FACTORS AFFECTING KNEE JOINT MUSCLE ACTIVATION PATTERNS DURING GAIT IN INDIVIDUALS WITH KNEE OSTEOARTHRITIS

by

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Signature of Author

This dissertation is dedicated to my wife and children,
Diana, Mackenzie and Oliver and to my parents
Jim and Lorraine Rutherford

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ABSTRACT

Knee osteoarthritis (OA) is a progressive disease and a leading cause of morbidity in older adults, resulting in severe mobility limitations. While the osteoligamentous and neuromuscular systems are altered in knee OA, little data is available to illustrate an association among these systems. The objective of this dissertation was to improve our understanding of how muscle activation patterns during gait are altered across the knee OA severity spectrum and to examine how factors related to the OA process are associated with these alterations. Three independent but related studies were conducted.

Muscle activation of the medial and lateral orientations of the gastrocnemii, quadriceps and hamstrings were recorded during gait using surface electromyography for all three studies. Key activation features were identified using principal component analysis. First, participants selected from a large group (n=272) of individuals classified as asymptomatic, ii) moderate ii) severe knee OA were matched for walking velocity. Significant amplitude and temporal activation characteristics were found, supporting that differences among OA severities exist and were not the result of walking velocity only. Secondly, individuals with moderate OA were sub-grouped based on structural severity determined using Kellgren-Lawrence radiographic scores (II-IV) and were compared to a velocity-matched asymptomatic group. Medial gastrocnemius, lateral hamstring and quadriceps amplitudes and temporal patterns were significantly altered by structural severity where significant activation imbalances between the lateral:medial gastrocnemii and hamstrings were found with greater structural impairment (score>II). Thirdly, individuals with moderate OA were prospectively evaluated and divided into knee effusion and no effusion groups, based on a positive bulge test. A significantly higher knee flexion angle during mid-stance, higher quadriceps amplitudes and prolonged hamstrings amplitudes were found when effusion was found.

These studies showed that muscle activation patterns during walking were related to i) OA presence and severity based on functional, symptoms and radiographic evidence, ii) structural severity and iii) knee joint effusion. These findings improve our understanding of the interrelationships between alterations in joint structure and function associated with knee OA and muscle activation patterns during gait. These data can contribute to the development of gait-based metrics that can facilitate knee OA diagnosis and monitor progression.

LIST OF ABBREVIATIONS USED

ANCOVA – Analysis of Covariance

ANOVA – Analysis of Variance

ASYM – Asymptomatic

BMI – Body Mass Index

cc – Cubic Centimeters

CCI – Co-Contraction Index

cm – centimeter

CMRR – Common Mode Rejection Ratio

dB – Decibels

EMG - Electromyography

HTO – High Tibial Osteotomy

Hz - Hertz

ICF – International Classification of Function

IRED – Infrared Light Emitting Diode

ISEK – International Society of Electrophysiology and Kinesiology

KFA – Knee Flexion Angle

kg – Kilogram

KL – Kellgren Lawrence

L – Eigenvalue

LG – Lateral Gastrocnemius

LH – Lateral Hamstring

LK3.1 – Likert Scale Version 3.1

m – Meter

mm - Millimeter

Ma – Moment Arm

ms – Millisecond

MG – Medial Gastrocnemius

MH – Medial Hamstring

MVIC – Maximal Voluntary Isometric Contraction

Nm – Newton Meters

OA – Osteoarthritis

PCA – Principal Component Analysis

PP – Principal Pattern

R^2 – Regression sum of squares

RF – Rectus femoris

S – Cross product matrix

SD – Standard deviation

SENIAM – Surface EMG for the Non-Invasive Assessment of Muscles

TKR – Total knee replacement

U – Eigen vector

V – Volt

VAS – Visual Analog Scale

VM – Vastus medialis

VL – Vastus lateralis

WOMAC – Western Ontario McMaster Osteoarthritis Index

GLOSSARY

ASYMPTOMATIC

Individuals over age 35 had no fracture or previous lower extremity injury other than a sprain or strain. Individuals had no lower extremity injuries within six months prior to data collection and no symptoms of lower extremity degenerative joint disease including knee pain, morning stiffness or no prior knee surgery or fracture. These individuals did not have radiographs completed for their knees.

MODERATE KNEE OSTEOARTHRITIS

Moderate knee osteoarthritis was defined using a composite of three metrics. First, knee OA was identified using i) American College of Rheumatology guidelines [3] and ii) evidence of knee OA through diagnostic imaging. Levels of structural impairment (structural severity), based on the Kellgren Lawrence ordinal radiographic scale ranged from KL I to KL IV. Individuals did not have a current or previous anterior cruciate ligament injury and had dominant medial tibio-femoral compartment knee OA. Secondly, all individuals reported that their ability to perform three functional tasks; i) jog five meters, ii) walk one city block and iii) reciprocally ascend and descend 10 stairs would not be encumbered by their knee OA symptoms. Thirdly, individuals were not scheduled for total joint arthroplasty at the time of testing.

OSTEOARTHRITIS

Osteoarthritis is a progressive disease of synovial joints that results from failed repair of joint damage that can arise as a result of biomechanical, biochemical and/or genetic factors [145]. Stresses can be initiated in any of the synovial joint tissues, including articular cartilage, subchondral bone, ligaments, menisci, periarticular muscles, peripheral nerves, or synovium. This ultimately results in the breakdown of cartilage and bone, leading to symptoms of pain, stiffness and functional disability. While the osteoarthritis process is progressive, the reparative process can also be successful leading to a functional, painless joint [27,199]. Hence, OA is an active process of knee joint tissue degradation and synthesis.

STRUCTURAL SEVERITY

Structural impairments considered pathognomonic with knee OA include articular cartilage lesions, joint margin and tibial spine osteophytosis, subchondral bone sclerosis, and bone attrition [5,105,125,195,224]. These impairments are also progressive. Standard anterior-posterior and lateral radiographs have been used to capture the appearance and level of the structural impairments associated with knee OA [5,125,195,224]. For this dissertation, the Kellgren Lawrence ordinal radiographic scale was used to define the level of structural impairment. Structural severity was used to describe the general state of structural impairments characterized in the OA knee.

Severe Knee Osteoarthritis

Severe knee osteoarthritis was defined using a composite of two metrics. First, knee OA was identified using i) American College of Rheumatology guidelines [3] and ii) evidence of knee OA through diagnostic imaging. Levels of structural impairment (structural severity), based on the Kellgren Lawrence ordinal radiographic scale ranged from KL III to KL IV and individuals had medial compartment knee OA. Secondly, individuals received a total knee arthroplasty within one-week after testing.

Stability

The ability of a system (i.e. the knee joint) to remain within a boundary of control after a perturbation (i.e. moment of force or translation) is applied. The definition was adopted from Panjabi [189,190] and McGill[167].

ACKNOWLEDGMENTS

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CHAPTER 1

INTRODUCTION

Osteoarthritis (OA) is a chronic, progressive disease that has world wide prevalence [19,68,83,108,121,208]. For decades, the knee has been recognized as the most common lower extremity joint affected [48,182] with knee OA associated with significant ambulatory disability [81,227]. Few objective metrics exist to aid in clinical decision-making for the management of knee OA. Metrics currently employed to capture knee OA associated disability assess structural changes primarily based on radiographic scoring [65,285] or are largely self-reports of symptoms and physical function [130,185]. The discordance between the disease (joint structure and function) severity and symptom severity [21,54,248] makes clinical decision making of knee OA management difficult. The interrelationships between impairments to joint structure and function and activity limitations are not clearly delineated.

The aim of this dissertation is to improve the understanding of how muscle activation patterns across the knee OA severity spectrum are altered during gait and to examine how factors related to the OA process are associated with these alterations. The goal of this research is to contribute to the development of gait-based metrics that can facilitate knee OA diagnosis and monitor knee OA progression.

THE PROBLEM

Arthritis of the lower extremity contributes significantly to adult ambulatory disability [12,18]. The annual economic burden of arthritis in Canada is estimated to be over 6 billion dollars, representing almost one third of the total cost of musculoskeletal diseases [142]. Estimates suggest one in six individuals are affected with arthritis and an estimated 1 in 10 individuals have been diagnosed with osteoarthritis (OA) [143]. In the United States, a projected 27 million adults live with osteoarthritis [147] where annual medical care expenditures for OA may exceed 185 billion dollars [138]. The most prevalent arthritic condition is OA which affects any synovial joint and currently has no cure [145]. Knee OA has been recognized for decades as a leading cause of mobility related disability in older adults [81,182] and the knee continues to be the most prevalent lower extremity joint affected [48,182]. In Canada, there was a 140-fold increase in hospitalizations over the past decade for total knee replacements, with over 90% of primary total knee

replacements performed because of knee OA [48]. Given the current numbers and projections, based on increasing prevalence of total knee arthroplasty in younger adults and with our aging population, this management approach cannot be sustained [141].

Knee OA is a progressive disease resulting from the failed repair of joint damage arising as a result of biomechanical, biochemical and/or genetic factors [145]. Stresses can be initiated in any of the synovial joint tissues, including articular cartilage, subchondral bone, ligaments, menisci, periarticular muscles, peripheral nerves, or synovium [27,145]. These stresses ultimately result in the breakdown of cartilage and bone, leading to symptoms of pain, stiffness and functional disability. While the osteoarthritis process is progressive, the reparative process can also be successful leading to a functional, painless joint [27,199]. Hence, OA is an active process of knee joint tissue degradation and synthesis where joint biomechanics are important in the pathophysiology of knee OA [27]. Ameliorating the abnormal biomechanical environment provides the foundation for this dissertation work.

Given the mechanical demands of gait and the frequency with which it is performed, gait analysis has been used as a model to study knee OA joint biomechanics [11,266]. It is estimated that healthy older adults take between 6000 and 8500 steps in a day where individuals with disabilities and chronic illnesses can take up to 5500 steps in a day [252], making the ability to walk the single most important daily physical activity. Twenty eight years ago, Cappozzo [38] stated, "Gait evaluation must overcome the stage where it supplies information on the way an individual walks and begin to answer the relevant whys." By in large, describing the way individuals with knee OA walk is still dominant in knee OA gait literature, and only recently have we begun to understand the "relevant whys."

Much of what we know about *in vivo* knee joint mechanics and knee OA has been gained through biomechanical studies of walking with a major focus on one variable, the net external knee adduction moment. The knee adduction moment provides a surrogate measure of medial compartment loading, with characteristics of this moment related to medial compartment cartilage and bone defects [53], reduced cartilage thickness [133] and clinical outcomes [261] but only one longitudinal study has showed a relationship to progression [173]. Although less studied, sagittal plane biomechanics of the knee showed

reduced flexion moments and angles with knee OA and OA progression based on cross-sectional studies [15,16,20,58,77,86,123]. Many studies have focused on joint biomechanics during gait but only recently has the role of the knee joint musculature during gait been considered in the study of knee OA [25].

Muscle forces are important when trying to understand the mechanical environment of the joint as they create moments of force that produce motion and maintain joint stability, [7,189,239] but can alter joint loading [7,160,229] and metabolic demand [78,171] during gait. Hence understanding muscle activation patterns can provide a more comprehensive picture of the joint mechanical environment. In addition, muscle force generation is of particular interest, because it can be controlled consciously by the individual and can be altered with training [25]. This dissertation therefore focused on examining knee joint muscle activation patterns during walking in individuals with medial compartment knee OA in an attempt to understand knee OA related factors that could potentially alter these activation patterns.

THE FRAMEWORK

The International Classification of Function (ICF) provides a standard language and framework for describing health and health-related states [264]. Figure 1.1 provides the framework developed by the World Health Organization. This framework has been modified to capture the knee OA process.

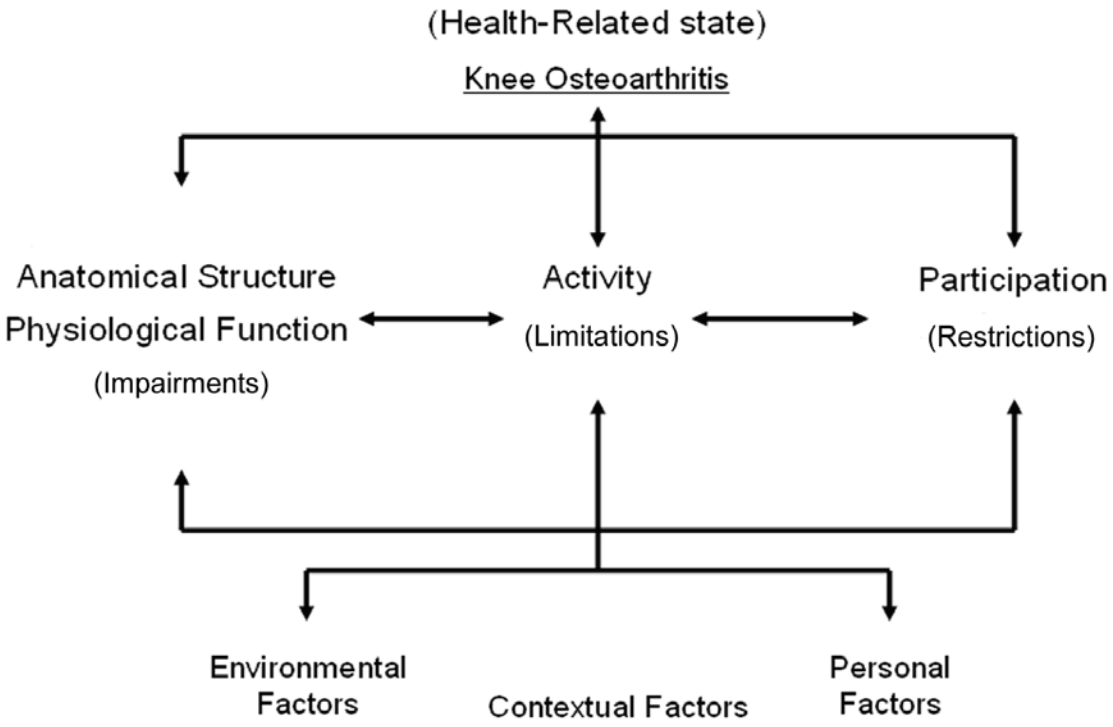

Figure 1.1: An adopted version of the International Classification of Function applied to the health related state of Knee Osteoarthritis to provide a standard framework and context for the relationship between impairments in body structure and function and activity limitations. Further discussed in Section 2.3.

In knee OA, impairments to anatomical knee joint structure exist and include articular cartilage lesions, joint margin and tibial spine osteophytosis, subchondral bone sclerosis, and bone attrition [5,105,125,195,224]. In addition, impairments to physiological functions of the knee joint and surrounding tissue include the muscular and neurological systems [25,210] and synovium [17,192,225]. Together these impairments provide a foundation to understand the knee OA process [27] and its relationship with activity.

Central to this dissertation is developing an understanding of the reciprocal relationship between joint impairments and limitations in joint function during fundamental activities, in this case walking, in those with different severities of medial compartment knee OA. Self-reported measures of physical function/disability and symptoms are commonly utilized to evaluate the knee OA process [145,185] despite their poor relationship to joint impairment [21,54,248]. While symptoms provide information on the "illness" component of knee OA [145], treatments that have focused on reducing symptoms

alone have not been shown to prevent ongoing structural damage [80,145]. In fact, there is evidence that addressing symptoms increases joint loads during gait [222] and can accelerate progression [146,207]. It has been hypothesized that improving the abnormal biomechanical environment has the potential to attenuate knee OA progression [11,27]. However, few systematic studies exist that have quantified the relationship between knee joint impairments characteristic of knee OA and knee OA severity with objective gait measures, specifically muscle activation.

At the knee, a balance must be established between knee joint stability and knee mobility where the passive osteoligamentous, muscular, and the neurological subsystems are thought to be fundamental to this process [239]. An initial framework is provided in Figure 1.2, modified from its original description of spinal stability [189] and emphasizes the interaction between these three subsystems to promote normal knee joint mechanics.

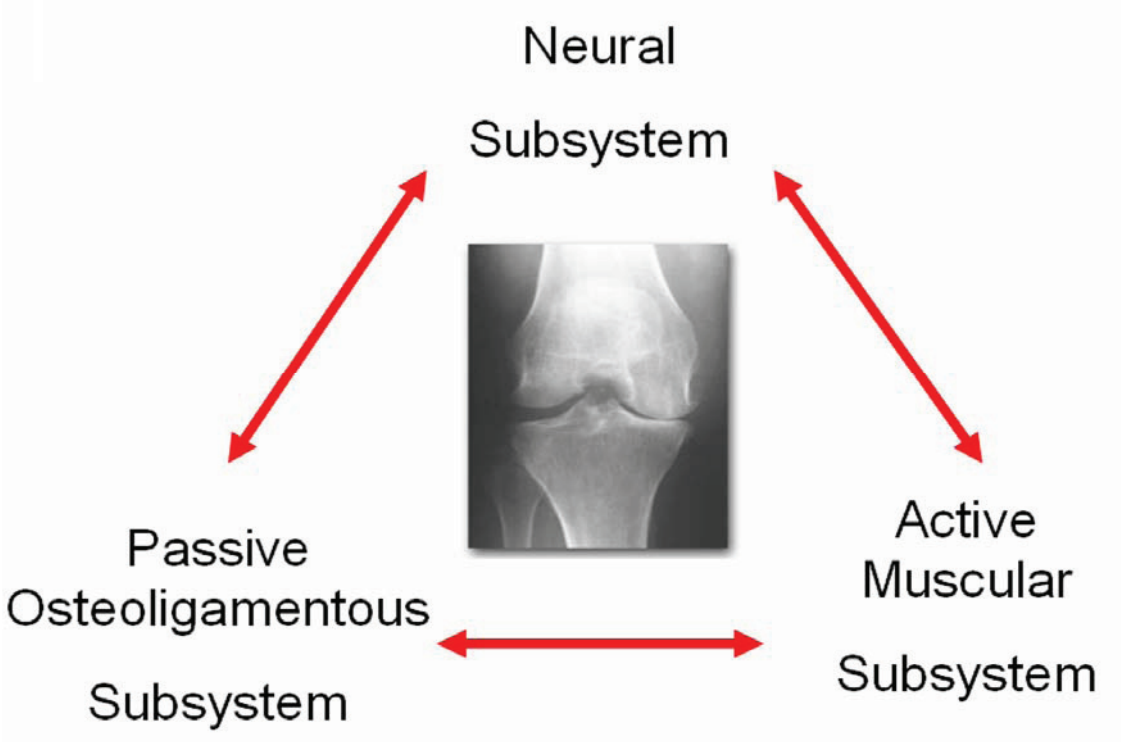

Figure 1.2: A conceptual framework, adopted from Panjabi [189], of the interaction between the passive osteoligamentous, active, and the neurological subsystems to maintain knee joint mobility and stability during gait.

Osteoligamentous structures are the primary tissues compromised with knee OA and OA progression [5,125]. Thus, there is a need for the neuromuscular system in this

interaction to adjust its contribution as shown in Figure 1.2. The relationship is reciprocal, in that alterations to the generation of muscle forces can create both negative and positive mechanical environments that have been associated with knee OA development and progression [89,118]. The muscles are required to produce forces through appropriate activations and the neural subsystem provides the control of appropriate responses through feedforward and feedback mechanisms. Quantifying knee joint muscle activation amplitudes and patterns across the gait cycle and their relationship to impairments of joint anatomical structural and physiological function can help determine how these factors challenge the neuromuscular system, influence gait mechanics and provide insight on knee OA progression. At present, the assessment of the neuromuscular system during gait is not contained in current diagnostic and evaluative criteria used to assess knee OA [5,125,145,285].

THE RATIONAL

Only a few studies have examined muscle activation, but the consensus from their findings show that knee joint muscle activation characteristics are altered during gait in individuals with knee OA compared to healthy individuals. While, methodological inconsistencies between studies make it difficult to compare findings, some general trends are found. The most notable findings are higher quadriceps and lateral hamstring amplitudes [103,284], greater co-activity [86,103,154,212] and longer durations of activity during stance [44,102] in individuals with knee OA. More recently, muscle activation imbalances have been found between medially and laterally oriented knee joint muscles for those with primary medial compartment knee OA [102,154,161,212,214]. The differences were more subtle for those with mild to moderate knee OA [102] with larger differences for severe OA [103].

Various explanations have been offered as to why muscle activation patterns are altered during gait in those with medial compartment knee OA. Mechanical factors include tibial adduction features during stance [7,86,161], medial compartment laxity [154,203], osteophytosis [284], muscle strength [102,103,212], gait velocity [16,214], and compressive medial joint loading [16,102]. As well, explanations related to OA symptoms including pain [13],

instability [154] and stiffness [102] have been provided. Several studies report proprioception deficits in knee OA [22,135,228] and greater dynamic knee stiffness [61] during gait. Together, these factors suggest that the interrelationships among the passive, active and neural subsystems are altered. What is currently unclear however is whether knee joint muscle activation patterns during gait are in fact related to structural and functional knee joint impairments characteristic of individuals with knee OA. This information is useful to substantiate the use of gait-based metrics to facilitate knee OA diagnosis and monitor knee OA progression.

Knee Osteoarthritis Severity and Gait Velocity

While medial compartment OA is the focus of most studies, participants with knee OA are often reported as a homogenous grouping with only a few studies recognizing the need to differentiate for the degree of OA severity [13,16,103,176,250,283,284]. The consensus from a small number of papers that focus on muscle activation is that alterations are related to OA severity [16,103,284]. The difficulty in drawing conclusions across these studies is that different definitions for classifying knee OA severity were used. Furthermore, self-selected walking velocities were different between the subgroups within these studies, where increasing severity was associated with a slower walking velocity [16,103,284]. Thus, separating OA severity effects from walking velocity effects is further confounded given that lower extremity muscle activation characteristics can be independently altered by changing walking velocity [94,231,278]. Whether muscle activation differences occur without the confounding effect of walking velocity is needed to understand how the three subsystems interact during gait across knee OA severity.

Two main approaches have been employed to separate and interpret OA effects from walking velocity effects on muscle activation during gait, including velocity constraints and statistical models [44,98,284]. The interpretation of these analyses, in the context of understanding the influence of knee OA severity on muscle activation characteristics is difficult given that walking velocity is largely self-governed where both joint impairments and symptoms can explain slower gait. Understanding whether muscle

activation differences exist with increasing knee OA severity provides the basis for the first objective of this dissertation.

The first objective of this dissertation was to determine whether alterations in knee joint muscle activation patterns exist among knee OA severity classifications that had similar average self-selected walking velocities during gait.

Structural Severity

Structural impairments to the knee joint and symptoms that individuals with knee OA experience are an integral part of the OA process. For instance, a Kellgren-Lawrence score greater than II (structural impairment), concurrent with knee pain intensity greater than 60/100 (symptoms) are predictors of future total joint replacement [49]. While symptoms and impairments to joint structure can progress in parallel, a known discordance exists [21,54,248]. Given experimentally induced quadriceps pain [87] and knee pain relief [88,111,222] can alter gait mechanics and muscle activation characteristics, controlling for symptom severity is a potential approach to isolate the influence of structural severity, defined as level of knee joint structural impairment, on muscle activation patterns during gait.

Structural impairments considered pathognomonic with knee OA include articular cartilage lesions, joint margin and tibial spine osteophytosis, subchondral bone sclerosis, and bone attrition [5,105,125,195,224]. Articular cartilage lesions are thought to result in joint space narrowing and promote an unstable joint where alterations in muscle activation would be required to maintain stability [154]. In contrast, medial compartment osteophytosis may reduce requirement of muscle activation levels typical of asymptomatic knees by increasing the contribution of the passive osteoligamentous system to maintain knee joint stability [284]. Structural impairments are asymmetrically distributed across the medial and lateral tibio-femoral condyles, where distinct medial and lateral knee joint muscle activations across the gait cycle have been found.

Classifying the level of knee OA structural severity using radiographic scores has been a major part of clinical investigation, study methodology and subject inclusion criteria and analysis. Several other approaches have been used or are developing and

include arthroscopic procedures [28,259] and magnetic resonance imaging (MRI) techniques [63,122,134]. While these methods provide a detailed account of specific impairments, the former is invasive and the latter expensive and have not been routinely used evaluate the OA knee. The Kellgren-Lawrence (KL) radiographic scale [125], is the most widely used method of classifying structural severity across many research foci [31,65,218,263,286] and is considered the standard for assessing radiographic knee OA by the World Health Organization. Joint space narrowing, osteophytosis, bone sclerosis and deformity are assessed using this five-point ordinal scale. The level of these impairments are considered together for the assignment of a KL-score (0 = normal to IV = severe) [125].

Knee joint muscle activity is altered in individuals with knee OA in comparison to an asymptomatic cohort [16,102,154,161,214,284] however, the role of impaired joint structure to provide a mechanism for these differences is not established. Currently, only two studies have examined muscle activation characteristics that coincide with structural impairment. Zeni *et al*., [284] utilized the KL radiographic scale where Astephen *et al*., [13] employed a proprietary radiographic visual analog scale to characterize impairment level. Understanding the influence of structural severity on knee joint muscle activity in a homogeneous group with similar clinical status, symptoms and physical function but a wide variation in structural impairments provides the foundation for the second objective of this dissertation.

The second objective of this dissertation was to determine whether alterations in knee joint muscle activation patterns were associated with structural severity determined using KL-scores, for those with a moderate knee OA classification based on clinical status, symptoms and physical function.

KNEE JOINT EFFUSION

There is evidence that knee joint effusions can provide a mechanism for knee OA progression [17,49]. In contrast to structural impairments associated with knee OA, knee joint effusions can occur secondary to a wide range of intra-articular pathologies [66,120,169,206,209]. Effusions are thought to represent an impairment to knee joint physiological function that has implications for understanding the knee OA process

[17,27,49]. While not found in everyone with knee OA, knee effusions have been reported in over half of the individuals treated for this disease [49,139,169]. Determining whether knee joint effusion in individuals with moderate knee OA is associated with unique muscle activation patterns and joint mechanics during gait provided the basis for objective three of this dissertation.

Most of what is known about the effect of knee joint effusion on muscle activation is based on experimental investigations of the quadriceps muscles [6,97,187,241,245]. Static, experimental acute effusion models have shown that the quadriceps force generating capacity is consistently reduced and is independent of pain. This reduction has been attributed primarily to a neurophysiological inhibition mechanism [97,187,241]. The effect of an acute effusion on the hamstrings and gastrocnemii has not been studied. Furthermore, only one study was found to address the effect of effusion on biomechanical and muscle activation patterns during a fundamental task. Torry *et al*., [251] found that gait mechanics and muscle activity were altered with an acute knee effusion in healthy individuals, and this was progressive with the amount of effusion.

