (Bertec Corp., Columbus, OH). Kinematics were recorded at 60 Hz by an eight camera motion capture system (Motion Analysis, Santa Rosa, CA) using a modified Helen Hayes marker set. Kinetic data from both force plates was collected at 1080 Hz. Each subject’s self-selected walking speed was calculated from a 10 m overground walk. Once familiarized with treadmill walking (Zeni and Higginson 2010), data was recorded while subjects walked for 30 s at their self-selected speed. As a safety precaution, all subjects were secured to an overhead safety harness with no body weight support.

All marker coordinate data was filtered using a 4th order, phase-corrected, Butterworth filter with a 6 Hz cutoff frequency (Cortex 1.3, Motion Analysis). Joint moments were determined by inverse dynamic calculations using Orthotrak 6.3.4 (Motion Analysis) and normalized to each subject’s body mass. All moments are reported as internal joint moments. Every gait cycle collected during a trial was time normalized to 101 points and then averaged for each variable to give one representative gait cycle for each subject.

Total support moment was calculated as the summation of the hip, knee, and ankle internal extensor moments at each time step (Winter 1980) (Fig. 3.1). Peak total support moment was defined as the maximum total support moment during the representative gait cycle. Individual joint contributions were determined as a percent of the total support moment at the instant of peak total support.
Total Support Moment = \( M_h + M_k + M_a \)

**Figure 3.1.** Total support moment is defined as the summation of the internal extensor moments at the hip, knee, and ankle.

The angular impulse of the total support moment was calculated as the integral of the total support moment curve over the single support phase of the gait cycle (Stefanyshyn et al. 2006; Thorp et al. 2006) (Fig. 3.2). Single support was defined as the period from contralateral toe off to contralateral heel strike.

**Figure 3.2.** Angular impulse of the total support moment (highlighted) was calculated as the integral of the total support moment curve over the single support phase of gait.
Paired t-tests were used to assess interlimb differences for peak total support moment (magnitude and timing), individual joint contributions to peak total support moment, and angular impulse of total support moment. P values of $\leq 0.05$ were considered to represent significant differences. All statistical tests were performed using SPSS v.18 (Chicago, IL).

3.3 Results

The average self-selected walking speed for all subjects was $1.14 \pm 0.13$ m/s. Subjects were symmetric with respect to spatio-temporal parameters showing no interlimb differences in stride length ($p = 0.106$), cadence ($p = 0.231$), percent stance ($p = 0.096$) or percent single support ($p = 0.722$).

Comparison between the OA symptomatic and contralateral limb for peak total support moment revealed no significant differences ($p = 0.354$) (Table 3.2; Fig. 3.3). However, the timing of the peak total support moment on the OA symptomatic limb was significantly later in gait cycle than the contralateral limb ($p = 0.014$) (Table 3.2). The OA symptomatic limb provided a significantly reduced knee contribution to peak total support moment when compared with the contralateral limb ($p = 0.004$) (Table 3.2; Fig. 3.3). The ankle contribution to peak total support moment on the OA symptomatic limb was greater than that of the contralateral limb ($p = 0.004$) (Table 3.2; Fig. 3.3). Subjects demonstrated interlimb symmetry for percent hip contribution to peak total support moment ($p = 0.104$) (Table 3.2; Fig. 3.3).
Although no significant differences were present between the OA symptomatic and contralateral limbs for angular impulse of the total support moment over single support, the data displayed a trend towards a larger angular impulse on the OA symptomatic limb ($p = 0.103$) (Table 3.2).
Table 3.2. Symptomatic and contralateral limb values for all total support moment parameters. Interlimb difference values of all subjects (contralateral – symptomatic). All data presented as mean (SD). All significant interlimb differences denoted with (*).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Symptomatic</th>
<th>Contralateral</th>
<th>Interlimb Difference (Contra. – Sympt.)</th>
<th>p value</th>
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<tr>
<td>Peak Total Support Moment (Nm/kg)</td>
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<td>0.94 (0.36)</td>
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<tr>
<td>Percent Knee Contribution (%)</td>
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<td>35.7 (43.1)</td>
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<tr>
<td>Percent Ankle Contribution (%)</td>
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</tr>
<tr>
<td>Timing of Peak Total Support Moment (% GC)</td>
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<td>16.7 (1.1)</td>
<td>-11.4 (17.1)</td>
<td>0.014 *</td>
</tr>
<tr>
<td>Angular Impulse of Total Support Moment ((Nm/kg)*s)</td>
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3.4 Discussion