The effect of effusions, characteristic of arthritis, on quadriceps inhibition during static testing was more variable, with evidence that both supported and refuted that inhibition was associated with effusion [66,120,170]. In addition, the role effusion for altering joint mechanics and muscle activation during activities, such as gait, has not been studied in individuals with knee OA. Whether the results of the acute effusion studies reflect the role of effusion present in individuals with knee OA to alter muscle activation characteristics, gait mechanics or muscle strength has yet to be established.

The third objective of this dissertation was to determine whether knee joint effusion in individuals with moderate knee OA was associated with altered sagittal plane knee joint mechanics and knee joint muscle activation patterns during walking.

In summary, knee OA is a chronic, progressive disease that has worldwide prevalence and is associated with significant ambulatory disability. The ICF framework provides the basis for understanding functioning and disability where the reciprocal relationship between joint impairments, characteristic of the knee OA process, and activity limitations, in this case walking became the focus of this dissertation.

Osteoligamentous structures are compromised with knee OA presence and progression. Thus, the potential exists for increased reliance on the neuromuscular system to maintain knee joint stability during gait. The role of the knee joint musculature in knee OA development and progression is beginning to emerge yet how muscle activation patterns are altered during walking and what factors contribute to these alterations is not well understood. Muscle forces are important to consider as they create moments of force to produce motion, maintain joint stability but have implications for joint loading and metabolic demand during gait.

The specific aim of this dissertation is to improve our understanding of how muscle activation patterns during gait are altered across the knee OA severity spectrum and to examine how factors related to the OA process are associated with these alterations. The goal of this research is to contribute to the development of gait-based metrics that can facilitate knee OA diagnosis and monitor knee OA progression.

1.1 PURPOSE

The overall objective of this dissertation was to investigate how the knee OA process including progressive structural and functional impairments, alters knee joint muscle activation patterns during self-selected gait. Given the high prevalence, only individuals with radiographic evidence of primary medial compartment knee OA were examined. Three independent but related studies were designed to address this overall objective by examining muscle activation patterns during gait associated with 1) knee osteoarthritis severity and gait velocity, 2) structural severity and 3) knee joint effusion. Muscle activation patterns during self-selected gait were quantified for the medial and lateral orientations of the gastrocnemii, quadriceps and the hamstrings using principal component analysis (PCA) as a pattern recognition methodology. A standard approach, including data collection, processing and analysis methodology was utilized to address all three objectives.

1.2 Research Objectives and Hypotheses

Objective One – Knee Osteoarthritis Severity and Gait Velocity

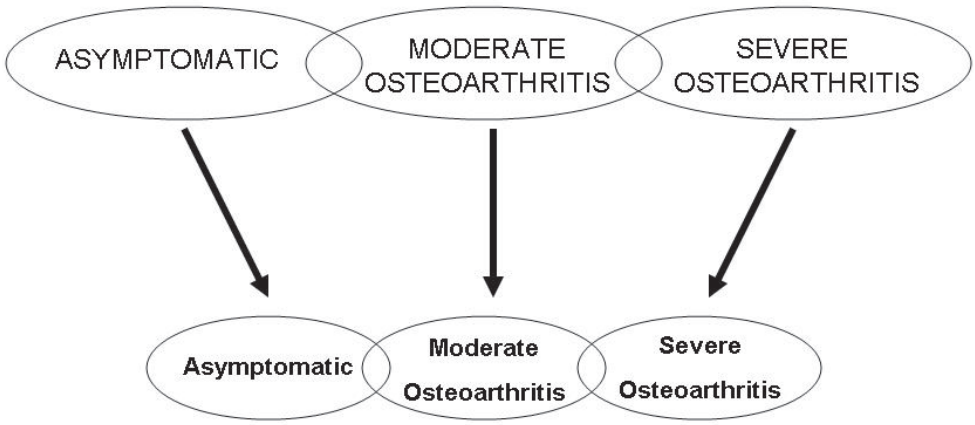

Figure 1.3: Population sampling framework for Objective One. The asymptomatic group had no signs or symptoms of knee osteoarthritis. The moderate osteoarthritis group was homogeneous regarding clinical status, physical function and symptoms and heterogeneous regarding structural severity. All individuals in the severe osteoarthritis group received a total knee replacement within one week of gait testing and were heterogeneous regarding structural severity. Samples were selected from these large groups based on similar self-selected waking velocity.

The first objective was to determine whether alterations in knee joint muscle activation patterns exist among knee OA severity classifications that had similar average self-selected walking velocities during gait. This study included asymptomatic individuals as well as individuals with moderate and severe knee OA (Figure 1.3). Groupings were based on a combined radiographic and functional assessment. The following null hypotheses were tested:

- Knee joint muscle amplitude and temporal activation patterns are not different among the asymptomatic and the two distinct OA severity groups when walking at similar average self-selected walking velocities.
- Lateral and medial knee joint muscle activation patterns are not different within each muscle grouping (gastrocnemii, quadriceps, hamstrings) across the knee OA classification groups.

OBJECTIVE TWO –STRUCTURAL SEVERITY

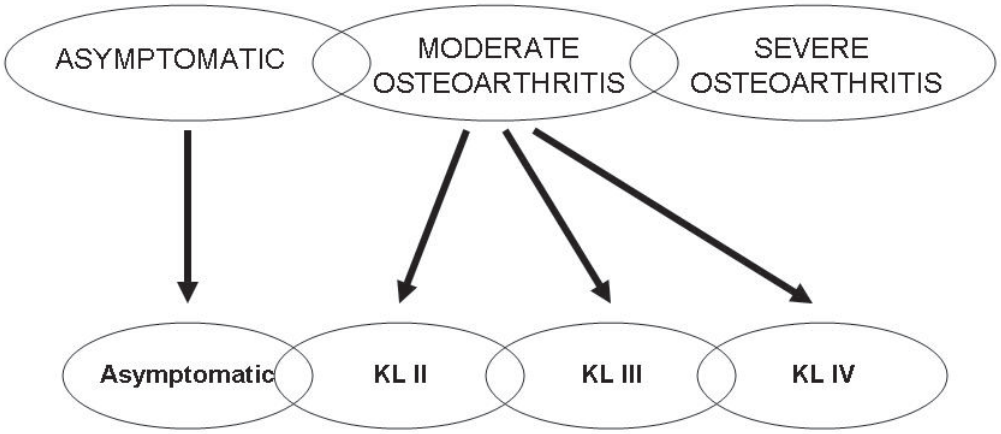

Figure 1.4: Population sampling framework for Objective Two. The moderate osteoarthritis group was divided based on structural severity assigned using Kellgren Lawrence ordinal radiographic scores. The asymptomatic group was matched to the moderate osteoarthritis group for age and walking velocity.

The second objective was to determine whether alterations in knee joint muscle activation patterns were associated with structural severity for those within a moderate knee OA classification based on clinical status, symptoms and physical function. Sub-groups with different structural severity were identified based on Kellgren Lawrence ordinal radiographic scores (Figure 1.4). A sub-objective was to determine if all OA sub-groups differed from asymptomatic controls. The following null hypotheses were tested,

- Knee joint muscle amplitude and temporal activation patterns are not different between asymptomatic and moderate knee OA individuals or among individuals with moderate knee OA sub-grouped based on KL-scores of II, III and IV.
- Lateral and medial knee joint muscle activation patterns are not different within each muscle grouping (gastrocnemii, quadriceps, hamstrings) across the participant sub-groups.

OBJECTIVE THREE – KNEE JOINT EFFUSION

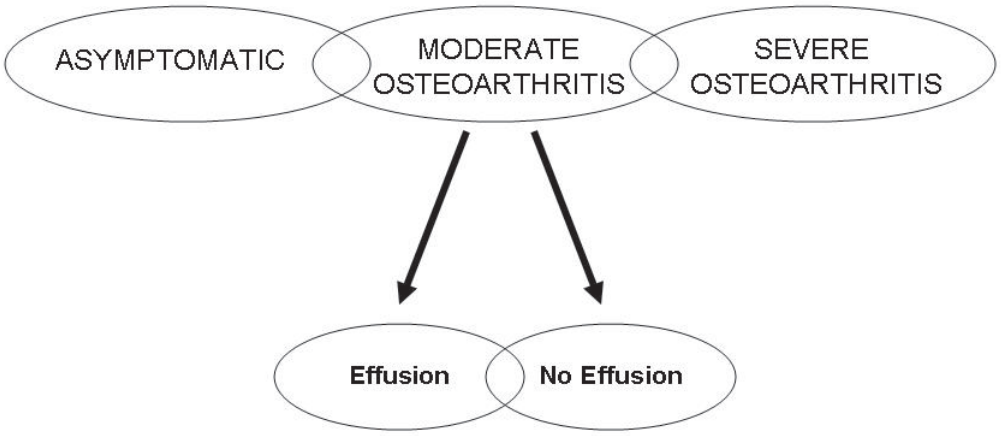

Figure 1.5: Population sampling framework for Objective Three. The moderate osteoarthritis group was prospectively assessed and divided based on effusion/no effusion status using the bulge sign.

The third objective was to determine whether knee joint effusion in those with moderate knee OA was associated with altered sagittal plane knee joint mechanics and knee joint muscle activation patterns during walking (Figure 1.5). The following null hypotheses were tested,

- Sagittal plane knee angle and moments of force characteristics are not different between individuals with and those without knee effusion during self-selected walking.
- Knee joint muscle amplitude and temporal activation patterns are not different between individuals with and without knee effusion.
- Lateral and medial knee joint muscle activation patterns are not different within each muscle grouping (gastrocnemii, quadriceps, hamstrings) between individuals with and without knee effusion.

1.3 DISSERTATION STRUCTURE

Chapter 1 introduces the dissertation, the topic of knee osteoarthritis and the rational for studying structural and functional knee joint impairments associated with knee OA severities that may alter knee joint muscle activation patterns. The three main objectives and null hypotheses are stated. The dissertation structure is described.

Chapter 2 provides an overview of the background literature relevant to this dissertation. The literature establishes the need to understand knee OA pathomechanics for the development and progression from the perspective of knee joint muscle activation characteristics. Topics reviewed include, the burden of OA, joint structural changes, knee joint function through biomechanics and electromyographic studies of gait and pertinent methodological considerations, limitations and gaps in current knowledge regarding muscle activation during gait.

Chapter 3 provides an overview of the general methodology employed to carry out the three objectives of the dissertation. More specifically, this section was divided into three sub-sections. Section 3.1 describes the subject selection, methodology and considerations for the analysis of kinematic, kinetic and electromyographic gait variables. Section 3.2 explains the methodological aspects for the radiographical evaluation of the knee OA process using the Kellgren Lawrence ordinal radiographic scale and identification of joint effusion presence. Finally, Section 3.3 describes general gait analysis procedures, including pattern recognition methods and statistical analyses.

Chapter 4 contains an original scientific paper titled, “Neuromuscular alterations exist with knee osteoarthritis presence and severity despite walking velocity similarities” and authored by Derek J Rutherford, coauthors Dr’s Cheryl Hubley-Kozey, William Stanish and Michael Dunbar. This manuscript addresses objective one of this dissertation and has been published in Clinical Biomechanics 26 (2011) 377-383.

Chapter 5 contains an original manuscript, intended for scientific publication titled, "Changes in knee joint muscle activation patterns during walking are consistent with structural severity in knee osteoarthritis." This manuscript addresses objective two of this dissertation and has been prepared for publication.

Chapter 6 contains an original manuscript, intended for scientific publication titled, "Knee joint effusion affects knee mechanics and muscle activity during gait in individuals with knee osteoarthritis," and is authored by Derek J Rutherford and co-authored by Drs. Cheryl Hubley-Kozey and William Stanish. This work was presented at the Congress of the International Society of Electrophysiology and Kinesiology, Aalborg, Denmark, June 16-19, 2010 and the Canadian Institute of Health Research Poster Competition at the Canadian Student Health Research Forum, Winnipeg, Manitoba, June 1-4, 2010. This manuscript addresses objective three of this dissertation and has been prepared for publication.

Chapter 7 concludes the dissertation by providing a general discussion to integrate the findings among the three studies, concluding summary of key results, future directions and recommendations for studying knee joint muscle activation to understand impairments in joint structure and function in individuals with knee OA.

Appendix A is divided into two parts. A summary of the manuscript titled "Maximal Voluntary Contraction Exercises: A Methodological Investigation in Knee Osteoarthritis" authored by Derek J Rutherford, co-authored by Drs. Cheryl Hubley-Kozey and William Stanish is included in Appendix A.1. This manuscript was published in the Journal of Electromyography and Kinesiology 21 (2011) 154-160. On a sub-group of individuals, Appendix A.2 illustrates the influence of exercise selection on amplitude normalization of the gait electromyogram for each muscle group. This topic of EMG normalization is a particularly pertinent one and highly relevant to the study of EMG in OA and pathological conditions.

Appendix B provides a summary of principal component analysis methodology for electromyographic waveform analysis and interpretation. The data for this summary was obtained from the analysis contained in Chapter 4.

Appendix C provides an electromyographic waveform analysis completed on 25 participants with knee OA to delineate potential differences in low-pass filtered (Butterworth, 6Hz, 4^{th} order) data that would be expected using down sampled data at 1000Hz from data originally collected at 2000Hz.

Appendix D was included in this dissertation as an adjunct to the analyses completed in Chapters 4, 5 and 6. Individual waveforms used in the principal component analyses, the principal patterns and the mean of five waveforms to represent high and low principal pattern scores can be found in this appendix.

Appendix E contains the license agreements with Elsevier Limited for the use of published manuscripts in this dissertation.

The authors of the manuscripts contained within this dissertation were involved in various stages throughout the course of this work. I was responsible for formulating the hypotheses, methodology, data analysis, interpretation, writing and preparation for submission of all manuscripts. Individuals that assisted with recruitment, data collection and processing are acknowledged in the appropriate section.

CHAPTER 2

REVIEW OF RELEVANT LITERATURE

This chapter provides an overview of the relevant background literature for this dissertation. The literature establishes the role that gait analysis has played in understanding knee OA pathomechanics with respect to both development and progression of knee OA and in particular examines the need to understand knee joint muscle activation characteristics. Topics reviewed include, the burden of OA, joint structural changes, knee joint function through biomechanics and electromyographic study of gait and pertinent methodological considerations, limitations and gaps in current knowledge regarding muscle activation during gait.

2.1 THE BURDEN OF OSTEOARTHRITIS

"Arthritis Deformans" was described by Sir William Osler (1849-1919) as "a chronic disease of the joints of doubtful etiology, characterized by changes in the cartilage and synovial membranes, with periarticular formation of bone and great deformity". First illustrated by Rudolf Virchow (1821-1902), the term "arthritis deformans" included osteoarthritis (OA) and perhaps many other arthritic diseases of current day medicine [60]. It is clear from the description outlined by Osler that pathognomonic characteristics of OA were emphasized including "chronic disease", "changes in cartilage", "periarticular formation of bone and great deformity." The term "osteoarthritis" became modernized and widely accepted in the early 1900's as a result of the work by A.E. Garrod [74]. There have been many names for the present day osteoarthritis including arthrosis, arthritis, arthritis deformans and degenerative joint disease, which perhaps lead to its controversial beginnings and current difficulties capturing the true extent of this disease process.

In Canada, the estimated yearly costs associated with arthritis are over 6 billion dollars, representing almost one third of the total cost of musculoskeletal diseases [142]. Osteoarthritis is the most prevalent form of arthritis where a projected 1 in 10 individuals have OA [143] . In the United States, a similar situation exists. An estimated 27 million adults live with OA [147] where annual medical care expenditures exceed 185 billion dollars [138]. Many of these costs are encountered as individuals affected with OA are more

likely to need help with daily activities, incur greater economic stress and contact health care professionals with greater frequency [18,82].

Of all lower extremity joints, OA is most prevalent in the knee joint and has been recognized for decades as a leading cause of disability in older adults [81,182]. Currently there is no cure for OA [145] with arthroplasty, the treatment of choice for severe cases. In Canada, there has been a 140-fold increase in hospitalizations over the past decade for total knee replacements, where over 90% of primary total knee replacements were performed because of knee OA [48]. Given the current numbers and projections, based on increasing prevalence of total knee arthroplasty in younger adults plus the aging population, managing individuals with knee OA may be the largest challenge for orthopaedic care in future decades [141]. Thus, methods to facilitate early knee OA diagnosis, monitor progression and devise treatments to slow down progression are relevant to reduce this burden on Canada's population and heath care system.

2.2 WHAT IS KNEE OSTEOARTHRITIS?

The knee joint is composed of two distinct articulations located within a single joint capsule. The knee consists of several different tissues (articular cartilage, ligaments, meniscus, bone, synovium, joint capsule, afferent receptors and periarticular musculature) that allow relatively frictionless, painless movement to occur during gait. The tibio-femoral articulation is the focus of this dissertation. The mechanics of this articulation are important for the health of these tissues. *In vitro* [114], *in vivo* [9] and computer simulation studies [23] provide evidence that intermittent mechanical loads within normal physiological limits contribute to normal knee joint function and balance between tissue synthesis and degradation. In contrast, excessive joint loads have led to articular cartilage fissuring [200,257], subchondral bone remodeling and microfractures [36,201], and articular cartilage vascularization [33,244]. In addition, altered spatial orientation of the tibial and femoral articular surfaces [8,9,11] and/or joint unloading and immobilization [181,254] have been shown to result in knee joint degeneration. Knee OA has been considered an attempt to contain these mechanical problems of the joint [27]. The importance of intra-articular

biomechanical stress has been emphasized in many recent reviews on the mechanics of knee OA [10,27,41,266].

Knee OA occurs in all compartments of the knee joint, including patello-femoral, lateral and medial tibio-femoral surfaces [5,128,249], however medial knee OA is more frequently reported [64,249] and has received a great amount of investigation. Pathognomonic impairments to anatomical knee joint structure exist and include articular cartilage lesions, joint margin and tibial spine osteophytosis, subchondral bone sclerosis, and bone attrition [5,105,125,195,224]. The complexity of structural involvement make capturing the disease with any one feature difficult, as has been discussed in the case with isolating knee OA structural impairments to articular cartilage degeneration [27]. In addition, impairments to physiological functions of the knee joint and surrounding tissue include the muscular and neurological systems [25,210] and synovium [17,192,225]. Together these impairments to joint structure and function provide a foundation to understand OA [27].

Knee OA is a progressive disease that results from failed repair of joint damage that can arise as a result of biomechanical, biochemical and/or genetic factors [145]. While considered progressive, the reparative process can also be successful leading to a functional, painless joint [27,199]. Therefore, the balance between tissue synthesis and degradation is not constant. It has been discussed that stresses (physical and/or biochemical) can be initiated in any of the synovial joint tissues, including articular cartilage, subchondral bone, ligaments, menisci, periarticular muscles, peripheral nerves, or synovium [27,145]. This ultimately results in the breakdown of cartilage and bone, leading to symptoms of pain, stiffness and functional disability.

Knee OA is a multifaceted disease process that impairs joint structure and function, limits the performance and capacity of weight-bearing activities and ultimately restricts societal participation. The International Classification of Function provides a framework to organize the interrelationship between these levels of human function affected by this disease.

2.3 INTERNATIONAL CLASSIFICATION OF FUNCTION

The International Classification of Functioning, Disability and Health (ICF) provides a standard language and framework for describing health and health-related states [264]. The ICF is a biopsychosocial model of health states from a biological, personal and societal perspective [264] (Figure 1.1). Three levels of human functioning are recognized; i) level of body or body part ii) the whole person and ii) the whole person in a social context. Disability involves a dysfunction at one or more of these levels including i) impairments to structure and function, ii) activity limitations and ii) participation restrictions. Within the ICF, contextual factors include aspects of the human environment (i.e. physical, social) as well as personal factors (i.e. physical, emotional) that can influence how disablement is experienced by the individual [119,264]. Given that impairments to knee joint structure and function are central to the knee OA process and many individuals are disabled by this disease, the ICF framework provides the basis for understanding functioning and disability in individuals with knee OA for this dissertation.

Central to this dissertation is developing an understanding of the reciprocal relationship between joint impairments and activity limitations, in this case walking. It is estimated that healthy older adults take between 6000 and 8500 steps in a day where individuals with disabilities and chronic illnesses typically take up to 5500 steps in a day [252], making the ability to walk the single most important daily physical activity. Joint mechanics are integral to the knee OA process [27]. The cyclic, weight-bearing nature of human gait has served as a good model to study the knee joint in individuals with knee OA [11,27,266]. Joint loads during gait in the tibio-femoral joint are asymmetrically distributed where the majority of weight-bearing compressive load is transferred through the medial compartment [219,229,287,288]. Schipplein and Andriacchi [219] predicted that 70% of the total load passes through the medial compartment. A similar load distribution was found using *in vivo* measurements [288]. Concomitantly, it has been recognized for many decades that OA prevalence within the medial compartment of the tibio-femoral joint is greater than the lateral compartment [64,249]. This in part, provides the basis for evaluating "walking related" factors of the knee OA process [11,25,27,266].

A knowledge gap exists in understanding how anatomical and physiological impairments limit activities such as walking in individuals with medial compartment knee OA. Biomechanical insults impair joint structure and function and play an important role in the development and progression of knee OA [27,29,145,266]. Amelioration of the abnormal biomechanical environment has the potential to attenuate knee OA progression [27] however, a lack of systematic studies exist to quantify the relationship between knee joint impairments and activities, such as walking.

The next section of this review will look at gait mechanics, including both kinematics and kinetics. A particular emphasis on joint loading and abnormal variations thereof, studied to understand knee OA development and progression [11,27] will be discussed.

2.4 JOINT MECHANICS DURING GAIT IN KNEE OA

Gait mechanics have been studied to understand the impact of the knee OA process on how an individual walks. Conversely, joint mechanics, particularly those that provide a surrogate measure of joint loading have been studied to understand the role of walking in the development and progression of this disease. For understanding gait mechanics, biomechanical analyses have used kinematic and kinetic evaluations. A general overview of knee joint kinematics and kinetics pertaining to knee OA gait will be covered in the following sections.

2.4.1 Knee Joint Kinematics

Biomechanical research methodologies for the study of gait in individuals with knee OA are well established. Many studies have recorded, using state of the art motion capture systems, movement profiles (kinematics) of individuals with varying severities of knee OA [15,44,77,86,123,144,154,164,176].

Sagittal plane knee joint angles are altered in the presence of knee OA however; the amount of change, where the change occurs in the gait cycle and the direction of change varies among studies. The most common finding is a reduced knee flexion angle

during the loading response (early stance) for those with knee OA [15,44,58,77,123,154] compared to asymptomatic controls. A progressive decrease in the flexion angle with increasing knee OA severity has also been found [15]. Others however, have reported no differences [20] or greater stance phase peak knee flexion angles [86] between asymptomatic individuals and those with knee OA. Heiden *et al*., [86] also found a greater knee flexion angle at heel strike, consistent with the findings of Childs *et al*., [44] and greater knee flexion during mid to late stance. These findings contrast with Mundermann *et al*., [176] where individuals with both moderate and severe knee OA made initial contact with the ground in more knee extension and no differences were found for the mid to late stance peak angles. Sagittal plane knee angle waveforms presented in Astephen *et al*., [15] demonstrate no differences between asymptomatic individuals, and individuals with moderate and severe knee OA at heel strike and during mid to late stance. Reduced sagittal plane knee motion is most frequently reported and in general, individuals with knee OA walk with reduced overall knee motion. There are however, a number of factors, including subject demographics and knee OA severity [15,283], gait velocity [144,283], motion capture methodology and waveform analyses that currently exist that can explain these differences between studies.

While the greatest range of motion about the knee occurs in the sagittal plane during gait, frontal and transverse plane joint motions have also been evaluated. Varus thrust is known to occur in individuals with knee OA, characterized by the rapid change in tibial adduction angle during early stance [42]. While typically identified through visual observation [42], others have reported Euler angle derived frontal plane motion [2,75] and frontal plane motion in two-dimensions through a dynamic hip-knee-ankle angle calculation [140]. Varus thrust was found to be a significant predictor of medial knee OA progression [42] and was also related to the level of knee joint structural impairment as determined using the Kellgren-Lawrence (KL) ordinal radiographic scale [140]. The amount of varus thrust increased with greater KL-scores [140]. While this factor alone suggests frontal plane joint mechanics are abnormal, varus thrust can also provide a mechanism for altered muscle activation patterns during gait [32].

Less well understood are the alterations that occur in transverse plane motion (i.e. internal and external tibia on femur rotation). Transverse plane tibio-femoral motion has

not been reported for individuals with knee OA. This motion may be reduced in individuals with knee OA, given the reduced transverse plane moment of force [15], reduced sagittal plane motion [15,44,58,77,123,154] and greater levels of quadriceps and hamstrings activity in individuals with knee OA [103]. Studies however, have not included this motion in their analyses and further work is required to understand how transverse plane motions are altered in individuals with knee OA.

Currently, state of the art motion capture systems rely on capturing rigid segment movement through skin surface marker motion in a particular volume of space [40]. The accuracy of identifying boney landmarks used for skin surface marker placement, virtual point digitization and soft tissue artifact can affect the calculation and accuracy of resultant joint angles [57]. Kinematic crosstalk can severely affect the interpretation of non-sagittal plane motion [57,196,204] where large excursions about the knee flexion and extension axis cross talk with smaller excursions in the other planes. Frontal and transverse plane knee joint angles are small in relation to sagittal plane movement, where frontal plane movements less than five degrees have been reported [2,75,140]. Error magnitudes can be greater than the movement itself [59] limiting a general understanding of frontal and transverse plane motions and how they might be affected by the knee OA process. In fact, Landry *et al*., [144] did not measure these motions for this reason. Given individuals with knee OA typically have greater BMI, larger amounts of lower extremity soft tissue can be suspected in comparison to asymptomatic counterparts, making landmark identification and soft tissue artifact a consideration in interpreting all joint angles, most notably those that occur in the frontal and transverse planes.

Joint kinematics provide a description of the motion and the literature supports altered knee joint kinematics with knee OA, particularly in the sagittal plane. To understand factors that relate to joint loading however, a kinetic analysis is needed as kinematics do not provide information that allows an understanding of the forces that create, maintain and terminate motion during gait. Gait kinetics provides a joint specific analysis of the forces and moments of force during gait. Together, kinematics and kinetics have been used to evaluate gait pathomechanics.

2.4.2 Knee Joint Kinetics

Knee joint moments of force have been widely studied in knee OA gait. Frontal and sagittal plane moments have been primarily interpreted to estimate the mechanical load on the knee joint tissues (i.e. articular cartilage and musculature). During gait, moments of force have been most commonly quantified through the use of traditional Newton-Euler inverse dynamics [15,20,77,86,91,92,123,144,173,177,250]. For the inverse dynamics problem, the motion of the mechanical system is defined and the goal is to determine the forces causing the motion through a linked, rigid body analysis [253,255,269,281].

Inverse dynamics are based on a representation of the lower extremity as a set of rigid segments connected by a set of articulations [253,255,269]. Segment inertial characteristics and ground reaction forces are used to derive, through the evaluation of Newton-Euler equations ($\sum F=ma$ and $\sum M=I\alpha$), resultant net joint moments. The calculations follow a distal (ankle joint) to proximal (hip joint) sequence of evaluations where four sets of information are required; i) ground reaction forces, ii) joint centers of rotation, iii) linear and angular acceleration data of each segment and iv) segment anthropometry [255,269]. Assumptions exist for these calculations [253,255,269,281] and while many can be universally applied to both individuals with knee OA and asymptomatic counterparts, those pertaining to segment anthropometry and joint center locations can differ between populations and significantly affect inverse dynamics interpretations [95]. Despite these considerations, a great amount of information has been gleaned by the study of frontal and sagittal plane net external moments of force about knee OA gait pathomechanics.

The net external knee adduction moment, a moment of force tending to adduct the tibia during the stance phase of the gait cycle, has been calculated as a surrogate for medial:lateral tibio-femoral compressive loading [20,112,173,177,261,288]. The peak net external adduction moment has been found to be highly correlated (R^2=0.77) to *in vivo* medial contact loads, however the loading patterns and where the peaks occurred did not always correspond with *in vivo* measures [288]. These findings emphasize that more information is contained within the net external knee adduction waveform than what peak measures provide.

Discrete net external knee adduction moment waveform characteristics [15,86,123], impulse [250,260], as well as moment of force patterns [13,58,144] have been extracted from the dynamic waveforms. The moments are typically elevated in individuals with knee OA [15,20,86,123,176,250] although where these differences occur has not been consistent. Peak magnitudes, typically found during early stance, are reported to be greater in individuals with knee OA compared to an asymptomatic group [20,123,250]. Thorp *et al*., [250] found the impulse measure to be greater for individuals with KL III compared to KL II scores, the first study, to my knowledge that separated groups based on structural impairment associated with KL II and KL III scores. In contrast, no differences in peak moments have been found [15,86]. In addition, Astephen *et al*., [15] found that the bi-modal pattern in asymptomatic individuals became more uni-modal with increasing knee OA severity [15]. This indicates that the dynamics of how the tibio-femoral joint is experiencing this load is altered.

The net external knee adduction moment is not the only moment that contains a joint compression component (i.e. joint contact forces). *In vivo* medial contact force peaks were best predicted by a combination of net external knee adduction and flexion moments (R^2=0.93) [260]. The net external knee flexion moment has been investigated, although to a much lesser extent than the net external knee adduction moment, during gait in individuals with knee OA [16,20,58,77,86,93,123,144,175,237,279].

Net external sagittal plane moment characteristics have differed between asymptomatic individuals and individuals with moderate and severe knee OA [15,16,20,58,77,86,123]. A reduction in the peak early stance moment was the most common finding however this reduction was not always related to knee OA severity progression [15,283]. In addition, the early stance flexion moment is increased with a faster walking speed [144,283] suggesting gait velocity should be considered for the interpretation of this moment. Compared to early stance, a net external extension moment has been shown to peak during mid to late stance. A reduction in this mid to late stance moment of force has been found for individuals with knee OA compared to an asymptomatic cohort [20,86,123] and in individuals with severe knee OA compared to individuals with lesser knee OA severity [15]. These findings suggest that not only are mechanics that occur during early stance important to understand, but also joint mechanics occurring during mid to late

stance; a period of stance where individuals are on a single leg stance, transferring their mass to their contra-lateral limb and providing propulsion.

The net external knee flexion moment during early stance has been associated with knee flexion motion. A significant correlation between the net external knee flexion moment and flexion angle (r=0.813) in a combined asymptomatic and knee OA group has been reported [20], hence 66% of the variance in the moment. Some of the unexplained variance may be accounted for by muscle forces. A reduction in both flexion moment and angle during early stance has been equated with a quadriceps avoidance gait [20]. Kauffman *et al*., [123] concluded that individuals reduce their internal knee extensor moment as an attempt to reduce their pain by minimizing knee joint load. Unfortunately, these studies do not evaluate knee extensor muscle contributions and pain during walking, limiting the general applicability of the "quadriceps avoidance" interpretations. Unlike the net external knee adduction moment, the net external knee flexion moment has been interpreted in the context of musculature contributions during gait. Hence the later has been included as part of the analysis in Chapter 6 of this dissertation.

Net transverse plane rotation moments are less studied and have not been typically included in the biomechanical analysis of knee OA gait. Differences have been found in this moment between individuals with knee OA and asymptomatic individuals [15,16,77,144,168]. Gok *et al*., [77] found a greater internal rotation moment during the stance phase in individuals with knee OA compared to healthy individuals. Where this occurred in the stance phase and the frame of reference was not provided [77]. The other four studies analyzed the net external transverse plane moments. The results are inconsistent. A progressive decrease in late stance internal knee rotation moment in individuals with increasing knee OA severity was found [15]. The only significant difference was found for the severe OA group compared to asymptomatic and individuals with lesser severity [15]. In another study by the same author, individuals with moderate knee OA had higher knee internal rotation moments during late stance compared to asymptomatic individuals [16]. This conflict could be a result of the analysis methods that were utilized. McKean *et al*., [168] found no early or late stance differences to exist between asymptomatic individuals and those with moderate knee OA where Landry *et al*., [144] did find a significant decrease in the external rotation moment during early stance for individuals with moderate knee

OA . Collectively, it remains unclear if a systematic difference occurs in the tibio-femoral transverse plane moments of force with knee OA and with increasing severity. What information these differences are providing, in comparison to sagittal and frontal plane moments of force have not been clearly discussed.

In summary, gait kinematics and kinetics are altered in individuals with knee OA during self-selected gait. These alterations occur about the flexion/extension, abduction/adduction and internal/external rotation knee joint axes however; the internal/external tibial rotation biomechanics remain unclear. While many studies also find hip and ankle mechanics are altered in individuals with knee OA, knee mechanics directly correspond to the biomechanical environment of the OA knee.

Understanding the dynamic loading of the knee joint during walking has its limitations. First, intersegmental moments of force are conceptual quantities that are not necessarily physically present in any one single anatomical structure [55]. This makes interpretation of these findings, directly in context with impaired knee joint structure and function difficult. Secondly, muscle forces play a role in creating moments of force to produce motion, maintaining joint stability [189,239]. These forces influence joint loading [7,160,229] and metabolic demand [78,171] during gait. Despite the interpretation of quadriceps avoidance gait stemming from reduced net external knee flexion moments in gait studies [20,251], moment of force computations do not include muscle forces.

Two recent reviews [25,210] highlight the importance of understanding alterations in the neuromuscular system associated with the knee OA process. While less studied than knee joint biomechanics, over the past 6-8 years, studies have shown that the knee joint muscle activation characteristics are altered in patients with knee OA during walking. Together with work on understanding joint biomechanics, this information will provide a comprehensive understanding of the dynamic mechanical environment of the knee joint during gait and add to our understanding of OA pathomechanics.

2.5 Muscle Activation During Gait in Knee Osteoarthritis

During gait, a balance must be established between knee joint stability and mobility where the passive osteoligamentous, muscular, and the neurological subsystems

are thought to be fundamental to this process [239]. An initial framework is provided in Figure 1.2, modified from its original description of spinal stability [189], and emphasizes the interaction between these three subsystems to promote normal knee joint mechanics.

Panjabi [189] described the basic biomechanical functions of the spine, for which mechanical stability is required for successful performance. The spinal system has to i) allow movements between body parts, ii) carry loads, and iii) protect the spinal cord and nerve roots [189]. Parallels can be drawn to functions of the knee joint during gait where i) movements have to be allowed between tibia, femur and patella, ii) the knee joint has to carry the load of the body, and iii) the internal structures of the knee have to be protected. As described for the spinal system, three subsystems are defined, including the passive, active, and the neural subsystems.

Panjabi states that normal joint function is to provide sufficient stability to match the instantaneously varying demands due to changes in posture and static and dynamic loads [189]. Specifically, the passive subsystem is thought to contribute to the maintenance of stability towards the ends of the range of motion. This subsystem is passive as it does not generate or produce joint motions [189]. The active subsystem is the means through which the body can generate forces through muscle contraction and maintain joint stability. Finally, the neural subsystem receives information from the passive and active subsystems among others, including the vestibular and visual apparatii [210], to determine specific stability requirements, causing the active subsystem to achieve the given stability goal [189]. The relationships between subsystems are reciprocal whereby a dysfunction in one subsystem requires adaptations in the other subsystems to maintain joint stability and the performance of joint functions as described for the knee above.

Osteoligamentous structures are compromised with knee OA in a progressive manner [5,106,106,125,194]. Thus, the potential exists for increased reliance on the neuromuscular systems to maintain knee joint stability during gait as the structural changes become more apparent as the disease progresses. The neuromuscular system has been assessed during gait using surface electromyography. This techniques has been used for decades to quantify muscle activation characteristics during kinesiological investigations [191,274,278]. More recently, these techniques have provided information on activation amplitudes [44,86,103,154,161,212,284], co-activation [44,86,98,103,124,154,156,157,202,203,212,220],

onset and offset latencies [44], and patterns of activity during the gait cycle in individuals with knee OA [13,16,102,103,214]. The most notable differences include increased quadriceps and lateral hamstrings amplitudes [102,103,161,214,284], reduced overall medial gastrocnemius amplitudes [102], greater agonist/antagonist co-activity [86,103,154,212] and longer durations of activity during stance for those with knee OA compared to an asymptomatic cohort [44,102,214]. In addition, muscle activation amplitude and timing differences have been found between medially and laterally oriented knee joint muscles in individuals with medial compartment knee OA [102,161,214]. These general alterations are related to the presence of knee OA, however a small number of studies found that alterations to muscle activation were also related to knee OA severity [13,16,103,284]. To note; participants with knee OA were often reported as a homogenous grouping with only a few studies sub-classifying samples based on the degree of OA severity [13,15,16,103,176,250,284]. Regarding gait EMG studies, knee OA severity has been defined using inconsistent metrics that can include radiographic scores only [284] or radiographic scores in combination with symptoms, function and treatment [13,16,103]. This makes drawing conclusions across these studies, regarding the effect of knee OA severity difficult. Knee OA severity is reviewed in more detail in Section 2.6 and Section 2.7.

2.5.1 Activation Characteristics of Specific Muscle Groups

Electromyographic waveform data during gait have high dimensionality, variability, highly correlated within muscle groups, and temporally dependent [43]. Determining how muscle activations change across different phases of the gait cycle (Figure 3.8), phases that correspond to changing joint mechanics (motion and moments of force), is of particular interest as it helps us to understand the factors that can alter knee joint muscle activation.

Alterations found in knee joint muscle activation characteristics during walking in knee OA have been largely based on electromyogram amplitude differences. This includes measures of overall amplitude, whether captured using mean or peak values obtained over the stance phase, or captured as amplitude time histories using pattern recognition methods, namely Principal Component Analysis (PCA). Amplitude measures

have also been taken for specific periods within the gait cycle. For instance, a mean value calculated during the loading response [212]. Restricting analyses to a defined interval limits the identification of how amplitudes transition from phase to phase. Principal component analysis has been used to capture pattern dynamics across the gait cycle. Amplitude difference operators (i.e. the relative amplitude differences between gait cycle phases (early, mid and late stance) have been reported for the gastrocnemii, quadriceps and hamstrings [13,102,214], as well as muscle activity phase shifts [102,214], primarily of the gastrocnemii and hamstrings.

Studies have focused on quadriceps and hamstrings activation characteristics, with fewer studies on the gastrocnemii, where representative muscles are often assessed for these muscle groups [44,98,284]. The vastus lateralis, medialis, and rectus femoris, along with the medial and lateral muscles of the hamstrings and gastrocnemii have been also been investigated separately. The following section will provide a summary of the current literature pertaining to muscle activation during gait in individuals with knee OA.

2.5.1.1 Hamstrings Activation

Increased overall lateral hamstring amplitudes are the most consistent knee joint muscle activation alteration reported between individuals with knee OA and an asymptomatic cohort [16,98,102,103,161,212,214]. Lateral hamstring activation was also more prolonged (Phase Shift) during early to mid-stance in individuals with moderate knee OA [102,214] compared to an asymptomatic cohort. Peak lateral hamstring activation has been found to occur after heel strike in individuals with moderate knee OA compared to the lateral hamstring of asymptomatic individuals [102]. Furthermore, Hubley-Kozey *et al*., [103] found that overall LH amplitudes are increased progressively with increasing knee OA severity. These findings indicate that lateral hamstring amplitudes were affected by the OA process. These preferential increases altered medial and lateral hamstring activation dynamics.

Differences between lateral and medial hamstring amplitudes [86,102,161,214], as well as prolonged activation of lateral hamstrings compared to medial hamstrings have been reported [102,214]. Lynn *et al*., [161] found that during the stance phase, the medial:lateral

hamstring activity ratio was reduced. Heiden *et al*., [86] found in each of the loading, early and mid-stance phases, this difference occurred. A greater lateral hamstring to medial hamstring activation ratio for each period of the stance phase was related to lower scores on the physical component of the Short-Form 36 [86]. This indicates lower self-reported function in individuals with greater medial:lateral hamstring activation differences. In addition, this difference was associated with greater early stance peak knee adduction and flexion moments and greater late stance peak extension moments [86]; joint mechanics that are directly related to *in vivo* medial compartment contact forces[260].

Elevated and prolonged lateral hamstring activity in individuals with medial compartment knee OA may be related to structural impairments associated with this disease, namely medial compartment articular cartilage degeneration. Various explanations for these differences have been provided. Mechanical explanations include, i) a response to reduce medial compartment compressive loading [102], ii) an outcome of muscle mechanics [161], as lateral hamstring has a smaller physiological cross sectional area [262] and smaller moment arm length [242] in comparison to medial hamstring and/or iii) a reflex response or learned response to the tensile stress on the lateral tibio-femoral compartment [86] during stance. In addition, neurophysiological responses may also occur. While not currently discussed, greater lateral hamstring activity could be a result of a heightened flexor withdrawal reflex that was found for biceps femoris in individuals with knee OA [51]. As well, non-weight bearing proprioception can be impaired in individuals with knee OA [22,135,228]. Swing to stance transitions may be affected by impaired proprioception and provide an explanation for the delayed peak activity previous found [102].

While the hamstrings are estimated, through modeling, to provide knee stability [219], lateral tibio-femoral compartment tensile stress may be a plausible explanation for preferential lateral hamstrings activation, given that varus thrust during loading was found to increase with increasing structural severity (KL-score) [140]. Despite these hypotheses, how hamstrings activation amplitudes change and how these dynamics are altered during stance with respect to structural severity, including joint space narrowing, remains to be determined.

In contrast to the lateral hamstrings, many studies have found that medial hamstring amplitudes are not significantly altered with moderate knee OA [102,161,214,284]. However, Childs *et al*., [44] analyzed the duration of activity during stance and found that the medial hamstring was active ~1.6x longer in individuals with knee OA compared to asymptomatic individuals. This partially supports the prolonged lateral and medial hamstring activity found in individuals with moderate knee OA compared to asymptomatic individuals [214]. In addition, individuals with severe knee OA had greater overall medial hamstring amplitudes compared to asymptomatic individuals and individuals with moderate knee OA [103]. In contrast, Zeni *et al*., [284] did not find differences in medial hamstring activation between these group classifications. This supports that knee OA severity differences in medial hamstring amplitudes are not as consistent as those found for the lateral hamstrings. Differences between these studies could be attributed to the sample size differences, reducing statistical power, and differing gait velocities, indicating different levels of participant function between studies [284]. In addition, Hubley-Kozey *et al*., [100] also reported reduced hamstrings strength for individuals with severe knee OA that may explain the greater lateral and medial hamstrings activation amplitudes found in this group.

Muscle strength, amplitude normalization and gait velocity may explain hamstrings amplitude differences. First, lower hamstrings strength can elevate activation amplitudes during sub-maximal tasks, as individuals will need to work at a higher percentage of maximum to produce the same torque output. Muscle strength is defined as the maximum ability of a muscle or group of muscles to produce a force at a specified velocity [132]. Strength was not reported in many knee OA gait studies, however when hamstrings activation increases were found between groups, strength deficits were not [102]. Secondly, lower amplitudes because of a sub-maximal effort during the amplitude normalization exercises could also explain higher amplitudes. Amplitude normalization is an important aspect of surface electromyography methods and is discussed separately in Section 2.9. Finally, studies find that walking velocity is slower in individuals with knee OA [16,103,214,284]. Elevated hamstrings activity was, however, contrary to what was expected with slower gait, where amplitude reductions were found when asymptomatic individuals reduce velocity [94,231,278]. While overall hamstrings amplitudes could be

influenced by these factors, medial:lateral muscle site activation amplitude differences and prolonged stance phase activity can not be fully explained through these mechanisms.

In summary, both amplitude and temporal activation features of the hamstrings electromyograms during gait are altered with knee OA presence and severity that was based a combined functional, symptomatic and radiographic criterion. Overall, increased lateral hamstring amplitudes and prolonged mid-stance hamstrings activity are the most commonly reported findings. Differences between medial and lateral hamstrings exist and demonstrate asynchronous activation in individuals with knee OA. A gap exists however to understand if many of these differences with increasing knee OA severity were merely a result of different walking velocities among groups. In addition, while knee mechanics pertaining to medial compartment articular cartilage degeneration have been discussed as a factor to influence the lateral hamstring activity consistently reported, the association between increasing level of structural impairment and hamstrings activation patterns has not been determined.

2.5.1.2 Quadriceps Activation

Quadriceps are estimated to provide primary control of knee stability during early to mid-stance [219,229]. As with the hamstrings, amplitude increases are typically found for these muscles, however these increases are not systematic across the gait cycle and medial:lateral muscle site activation differences have not been consistently reported.

Greater peak [98] and overall vastus lateralis [102,103] amplitudes have been reported in individuals with moderate knee OA compared to an asymptomatic cohort. In addition, Hubley-Kozey *et al*., [102] also found a difference in overall activation between vastus lateralis and medialis. Greater vastus lateralis activity has been thought to provide a counter abduction moment during stance to unload the medial compartment in combination with the greater lateral hamstring amplitudes as discussed previously [102]. This finding has not been repeated for amplitude measures of VL/VM [99,103,212,214] where either both vastii amplitudes were increased [103,212] or no differences were found [214]. Andriacchi *et al*., [7] suggested the position of the tibio-femoral contact force influences

the quadriceps moment arm to produce frontal plane torques to maintain knee joint stability during gait. This suggests that vastus laterialis, medialis and medial:lateral quadriceps activation differences can be related to level of joint impairment. This however would be dependent on the medial:lateral position of the contact force that would theoretically vary depending on the amount of medial compartment articular cartilage degeneration. Thus, the level of structural impairment associated with medial compartment knee OA, while currently heterogeneous in all knee OA EMG studies, with the exception of Astephen *et al*., [13] and the severe group studied by Zeni *et al*., [284] , can explain this variation yet this association remains to be determined.

The effect of knee OA severity on quadriceps activity is less clear. Hubley-Kozey *et al*., [103] reported a progressive increase in overall vastus lateralis activity with increasing knee OA severity. No differences were found between vastus medialis and lateralis for the moderate and severe knee OA groups. These findings support that greater contributions of the quadriceps are needed for knee stability as knee OA severity increases. In contrast, Zeni *et al*., [284] found no differences in mean or peak vastus lateralis activity across the gait cycle between asymptomatic individuals and individuals with moderate and severe knee OA. As discussed for the hamstrings results, differences between these studies could be attributed to the sample size, gait velocities and functional abilities. In addition, when asymptomatic individuals and individuals with moderate knee OA, based on KL II and III scores walked faster than their self-selected speed, corresponding increases in vastus lateralis activation occurred [284]. This was expected given previous findings in asymptomatic individuals [231,278]. In the severe knee OA group (KL IV), despite a 0.4 m/s increase in walking velocity, vastus lateralis activity did not increase. The authors suggest that other mechanisms (i.e. osteophytosis) can be maintaining stability and subsequently, quadriceps amplitude increases were not required [284]. This conclusion was the first to suggest that osteophytosis may be involved in altering muscle activity, by increasing the contribution of the passive osteoligamentous system to maintain knee stability. This provides a potential connection between structural severity and knee joint muscle activity.

As discussed in the context of hamstrings amplitude measures, muscle strength and amplitude normalization may explain alterations in overall quadriceps amplitude

differences associated with knee OA, most notably individuals with severe knee OA [100]. Quadriceps muscle atrophy [69], inflammation [153], and inhibition [120] have been reported for individuals with knee OA. This may specifically lead to the findings of impaired muscle force generating capacity of the quadriceps in many individuals with knee OA [70,110,158,236]. For gait velocity, the effect was unclear. Lower amplitudes, as shown for the severe OA group in Zeni *et al*., [284], would be expected given the slower gait velocities reported, but this association was not always found [103]. In addition to these factors, impaired proprioception has been found in individuals with knee OA [22,135,228]. Given the role of the quadriceps in maintaining knee stability during gait, reduced proprioception may result in increased overall quadriceps activity. Furthermore, knee effusion has been shown to influence the force generating capacity of the quadriceps and promote a "quadriceps avoidance" gait pattern in healthy subjects [251]. The effect of knee effusion on gait mechanics and muscle activity has not been previously considered and was included as objective three of this dissertation and further reviewed in section 2.8.

In contrast to overall amplitude measures, two studies have specifically evaluated the dynamics of vastus lateralis, medialis and rectus femoris activation across the gait cycle using PCA. Amplitude difference measures between gait cycle phases (i.e. early, mid and late stance) are different in individuals with knee OA. Greater mid-stance amplitudes were found with respect to late stance for the vastus lateralis, medialis and rectus femoris individuals with moderate knee OA compared to an asymptomatic cohort [214]. This supports a previous finding with respect to the vastii amplitudes in individuals with moderate knee OA [102]. Greater quadriceps activity during mid-stance, where lower amplitudes for asymptomatic individuals were found, could be required to maintain knee stability during single leg support. These results were novel, and while muscle strength, amplitude normalization and gait velocity differences were not expected to influence these measures, their relationship to gait mechanics and joint impairments characteristic of individuals with knee OA remain to be fully understood.

In summary, quadriceps amplitude alterations reported during gait in individuals with knee OA are generally inconsistent. Activation differences were found between vastus lateralis and medialis and typically, rectus femoris has lower amplitudes than the vastii in all groups evaluated. Furthermore, activation dynamics are altered, particularly

mid-stance amplitudes with respect to late stance in individuals with moderate knee OA. The current differences from asymptomatic individuals or between severities are thought to be dependent on factors that challenge knee stability. The role of knee joint impairments, including structural severity as well as knee effusion have not been entirely determined and provide the motivation for objective two and three of this dissertation.

2.5.1.3 Gastrocnemii Activation

Currently, only a small group of studies has investigated gastrocnemii activation during gait in individuals with knee OA. In contrast to the increased amplitudes of the hamstrings and quadriceps, a trend existed for an overall amplitude reduction in the gastrocnemii.. Hubley-Kozey *et al*., [102] found medial gastrocnemius amplitudes were reduced in individuals with moderate knee OA compared to an asymptomatic group and no differences for lateral gastrocnemius. This is similar to the trend found in Rutherford *et al*., [214] however his results were not significant and could have been due to a smaller sample size in comparison to Hubley-Kozey *et al*., [102]. The waveforms presented in Hubley-Kozey *et al*., [103], illustrated that this reduction in overall medial gastrocnemius amplitude was associated with knee OA severity. This reduced amplitude was not significant and could have been based on PCA waveform analysis methods.

While not as extensively studied as the hamstrings and quadriceps, the gastrocnemii amplitude decreases and in particular the medial gastrocnemius found in those with medial compartment knee OA are thought to reflect a strategy to reduce the medial compartment compressive loads [102,214]. Furthermore, this strategy may be linked with knee OA severity [103] defined using a radiographic, function and symptomatic criterion where lower medial gastrocnemius amplitudes were shown with greater severity level. Muscle strength, amplitude normalization efforts and gait velocity cannot fully explain reduced MG amplitudes in these studies. Temporal gastrocnemii activation characteristics shown to also occur in individuals with knee OA [102,214], would not be affected by these factors.

The use of PCA to analyze gastrocnemii electromyograms has consistently identified an activation phase shift and an early to late stance amplitude difference

operator. In asymptomatic individuals and individuals with moderate knee OA, the medial gastrocnemius increases activity during mid to late stance before the lateral gastrocnemius [102,214]. How, or if, this temporal asynchrony of the gastrocnemii is altered with increasing knee OA severity has not been determined. Earlier medial gastrocnemius activity may reflect the role of this muscle to control hind foot mechanics during gait [150] and transverse plane tibial rotation [197]. These hypotheses remain to be fully explored.

In contrast to the activity phase shift, elevated gastrocnemii activity during early stance, specifically or in relation to late stance, has been found for individuals with moderate knee OA. Rudolph *et al*., [212] found that during the loading phase (approximately 0-20% of the gait cycle) gastrocnemii amplitudes were elevated, most notably the lateral gastrocnemius. This partially corroborates Rutherford *et al*., [214] where individuals with moderate knee OA had greater early stance gastrocnemii amplitudes compared to late stance amplitudes, captured using PCA. Elevated gastrocnemii amplitudes found during the loading phase may act to maintain joint stability at that period of the gait cycle [16,212,214].

Gastrocnemii amplitudes were reduced, most notably for the medial gastrocnemius. Temporal asynchrony between the medial and lateral gastrocnemii activations existed in asymptomatic individuals and were not altered in individuals with moderate knee OA. Elevated early stance and reduced late stance patterns have also been identified for individuals with knee OA. Since fewer studies have examined the gastrocnemii, mechanisms for these findings have not been fully formulated but the waveforms presented by Hubley-Kozey *et al*., [103], would suggest that these alterations are related to knee OA severity.