Although considerable research has been dedicated to the gait of individuals with knee OA (Al-Zahrani and Bakheit 2002; Astephen et al. 2008; Baliunas et al. 2002; Childs et al. 2004; Gök et al. 2002; Kaufman et al. 2001; Landry et al. 2007; Messier et al. 1992; Mündermann et al. 2005; Weidow et al. 2006; Zeni and Higginson 2009), these analyses have almost exclusively focused on the more symptomatic limb. Recently, two studies have examined the interlimb symmetry between the OA symptomatic and contralateral limbs during gait (Creaby et al. 2012; Richardson 2012, Ch. 2, IN REVIEW), however the differences identified in these studies were for discrete kinematic and kinetic parameters at a single joint. While these findings are valuable, the insight is limited to a localized, joint level understanding. The current study aimed to evaluate interlimb symmetry of OA gait on a more global limb level by
examining the total support moment which accounts for the inherent synergy between hip, knee, and ankle joints.

Previous research has utilized the total support moment to examine the OA symptomatic limb in comparison with limbs of healthy individuals (Zeni and Higginson 2011). In that study, Zeni and Higginson (2011) investigated the peak total support moment along with the relative contributions of the hip, knee, and ankle to the peak total support moment and found that while there were no differences between groups in peak total support moment, the OA limb utilized a decreased knee contribution and an increased ankle contribution. Similar to these findings, our results showed that there was no difference in peak total support moment between the OA symptomatic and contralateral limbs. Our finding in conjunction with that of Zeni and Higginson (2011) provides evidence that there is no difference in peak total support moment between the OA symptomatic and contralateral limbs and the limbs of healthy controls, which implies that normalized magnitude of limb loading may not be a risk factor for disease progression.

Our findings suggest that while there is not an interlimb difference in peak total support moment, the subjects appear to be employing a strategy that reduces the knee contribution on the OA symptomatic limb. Many previous studies have found that individuals with knee OA display reduced peak internal knee extension moments when compared with healthy control subjects (Astephen et al. 2008; Gök et al. 2002; Kaufman et al. 2001; Landry et al. 2007; Weidow et al. 2006). As internal knee extension moments increase, greater quadriceps activity is necessary to maintain support. Increased muscle forces across the knee result in greater loading on the joint, which may expedite cartilage deterioration (Herzog et al. 2003; Kellis 2001; Taylor
and Walker 2001). Therefore the reduction of knee contribution to total support moment may be indicative of a compensatory strategy to reduce quadriceps activity in order to minimize forces across the joint and associated pain. Another explanation for the diminished knee contribution to total support moment may be quadriceps weakness. Several studies have established links between knee OA and subsequent quadriceps weakness (Hassan et al. 2001; Hurley et al. 1997; Lewek et al. 2004; Messier et al. 1992). In order to compensate for diminished quadriceps strength, subjects often walk with a more extended knee during the stance period (Lewek et al. 2002). This quadriceps avoidance gait pattern may be responsible for the observed decreased knee contribution to total support moment in the OA symptomatic limb.

The peak total support moment on the OA symptomatic limb occurred significantly later in the gait cycle than on the contralateral limb. This difference in timing could explain the redistribution of peak total support moment between the knee and ankle. The timing of peak total support moment on the contralateral limb occurred during early mid-stance; however the timing on the OA symptomatic limb occurred near the end of mid-stance. Throughout the mid-stance phase of gait the internal knee extension moment is typically decreasing whereas the internal ankle plantar flexion moment is typically increasing. This natural pattern would result in smaller knee moments and larger ankle moments at late mid-stance, which corresponds with our observed redistribution of total support moment. Thus peak total support moment may be occurring later on the symptomatic limb in an effort to minimize the knee’s contribution to support.