In summary, individual knee joint muscle activation amplitudes and temporal features have been investigated during self-selected gait in individuals with medial compartment knee OA. These investigations have included both discrete waveform parameterization and pattern recognition. Medial and laterally oriented muscle group amplitudes and temporal features of the gastrocnemii, quadriceps and hamstrings are altered, supporting that changes to the neuromuscular system are occurring and affecting all major knee joint muscles during self-selected gait. What remains to be determined however, are objective *in vivo* measures to understand the reciprocal relationship between

knee joint impairments and limitations in walking using surface electromyography of the knee joint musculature. The role of knee OA severity to alter knee joint muscle activation patterns remains inconclusive given the severity metrics and walking velocity differences found among previous groups and studies. In addition, the association of structural severity and knee effusion to individual knee joint muscle activation patterns during gait is not clear. These knowledge gaps formed the foundation for this dissertation work.

2.5.2 Knee Joint Muscle Co-activation

In contrast to assessing individual muscles, a group of studies has considered how amplitude levels between knee joint muscle pairs or groups of muscles compare to provide information on co-activity. Co-contraction is considered the algebraic sum of agonist (prime mover) and antagonist (stabilizer) moments where the lesser of the two opposing muscle moments is always the antagonist [67,126]. Given the difficulty and complexity of calculating muscle moments in practice, muscle activity has been assessed through electromyography to understand co-activity [67,126]. Co-activation and co-contraction have been used interchangeably in the literature. For this dissertation, the term co-activation will be used unless the literature has specifically used the term co-contraction.

The co-contraction index (CCI) is the most widely used method for examining co-activation in individuals with knee OA [44,103,124,154,156,157,202,203,212,220]. Co-contraction, using this index was defined as the simultaneous activation of two muscles [211]. High co-contraction values provide an indication of generalized muscle activation and high levels of activation in both muscles in the pairing. Low co-contraction values indicate selective muscle activation and could be generated by low activations in both muscle pairs or high activation in one muscle and low activation in the other muscle of the pairing [211]. Co-contraction was calculated from 100ms prior to heel strike to the peak net external knee adduction moment [103,103,154,203,212], but variations in this time signature exist [44,284]. Proprietary co-contraction ratios have also been calculated [86]. Using these methods, the resultant co-contraction index/ratio has not provided an indication of which muscle in the pair was higher or lower. It was however assumed that in general, higher levels of co-

activation resulted in higher joint compression [211] and thus stability, as co-activation has been used to understand in the context of knee OA gait [154,202,221].

Most studies have reported higher CCI values for individuals with knee OA with the exception of the vastus medialis-medial hamstring pairing [154,156,203,212]. In addition, the greatest CCI's are typically found for the vastus lateralis-lateral hamstring [103,154,156,202,203,212], a CCI that has been positively related to amount of tibio-femoral varus angulation [202]. These general CCI findings corroborate the individual muscle findings discussed above. Some specific findings do not necessarily follow this general trend. These differences can be a result of differing levels of frontal plane medial compartment laxity [154], level of structural impairment [284], alignment [202,203], knee OA classification criteria [103,284], CCI muscle pairing [44,284] or amplitude normalization criteria [124,157,220,221]. For instance, a group of four studies assessed knee joint muscle activation amplitudes for individuals with knee OA, with the co-contraction index as previously described, using EMG data amplitude normalized to peak activation obtained during the gait trials [124,157,220,221]. The co-contraction indices are larger than previously found and do not correspond to the general trend found for CCI's calculated using MVIC normalized data [103,154,156,203,212]. A waveform derived normalization measure reflects the muscle activity patterns within a trial however amplitude comparisons between trials, individuals or groups are meaningless because of the constantly changing denominator [34,35]. Amplitude normalization will be specifically addressed in section 2.9.

Symptoms of knee instability are commonly reported for individuals with knee OA [71]. Several studies have found that individuals with measurable frontal plane passive knee joint laxity, medial compartment joint space narrowing and symptoms of instability had a greater vastus medialis-medial gastrocnemius CCI (calculated during weight acceptance) compared to control subjects [154,156,203,212]. Lewek *et al*., [154] concluded that this increased CCI indicated greater muscular control of medial compartment laxity during this period of the gait cycle. In addition, Lewek *et al*., [154] found lateral compartment laxity the knee OA group to be similar to asymptomatic individuals and no significant differences in lateral co-contraction were found between these groups. In support of this conclusion, Ramsey *et al*., [203] found that after patients underwent an opening wedge high tibial osteotomy, a significant reduction in medial compartment

laxity resulted and a corresponding reduction in the vastus medialis-medial gastrocnemius CCI was found. As well, no change in lateral laxity was found and corresponded to no change in lateral co-contraction. These results are in contrast to the findings of Heiden *et al*, [86] where greater lateral site co-activation was associated with greater early stance peak knee adduction moments. Previous findings relate to a time interval from 100ms prior to heel strike to the peak knee adduction moment [154,156,203,212]; a period of stance were lateral compartment instability may not be apparent. Heiden *et al*., [86] included the loading and early stance periods separately, providing a partial explanation for the differences between studies. In addition, Heiden *et al*., [86] did not consider the assessment of instability and measurements of resistance to passive knee motion, factors that have been important for understanding co-activation in previous studies.

The CCI has also been used to understand knee joint muscle co-activation with increasing knee OA severity. Hubley-Kozey *et al*., [103] found that during the loading phase, individuals with severe knee OA had greater vastus medialis-medial hamstrings, vastus medialis-medial gastrocnemius, vastus lateralis-lateral hamstring and vastus lateralis-lateral gastrocnemius CCI's compared to asymptomatic individuals and individuals with moderate knee OA. Only the vastus lateralis-lateral hamstring CCI was greater in the moderate knee OA group compared to asymptomatic individuals [103]. Explanations for greater co-activity can be modeled after those provided for the individual muscles in response to medial compartment knee OA. This study also evaluated co-activity using PCA to identify a single pattern that captured the overall shape and amplitude of knee joint musculature activity during gait. Hubley-Kozey *et al*., [103] attempted to understand amplitude and temporal components of co-activation among muscles and between knee OA severity groups. Generally, within-muscle-group co-activity was found for asymptomatic individuals and as knee OA severity increased, between-muscle-group co-activity increased, most notably for the vastii and lateral hamstrings. Knee joint muscle co-activity was different between knee OA severity groups where strategies to unload the medial compartment, control medial joint stability and the role of muscle strength and walking velocity could be potential mechanisms for this altered co-activity across the knee OA severity spectrum.

In contrast, Zeni *et al*., [284] evaluated the vastus lateralis-medial hamstring CCI in individuals with medial compartment knee OA. This muscle pairing captured the extensors and flexors that have the greatest force generating capability, however was limited to understand the medial:lateral muscle activations found for individuals with medial compartment OA. Zeni *et al*., [284] found that individuals with moderate knee OA had greater a CCI than asymptomatic individuals. No differences were found between asymptomatic individuals and individuals with severe knee OA at self-selected (1.25 m/s and 1.05 m/s) and fast walking speeds (1.75m/s and 1.40 m/s) [284]. Zeni *et al*., [284] concluded that individuals with severe knee OA had an increased passive osteoligamentous contribution to stability, thus reducing the need to increase muscle activity when compared to the other groups. Knee OA severity is a complex multifactorial construct and understanding elements within the definition of severity including structural impairments, symptoms or functional limitations are important for providing a context for muscle activation during gait as exemplified by the studies of Zeni *et al*., [284] and Hubley-Kozey *et al*., [103].

There are certain challenges to understand muscle activation characteristics through currently employed co-activation methods despite similar results from across studies that have used this measure. First, many combinations of muscle activation characteristics can lead to a similar CCI [103] or co-contraction ratio presented by Hieden *et al*. [86]. A unique solution is not possible given these indices are indicating simultaneous activity of selected muscle pairs [211]. Therefore, a loss of information is inevitable. Many definitions of co-activity exist and the current reliance on amplitudes at specific phases of gait does not address temporal characteristics. Understanding strategic adaptations employed by individuals with knee OA across the gait cycle to control their knee is however difficult to translate from these measures [212].

In summary, co-activation studies have shown that increased amplitudes occur between muscle pairs or muscle groups in individuals with knee OA. These increases are largely thought to maintain stability of the tibio-femoral joint in response to impaired joint structure and function. Co-contraction indices/ratios are however limited, as currently calculated, to provide information on individual muscle activation characteristics and contributions over the entire gait cycle. Explanations for individual

muscle amplitudes, temporal activation features and co-activation findings have been largely directed towards the mechanical environment of the knee joint during gait. Understanding how knee OA severity influences muscle activation characteristics has not been a large focus of the current investigations despite the progressive nature of this disease.

The goal of this dissertation is to contribute to the development of gait-based metrics that can facilitate knee OA diagnosis and monitor knee OA progression. While some muscle activation characteristic changes appear to be related to knee OA severity, isolating factors contributing to those changes have not been fully explored.

2.6 Knee Osteoarthritis Severity and Gait Velocity

While medial compartment OA was the focus of most studies, participants with knee OA were often reported as a homogenous grouping with only a few studies sub-classifying samples based on the degree of OA severity [13,15,16,103,176,250,284]. The consensus from a small number of papers that focus on muscle activation was that alterations were related to OA severity [16,103,284]. The results of these studies have been integrated above. The difficulty however, in drawing conclusions across these studies was that different definitions for classifying knee OA severity were used.

In two of these three studies, a similar method to define knee OA severity was employed. Hubley-Kozey *et al*., [103] and Astephen *et al*., [16] defined moderate knee OA based on a combined radiographic and functional assessment and severe knee OA based on functional assessment and treatment prescription (total knee arthroplasty). This classification recognized joint structural impairments, quantified through Kellgren Lawrence scoring where the moderate groups contained individuals with scores from KL I to KL IV. KL III and KL IV scores were suspected for the severe group given their clinical management. In addition, symptoms associated with knee OA through activity limitations and treatment options were included in this classification. This classification captured the multidimensional presentation of function and disability associated with knee OA severity. In contrast, Zeni *et al*., [284] classified moderate and severe knee OA based solely on radiographic evidence where individuals with moderate knee OA had KL

II or KL III scores and individuals with severe knee OA had KL IV scores. Zeni *et al*., [284] however did not specifically include information on symptoms and clinical management strategies. In addition, three different analysis methods were utilized to understand knee joint muscle activations. Thus, we are currently uncertain of how knee OA severity and the factors that are considered in this definition alter muscle activation characteristics during gait, making definitive conclusions difficult.

In these previous studies, self-selected walking velocities were different between the subgroups (up to 33%), where increased severity was associated with a slower walking velocity [16,103,284]. Most electromyographic studies have showed that muscle activation during gait was altered with increasing walking velocity in asymptomatic individuals. Amplitude changes were the most prominent alteration, namely increased overall activity as individuals walked faster [94,231,278], although minor changes in shape and duration of activation were also shown [232].

Two methods have been utilized to address gait velocity differences when studying knee joint muscle activity during gait in individuals with knee OA. An *a priori* velocity target has been selected for all individuals to ambulate [44,98,284]. The limitation to this approach is that the predetermined walking velocity can unknowingly alter habitual gait patterns influencing intra-subject variability [231]. In general, self-selected walking speeds are highly reliable (ICC=0.973 95%CI (0.937-0.988)) in older adults [96]. As individuals volitionally slow their gait velocity, the variability to signal ratio increases, most notably for the quadriceps and hamstrings [231]. Others have elected to consider an analysis of covariance (ANCOVA) for statistical hypothesis testing to correct for baseline differences in walking velocity to understand gait biomechanics and muscle activity [154,212,284]. However, when a variable co-varies with a disease process, the use of an ANCOVA model will adjust disease effects for differences caused by the disease (i.e. slower walking velocity) [52] and can remove part of the disease signal. The treatment (knee OA) should have no effect on the covariate (velocity) and a linear relationship between covariate and dependent variable should exist [179]. These assumptions were not satisfied with the current use of this technique.

Currently, a single method has not been recognized as a standard to address the influence of self-selected gait velocity for assessing muscle activity during gait. Thus,

separating OA severity effects from walking velocity effects was further confounded given that lower extremity muscle activation characteristics can be independently altered by changing walking velocity [94,231,278].

Self-reported measures of physical function/disability and symptoms are commonly utilized to evaluate the knee OA process [145,185] despite their poor relationship to joint impairment [21,54,248]. While symptoms provide information on the "illness" component of knee OA [145], treatments that have focused on reducing symptoms alone have not been shown to prevent ongoing structural damage [80,145]. There is evidence that addressing symptoms increases joint loads during gait [222] and can accelerate progression [146,207]. Few systematic studies exist to evaluate the influence of knee OA severity on the neuromuscular system with objective gait measures, specifically muscle activation.

Whether muscle activation differences occur without the confounding effect of walking velocity is needed to understand how the neuromuscular system is altered with increasing knee OA severity. In addition, using a knee OA severity metric that includes symptoms, functional abilities, treatment strategies and level of structural impairment provides a framework to understand the multidimensional nature of knee OA as discussed previously in the context of the International Classification of Function. Addressing this deficiency in knowledge became the first objective of this dissertation.

2.7 Structural Severity

Structural impairments and symptoms are an integral part of the knee OA process. A Kellgren-Lawrence score greater than II, concurrent with knee pain intensity greater than 60/100 were predictors of future total joint replacement [49]. While symptoms and impairments to joint structure can progress in parallel, a known discordance exists [21,54,248]. Given experimentally induced quadriceps pain [87] and knee pain relief [88,111,222] can alter gait mechanics and muscle activation characteristics, controlling for symptom severity is a potential approach to isolate the influence of structural impairments on muscle activation patterns during gait.

Structural joint impairments occur in the presence of knee OA, change in a progressive manner and have been a component of understanding knee OA severity. For

the purpose of this dissertation, structural severity will be used to define the general state of impaired knee joint characteristic of knee OA. Structural impairments considered pathognomonic with knee OA include articular cartilage lesions, joint margin and tibial spine osteophytosis, subchondral bone sclerosis, and bone attrition [5,105,125,195,224]. Articular cartilage lesions are thought to result in joint space narrowing and promote an unstable joint where alterations in muscle activation would be required to maintain stability [154]. In contrast, medial compartment osteophytosis may inherently reduce the requirement of muscle activation levels typical of asymptomatic knees by increasing the contribution of the passive osteoligamentous system to maintain knee joint stability. This latter association was discussed by Zeni *et al*., [284]. Structural impairments are asymmetrically distributed across the medial and lateral tibio-femoral condyles, where distinct medial and lateral knee joint muscle activations could result.

Structural severity has been detected and understood primarily through diagnostic imaging methods and arthroscopic procedures. While arthroscopic procedures [28,259] and magnetic resonance imaging (MRI) techniques [63,122,134] can be used to identify specific impairments, these methods are invasive, expensive and not routinely used to provide a score on structural severity associated with the OA knee.

There are many arthroscopic grading methods available to assess articular cartilage lesions [30,137,180,186]. The Outerbridge classification [186], originally designed to understand grade of chondromalacia patellae, is often used to grade articular cartilage degeneration associated with knee OA on a five-point ordinal scale [28,37,265]. While good to excellent reliability and agreement has been found for this scale [37], the Outerbridge classification and many other arthroscopy based grading measures are limited. These grading scales do not account for other structural impairments that may influence muscle activity, namely extra-capsular impairments (i.e. osteophytosis) associated with knee OA.

Magnetic resonance imaging is becoming increasingly popular for investigating the OA knee. The Osteoarthritis Research Society International OA imaging working group recently discussed the development of a definition of knee OA on MRI. These characteristics included articular cartilage loss, osteophytosis, bone attrition, meniscal pathology and subchondral bone marrow lesions [105]. MRI-based osteoarthritis knee scores are evolving including the MRI OA Knee Score (MOAKS) [106], MR Knee

Osteoarthritis Scoring System (KOSS) [136], Whole-organ MRI score (WORMS) [194] and the Boston Leeds OA knee score (BLOKS) [107]. These classifications divide the patella, femur and tibia in to regions of interest to which ordinal scores have been assigned to identify the level of impairment associated with for example, bone mineral lesions, articular cartilage loss, osteophytes, synovitis and effusion. This scoring provides a detailed assessment of specific structural impairments however, a single composite knee OA score has not been presented to provide an appreciation for the general state of knee OA structural impairment.

Radiographic scoring has been a major part of clinical investigation, study methodology and subject inclusion criteria and analysis. Joint space narrowing, both a linear measure [184] or an ordinal grade [4,224], as well as degree of bone attrition, using the Ahlbäck criteria [1,195] have been used to establish specific aspects of structural severity. As mentioned above, these scores do not reflect the general state of structural impairment associated with knee OA, including both articular cartilage loss and osteophytosis, elements of impaired joint structure that may alter muscle activation during gait.

Kellgren and Lawrence [125] first established a criterion for radiological assessment where key features were considered evidence of OA. These features are based on structural impairments to the knee joint evident on lateral and anterior-posterior radiograph views. Five grades were established, (0) none, (I) doubtful, (II) minimal, (III) moderate and (IV) severe depending on the extent of the following alterations.

1. Formation of osteophytes on the joint margins or tibial spines
2. Narrowing of the articular cartilage associated with sclerosis of the subchondral bone
3. Small pseudocystic areas with sclerotic walls situated usually in the subchondral bone
4. Altered shape of the bone ends particularly the head of the femur

The Kellgren-Lawrence ordinal radiographic scale [125], is the most widely used method of classifying radiographic disease and structural severity across many research

foci [31,65,218,286] and considered the standard for assessing radiographic knee OA severity by the World Health Organization. This scale however, is not without limitations.

There has been criticism in defining structural severity of OA using KL-scores alone. The inconsistent description of grade II alterations [218] and the reliance on osteophytosis preceding joint space narrowing remain problematic [46,240]. The chronological sequence of alterations to knee joint structure evident on the radiograph remains inconclusive and thus having a graded sequence of observations can lead to uncertain classifications, especially for early knee OA detection [84]. In addition, conflicting evidence exists to relate KL-score to articular cartilage damage evident during arthroscopic procedures. Wada *et al*., [259] found that KL-scores (I-IV) highly correlate with cartilage lesions in the medial compartment, in individuals with medial compartment OA. In contrast, Brandt *et al*., [28] found that compared to arthroscopic evidence of articular cartilage deficits in individuals with chronic knee pain, joint space narrowing scores and KL-scores did not provide a good assessment in patients with early knee OA.

It is well documented that radiographic procedures and joint positioning can significantly alter the perception of joint space narrowing [166,205], a component of the radiograph score thought to represent cartilage degeneration. This, in addition to not representing the other characteristics of impaired knee joint structure associated with knee OA, is a limitation of relying solely on joint space width as a measure of structural severity. It is less clear how these technical considerations would affect the KL-scoring that, in addition to joint space narrowing, relies on other signs of disease.

Despite these limitations, progressive impairments to joint structure must occur for the assignment of increasingly greater KL-scores, making this metric sensitive to gross structural impairments [125]. It was estimated, from previously published reports that the risk of a 1 KL grade progression was under 6% per year [65]. While the KL-score identifies structural impairment, these impairments are gross and take a long time to become evident and progress. Smaller increments of progression maybe occurring (i.e. joint space narrowing > 0.5mm) [184] that the KL-score cannot account for, providing the basis for the argument that other metrics are more sensitive to capture progression of structural impairment.

Few studies have examined the relationship between knee joint mechanics or muscle activation during functional tasks with respect to levels of structural impairment associated with knee OA. Only one study, Astephen *et al*., [13], assessed whether gait biomechanics and knee joint muscle activation patterns, determined using PCA, explain significant variability in pain, assessed using the Western Ontario Osteoarthritis Index (WOMAC) and radiographic severity assessed using a proprietary visual analog radiographic scale in a group of individuals with moderate knee OA (KL I - IV). A moderate relationship between this scale and KL grade existed (r=0.64) however authors found that knee joint muscle activation patterns did not explain a significant amount of variance in radiographic severity. The WOMAC pain score was however related to altered amplitudes of lateral gastrocnemius and medial hamstrings. While the visual analog scale provided a continuum of structural severity, it was difficult to ascertain the specific components of structural impairment associated with differing levels of radiographic severity. Approximately 60% of the variance in KL-score was not accounted for by the visual analog score. In addition, whether level of medial compartment structural impairment knee OA progressed along this scale was difficult to determine. The multidimensional model used and the small sample size potentially explains this lack of relationship found.

As previously stated, medial joint articular cartilage loss and osteophytosis are structural impairments thought to alter knee joint muscle activation characteristics in individuals with knee OA. The Kellgren-Lawrence ordinal radiographic scale provides a metric to capture this level of impairment and provide a global score of knee OA structural severity. While self-reported activity limitations are more likely to occur with KL-score worsening [263], the known discordance between knee OA symptoms and impairments to knee joint structure [21,24,54,248] provides support for identifying a knee OA group, that have similar knee OA symptoms and activity limitations, yet a wide spectrum of structural impairments. Understanding the impact of structural impairments on knee joint muscle activation patterns in individuals with moderate knee OA, a relatively homogeneous group pertaining to knee OA symptoms, provided the impetus for objective two of this dissertation.

2.8 KNEE JOINT EFFUSION

In addition to structural impairments, knee joint effusions have been known to occur because of arthritis [66,120,169], meniscal [209] and ligament injuries [206]. While not found in everyone with knee OA, knee effusions have been found in a number of individuals (30-81%) [49,139,169] and have been associated with increased knee OA progression [17,49]. Given this prevalence and our understanding of the effects of effusion on muscle activation in static experimental testing, examining whether effusions alter muscle activation characteristics and knee joint mechanics during gait can assist to understand knee OA development and progression.

Most of what is known about the effect of knee joint effusion on muscle activation is based on experimental investigations of the quadriceps muscles [6,97,187,241,245]. Static, experimental acute effusion models have shown that the quadriceps force generating capacity was consistently reduced and occurred independent of pain. This reduction has been attributed primarily to a neurophysiological inhibition mechanism [97,187,241]. Acute effusion effects on the hamstrings and gastrocnemii have not been studied.

Static experimental studies have found that acute knee effusions reduced the Hoffmann (H-reflex) response amplitude, supporting an inhibition of the quadriceps alpha motor neurons [97,188,241] occurred. The H-reflex is characterized by the projection of 1a afferents onto homonymous motor neurons, an electrical analog to the patellar tendon tap reflex of the quadriceps [172]. A reduction in the amplitude of this reflex is thought to indicate an increased level of inhibition [172]. An inhibitory signal can come from many of the knee joint mechanoreceptors including the pacinian corpuscles, golgi joint receptors and ruffini endings in response to joint distension [239]. While pacinian corpuscles can be involved in the immediate response to joint distension, H-reflex amplitude reductions have been shown to persist after initial effusion despite a reduction in intra-articular pressure, leading authors to believe that slowly adapting ruffini endings were also involved to impair the quadriceps [97,241]. These findings support the possible role of distension sensitive mechanoreceptors in the subsequent inhibitory influence on quadriceps activation during voluntary contractions in the presence of an acute effusion.

The effect of effusions, characteristic of arthritis, on quadriceps inhibition during static testing was more variable, with evidence that both supported and refuted that inhibition was associated with effusion [66,120,170]. Jones *et al*., [120] found that inhibition in individuals with various types of arthritis, assessed using the interpolated twitch technique, was greater when knee extensor strength was tested in a position of knee extension compared to mid-range (90^{o}) however; no obvious relationship was found between amount of inhibition and size of effusion, pain experienced during contraction or muscle strength. In addition, aspiration did not alter the inhibitory effect [120]. These findings corroborate those of Merry *et al*., [170] supporting that non-acute effusions do not consistently have the inhibitory influence on voluntary quadriceps contraction that acute effusions do. Furthermore, the central activation ratios of individuals with knee OA, calculated using the knee extensor force generated during burst superimposition testing were shown to be within 10% of asymptomatic individuals [72,155,174,212]. While knee effusion effects have not been specifically tested, effusion could have been present and yet, a significant activation ratio reduction was not found.

The quadriceps have been the focus of many studies, so less is known if or how effusion affects hamstrings and gastrocnemii, both of which cross the knee joint. The neurophysiological mechanisms of non-acute effusions and their role to alter the musculature have not been as extensively studied when compared to acute effusions. In the presence of non-acute effusions, joint capsule mechanoreceptors can become habituated and insensitive to alterations in distension, given that the joint pressure-volume relationship varies with time [152] supporting the work of Jones *et al*., [120] and Merry *et al*., [170]. Together, these findings suggest that there are limitations in using an acute, experimentally controlled effusion model to understand the effects of non-acute, effusions in individuals with knee OA.

With respect to the effect of effusion on biomechanical and muscle activation patterns during a fundamental task, only one study was found that studied walking. Torry *et al*., [251] found that gait mechanics and muscle activity were altered with an acute knee effusion model in healthy individuals, and alterations were progressive with the amount of fluid injected. During the first half of the stance phase, average quadriceps activation was reduced and average hamstrings activation increased when an intra-articular saline

injection greater than 50cc was administered to the knee joint of otherwise healthy individuals. An associated reduction in knee flexion range of motion and extensor moments were found, leading authors to conclude that effusion caused a quadriceps-avoidance gait pattern. It was unclear whether knee effusion was the only difference between the gait trials as walking velocity was not reported and could influence muscle activity and gait biomechanics as previously discussed. This study did show an association among effusion, joint mechanics and muscle activation and provides evidence, in combination with experimental studies, that knee joint effusions can alter knee joint mechanics and muscle activation during gait.

Cho *et al*., [45] found that joint effusion impairs knee joint proprioceptive function in individuals with knee OA. Greater non-weightbearing, compared to weightbearing proprioceptive deficits were found [45]. Thus, effusion can impair the body's ability to sense and respond to mechanics associated with swing phase to heel strike transitions. Furthermore, Simkin *et al*., [234] provided a theoretical rational, based on available evidence, to support that effusions reduce the stabilizing features of sub-atmospheric intra-articular pressure in synovial joints. This may also influence proprioception and explain findings of Cho *et al*., [45]. In combination, these effects would increase the requirement of the neuromuscular system, particularly the quadriceps, to maintain knee stability. What remains to be determined however is whether effusion is associated with altered knee joint mechanics and muscle activation patterns in individuals with knee OA.

Knee effusions have been reported in over half of the individuals treated for knee OA [49,139,169]. Given this, the assessment of knee joint effusion has been considered part of an overall knee OA assessment [47]. Various methods exist to detect effusion and quantify fluid volume. Studies attempting to understand the effect of effusion on knee joint function have focused primarily on acute effusion models where known amounts of fluid are injected into the joint capsule [45,188,251]. In addition, aspiration studies have been conducted on individuals with pre-existing effusion to determine the effect of removing fluid on quadriceps function [66,120]. Various imaging modalities, including magnetic resonance imaging [169,209,223] and ultrasonography [49,113,149] have also been utilized to quantify the presence and amount of knee joint effusion. Specific resolutions and reliability measures have been reported, particularly for ultrasonography [56].

Less sophisticated tests have also been developed. Sturgill *et al*., [243], found the stroke test, also called the Bulge test/sign [47,162] was a reliable method of assessing grade of knee joint effusion with substantial agreement found between raters (Cohen Kappa = 0.61). Only one of 75 sets of ratings different for identifying effusion/no effusion. These findings were corroborated by Cibere *et al*., [47] who also found the bulge sign for identifying effusion/no effusion was reliable (R_c= 0.97) in individuals with knee OA. Furthermore, Hauzeur *et al*., [85] found moderate agreement between a clinical evaluation, which included the bulge sign, and ultrasonography for assessing knee effusion/no effusion. For detecting the amount of effusion, whether on a three [85], four [47] of five [243] point scale, the accuracy and reliability were diminished when compared to a dichotomous grading of effusion/no effusion. Despite this support, false negative tests can occur. Individuals classified as not having effusion may have a small or conversely a very large effusion not detectable using the bulge sign. Together these studies support the use of clinical testing through the bulge sign as a reliable and valid method for identifying knee effusion in individuals with knee OA.

In summary, acute effusion models have demonstrated reduced muscle activation and force generating capabilities of the quadriceps with increased amounts of effusion in healthy individuals. Evidence suggests that non-acute effusions, such as those found in individuals with knee OA do not have consistent reductions. Only one study has examined the role of knee effusion to alter gait mechanics and muscle activation in healthy individuals using an acute effusion model but many factors preclude generalizing the results to individuals with knee OA. Knee effusion can create an environment that increases knee OA progression [17,49] and muscle inhibition has been discussed as a factor in the knee OA process [90,109,245,280]. Hence, the question of whether effusion is associated with altered knee joint mechanics and muscle activation patterns during gait in individuals with moderate knee OA became the third objective of this dissertation.

2.9 Amplitude Normalization Procedures

To compare knee joint muscle activation levels between different muscles, individuals, studies and across time, electromyogram amplitude normalization is required

[34]. Consistent with the literature on asymptomatic individuals, various methods have been utilized to normalize the electromyogram during gait in individuals with knee OA. These include waveform measures (peak or mean) [124,157,220,221] and both maximum voluntary isometric [16,44,100,102,103,154,156,202,203,212,214,284] and isokinetic contraction methods [98,161].

Normalization techniques based on waveform characteristics (peak or mean) have been typically employed to reduce intersubject variability [34,35,277] when compared to un-normalized data given the volume conducting properties of the electrode-muscle interface can influence peak to peak amplitudes [73] and can vary widely from subject to subject. A waveform derived normalization measure reflects the muscle activity patterns within a trial however; this technique could not be used to compare amplitude measures between trials, individuals or groups because of the constantly changing denominator [35]. Unfortunately, this method has been used for this purpose in individuals with knee OA [124,157,220,221] making gait electromyogram interpretation difficult in these studies.

In contrast, normalizations through maximal isometric voluntary contraction (MVIC) amplitudes are designed to reveal how active muscles are compared to a maximum state [34]. In a recent detailed review of the literature, Burden *et al*., [34] endorsed the MVIC as an amplitude normalization reference value. Knutson [131] concluded that by virtue of an unchanged physiologically relevant denominator, maximal voluntary contraction normalization is the only method that has the potential to reveal how active a muscle is during gait. The MVIC is the most common normalization technique to investigate muscle activation characteristics of individuals with knee OA and allows amplitude comparisons to be made between muscles and groups of individuals.

Currently, a standard does not exist for MVIC procedures and generally, normalization exercises/protocols are not well described in the literature. During MVIC normalization exercises, individuals are instructed to produce a maximum voluntarily effort during an isometric contraction for a given muscle group [238]. In knee OA studies, the quadriceps, hamstrings and gastrocnemii normalization exercises largely encompass an open kinetic chain mode [16,44,100,102,103,214,284] with the exception of standing plantar flexion [102]. Many studies have not reported exercise specifics [154,156,202,203,212] or they employed a single standard exercise for each muscle grouping [44,284]. This normalization protocol variation needs to be considered when interpreting amplitude measures or when

comparing these measures across studies [215]. While each protocol generates a maximal level of activation, exercise selection can considerably affect this level (Appendix A.1) and subsequent gait electromyogram amplitudes (Appendix A.2). This has implications for asking questions related to muscle activity levels required during gait.

Hubley-Kozey *et al*., [102] originally described a sequence of exercises for normalization purposes. In a recent publication [215] (summarized in Appendix A.1), we determined that one exercise per muscle group would not be sufficient to ensure maximal levels of activation, supporting the value of using a standard exercise series for normalization purposes. Individuals with knee OA and asymptomatic individuals obtained maximum values from similar exercises. These data support the use of an exercise series to determine maximal amplitude levels for normalization.

While limitations exist for using MVIC normalization methods in individuals with knee OA, amplitude based waveform features are comparable across studies [103,154,202]. Studies have found that with standardized verbal encouragement to produce a maximum effort, individuals with moderate knee OA were able to volitionally generate 93% of the force generated during burst superimposition testing as calculated by the central activation ratio [72,155,212]. Electrical stimulation testing procedures have their limitations [246,247] however, in general, individuals with various severities of knee OA have been within 10% of the volitional force generating capacity of asymptomatic individuals. At present, the MVIC amplitude normalization this is the only method that allows group and muscle comparisons to be made based on amplitude measures of the electromyogram.

2.10 General Summary

Osteoarthritis is a chronic, progressive disease that has worldwide prevalence. For decades, the knee has been recognized as the most common lower extremity joint affected with knee OA; a disease associated with significant ambulatory disability. The International Classification of Function framework provides the basis for understanding functioning and disability in individuals with knee OA for this dissertation. Central to this dissertation is developing an understanding of the reciprocal relationship between joint

impairments, characteristic of the knee OA process, and activity limitations, in this case walking.

Stability is required of the knee joint to match the instantaneously varying mechanical demands due to changes in posture and static and dynamic loads during gait. Osteoligamentous structures (passive) are compromised with knee OA in a progressive manner and proprioception deficits (neural) have been found in many individuals with knee OA. Thus, the potential exists for an increased reliance on the neuromuscular system to maintain knee joint stability and produce appropriate motions during gait.

An understanding of how muscle activation patterns are altered during walking is emerging but what factors contribute to these alterations is not well understood. Altered muscle forces can create an improved mechanical environment, but can also have implications for increasing joint loading and metabolic demand during gait. Structural impairments form the basis for understanding knee OA progression yet how these impairments specifically relate to muscle activation patterns during gait is yet to be established. Impairments in knee joint physiological function, resulting in knee joint effusions have not been considered in studying knee OA gait. Effusion is involved in knee OA progression, making this knowledge significant for understanding muscle activation patterns during gait and their association to knee OA progression.

The aim of this dissertation is to improve our understanding of how muscle activation patterns during gait are altered across the knee OA severity spectrum and to examine how factors related to the OA process are associated with these alterations. The focus is on walking velocity, structural severity and knee joint effusion. The goal of this research is to contribute to the development of gait-based metrics that can facilitate knee OA diagnosis and monitor knee OA progression.

CHAPTER 3

GENERAL METHODOLOGY

3.1 General Methodology

The dissertation objectives focused on understanding factors that affect muscle activation patterns during walking in individuals with primary medial compartment knee OA of varying severities. The general dissertation methodologies are described in the following sections. Section 3.1 outlines the methodological considerations and details of the research, including the participant selection, collection and processing of kinematic, kinetic and electromyographic data. Section 3.2 describes specific methods pertaining to determining the KL-score and effusion. Section 3.3 provides gait waveform analysis procedure details. Gait data collection procedures have been completed using standardized protocols and state of the art motion, force and electromyogram analysis equipment located in the Dynamics of Human Movement Laboratory, Dalhousie University, Halifax, Nova Scotia, Canada.

3.1.1 Participant Recruitment

Asymptomatic participants for objectives one and two were recruited from the general community using email, website and poster board advertisements from 2003 to 2007. These individuals reported no lower extremity injuries within six months prior to data collection and no symptoms of lower extremity degenerative joint disease including morning stiffness, knee pain; and no prior knee surgery or fracture. Participants with knee OA were recruited from local orthopaedic clinics between 2003 to 2010. Knee OA was identified using i) American College of Rheumatology guidelines [3] and 2) evidence of knee OA through diagnostic imaging. For this dissertation, Kellgren Lawrence scores for radiographic evidence of knee OA [125] were assigned to all individuals, with the exception of four participants those radiographs were either not available or a magnetic resonance image of the knee was investigated. Individuals with lateral compartment joint space narrowing greater than medial compartment joint space narrowing[224] were not included in this dissertation. For all three objectives, participants with moderate knee OA were required to meet a functional status consistent with a moderate OA classification [102] based on self-report, including the ability to i) reciprocally ascend and descend 10 stairs, ii) safely walk one city block, and iii) jog five meters and were not scheduled for total

knee arthroplasty at the time of testing. For objective one only, participants with severe knee OA had radiographic evidence of medial compartment disease and were receiving a total knee replacement within one-week after testing. This classification method has been previously utilized to define severe knee OA [16,103]. In addition to the above criteria, participants were required to be 35 years of age or older, have no cardiovascular/respiratory disease or neurological disorders that would affect their ability to safely complete the data collection protocol (i.e. stroke, Parkinson's disease, myocardial infarct, arrhythmias), and not sustain a fracture or injury other than a sprain or strain (within one year). Individuals were excluded if they had sustained an anterior cruciate ligament injury. Written informed consent to participate was attained. All procedures were approved by the local institutional ethics review boards (Dalhousie University Health Sciences Research Ethics Board and Capital Health Research Ethics Board).

3.1.2 General Data Collection Procedures

The Western Ontario McMaster Osteoarthritis Index (WOMAC-LK3.1) was completed by all participants upon arrival to the lab. Height, mass and lower limb anthropometrics (thigh and shank circumference and foot width) were also recorded. For individuals with knee OA, the most affected lower extremity was tested. For asymptomatic individuals, the tested lower extremity was randomly assigned. All participants wore a loose fitting tee shirt, tight-fitting (Spandex® / Lyra®) shorts, low ankle socks and their self-selected footwear for gait data collection. Participants were introduced to the laboratory environment, equipment and general procedures prior to testing.

Walking trials were completed across a six-meter walkway in which all individuals were asked to walk at their self-selected pace. Familiarization time was given prior to data collection. During the walking trials, muscle activity was monitored in real-time by a clinician and engineer for artifact and proper signal acquisition. Photoelectric timers, positioned at known distances on the walkway, monitored walking velocity during the data collection. Walking trials were repeated if artifact was apparent or walking velocity varied greater than 10% of familiarization trials. Following the walking

trials, motion and ground reaction force data were visually inspected for errors in collection (i.e. missing marker data, double foot strike on force plate etc.) and heel strike detections were preformed. If required, walking trials were repeated to ensure at least five trials were available for processing. For the majority of participants, five trials were used in the analysis however four and three trials were averaged for the analysis in 7/150 and 1/150 participants respectively.

3.1.3 Motion Data Acquisition and Processing

Triangular sets (triads) of active Infrared Emitting Diode (IRED) skin surface markers were secured to the sacrum, thigh, lower leg and foot of the participant's most affected lower extremity or a randomly assigned lower extremity in the case of asymptomatic individuals. This marker cluster and the motion capture procedures have been previously described [144,168,213]. Individual IRED markers were placed on the greater trochanter, lateral epicondyle, lateral malleolus, and shoulder while eight virtual points were digitized on predefined anatomical landmarks. Virtual points included the right and left anterior superior iliac spine, medial epicondyle of the femur, fibular head, tibial tuberosity, medial malleolus, second metatarsal and middle posterior calcaneous as shown in Figure 3.1. Virtual points were required to complete the joint axis definitions and considered invariant. These points could not be directly captured using the camera system currently employed in the lab and are subsequently measured relative to the rigid body coordinate systems derived from the laterally positioned IRED markers captured during gait. All skin surface markers were affixed with adhesive tape. Two optoelectronic motion analysis sensors (Optotrak™, Northern Digital Inc., Waterloo, ON, Canada), calibrated and standardized to laboratory position and orientation, were employed to monitor marker movement at a frame rate of 100Hz during the one-second standing calibration trial and the walking trials. After completing the walking trials, all Optotrak IRED markers were removed.

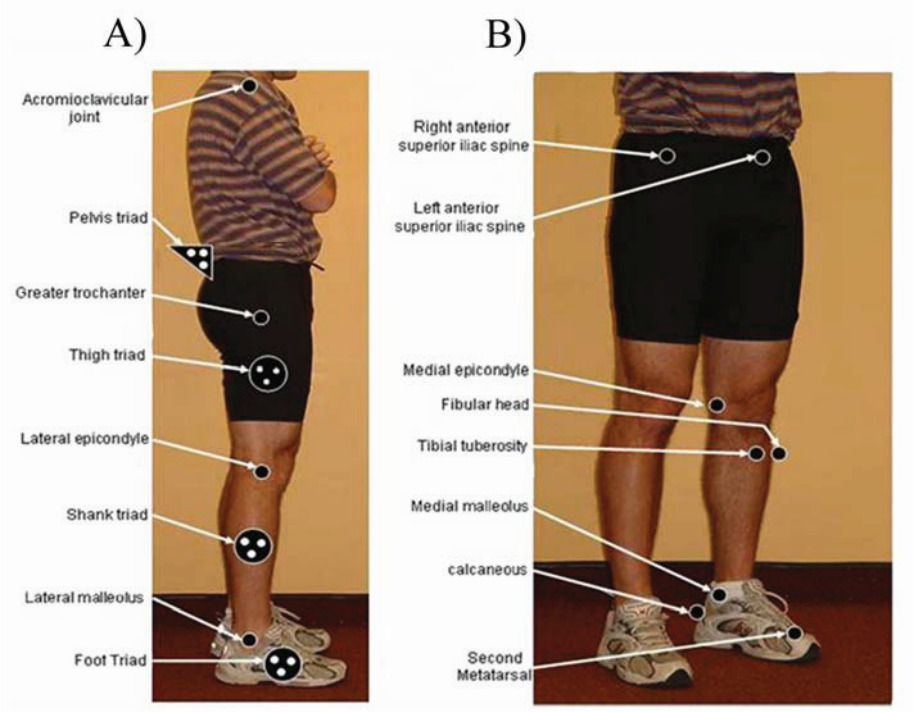

Figure 3.1: IRED marker placements attached to the skin (A) and virtual points (B) utilized during motion capture.

Three-dimensional motion capture utilized a Cartesian coordinate system [79,255,282] and is considered a standard in reporting kinematic data as recommended by the International Society of Biomechanics (ISB) [275,276]. This right-handed coordinate system was derived on each rigid body segment by the use of IRED marker clusters located on the skin and virtual points [39] (Figure 3.1 and 3.2). All lower extremity motion data was low-pass filtered (Butterworth 4th order recursive) at 8Hz and processed using custom programs, written in MatLab™ version 7.1 (The Mathworks Inc., Natick, Massachusetts, USA) that have been used in the Dynamics of Human Movement Laboratory, Dalhousie University [15,144]. The position and orientation of each rigid segment was described relative to a reference pose. For instance, the anatomical coordinate system of the tibia [T tibia] was described with reference to the femoral anatomical coordinate system [T femur]. A schematic of this is shown on Figure 3.2. The resultant 4x4 pose matrix that describes the position and orientation of the tibial anatomical coordinate system with respect to the femoral coordinate system was utilized to calculate three-dimensional joint angles using currently accepted Euler angle principles [79,282]. A flexion/extension – adduction/abduction – internal/external rotation sequence was utilized, where flexion,

adduction, and internal rotations were derived as a positive angle. For this dissertation, sagittal plane knee joint angles were utilized for the analysis of objective two and three.

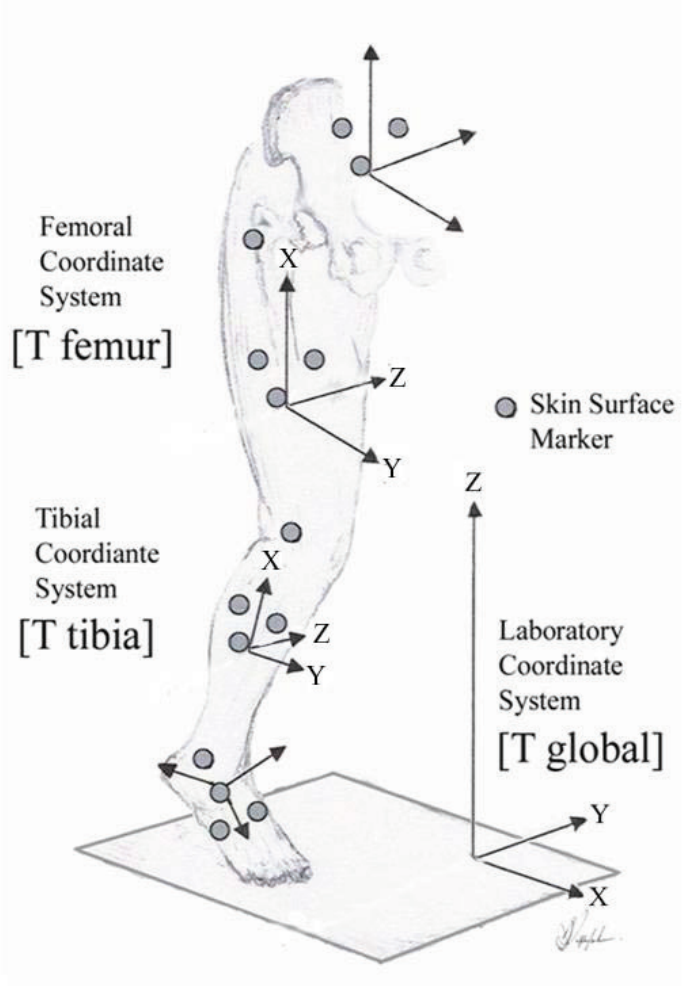

Figure 3.2: The coordinate system derived from the marker clusters on each rigid body in the lower extremity. The technical femoral, tibial and global coordinate systems are further illustrated.

3.1.4 Gait Kinetics Data Acquisition and Processing

Three-dimensional ground reaction forces and moments were collected using a single AMTI™ force plate (Advanced Mechanical Technology Incorporation, Newton, MA, USA) embedded in the laboratory walkway and aligned with the global coordinates of the motion capture system. Force plate signals were sampled at 1000Hz or 2000Hz[#]

[#] The sampling rate was changed in September 2008.

using the analogue data capture feature of the Optotrak system. Raw force and moment data were low pass filtered (Butterworth 4th order recursive) at 60Hz and processed using pre-programmed software, written in MatLab™ version 7.1 (The Mathworks Inc., Natick, Massachusetts, USA). Ground reaction forces were used in conjunction with segment linear and angular accelerations, subject anthropometrics and inertial properties for the evaluation of Newton-Euler equations ($\sum$F=mass (kg) * linear acceleration (m/s^2) and $\sum$M= Moment of Inertia (I) (kgm^2) * angular acceleration (α) (rads/s^2)), to derive moments of force about the knee joint center [255] (Figure 3.3).

The calculations began at the foot segment where five sets of information were required to complete the three dimensional moment calculations; 1) ground reaction forces and moments, 2) center of pressure 3) ankle joint center of rotation (defined, as mid-way between the medial and lateral malleoli), 4) segment anthropometry and 5) segment velocities and accelerations obtained from differentiating, using a finite differences method, the segments kinematic displacements [255,269]. To calculate net knee joint moments of force, ankle joint reaction forces and moments (equal in magnitude and opposite in direction – Newton's Third Law), the ankle joint center, knee joint center (defined, as mid-way between the medial and lateral malleoli), segment anthropometry, segment velocities and accelerations were required. Three dimensional net knee joint moments of force were calculated in the laboratory frame of reference and projected in to a non-orthogonal joint coordinate system where by the flexion/extension axis was embedded in the femur (sagittal plane), the internal/external rotation axis was embedded in the tibia (transverse plane) and the adduction/abduction axis was considered a floating axis (frontal plane), a mutual perpendicular to the flexion/extension and internal/external rotation axes [79].

A free body diagram illustrating the transfer of joint reaction forces and muscle moments through the lower kinetic chain is shown in Figure 3.3(A). Figure 3.3 (B) provides the required parameters for completing the Newton-Euler equations for the shank segment in three dimensions. Net muscle moments of force were multiplied by negative one, to present net external moments of force [14,58,144,159,164,168]. Amplitudes were normalized to body mass to standardize the known effect of mass on the net external sagittal plane moments. The direction conventions of these resultant normalized net

moments were equivalent to those shown for the kinematics of the lower extremity. For this dissertation, sagittal plane knee moments of force were utilized for the analysis of objective three.

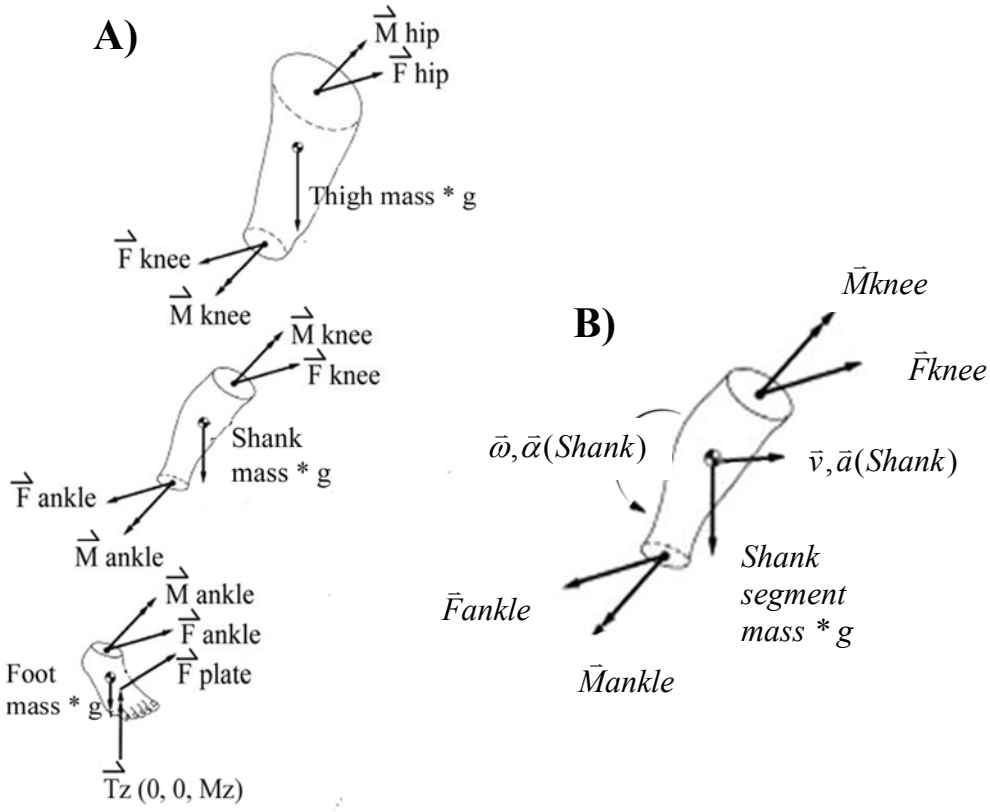

Figure 3.3: A) A general free body diagram showing the external moments ($\vec{M}$) and forces ($\vec{F}$) calculated through linked segment modeling of the lower extremity during gait. B) A representative shank segment illustrated with the required parameters for the inverse dynamics calculations (Subject anthropometrics not illustrated (segment centers of mass and moments of inertia (I)). In A), $\vec{T}$ z = moment of force applied to the foot about the vertical axis (Free moment), $\vec{F}$ plate = the resultant force on the plate and g = acceleration of gravity. In B), g = acceleration of gravity, $\vec{\omega}$ = angular velocity, $\vec{\alpha}$ = angular acceleration, $\vec{v}$ =linear velocity, $\vec{a}$ = linear acceleration. All vectors include x, y and z, components. Adopted from Vaughan [255].

3.1.5 Electromyography Data Acquisition and Processing

An AMT-8 (Bortec, Inc., Calgary, Alberta, Canada) eight channel EMG measurement system (Input Impedance: ~10GΩ, CMRR: 115dB at 60 Hz, Band-pass (10-1000Hz)) was utilized to amplify surface EMG recordings. A standardized protocol

for instrumentation set up and electromyographic data collection procedures was employed and consistent with accepted guidelines as suggested by the International Society of Electrophysiology and Kinesiology (ISEK) and SENIAM (Surface EMG for the Non-Invasive Assessment of Muscles) [226].

Electrodes were placed over the knee joint musculature and included lateral and medial gastrocnemius, vastus lateralis and medialis, rectus femoris, biceps femoris and semitendinosus/membranosus. Preparation procedures included,

- Medial and lateral tibio-femoral joint line identification.
- The location of standardized electrode placements with non-indelible ink (Table 3.1, Figure 3.4).
- Shaving the skin of the selected electrode location, abrading with alcohol-water solution and applying the electrodes parallel to the underlying muscle fibers in accordance to standardized guidelines (Table 3.1, Figure 3.4). These procedures are required to reduce skin impedance to less than one percent of amplifier input impedance [268] and maximize the capture of directional propagation of electrical activity in the corresponding muscle.
- Bipolar skin surface electrodes were affixed to the corresponding muscle sites (Figure 3.4) (Ag/AgCl, 10 mm diameter, 0.79cm2 surface area, 20-30mm interelectrode distance).
- Lead wires with pre amplification (500x) were connected to the electrode pairs of each muscle and a single ground was affixed to the anterior tibia shaft.
- Manual muscle testing was performed to validate electrode position, the EMG signal and assess crosstalk potential as suggested by Winter [270]. Throughout the manual muscle testing, amplifier gains (500-5000x) were set for each channel separately to maximize the signal amplitude but to avoid signal saturation (+/- 2V).
- Manual muscle testing included,
  - Unilateral heel rise for gastrocnemii activation.
  - Isometric knee extension and mini squat for quadriceps activation.
  - Isometric knee flexion at ~60^{o} for hamstrings activation.