Although there appeared to be asymmetry in hip contribution to peak total support, there was not a statistical difference between limbs. This is likely due to the
large amount of variability associated with this parameter, which suggests that a larger sample size may provide an improved understanding of the hip’s role in support. The ankle contribution to peak total support moment was significantly greater on the OA symptomatic limb in comparison with the contralateral limb. This asymmetry is likely due to the peak total support moment occurring later in gait cycle. An alternative explanation may be that the increased ankle contribution is compensating for the reduced knee contribution in an effort to maintain an adequate total support moment. An increased ankle contribution may reflect a greater ankle plantar flexion moment on the OA symptomatic limb at the time of peak total support, which could have detrimental repercussions at the ipsilateral knee joint. It has been hypothesized that greater ankle plantar flexion moments result in larger compressive forces within the knee joint (Fisher et al. 1997; Robon et al. 2000) which may be a risk factor for OA progression (Herzog et al. 2003). Additionally, increased loading on the ankle may result in injury or degradation of the articular cartilage of the ankle and surrounding joint structures.

We found no interlimb difference in peak total support moment, however this measure only represents one instant during gait and does not account for duration of loading. In order to gain insight into limb load over a larger period of time, we integrated the total support moment curve over the single support phase of gait to obtain the angular impulse of total support moment. By choosing to integrate over the single support period of gait we were able to isolate one limb and prevent any direct compensation from the opposite limb. Our results indicated that there were no interlimb differences for angular impulse of total support moment during single support; however the data demonstrated a trend towards significance with the OA
symptomatic limb possessing a larger angular impulse. Any observed asymmetry cannot be attributed to duration of loading as there was no interlimb difference in percent single support. Although we did not observe any asymmetry in limb level parameters (i.e. peak total support moment and angular impulse of total support moment), a previous knee OA study found that knee adduction moment angular impulse increases with OA severity (Thorpe et al. 2006). This suggests that interlimb asymmetries in the knee OA population may be limited to the joint level.

This study successfully evaluated the interlimb symmetry between the OA symptomatic and contralateral limbs; however it is unknown as to whether the observed interlimb differences are the result of changes in one or both limbs. Future research comparing the OA symptomatic and contralateral limbs with limbs of healthy controls could be used to better understand these interlimb differences. For peak total support moment and joint contributions, our contralateral limb values appeared to be very similar to the values reported by Zeni and Higginson (2011) for healthy individuals; although the symptomatic limb had similar magnitude of peak total support, the joint contributions were markedly different. Our determination of the OA symptomatic limb was based on the subject’s self-described more painful knee and was radiographically confirmed to exhibit more severe OA than the contralateral knee. Although this method gives insight to the role of pain in gait modifications, a more robust pain scale could provide an enhanced understanding. Lastly, while adequately powered, this study analyzed a moderately small sample size. Given the relatively high variability in some of these parameters, an increased sample size would yield a better representation of the knee OA population.
In conclusion, our hypotheses for peak and angular impulse of total support moment were partially supported as we found no interlimb differences for either parameter. While this suggests that limb level loading is similar between the OA symptomatic and contralateral limbs, the symptomatic limb exhibited a reduced knee contribution and a concurrent increase in ankle contribution to peak total support moment, thus supporting our hypotheses for joint contributions to peak total support moment. This redistribution of loading from the OA symptomatic knee to the ipsilateral ankle may represent a compensatory strategy to alleviate loading on the painful knee, which may result in increased loading and risk of OA on the contralateral knee.
Chapter 4

CONCLUSIONS

When investigating the pathogenesis of knee OA, the mechanics of gait are extremely important as ambulation involves the repetition of substantial forces across the joints and segments of the lower limb (Anderson and Pandy 2001; D’Lima et al. 2007; Schippein and Andricacchi 1991). The anatomical structures of the lower limbs are designed and well adapted for the motion and forces associated with healthy ambulation, however the presence of pain or other symptoms of knee OA can change an individual’s gait mechanics. Even minor gait alterations can displace loading to joints of the ipsilateral and contralateral limbs, which is of concern as articular cartilage degeneration has been shown to be influenced by changes in magnitude (Jeffrey et al. 1995), rate (Ewers et al. 2002), and location of joint loading (Biswal et al. 2002). Previous knee OA studies have identified many specific gait alterations exhibited by individuals with knee OA, but past research has only evaluated the contralateral limb to a very limited capacity. The findings of studies that have considered the contralateral limb do, however, suggest that the contralateral knee is at an increased risk of OA initiation and progression (Creaby et al. 2012; Messier et al. 1992; Shakoor et al. 2002; Sharma et al. 1997).