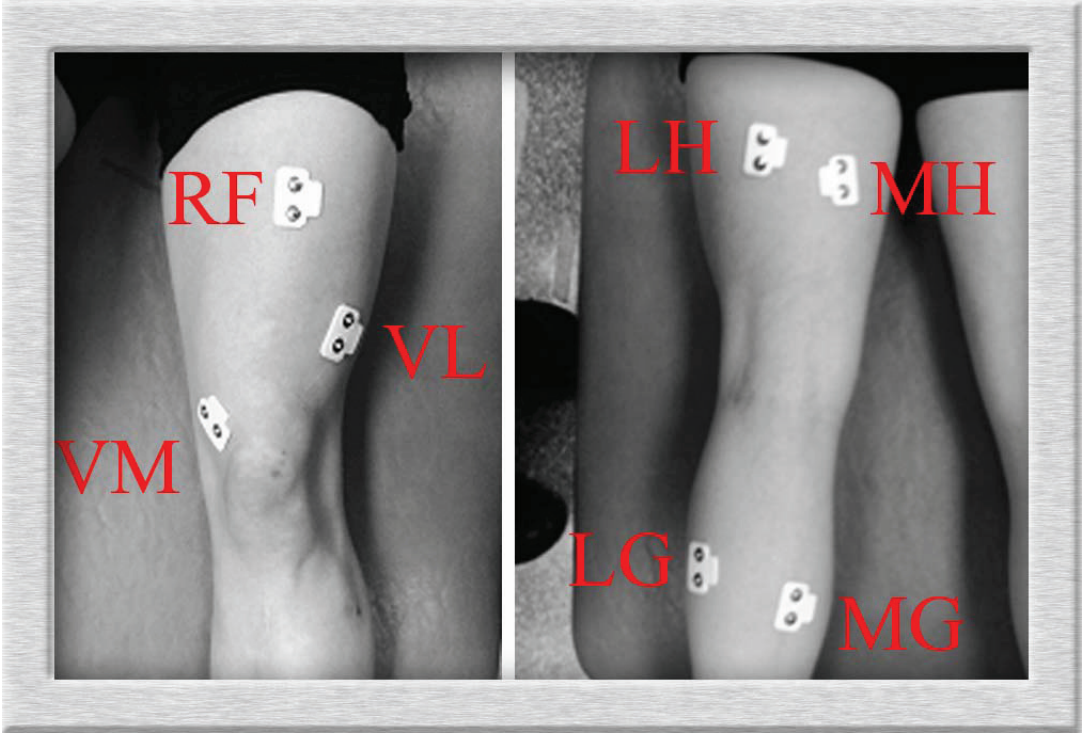

Figure 3.4: Electrode site location and orientation for lower extremity sites. References: Leveau [151], Hubley-Kozey and Smits [104], SENIAM [226].

Following the walking trials, participants completed a subject bias (resting EMG) recording in a supported supine position. A series of eight exercises were then completed to generate a maximal voluntary isometric contraction. Seven exercises were performed using a Cybex II™ Isokinetic dynamometer (Lumex, NY, USA) (Appendix A.1). This exercise series has been previously utilized for amplitude normalization purposes [102,214]. For the Cybex trials, subjects were securely fastened to the dynamometer chair and the dynamometer and joint axis of rotation were aligned. The dynamometer shin pad was located at the distal tibia at a known distance. This allowed for the standardized determination of torque (muscle strength) during each exercise (Section 3.1.6). Following at least one practice and warm-up contraction, two, three-second maximal isometric contractions were completed for each exercise. A 60-second rest period separated each contraction, and strong, standardized verbal encouragement/feedback was given to ensure consistent maximal effort [155]. Gravity correction trials were recorded in each position

(Section 3.1.6). All signals were sampled at either 1000Hz or 2000Hz[#] using the analogue data capture feature of the Optotrak system (16bit, +/- 2V). Data were stored for offline processing.

Table 3.1: Outline of muscle site, location and orientation utilized for the standardized placement of surface electrodes on the lower extremity. References: Leveau [151], Hubley-Kozey and Smits [104], SENIAM [226].

Muscle Site	Location	Orientation
Lateral Gastrocnemius (LG)	30% distance from lateral knee joint line to the tubercle of the calcaneous (Ankle in Neutral Position)	Along lead line
Medial Gastrocnemuis (MG)	35% distance from medial knee joint line to the tubercle of the calcaneous (Ankle in Neutral Position)	Along lead line
Vastus Lateralis (VL)	25% distance from the lateral joint line of the knee to the ASIS	45 degrees medial and inferiorly to lead line
Vastus Medialis (VM)	20% distance from the medial joint line of the knee to the ASIS	45 degrees lateral and inferiorly to lead line
Rectus Femoris (RF)	50% distance ASIS to superior border of patella	Along lead line
Bicep Femoris (LH)	50% distance from the ischial tuberosity to fibular head	Along lead line
Semitendinosus / Semimembranosis (MH)	50% distance from the ischial tuberosity to the medial joint line of the knee	Along lead line

[#] The sampling rate was changed in September 2008. Refer to Appendix C for details pertaining to sampling rate differences and EMG analysis

A visual depiction of the MVIC exercises can be found in Appendix A.1 and include,

1. Knee extension from sitting (knee position - 45 degrees flexion).
2. Knee extension/hip flexion from sitting (knee position - 45 degrees flexion).
3. Knee flexion from sitting (knee position - 55 degrees flexion).
4. Knee extension from supine lying (knee position - 15 degrees flexion).
5. Knee flexion from supine lying (knee position - 15 degrees flexion).
6. Ankle plantar flexion from long sitting (ankle position - zero degrees).
7. Knee flexion from prone lying (knee position - 55 degrees flexion).
8. Standing unilateral heel raise

Electromyographic data were processed through a custom program, written in MatLab™ version 7.1 (The Mathworks Inc., Natick, Massachusetts, USA). All signals were visually checked for artifacts in real time using an oscilloscope during data collection. Trials that contained movement artifact, dynamic range saturation or notable 60Hz signal were repeated. Off line, all signals were further checked for artifact and if 60Hz noise was found in the signal, removal using a digital, inverse Fast Fournier Transformation algorithm was completed. Fast Fournier Transformations were completed on random signals/subjects to verify the power spectrum [76]. Raw signals were corrected for bias (subtracting the subject bias) and converted to micro-volts (dividing by the actual signal gain), full wave rectified and low pass filtered (Butterworth Fc=6Hz, 4th order low-pass filter) [102,214]. A 100ms moving-average window algorithm (99ms overlap) was employed to identify the maximal amplitude for each muscle across all eight MVIC exercises [102,214]. Gait waveforms were amplitude normalized to the absolute maximal amplitude for each muscle regardless of MVIC exercise in which it was obtained. See Figure 3.5 for a schematic of the processing framework. Excellent within day reliability for asymptomatic participants has been reported [178] as well as excellent between day reliability for knee joint muscle activation patterns for 18 participants with moderate knee OA using this protocol, processing and analysis methodology [101]. For the latter, all but two ICC values were less than 0.80, with many above 0.90.

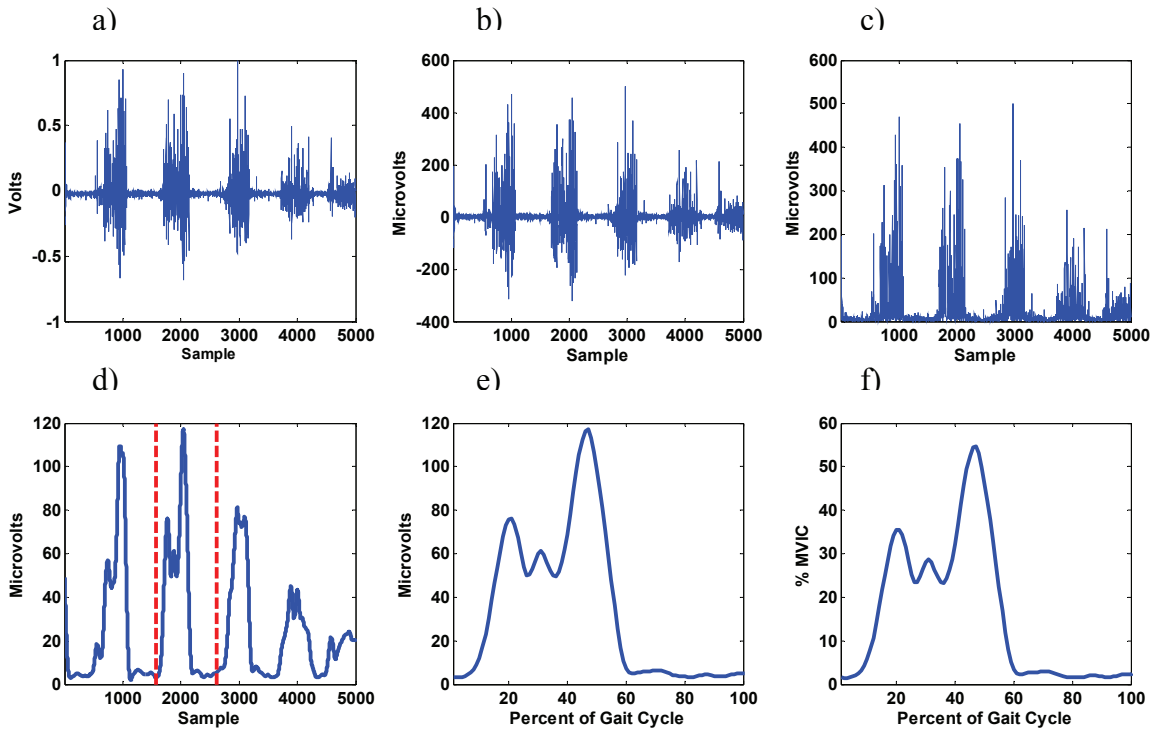

Figure 3.5: Example medial gastrocnemius electromyogram processing. a) Uncorrected Raw EMG signal b) Corrected Raw EMG signal c) Full wave rectified EMG signal d) Low pass filtered EMG signal with first and second heel strike indicated e) Time normalized to complete gait cycle (Section 3.3) f) MVIC Normalized for a complete gait cycle (0-100%).

3.1.6 Isometric Muscle Strength Data Acquisition and Processing

Isometric lower extremity torque data obtained from the Cybex isokinetic dynamometer during six of the eight MVIC procedures was processed through a custom program, written in MatLab™ version 7.1 (The Mathworks Inc., Natick, Massachusetts, USA). Compared to isotonic and isokinetic strength measures, the isometric method was chosen to 1) complete EMG normalization procedures within the same collection, 2) standardize the protocol across many severities of knee OA and 3) minimize the potential for pain that can occur with movement. Two maximal effort contractions were completed in each of the six positions. Prior to each contraction, the Cybex was reset and for each position, a gravity correction trial was recorded. To process torque, first a calibration constant (Cal_cons) was determined [3.1]. The torque/voltage difference between a

known mass (18kg) at a known distance (Ma) with the lever of the Cybex parallel to the ground and the lever perpendicular to the ground with no mass was calculated.

Cal_cons (Nm/V) = (((known mass*9.8)*Ma +1)) / (known mass (V) - 0kg (V))) [3.1]

Raw voltage signals were converted to torque (Nm) and were corrected for the effect of gravity [3.2]. Gravity correct torques were additive when the torque produced by the subject was against gravity and removed from the torque when the subject produced torque assisted by gravity.

Torque (Nm) = ((Trial (V) - 0kg (V))*Cal_cons (Nm/V)) ± Gravity correct (Nm) [3.2]

A 500ms moving-average window algorithm (0ms overlap) was employed to capture the maximum torque generated over the three-second steady state contraction [102]. The average value between the two trials was recorded as the maximal torque for each of the exercises. Linearity and hysteresis have been tested for this instrument (Figure 3.6) by placing increasingly greater mass (in 4.5kg increments) on the Cybex lever at a known distance (Ma) with the lever of the Cybex parallel to the ground. This was followed by removing this mass in 4.5 kg increments. The largest residual was 2.6 Nm corresponding to the 4.5 kg mass. This gives an independent non-linearity (i.e. maximal deviation of points from the least squares fitted line) of approximately 2% of full scale and 18% of the reading. Hysteresis was minimized during testing by resetting the Cybex after each isometric contraction.

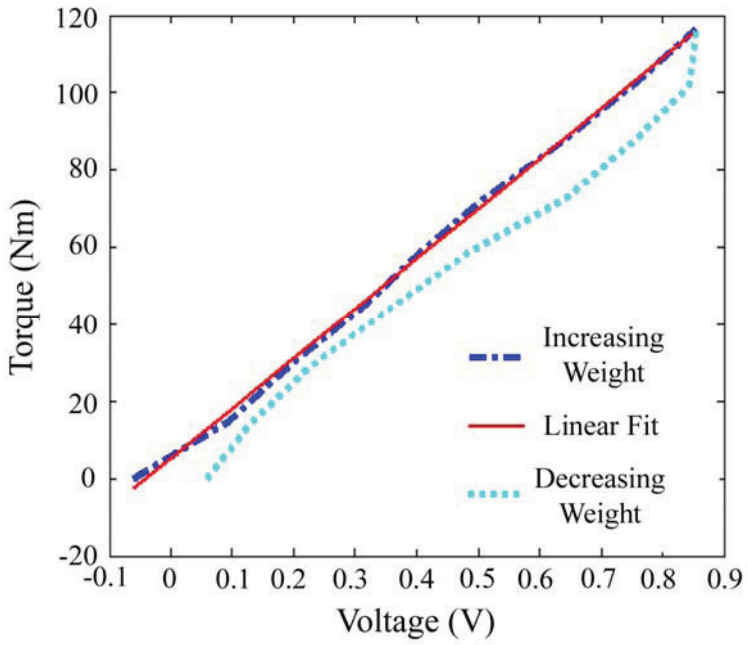

Figure 3.6: Association between voltage output of the Cybex™ Isokinetic Dynamometer and measured torque using known mass from 4.5kg to 36kg.

3.2 SPECIFIC METHODOLOGY

3.2.1 Radiographic Scoring of Knee Osteoarthritis

For objectives, one and three, radiographic scores were used for descriptive purposes. For objective two, they were utilized to sub-group individuals with moderate knee OA in to categories of structural severity. Standard weight-bearing anterior-posterior and lateral radiographs were acquired within one year of gait analysis for each participant included in this dissertation (with the exception of four individuals (Section 3.1.1)). All information that would identify the patient was removed. The Kellgren-Lawrence ordinal radiographic scale [125] (Table 3.2) was used to score each radiograph by a single experienced reader blinded to gait analysis outcomes (WDS) as recommended by Vigon *et al*., [258] . For the Kellgren Lawrence grading, fair to good reliability has been previously reported (ICC = 0.59) [168]. Comparing the reader who scored the radiographs in this dissertation, with another experienced reader, substantial reliability was found (Weighted Kappa statistic = 0.6).

For objective two, individuals with moderate knee OA were classified into sub-groups based on KL-score corresponding to KL II, KL III and KL IV and compared to an

asymptomatic cohort. This asymptomatic cohort did not have knee radiographs completed due to logistical reasons. It was thought that having asymptomatic individuals with KL II scores was minimal given i) the inclusion criteria for these subjects and ii) the prevalence of structural impairment characteristics of a KL II score is between 3-9% for the asymptomatic age group identified in this dissertation [148].

Table 3.2: Kellgren-Lawrence criteria utilized for scoring knee OA radiographs

Grade 0	• Normal
Grade I	• Doubtful narrowing of the joint space • Possible osteophytic lipping
Grade II	• Definite osteophytes • Possible narrowing of the joint space
Grade III	• Moderate multiple osteophytes • Definite narrowing of the joint space • Some sclerosis • Possible deformity of the bone contour
Grade IV	• Large osteophytes • Marked narrowing of joint space • Severe sclerosis • Definite deformity of bone contour

3.2.2 Knee Joint Effusion Detection

For objective three, a sub-group of individuals with moderate knee OA were recruited between 2007 and 2010 and assessed for the presence or absence of knee joint effusion. Figure 3.7 illustrates the clinical test for effusion presence that was employed for the current dissertation work. This test is described as the bulge, stroke or brush test by David Magee [162].

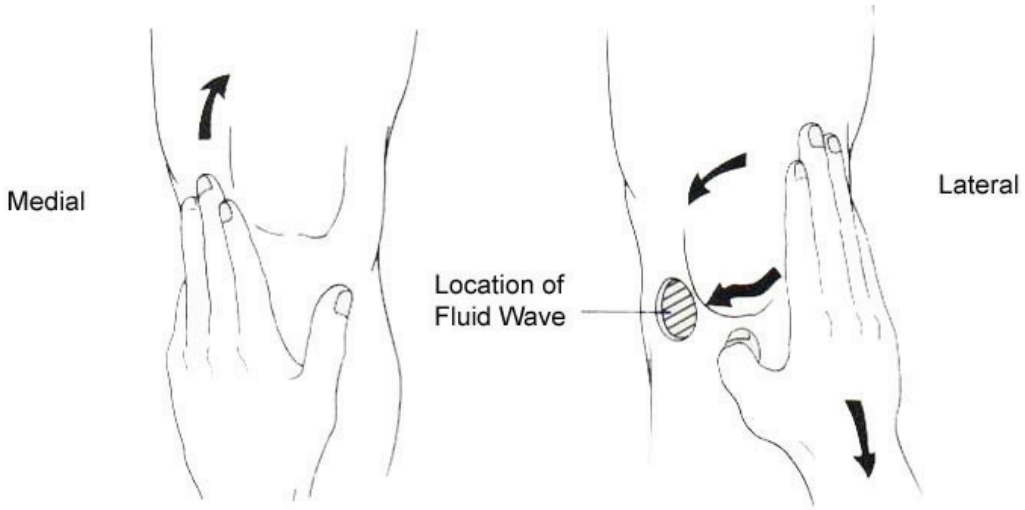

Figure 3.7: Brush test (Bulge sign) for knee effusion detection as described by Magee [162].

The examiner begins the brush/stroke just below the medial knee joint line on the medial side of the patella and moves proximally toward the thigh as far as the supra-patellar pouch at least three or four times. Using the opposite hand, the examiner immediately brushes down the lateral side of the patella noting the presence or absence of a bulge just below the medial joint line or medial border of the patella. This bulge is thought to represent the relocation of intra-capsular synovial fluid when the knee is effused.

Sturgill *et al*., [243], found this test [47,162] to be a reliable method of assessing grade of knee joint effusion (Cohen Kappa = 0.61) using a 5-point ordinal scale. The scores were; zero – no wave produced on downstroke, Trace – small wave on medial side with downstroke, 1+ - larger bulge on medial side with downstroke, 2+ - effusion spontaneously returns to medial side after upstroke, 3+ not possible to move effusion out of medial aspect of knee. Fifty-four of 75 sets of ratings had perfect agreement but only one set differed in identifying effusion/no effusion. Cibere *et al*., [47] found the bulge sign for effusion identification was reliable (R_c= 0.97) in individuals with knee OA. In addition, Hauzeur *et al*., [85] found moderate agreement between a clinical and ultrasonography evaluation for knee effusion/no effusion. For detecting the amount of effusion, whether on a three [85], four [47] of five [243] point scale, the accuracy and reliability were lower when compared to a dichotomous grading. Together these studies support the

use of clinical testing through the bulge sign as a reliable and valid method for identifying knee effusion in individuals with knee OA.

3.3 GAIT WAVEFORM ANALYSIS

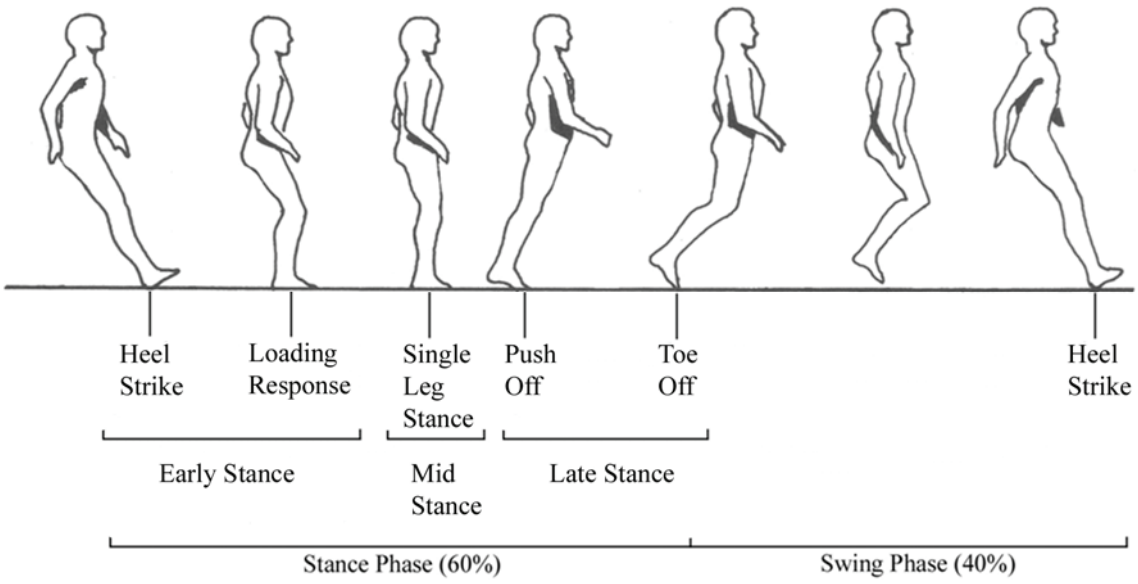

Figure 3.8: An illustration of the complete gait cycle beginning with heel strike and terminating with the subsequent ipsilateral heel strike. Adopted from Simoneau [235].

All electromyographic, kinematic, kinetic gait waveforms were time normalized to represent 100% of the gait cycle utilizing a cubic spline interpolation technique [102,144,214]. The gait cycle begins with heel strike (first contact on the force plate) and terminates with the second heel strike of the ipsilateral leg. The first heel strike was determined using a five Newton threshold in the vertical ground reaction force recorded during appropriate foot contact. The second heel strike was determined using positional data of the lateral malleolus IRED marker captured utilizing the Optotrak 3020™ motion sensors. Heel strike was demarcated as 0% of the gait cycle followed by stance and swing phases respectively. This is illustrated in Figure 3.8. For waveform analysis, discrete variables (peak values/differences) were used to analyze the kinematic, kinetic gait waveforms and pattern recognition techniques (PCA) were utilized to capture amplitude and temporal characteristics of the electromyographic waveforms.

3.3.1 Principal Component Analysis

Electromyographic waveform data during gait are multi-dimensional, variable, correlated within muscle groups and temporally dependent [43]; characteristics that are difficult to account for using discrete waveform analyses. Determining how muscle activations change during different phases of the gait cycle (Figure 3.8), phases that correspond to altered joint mechanics and the transition between these phases is of particular interest as it helps us to understand the factors that can alter knee joint muscle activation during gait. The ideal analysis method is one that is able to address the constant challenges of data volume, dimensionality and temporal dependence of electromyographic waveform data. Pattern recognition techniques, including Karhunen-Loeve expansion, cluster analysis, factor analysis, wavelet transforms, neural networks and PCA [102,115,183,193,198,230,233,273] have been utilized to quantify patterns of muscle activity during gait.

To answer questions related to amplitude and temporal waveform characteristics, PCA offers an optimal unbiased means of data reduction, identifying salient features in the original data not possible with previously utilized techniques in knee OA gait analysis. This reduced representation maximizes the preservation of original data variance, and identifies both amplitude and temporal muscle activation features, making this technique optimal to quantify principal muscle activity patterns during gait.

For this dissertation, amplitude and temporal activation features of the recorded lower extremity electromyograms were extracted using PCA. The method of PCA used for this dissertation is described in Appendix B. Briefly, ensemble average electromyographic waveforms were determined for each subject corresponding to each muscle [271]. Principal component analysis was performed using custom MatLab™ Ver.7.1 programs (The Mathworks Inc., Natick, Massachusetts, USA) using methods previously described in the literature [102,214]. Three separate PCA were performed, one for each muscle grouping. Time-normalized waveforms (101 points) from the corresponding individual muscles, and groups (dependent on the analysis) formed three matrices (X); 1) gastrocnemii 2) quadriceps and 3) the hamstrings. An eigenvector decomposition of the cross product matrix ($[S] = [X^T]*[X]$) was performed, using standard notation U'SU=L,

yielding the predominant orthonormal components (principal patterns) [102,117]. The principal patterns explaining the greatest percent of variation in the waveforms were retained and referred to as PP1, PP2 etc. A percent trace was calculated to determine how well the patterns represented the original waveform so that the correct numbers of patterns were retained. The number of principal patterns retained in the analysis is determined by the percent trace which is typically greater than 90% [102,214,216]. Principal pattern scores (*PP-Scores*) were computed for individual gait waveforms in each separate analysis (*PP-Score* = [X]*[U]). Physiological relevance of these patterns was assigned and based on various methods of investigating principal patterns and pattern scores for each group assignment (Appendix B). Principal patterns are determined by the structure of the waveform data across the entire gait cycle and in some cases, discrete differences recognized in the group ensemble-averaged waveforms are not identifiable using these patterns. The measured EMG waveform can be accurately reconstructed by the linear combination of principal patterns multiplied by the corresponding *PP-Score* (Appendix B). The individual *PP-scores* for each muscle within a grouping were scored against a common principal pattern thus allowing for statistical hypothesis testing to compare waveform characteristics between muscle sites within a muscle group and between participant groupings [102,214].

3.3.2 Statistical Analysis

All statistical procedures were completed on Minitab™ Ver.15 (Minitab Inc. State College, PA, USA). For gait waveform analysis, normality and equal variance of the *PP-scores* were determined from Kolmogorov-Smirnov and Levene's tests respectively. If assumptions were not met, data were transformed using one of two functions; a natural logarithm function or an inverse hyperbolic sine function as determined using the Johnston Transformation in Minitab™ Ver.15. For each objective, a two-factor mixed model ANOVA tested for significant group (between) and muscle (within) main effects and interactions (alpha=0.05). Significant findings were post hoc tested using a Bonferonni adjusted alpha level to determine pair-wise significant differences.

In summary, asymptomatic individuals and individuals with various severities of knee OA were recruited to the Dynamics of Human Motion Laboratory to assess walking mechanics and knee joint muscle activation associated with the knee OA process. The amplitude and temporal characteristics from the PCA of the electromyographic waveforms were used to address the three objectives of the current dissertation.

CHAPTER 4

NEUROMUSCULAR ALTERATIONS EXIST WITH KNEE OSTEOARTHRITIS PRESENCE AND SEVERITY DESPITE WALKING VELOCITY SIMILARITIES

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This manuscript has been modified from its original format to conform to the structure of this dissertation

Note: The term "neuromuscular function" was used in this chapter to describe "muscle activation". Upon reflection, this term does not clearly represent its intended meaning and confusion can exist. Given Chapter 4 is published; the term "neuromuscular function" and the context in which it is used has not been altered in this chapter of the dissertation.