The objective of the present study was to gain an improved understanding of the mechanics of the contralateral limb by assessing the interlimb symmetry during gait. In order to achieve this goal we investigated interlimb symmetry on a local joint level as well as a more global limb level. Aims 1 and 2 analyzed several kinematic
and kinetic parameters of interest. Aim 3 utilized the total support moment, which accounts for coordination between hip, knee, and ankle, to evaluate the mechanics of OA gait on a limb level.

4.1 Aim 1: Kinematics

The purpose of Aim 1 was to examine the motion of the OA symptomatic and contralateral limb during gait and to determine if the joints of the lower limb were moving differently. The primary focus was the knee joint during early stance as the highest magnitude and rate of loading occurs during this period of gait. The results showed that the knee joint of the OA symptomatic limb displayed reduced total knee excursion than the contralateral limb, however there were no interlimb differences at the hip or ankle joints for this measure. Additionally, the OA symptomatic limb exhibited greater knee flexion at initial contact than the contralateral limb. Decreased knee excursion during stance was also observed on the OA symptomatic limb when compared to the contralateral. Therefore, all three of our hypotheses for Aim 1 were supported.

These results show that individuals with knee OA utilize different patterns of knee motion with the symptomatic and contralateral limbs. In particular, the alterations in knee motion during initial contact and early stance are of specific interest due to their potential ability to modify kinetic loading parameters. Additional research assessing the role of knee kinematics on loading rate could provide valuable insight into disease initiation and progression.
4.2  **Aim 2: Kinetics**

The goal of Aim 2 was to assess the forces experienced by the OA symptomatic and contralateral limbs during gait. Our initial hypotheses for peak vertical ground reaction force and loading rate were supported as the OA symptomatic limb displayed lower values than the contralateral limb for both parameters. Contrary to our hypothesis, there were no interlimb differences for peak knee flexion moment.

The reductions in peak vertical ground reaction force and loading rate may be effective methods of unloading the symptomatic limb in order to slow the progression of OA, but these asymmetries could result in increased risk to the contralateral limb. Future research is necessary to determine if the contralateral limb possesses values above those of healthy controls for peak vertical ground reaction force and loading rate. The lack of interlimb differences in peak knee flexion moment directly contrasts with the finding of a similar study (Creaby et al. 2012). Differences in walking speeds, range of disease severity, and method of joint moment normalization may be responsible for conflicting findings. However, the high variability associated with this parameter and limited sample size of our study could have resulted in Type II error. A larger sample size may reveal significant interlimb differences for peak knee flexion moment.

4.3  **Aim 3: Total Support Moment**

The objective of Aim 3 was to study interlimb symmetry on a more global limb level. Where Aims 1 and 2 investigated parameters that were limited to a single joint, Aim 3 analyzed the total support moment which considered the hip, knee, and ankle and the coordination between these joints to gain information about the entire lower limb during gait. The results showed that although there were no interlimb
differences for peak total support moment, there were interlimb differences in the
distribution of the peak total support moment across the lower limb joints with the OA
symptomatic limb displaying decreased knee contribution and increased ankle
contribution when compared with the contralateral limb. Thus our hypotheses for
magnitude and distribution of peak total support moment were both supported. Our
hypothesis for angular impulse of the total support moment was not supported, as
there were no significant interlimb differences.

The results from this aim provide strong evidence for there being no difference
in the magnitude of sagittal plane limb level loading between the symptomatic and
contralateral limbs. This suggests that OA gait asymmetries may not be severe
enough to result in changes observable on a global limb level; however these findings
may be somewhat task-constrained as there is a minimum amount of total support
moment necessary to prevent the lower limb from collapsing during gait. Although
there were no differences at the limb level, the redistribution of loading from the knee
to the ipsilateral ankle on the symptomatic limb demonstrates that individuals with
knee OA are using their limbs differently at a joint level.

4.4 Future Work

The current study documented several interlimb asymmetries between the OA
symptomatic and contralateral limbs at both the joint and limb levels; however it was
limited by the inability to determine if the observed interlimb differences were due to
changes on one limb or both limbs. Past knee OA research has identified that the OA
symptomatic limb behaves differently than healthy limbs during gait, but it is still
largely unknown if the OA contralateral limb is similar to healthy limbs. Future work
should focus on comparing the contralateral limb with limbs of healthy individuals in
order to determine if the alterations on the symptomatic limb induce abnormal loading on the contralateral limb which would result in an increased risk of OA.

All three aims of this research focused entirely on sagittal plane gait parameters. While previous research has identified many sagittal plane alterations in OA gait, many other studies have found important changes in frontal and transverse plane measures, with the most prominent examples being the knee adduction and hip abduction moments. Based on the significant findings of previous research and the inherent three-dimensional nature of gait, it would be beneficial for future work to examine the symmetry of OA gait in the frontal and transverse planes.

This study assessed the differences between the OA symptomatic and contralateral limbs, however only individuals with mild to moderate OA (K-L Grade 2-3) were included and analyzed. Although this range of disease severity represents the majority of the OA population, it is unknown if the asymmetries observed in this study would intensify in individuals with end stage OA (K-L Grade 4). Future work is warranted to understand how interlimb gait asymmetries evolve as a function of disease progression.

4.5 Overall Conclusions

This thesis is one of the few knee OA research studies to investigate the contralateral limb and associated interlimb symmetry during gait. Specifically it is the first study to simultaneously evaluate OA gait symmetry at a local joint level as well as in a more global limb perspective. This research provides documentation of the existence of interlimb asymmetry for several OA gait parameters of interest. Specifically, the results demonstrate that the symptomatic and contralateral limbs utilize different patterns of knee joint motion and experience different magnitudes and
rates of loading. These observed asymmetries are likely a response to pain and/or morphological changes to the joint structure and surrounding musculature on the symptomatic limb, however it is unclear if these alterations result in detrimental changes to the contralateral limb. Future research comparing the contralateral limb to the limbs of healthy individuals is necessary to determine if clinical interventions should target one or both limbs in an effort to restore normal gait symmetry.
REFERENCES


Hirasawa, Y., 1981. Left leg supporting human straight (bipedal) standing. Saiensu. 6, 32–44.


Appendix A

DEMOGRAPHIC INFORMATION FOR ALL SUBJECTS

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## Appendix C

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Appendix E

IRB APPROVAL
DATE: July 10, 2012

TO: Jill Higginson, PhD
FROM: University of Delaware IRB

STUDY TITLE: [138671-5] Risk factors for progression of osteoarthritis of the knee

SUBMISSION TYPE: Amendment/Modification

ACTION: APPROVED
APPROVAL DATE: July 10, 2012
EXPIRATION DATE: October 19, 2012
REVIEW TYPE: Administrative Review

Thank you for your submission of Amendment/Modification materials for this research study. The University of Delaware IRB has APPROVED your submission. This approval is based on an appropriate risk/benefit ratio and a study design wherein the risks have been minimized. All research must be conducted in accordance with this approved submission.

This submission has received Administrative Review based on the applicable federal regulation.

Please remember that informed consent is a process beginning with a description of the study and insurance of participant understanding followed by a signed consent form. Informed consent must continue throughout the study via a dialogue between the researcher and research participant. Federal regulations require each participant receive a copy of the signed consent document.

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

All SERIOUS and UNEXPECTED adverse events must be reported to this office. Please use the appropriate adverse event forms for this procedure. All sponsor reporting requirements should also be followed.

Please report all NON-COMPLIANCE issues or COMPLAINTS regarding this study to this office.

Please note that all research records must be retained for a minimum of three years.

Based on the risks, this project requires Continuing Review by this office on an annual basis. Please use the appropriate renewal forms for this procedure.
If you have any questions, please contact Jody-Lynn Berg at (302) 831-1119 or jilberg@udel.edu. Please include your study title and reference number in all correspondence with this office.