4.1 INTRODUCTION

Knee osteoarthritis (OA) impairs lower extremity function, influencing ambulatory ability in older adults [81]. Reduced muscle strength [110,236] and endurance [70], reports of giving-way [71], and stiffness [102] suggest that neuromuscular function may be impaired. Studies have begun to explore lower extremity neuromuscular characteristics of the knee OA process during walking through surface electromyography however, isolating differences to disease presence or severity is difficult given factors that affect neuromuscular characteristics may differ between groups such as walking velocity.

Lower extremity neuromuscular characteristics are altered with walking velocity in asymptomatic individuals. Amplitude changes are the most prominent alteration [94,231,278], although minor changes in shape have also been shown [232]. Determining what changes are associated with the disease process can be a challenge since slower walking velocities have been reported for those with knee OA compared to asymptomatic controls [103,214,284]. Attempts have been made to account for walking velocity and include setting a threshold, [44,98,284], entering velocity as a covariate when making statistical comparisons [154,212,284] or describing velocity as self-selected and reporting the differences among groups [103]. All three approaches have merits and limitations when attempting to differentiate the effect of walking velocity that accompanies OA progression from changes associated with structural and symptomatic differences among groups at different stages of OA progression.

A predetermined walking velocity may unknowingly alter habitual walking patterns influencing intra-subject variability [231], as individuals will have to modify their walking velocity to meet the required threshold. While appealing, employing ANCOVA models to study walking in individuals with knee OA has the potential to mask group differences. Astephen *et al*., [15] argued that critical assumptions are violated since walking velocity is not independent of treatment/group (knee OA). When a variable co-varies with a disease process, the use of an ANCOVA model will adjust disease effects for differences caused by the disease (i.e. slower walking velocity) [52] and may remove part of the disease signal. Reporting results without considering walking velocity is also problematic.

In asymptomatic individuals, reduced walking velocity is associated with decreased muscle activation amplitudes [94,278]. However, for those with knee OA, despite reduced walking velocities, muscle activation amplitudes of the quadriceps and hamstrings were higher and more prolonged than faster walking asymptomatic controls [103,214]. Providing mechanisms for these alterations in muscle activation are still at an early stage in our understanding of OA and may include a response to nociceptive inputs and reflex activity [51], muscle inhibition during maximal normalization testing [66], joint loading [102], laxity [154] and walking velocity [284]. Given walking velocities in individuals with knee OA are typically reduced in comparison to asymptomatic cohorts, understanding neuromuscular function driven by the OA disease process rather than confounded by group differences in walking velocity may provide further information on disease mechanisms.

This study investigated amplitude and temporal characteristics using principal component analysis from surface electromyograms of seven lower limb muscles during walking in asymptomatic individuals and individuals with different severities of knee OA. To address the question of whether neuromuscular alterations are apparent in the electromyogram despite similarities in average self-selected walking velocity, three groups separated by their clinical status were selected based on matching average self-selected walking velocity. We hypothesized that increased amplitudes, medial and lateral site imbalances and temporal alterations would be found between asymptomatic controls and patients with knee OA and between knee OA severities.

4.2 METHODOLOGY

4.2.1 Participants

Surface electromyographic (EMG) data were collected from a large sample of individuals with asymptomatic knees and a clinical population with knee OA during self-selected, level-ground walking (N=230). Subjects over age 35 with no history of cardiovascular disease or neurological disorders were included. Subjects with knee OA were recruited from the practice of two orthopedic surgeons (WDS, MJD). Standard

anterior-posterior radiographs confirmed predominant medial compartment radiographic disease presence and were scored using the Kellgren-Lawrence global scoring algorithm [125]. Fair to good reliability for this assessment has been previously reported [168], but for these two surgeons, substantial reliability was found (Weighted Kappa statistic = 0.6). Asymptomatic subjects were recruited from the general community using email, website and poster board advertisements. Written informed consent approved by the local institutional ethics review committee was attained. All subjects were tested between 2003 and 2009 at the Dynamics of Human Motion Laboratory, Dalhousie University, Halifax, Nova Scotia.

Three groups, matched for walking velocity were identified from the sample including i) asymptomatic, ii) moderate knee OA and iii) severe knee OA. First, 15/62 individuals with severe OA were identified from the sample who walked at an average walking velocity greater than 1m/s. Their clinical prognosis was poor and they received a total knee arthroplasty within one-week after testing. Asymptomatic individuals reported no lower extremity injuries within six months prior to data collection and no symptoms of lower extremity degenerative joint disease including knee pain, morning stiffness, prior knee surgery or fracture. Of the 77 asymptomatic individuals, those with the slowest walking velocities who were the best match based on demographic factors to the severe knee OA group were identified (16). Of the 91 patients with moderate knee OA, 16 were matched to both the asymptomatic and severe knee OA groups based on self-selected velocity and demographics. These individuals self-reported their ability to perform three functional tasks; i) jog five meters, ii) walk one city block and iii) reciprocally ascend and descend 10 stairs and were being managed with conservative approaches.

4.2.2 Procedures

The Western Ontario McMaster Osteoarthritis Index (WOMAC-LK3.1) was completed by all participants. For individuals with knee OA, the most affected lower extremity was tested. For asymptomatic individuals, the tested lower extremity was randomly assigned. Surface electrode locations were identified as previously reported [102] and standard procedures consistent with recommended guidelines [226] were employed.

Skin was shaved and cleaned with alcohol wipes (70% alcohol) and 10 mm bipolar electrodes (Ag/AgCl, interelectrode distance 20 mm) were affixed to the lateral (LG) and medial (MG) gastrocnemius, vastus lateralis (VL) and medialis (VM), rectus femoris (RF), biceps femoris (LH) and semitendinosis/membranosis (MH). A reference electrode was affixed to the mid-anterior tibial shaft. Following electrode placement, muscle palpation and a series of isometric contractions for specific muscle groups [127] were used for EMG signal validation [270] and gain adjustment. In addition, active Infrared Emitting Diode (IRED) triangular sets of markers were affixed to the lower extremity segments, individual IRED markers were secured on the lateral malleolus, lateral epicondyle of the femur, greater trochanter and lateral aspect of the shoulder then virtual points were digitized as previously reported [144,213].

4.2.3 Data Acquisition

After three to five familiarization walking trials, subjects were instructed to walk along a six-meter walkway at their self-selected velocity. At least five walking trials with a consistent walking velocity (+/- 10%) and correct force plate contact were collected. Following the walking trials, baseline muscle activity was recorded in supine lying. Then subjects performed a series of eight maximal voluntary isometric contractions (MVIC) (seven against a Cybex™ dynamometer (Lumex, NY, USA)) to elicit maximal activation amplitudes for normalization purposes and to provide a measure of muscle strength for the ankle plantarflexors, knee extensors and flexors [102]. Following at least one practice and warm-up contraction, two maximal isometric contractions were completed for each exercise. Standard feedback was given to ensure a consistent maximum effort [155]. Exercises included; 1) knee extension in sitting (knee position 45 degrees flexion) 2) knee extension/hip flexion in sitting (knee position 45 degrees flexion) 3) knee flexion in sitting (knee position 55 degrees flexion) 4) knee extension in supine lying (knee position 15 degrees flexion) 5) knee flexion in supine lying (knee position 15 degrees flexion) 6) Ankle plantar flexion in long sitting (neutral ankle position) 7) standing unilateral heel raise and 8) knee flexion in prone lying (knee position 55 degrees flexion). The torque

from exercises one, three and six were used to quantify quadriceps, hamstrings and plantarflexion muscle strength.

Lower extremity motion was captured at 100Hz using two optoelectronic motion analysis sensors (Optotrak 3020™, Northern Digital Inc., Waterloo, ON, Canada). A single force plate (AMTI™, Advanced Mechanical Technology Incorporation, Newton, MA, USA), aligned to the global coordinates of the motion capture system recorded the three-dimensional ground reaction forces. Motion and ground reaction forces combined to demarcate heel strike and toe off events for electromyogram time normalization. EMG signals were amplified using an AMT-8 (Bortec, Inc., Calgary, AB, Canada), eight-channel EMG measurement system (CMRR: 115dB at 60 Hz, Input Impedance: ~10GΩ, Band-pass filter (10-1000 Hz)). A Cybex II™ Isokinetic dynamometer (Lumex, NY, USA) was utilized to record the torque associated with the maximal isometric contraction series. EMG, ground reaction force and dynamometer signals were analogue to digital converted (16bit, +/- 2V) at 1000Hz and stored for offline processing.

4.2.4 Data Processing

EMG signals were processed through custom software, written in MatLab™ version 7.0 (The Mathworks Inc., Massachusetts, USA). Raw EMG signals were corrected for subject bias, converted to micro-volts, full wave rectified and low pass filtered (Butterworth 6-Hz low pass filter). Maximal amplitudes recorded from a 100-ms moving-average window across the eight MVIC exercises were identified for each muscle for amplitude normalization [102]. The EMG waveforms (% MVIC) were time normalized to 101 data points, representing one complete gait cycle (0-100%). Muscle torque was determined using a static model that included the gravity correction torque and the torque recorded by the dynamometer during the three MVIC conditions. The maximum torque calculated over a 500ms moving window from the three-second steady state contraction was averaged for the two trials of each exercise and recorded as muscle strength (Nm) and normalized to body mass (Nm/kg).

4.2.5 Analysis

Ensemble average EMG waveforms were calculated for each subject for each muscle [271]. Principal component analysis (PCA) was used to capture amplitude and temporal features in the asymptomatic, moderate and severe knee OA EMG waveforms using custom MatLab™ Ver.7.1 programs (The Mathworks Inc., Natick, Massachusetts, USA). This multivariate statistical technique has been utilized previously [102,214]. Briefly, three separate PCA were completed, one for each muscle grouping (gastrocnemii, hamstrings, quadriceps). Three matrices (X) were formed from the time-normalized waveforms (101 points). An eigenvector decomposition of the cross product matrix ([S] = $[X^T]$*[X]) was performed, yielding the predominant orthonormal patterns called eigenvectors [117]. Eigenvectors are referred to as principal patterns (PP). Principal patterns explaining the greatest percent of variation, estimated by the percent trace were retained and referred to as PP1, PP2 etc. [102]. Principal pattern scores (*PP-Scores*) were computed for individual gait waveforms (*PP-Score* = [X]*[PP]) to provide a weighting coefficient for how each principal pattern related to each measured EMG waveform. *PP-scores* were utilized for statistical hypothesis testing.

4.2.6 Statistical Analysis

One-way analysis of variance (ANOVA) models tested group main effects for age, body mass index (BMI), self-selected walking velocity, stride length and strength measures. Independent student t-tests were employed to test for significant knee OA group differences in WOMAC sub-scores. A Mann-Whitney U-test tested for significant differences in Kellgren-Lawrence radiographic scores. Normality and equal variance of the *PP-scores* were determined from Kolmogorov-Smirnov and Levene's tests respectively. Two-factor mixed model ANOVA tested for significant group (between) and muscle (within) main effects and interactions (alpha=0.05). Significant findings were post hoc tested using a Bonferroni adjusted alpha level to determine pair-wise significant differences. Statistical procedures were completed on Minitab™ Ver.15 (Minitab Inc. State College, PA, USA).

4.3 RESULTS

Subject demographics, WOMAC scores, strength measures and stride characteristics are shown in Table 4.1. Significant differences are indicated. Asymptomatic individuals had a lower BMI ($P<0.05$) and greater ($P<0.05$) relative knee extensor and knee flexor strength (Nm/kg) compared to individuals with knee OA ($P<0.05$). Relative plantar flexor strength was greater in asymptomatic individuals compared to individuals with severe knee OA only ($P<0.05$). Significantly higher Kellgren-Lawrence radiographic scores and WOMAC physical function sub-scores were found for the severe knee OA compared to moderate knee OA group ($P<0.05$).

Table 4.1: Mean and standard deviation (SD) subject demographics, gait characteristics, knee joint strength and WOMAC scores.

	Group		
	Asymptomatic	Moderate OA	Severe OA
Sample Size	16	16	15
Gender (M/F)	8/8	8/8	10/5
Age (years)	56 (6)	61 (6)	61 (9)
BMI (kg/m^2)	24.6 (3.9) *	31.3 (3.6)	30.7 (5.4)
Velocity (m/s)	1.23 (0.09)	1.22 (0.10)	1.20 (0.14)
Stride Length (m)	1.36 (0.09)	1.35 (0.12)	1.36 (0.12)
KL-scores	---	2.4 (0.9) #	3.1 (0.7)
WOMAC Pain	---	6.6 (3.7)	8.3 (3.3)
WOMAC Stiffness	---	3.8 (1.6)	4.1 (1.3)
WOMAC Physical Function	---	21.2 (13.9) #	30.9 (9.2)
Knee Extension Strength (Nm)^	102.7 (35.7)	93.9 (36.7)	94.2 (18.4)
Knee Extension Strength (Nm/kg)^	1.4 (0.4) *	1.0 (0.3)	1.0 (0.3)
Knee Flexion Strength (Nm)^	47.2 (21.7)	45.6 (18.1)	43.5 (15.6)
Knee Flexion Strength (Nm/kg)^	0.7 (0.2) *	0.5 (0.2)	0.5 (0.2)
Ankle Plantarflexion Strength (Nm)^	73.9 (32.3)	74.7 (28.7)	59.7 (17.7)
Ankle Plantarflexion Strength (Nm/kg)^	1.1 (0.3)[&]	0.8 (0.2)	0.7 (0.3)

- * - indicates asymptomatic significantly different from knee OA groups
- [&] - indicates asymptomatic significantly different from severe OA group
- # - indicates difference between OA groups
- ^ Knee Extension Strength (1 - Asymptomatic and 1- SOA), Knee Flexion Strength (1-Asymptomatic) and Ankle Plantarflexion Strength (1-Asymptomatic and 2-SOA) patients removed due to data errors.

Ensemble average profiles for each muscle and each group are illustrated in Figures 4.1-4.3. Differences among groups are apparent, but differences are not systematic throughout the gait cycle or among the muscles. A description of the characteristic captured by the principal patterns and the statistical results are found in Table 4.2 along with the *PP-scores* in Table 4.3.

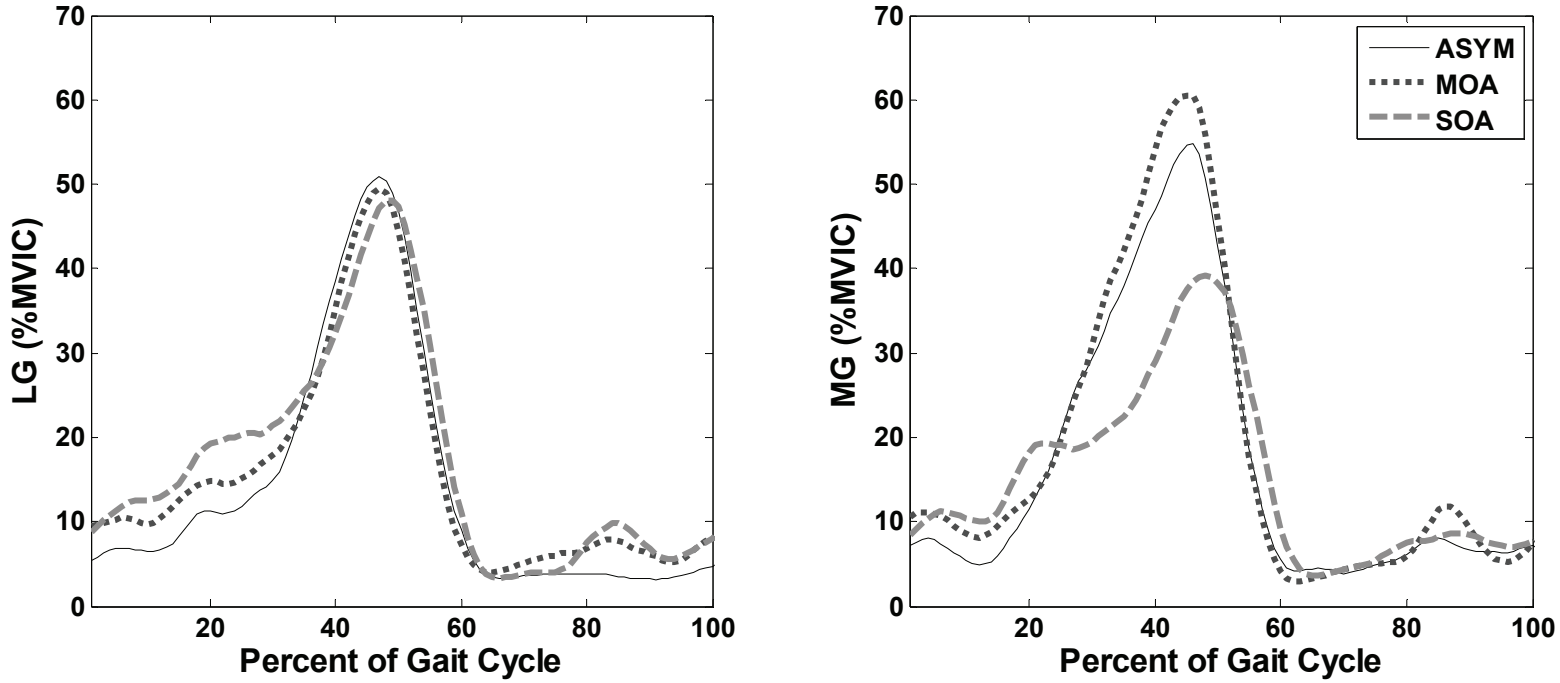

Figure 4.1: Ensemble-averaged electromyogram of lateral gastrocnemius (left panel) and medial gastrocnemius (right panel) for each group. Percent MVIC is on the y-axis and percent of gait cycle on the x-axis.

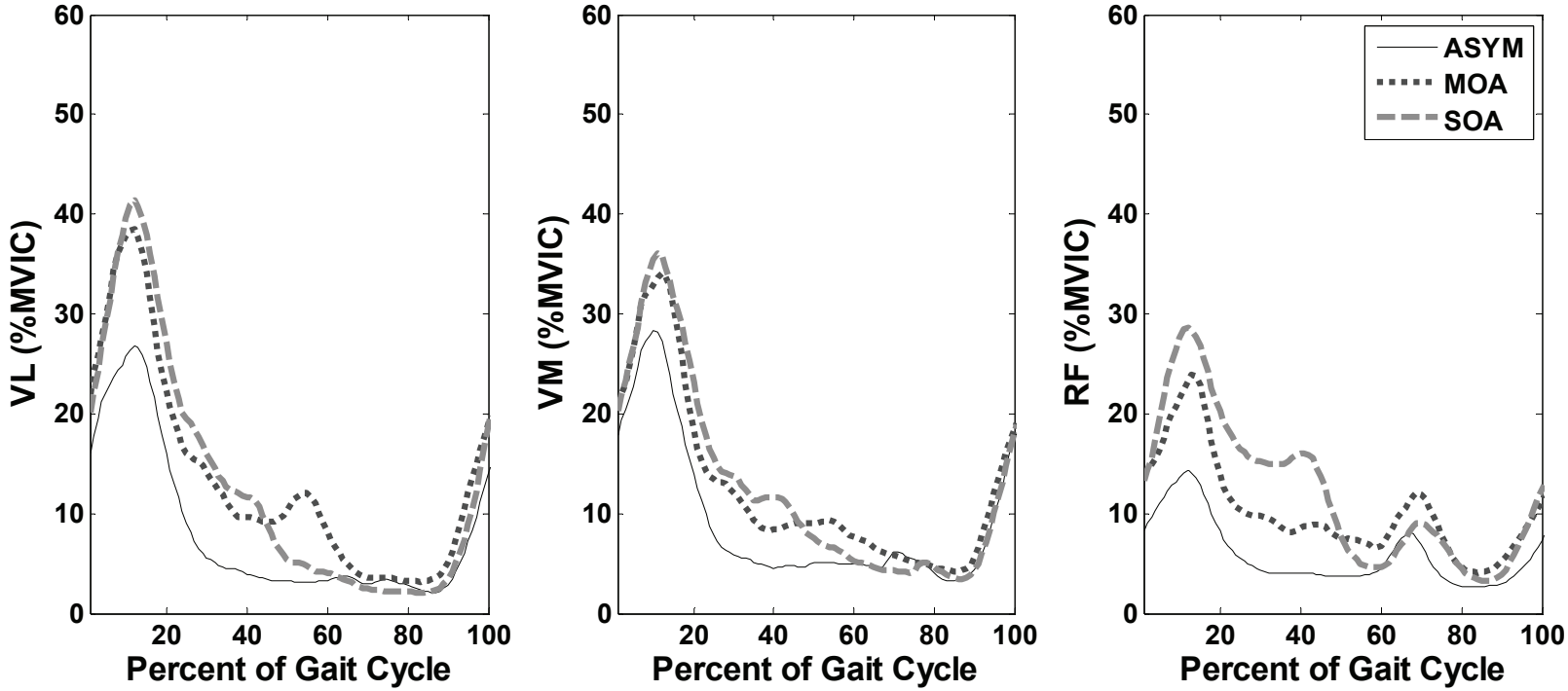

Figure 4.2: Ensemble-averaged electromyogram of vastus lateralis (left panel), vastus medialis (middle panel) and rectus femoris (right panel) for each group. Percent MVIC is on the y-axis and percent of gait cycle on the x-axis.

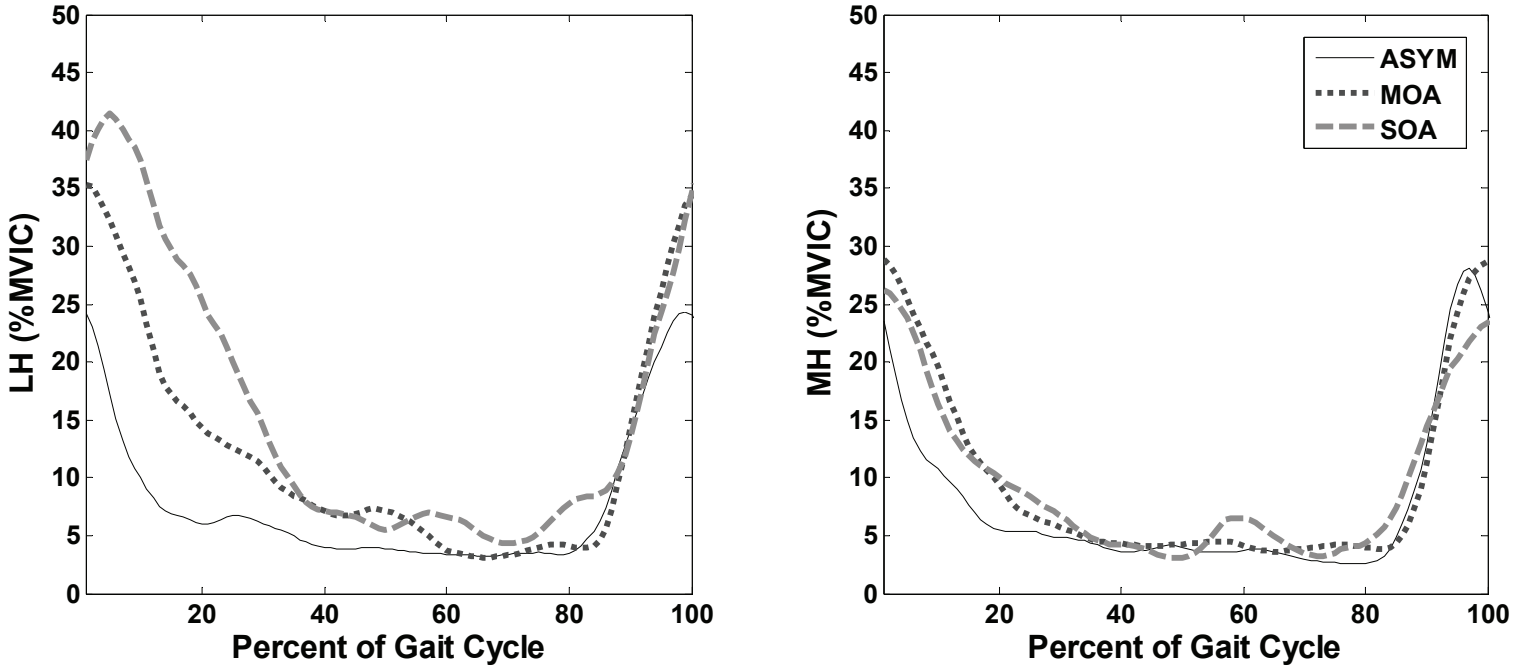

Figure 4.3: Ensemble-averaged electromyogram of lateral hamstring (left panel) and medial hamstring (right panel) for each group. Percent MVIC is on the y-axis and percent of gait cycle on the x-axis.

Table 4.2: P-values for *PP-score* main effects and interactions

	Principal Pattern Description	Group	Muscle	Group x Muscle
Gastrocnemius				
PP1 - scores	Greater scores = Greater magnitude	0.427	0.192	0.070
PP2 - scores	Greater scores = Earlier activity	0.040	0.000	**0.020**
PP3 - scores	Greater scores = larger difference between early and late stance activity levels	**0.002**	0.353	0.178
Quadriceps				
PP1 - scores	Greater scores = Greater magnitude	**0.015**	**0.000**	0.409
PP2 - scores	Greater scores = larger difference between early and mid-late stance activity levels	**0.045**	**0.000**	0.940
PP3 - scores	Greater scores = higher activity during late stance compared to mid-stance and swing phase	**0.032**	**0.000**	0.887
Hamstring				
PP1 - scores	Greater scores = Greater magnitude	0.028	0.006	**0.035**
PP2 - scores	Greater scores = greater activity during mid-stance and late swing burst of activity attenuation	0.007	0.001	**0.023**
PP3 - scores	Greater scores = greater differences between early and late gait cycle compared to mid gait cycle	0.299	0.914	0.950

*Significant findings that were post hoc tested are in **bold.**

A significant group by muscle interaction was found for Gastrocnemius *PP2-scores* ($P<0.05$). Post hoc analysis revealed significantly lower *PP2-scores* for LG compared to MG in the asymptomatic and moderate knee OA groups only ($P<0.003$). Medial gastrocnemius *PP2-scores* in the severe knee OA group were significantly lower than scores found for MG in the asymptomatic and moderate knee OA groups ($P<0.003$). A group main effect was found for *PP3-scores* ($P<0.05$). Post hoc analysis revealed that individuals with severe knee OA had significantly lower *PP3-scores* compared to asymptomatic and moderate knee OA groups ($P<0.017$).

Non-normality and unequal variance were found for quadriceps *PP-Scores* ($P<0.05$) and they were transformed. Significant group and muscle main effects were found for all three *PP-scores* ($P<0.05$). There were three pair wise comparisons for each main effect. *PP1-scores* were greater in individuals with knee OA compared to individuals with asymptomatic knees ($P<0.017$), indicating higher overall amplitudes. VL and VM *PP1-scores* were greater than RF *PP1-scores.* Lower *PP2-scores* were found in the severe knee OA group compared to asymptomatic and moderate knee OA groups ($P<0.017$) and in the moderate knee OA group compared to those with asymptomatic knees ($P<0.017$). *PP2-scores* for VM and VL were significantly greater than RF ($P<0.017$). Lower *PP3-scores* were found for the severe knee OA group compared to asymptomatic and moderate knee OA groups ($P<0.017$). Greater *PP3-scores* were found for VM and RF compared to VL ($P<0.017$).

Non-normality and unequal variance were found in the hamstring *PP-scores* ($P<0.05$). A significant group by muscle interaction was found for the transformed *PP1 and PP2-scores* ($P<0.05$). Post hoc analysis required 15 pair wise comparisons for each interaction. In the severe knee OA group, post hoc analysis revealed greater *PP1-scores* for LH compared to MH ($P<0.003$). Lateral hamstring *PP1-scores* were lower in the asymptomatic group, compared to those with knee OA ($P<0.003$) where no differences were found between individuals with moderate and severe knee OA ($P>0.003$). In the severe knee OA group, greater *PP2-scores* were found for lateral hamstrings compared to medial hamstrings ($P<0.003$). Lateral hamstring *PP2-scores* were also greater in the severe knee OA group compared to LH *PP2-scores* in the asymptomatic and moderate knee OA groups ($P<0.003$). No differences were found for MH *PP1-scores* and *PP2-scores* among all three groups ($P>0.003$).

Table 4.3: Mean and standard deviation (SD) *PP-scores* for each group and muscle

		Group		
		Asymptomatic	Moderate OA	Severe OA
Gastrocnemius				
PP1-scores	LG	214.2 (74.9)	200.3 (71.6)	208.7 (101.7)
	MG	245.0 (117.4)	253.0 (90.0)	181.6 (96.9)
PP2-scores	LG	-18.3 (42.5)	-15.9 (31.1)	-30.3 (61.0)
	MG	28.1 (47.3)	34.2 (49.3)	-22.0 (41)
PP3-scores	LG	25.1 (24.1)	-0.4 (33.8)	-18.0 (43.3)
	MG	9.0 (25.7)	6.7 (37.9)	-23.3 (24.1)
Quadriceps				
PP1-scores	VL	107.5 (43.5)	172.8 (51.6)	174.8 (51.6)
	VM	124.8 (74.6)	162.3 (89.9)	159.4 (87.1)
	RF	62.2 (27.8)	106.1 (63.1)	138.8 (92.2)
PP2-scores	VL	21.5 (13.5)	8.5 (35.5)	5.2 (39.0)
	VM	23.0 (22.1)	8.1 (24.4)	2.6 (37.2)
	RF	0.5 (10.4)	-9.9 (30.0)	-25.9 (40.1)
PP3-scores	VL	-4.7 (16.7)	-0.9 (25.8)	-24.3 (28.9)
	VM	11.3 (25.4)	9.7 (27.2)	-5.9 (24.3)
	RF	10.8 (9.3)	11.8 (17.8)	-1.9 (19.3)
Hamstrings				
PP1-scores	LH	98.8 (41.7)	159.5 (75.1)	195.9 (109.3)
	MH	99.9 (38.2)	126.4 (51.0)	116.6 (62.9)
PP2-scores	LH	-25.8 (24.7)	-0.8 (43.0)	35.3 (52.6)
	MH	-30.8 (19.8)	-12.4 (26.1)	-10 (44.3)
PP3-scores	LH	-4.5 (27.0)	2.02 (37.7)	-2.5 (36.0)
	MH	-2.6 (28.2)	8.5 (17.6)	-3.2 (19.2)

Gastrocnemius – PP1 explained 90%, PP2 explained 4% and PP3 explained 2% of the overall waveform variability. **Quadriceps** – PP1 explained 89%, PP2 explained 4% and PP3 explained 2% of the overall waveform variability. **Hamstrings** – PP1 explained 85%, PP2 explained 7% and PP3 explained 3% of the overall waveform variability.

4.4 DISCUSSION

This study confirmed that altered neuromuscular patterns during walking exist with knee OA presence and severity providing evidence that specific differences are found despite similarities in self-selected walking velocity. Individuals with severe OA were considered clinically appropriate for total knee arthroplasty in comparison to individuals with moderate disease who were being managed conservatively. The moderate knee OA group reported their ability to walk a city block, reciprocally ascend and decent stairs and jog 5-meters would not be encumbered by their knee OA. These clinical entities were previously used to determine group assignment [103], and while some classification methods have focused on radiographic evidence [284], the current approach identified two distinct groups as evidenced by the significant WOMAC function (symptoms) and KL-score (structural) differences between the two OA groups.

GASTROCNEMII

Overall amplitude differences (*PP1-scores*) were not found among groups with the elevated activity in the OA groups during early stance and to a lesser extent swing phase accounting for this finding. The asymptomatic and moderate knee OA groups however; displayed an earlier increase (phase shift - *PP2-scores*) in MG activation compared to LG consistent with findings reported when walking velocities were different between groups [102] whereas the severe group did not display this shift. This latter finding is consistent with reports from a severe OA group that walked at a slower walking velocity [100]. Shiavi *et al*., [232] found a trend for earlier gastrocnemius activity with increased walking velocity, but the current result suggests that this phase shift is also related to disease severity. Furthermore, individuals with severe knee OA had a reduced late stance to early stance activity differential (*PP3-scores*) compared to the other groups. While higher early stance activity was apparent in both gastrocnemius sites, only the MG had decreased activity in late stance. This decrease in activity may reflect an inhibition of MG in late stance (Figure 4.1), a strategy thought to reduce medial joint loading [102]. Increased gastrocnemius activity during early stance may provide active stiffness,

potentially improving the control of joint stability during weight acceptance and single leg stance consistent with higher vastus medialis-medial gastrocnemius co-contraction indices reported during early stance in those with frontal plane medial joint laxity [154]. While a mechanism is not established by this study, it is evident that severe knee OA disease processes influence MG strategies, more so than the moderate knee OA disease severity despite similar walking velocity.

QUADRICEPS

Quadriceps activity was greater in individuals with knee OA compared to asymptomatic knees, consistent with reports in which self-selected walking velocity was lower for OA groups [103]. Since decreased quadriceps activity with reduced walking velocities have been reported for asymptomatic controls [278], the higher quadriceps activity in this study, despite the similar average walking velocities among groups supports an OA related alteration. Increased activity during early to mid-stance may be necessary to counter external moments of force in the frontal plane [229] and internal flexion moments produced by knee flexor coactivity during early stance (Figure 4.2). Overall magnitudes were similar for those with moderate and severe knee OA contrasting previous findings [103]. The lack of significant differences in quadriceps strength between the OA groups may partially explain differences from previous findings in which group differences in average walking velocity were found and the severe group had lower strength values [102,103].

While overall magnitude differences were apparent, waveforms in Figure 4.2 illustrate a prolonged elevated activity in the OA waveforms, most notably in RF during mid-stance phase. *PP2-scores* captured this mid-stance activity, consistent with previous reports [102,214], supporting the finding of prolonged quadriceps activation in knee OA subjects by others [44]. This feature showed progressive traits, where all three groups were different and individuals with severe knee OA having the greatest mid-stance magnitude and asymptomatic individuals having the lowest mid-stance activity. The lower *PP3-scores* in individuals with severe knee OA also exemplifies the greater stance phase activity required by this group compared to asymptomatic and moderate knee OA

individuals. Mid-stance increases in quadriceps activity were specific to disease severity. Since walking velocities and muscle strength were similar between the OA groups, an alternate explanation for the higher mid-stance quadriceps activity for the severe group may be related to the need for active joint stiffness to prevent pain or giving away [71] as the severe group had greater joint changes based on higher KL-scores.

In summary, these results corroborate previous cross-sectional studies that show higher quadriceps activity for individuals with knee OA compared to controls despite slower self-selected walking velocity [103,212,284] and are not consistent with the reductions in early stance quadriceps amplitudes with reduced walking velocities found in asymptomatic subjects [278].

HAMSTRINGS

Recent studies found that activation levels and patterns of activity differ between medial and lateral sites during walking in the presence of both moderate and severe knee OA [103,161,214]. While overall magnitude of LH activity in those with knee OA was greater than asymptomatic individuals supporting previous work [102], differential levels of activation between LH and MH were only significant in the severe knee OA group despite the 10% higher LH compared to MH amplitudes in early stance in the moderate OA group (Figure 4.3). Differential recruitment patterns included both overall magnitude (*PP1-scores*) and prolonged activity during stance (*PP2-scores*). Asymmetric co-activity between LH and MH was expected given medial compartment dominated disease and the possible presence of a varus perturbations [32] along with greater knee adduction moments [86]. These characteristics may be more prevalent in individuals with progressing knee OA [42,173].

This lack of differential LH versus MH activity in moderate knee OA contrasts previous literature using PCA [102,214], where higher overall magnitude and prolonged LH compared to MH activations were found. Alterations in LH activity were related to disease severity however, no differences were reported for MH. This contrasts previous reports of higher overall MH amplitude in severe OA individuals compared to asymptomatic and moderate OA [103]. In asymptomatic individuals, increased hamstring

amplitude and prolonged activation during stance were related to increased walking velocity [115,278] but the current study illustrates an association with disease severity for the LH site. In summary, activation characteristics in the hamstring musculature are sensitive to presence and severity of medial compartment dominant knee OA despite similar walking velocity, strength and self-reported function.

In this study, self-selected walking velocity, WOMAC pain and stiffness sub-scores, lower extremity muscle strength, age and BMI were not different between individuals with a clinical diagnosis of moderate and severe knee OA. In contrast, neuromuscular patterns were sensitive to both the presence and severity of knee OA. This implies that objective neuromuscular function measures provides unique information for monitoring the disease process that addresses both symptomatic and structural progression with a particular emphasis on functional ability in individuals with knee OA.

Amplitude normalization to MVIC has its limitations, however the procedures employed were consistent with previous studies aiming to produce maximal activations [102,154,284] providing a standard for comparison [131]. Arthrogenic muscle inhibition may [66] or may not [120] significantly impair the quadriceps muscles during maximal testing for individuals with joint arthropathy. This study sought to minimize this effect as much as possible by utilizing a normalization protocol that provided feedback and positioned the leg differently from early studies of quadriceps inhibition [66]. In addition, this inhibition has not been reported for the hamstrings and gastrocnemii. Nevertheless, the potential that inhibition can lower both the force-generating properties of the quadriceps and amplitude of the EMG signal during normalization exercises can partially explain why individuals with knee OA have elevated quadriceps magnitude (*PP1-scores*) compared to asymptomatic individuals during walking. It is less clear as to how inhibition could alter the hamstrings and gastrocnemii activity or features other than magnitude (*PP1-scores*) that were found in the current study.

Although many consistencies were found between this study and previous studies that examined similar diagnostic groups walking at different self-selected velocities [102,103], there were notable differences. The small sample size resulted in lower statistical power than previous work, thus the results provide a conservative estimate of these differences. Difference detection, given the small sample and overlap of the groups (low

functioning asymptomatic and high functioning severe OA group), speaks to the strength of the findings. The current study found that despite the reported similarities in measures of symptoms (i.e. pain and stiffness) and function (i.e. muscle strength, self-selected walking velocity), neuromuscular patterns were different with OA presence, and some were progressive.

4.5 CONCLUSION

Walking velocity decreases are part of the disease process yet individuals with varying clinical presentations of knee OA who chose to walk at the same velocity still walk with altered neuromuscular patterns during walking. In particular, selective delay in medial gastrocnemius activity with severe knee OA, temporal synchrony of lateral and medial gastrocnemius, the increased and prolonged activation of the quadriceps muscles and the selective and prolonged activation of the lateral hamstring were all a function of the disease classification. This supports that differences are not the result of walking velocity only.

CHAPTER 5

CHANGES IN KNEE JOINT MUSCLE ACTIVATION PATTERNS DURING WALKING ARE CONSISTENT WITH STRUCTURAL SEVERITY IN KNEE OSTEOARTHRITIS

5.1 INTRODUCTION

Knee osteoarthritis (OA) is a leading contributor to chronic morbidity in older adults and managing end-stage OA places a considerable burden on health care systems [18,138]. Given there is no cure [145], and an exponential increase in the demand for end-stage treatment (i.e. arthroplasty) is projected [141], understanding the knee OA process before it reaches end-stage is important. Knee OA is a progressive disease of joint structure, largely considered to be a result of abnormal intra-articular biomechanical and biochemical stress on joint tissues [27,145]. While progressive, the reparative process may also be successful leading to a functional, painless joint [27,199]. Therefore, the imbalance between tissue synthesis and degradation is not a constant. Studying alterations to joint mechanics [11,266] and to the knee joint musculature [25,210] during gait have begun to be recognized and integrated into a framework to understand knee OA progression. The focus of this paper is on the knee joint musculature.

Panjabi [189] described the interrelationship between the passive osteoligamentous, muscular and the neural control systems to maintain joint stability. This interrelationship is fundamental to joint functions as muscle forces create moments of force that produce motion and maintain joint stability [189,239]. These forces have implications for joint loading [7,160,229] and metabolic demand [78,171] during gait. While other tissues such as muscles and the synovium are altered, the osteoligamentous structures are the primary tissues impaired with knee OA and OA progression [5,125]. Articular cartilage lesions, joint margin and tibial spine osteophytosis, subchondral bone sclerosis, and bone attrition are found [5,105,125,195,224]. Thus, adjustments to the neuromuscular system in response to impaired structure may provide information to assist in developing gait-based metrics that can facilitate knee OA diagnosis, monitor the progression of structural impairments and perhaps evaluate treatment.

Alterations to the neuromuscular system have been reported during gait in individuals with a knee OA based on surface electromyography. While, methodological inconsistencies between studies make it difficult to compare findings, some general trends are found. These include higher quadriceps and hamstrings amplitudes [103,284], greater co-activity [86,103,154,212] and longer durations of activity during stance [44,102]. More

recently, muscle activation imbalances have been found between medially and laterally oriented knee joint muscles for those with primary medial compartment knee OA [102,154,161,212,214]. The differences were more subtle for those with mild to moderate knee OA [102], with larger differences for more severe OA [103].

A variety of explanations have been offered as to why muscle activation patterns are altered with medial compartment knee OA. Mechanical factors include tibial adduction features during stance [7,86,161], medial compartment laxity [154,203], osteophytosis [284], muscle strength [102,103,212], gait velocity [16,214], and compressive medial joint loading [16,102]. As well, explanations related to OA symptoms including pain [13], instability [154] and stiffness [102] have been provided. Several studies report proprioception deficits in knee OA [22,135,228], greater dynamic knee stiffness [61] during gait and knee effusion [169], a factor that was shown to influence quadriceps and hamstrings activation amplitudes in healthy individuals during gait [251]. Together, these factors suggest that interrelationships among the passive, active and neural subsystems are altered in knee OA. What is currently unclear however is whether knee joint muscle activation patterns during gait are directly related to structural knee joint impairments characteristic of individuals with knee OA.

From a small group of studies and Chapter 4 of this dissertation, alterations appear to be influenced by OA severity [16,103,216,284]. The definitions of severity used in these studies were not comparable for structural impairments and/or symptoms. Thus, the link to structural impairment is not entirely clear. Given the relationship between structural impairments and symptoms is discordant [21,24,54,248], these two characteristics should be examined separately [145] or at the very least, both characteristics need to be considered, when examining their relationship to neuromuscular system alterations during gait.

Only one study examined structural severity separately, by testing a homogeneous group with a moderate OA classification based on functional and clinical criteria. They found no significant relationship between knee joint muscle activation patterns and structural severity based on a proprietary visual analog (VAS) assessment of the radiograph [13]. While the VAS was correlated to Kellgren Lawrence scores (r=0.64) over 60% of the variance was not accounted for by a linear relationship. Thus, while potentially useful for an overall assessment of knee impairment, the VAS was limited as

there was no weighting of how specific structural impairments contributed to the overall VAS score. Given osteophytosis [284] and joint space narrowing [154] have been thought to influence knee joint muscle activation, using a scale that includes a stepwise increase in severity of these impairments may provide a stronger link to muscle activity alterations during gait.

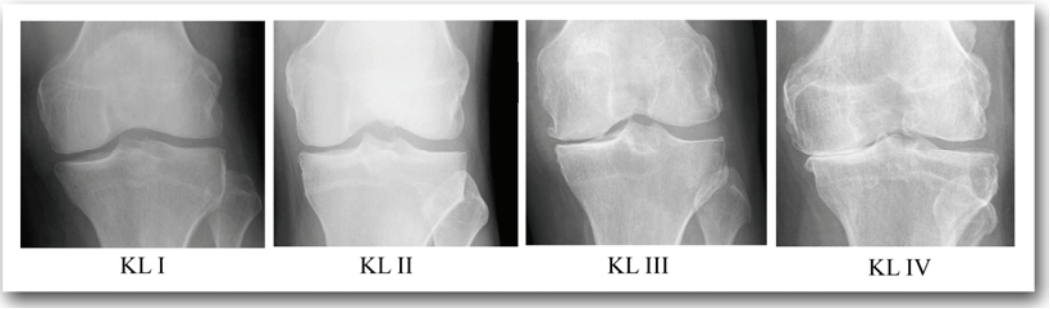

Figure 5.1: Anterior-posterior radiographs of individuals assigned KL I through to KL IV radiographic scores. Images have been modified to focus on the knee joint.

The present study focused on structural severity, defined as level of knee joint structural impairment. While arthroscopic procedures are used to evaluate these impairments [28,259] and magnetic resonance imaging techniques are developing, particularly for early cartilage degeneration and thickness measures [63,122,134], radiographic assessment, in particular the Kellgren-Lawrence (KL) ordinal radiographic scale [125] remains the most widely used method of classifying radiographic knee OA structural severity [31,65,218,286]. Through five discrete categories from none (0) through to severe (IV) (Figure 5.1), anterior-posterior and lateral knee joint radiographs are assessed for increasing osteophytosis, joint space narrowing, sclerosis and deformity of bone contour [125].

The discordance between knee OA symptoms and impairments to knee joint structure [21,24,54,248] provides support for identifying a knee OA group, that have similar knee OA symptoms and activity limitations, yet a wide spectrum of structural impairments. The objective of this study was to determine whether alterations in knee joint muscle activation patterns were associated with structural severity for those with a moderate knee OA classification. Sub-groups were based on Kellgren Lawrence ordinal radiographic scores. A sub-objective was to determine if all OA sub-groups differed from asymptomatic controls. Osteoligamentous structures are the primary tissues impaired by

the knee OA process, yet the interaction of the three subsystems is essential for maintaining joint function. Thus, we hypothesized that increased structural severity, as part of the OA process, would be associated with systematic changes to muscle activation amplitude and temporal activation patterns during walking. We further hypothesized that medial and lateral muscle site differences will exist and will interact with the sub-groups.

5.2 METHODOLOGY

5.2.1 Participants

Participants with knee OA were recruited from local orthopaedic clinics over the period of 2003-2010. Knee OA was determined using the American College of Rheumatology guidelines [3]. All participants were required to meet a functional status, consistent with a moderate OA classification, based on self-report and included the ability to i) reciprocally ascend and descend 10 stairs, ii) safely walk one city block, and iii) jog five meters [102]. Participants were clinically managed using non-surgical interventions and were not scheduled for total knee arthroplasty at the time of testing.

Asymptomatic participants were recruited from the general community using email, website and poster board advertisements over the period of 2003-2007. These individuals had no lower extremity injuries within six months prior to data collection and no symptoms of lower extremity degenerative joint disease including morning stiffness, knee pain, and no prior knee surgery or fracture. Seventy-seven asymptomatic individuals were identified, and a subset (n=35) was matched to the moderate knee OA group based on age and walking velocity.

In addition to the above criteria, all participants were required to be 35 years of age or older, have no cardiovascular/respiratory disease or neurological disorders that would affect their ability to safely complete the data collection (i.e. stroke, Parkinson's disease, myocardial infarct, arrhythmias), had not sustained a fracture or injury other than a sprain or strain (within one-year) or had a major injury or surgery to the knee joint including an ACL injury. Written informed consent was attained. All procedures were approved by the local institutional ethics review committee.

Standard weight-bearing anterior-posterior and lateral radiographs were acquired for each participant with knee OA. Radiographs were scored by a single experienced reader, as recommended by Vignon *et al*., [258], who was blinded to gait analysis outcomes (WDS). All information that would identify the patient was removed from the radiograph before reading. The Kellgren-Lawrence scale [125] was used to score each radiograph; 0 - Normal, I - doubtful narrowing of the joint space and possible osteophytic lipping, II - Definite osteophytes, minimal joint space narrowing, III - moderate osteophytosis, definite narrowing, some sclerosis, possible deformity of boney contour, IV - large osteophytes, marked narrowing of joint space, severe sclerosis, definite deformity of boney contour. Participants with lateral joint space narrowing greater than medial joint space narrowing [224] were excluded. Knee OA was defined as a KL-score ≥ II. Fair to good reliability for this assessment has been previously reported [168] (ICC=0.59, 95% CI (0.42-0.74)). All participants completed the gait analysis at the Dynamics of Human Motion Laboratory, Dalhousie University, Halifax, Nova Scotia.

5.2.2 Procedures

The Western Ontario McMaster Osteoarthritis Index (WOMAC-LK3.1) was completed by all participants with knee OA. Height and mass were measured and recorded. The most symptomatic lower extremity was tested in participants with knee OA and for the asymptomatic group; the tested leg was randomly assigned. Standardized procedures [102] were used for surface electromyographic (EMG) assessments and were consistent with published guidelines [226]. Standard skin preparation (light shave and abrasion with 70% alcohol wipes) and placement of surface electrodes in a bipolar configuration (Ag/AgCl, 10 mm diameter, 20 mm interelectrode distance) over the vastus medialis (VM), vastus lateralis (VL), rectus femoris (RF), semitendinosis/membranosis (MH), biceps femoris (LH), lateral gastrocnemius (LG) and medial gastrocnemius (MG) was completed. Refer to Rutherford *et al*., [215] for a complete description of placement guidelines (also see Table 3.1 and Figure 3.4). Muscle palpation and an isometric contraction series were used to validate electrode placement [270] and for setting appropriate gain adjustments. EMG signals were amplified using an AMT-8 (Bortec,

Inc., Calgary, Alberta, Canada), eight-channel EMG system (Input Impedance: ~10GΩ, CMRR:115dB at 60 Hz, Band-pass (10-1000 Hz)). Triangular sets of infrared emitting diode (IRED) skin markers were secured to the pelvis, femur, tibia and foot. Single IRED skin surface markers were placed on the lateral malleolus, lateral epicondyle and greater trochanter of the femur and lateral aspect of the shoulder. Eight virtual landmarks were defined, including right and left anterior superior iliac spines, medial epicondyle of the femur, fibular head, tibial tuberosity, medial malleolus, base of the second metatarsal and center of the posterior calcaneous. Lower extremity motion during gait was captured in three-dimensions at 100Hz using two optoelectronic motion analysis sensors (Optotrak™, Northern Digital Inc., Waterloo, ON, Canada). Marker motions were used to calculate knee joint angles and gait velocity. In combination with three-dimensional ground reaction forces, captured at 1000Hz or 2000Hz, from a single force plate (AMTI™, Advanced Mechanical Technology Incorporation, Newton, MA, USA) embedded in the walkway, marker motions were also used to identify heel strike and toe off events for waveform time normalization [144].

5.2.3 Data Acquisition

After at least three familiarization trials, participants were instructed to complete at least five walking trials at a consistent self-selected velocity (+/- 10%) along a six-meter walkway. Following the walking trials, baseline muscle activity was recorded in a relaxed supine position. Participants then completed a series of eight standardized exercises to elicit maximal voluntary isometric contraction (MVIC) efforts for normalization purposes [102]. These are shown in Rutherford *et al*., [215] (also see Appendix A.1). Following at least one practice and warm-up contraction, two, three-second maximal isometric contractions were completed for each exercise. A minimum 60-second rest period separated each contraction, and standardized verbal encouragement was given [155]. All electromyographic signals were analogue to digital converted at 1000Hz or 2000Hz[#] (16bit, +/-2V) and stored for processing.

[#] The sampling rate was changed in September 2008. Refer to Appendix C for details pertaining to sampling rate difference and EMG analysis

5.2.4 Data Processing

Raw EMG data was processed through custom MatLab™ Ver 7.1 programs (The Mathworks Inc., Natick, Massachusetts, USA). All signals were corrected for resting subject bias and converted to micro-volts to represent skin level voltage, full-wave rectified and low-pass filtered (Butterworth, non-recursive, 4th order, Fc-6Hz). Waveforms were time normalized to 100% of the gait cycle and amplitude normalized to MVIC. For amplitude normalization, a 100ms moving window algorithm (99ms overlap) identified the maximal amplitude for each muscle across all eight MVIC exercises [102]. Isometric torque values were corrected for gravity and the maximum torque for a 500ms window was identified for seated knee extension with knee at 45 degrees flexion, seated knee flexion with knee at 55 degrees flexion and plantarflexion from a long sitting position with ankle positioned at zero degrees. The average of the two trials was recorded as the maximal torque in Newton meters and normalized to body mass (Nm/kg).

Technical and local anatomical bone embedded coordinate systems for the thigh and tibia were derived from the skin surface markers and digitized points [39,50]. Sagittal plane knee joint angles were specified through Euler rotations using standard convention [79] where positive angles indicate knee flexion.

5.2.5 Analysis

Four groups were defined; i) asymptomatic individuals and three sub-groups of individuals with moderate knee OA based on KL-scores ii) minimal structural impairment (KL II), iii) moderate structural impairment (KL III) and iv) severe structural impairment (KL IV). For each subject, ensemble average waveforms were determined for each muscle [271]. Principal component analysis (PCA) was used to capture amplitude and temporal electromyographic waveform features using custom MatLab™ Ver.7.1 programs (The Mathworks Inc., Natick, Massachusetts, USA). This multivariate statistical technique has been previously described in detail [102,214]. Briefly, three separate analyses were performed, one for each muscle grouping (gastrocnemii (LG, MG), quadriceps (VL, VM, RF) and hamstrings (LH, MH)). For each muscle grouping, a

matrix of original waveform data was factored to yield a set of uncorrelated eigenvectors called principal patterns. A percent trace was calculated to determine how much variability was contained in each principal pattern. Principal patterns (PP1, PP2 etc) that together explained greater than 90% of the variability in the original waveforms were retained for further analysis. Principal pattern scores (*PP-Scores*) were computed to provide a weighting coefficient for how each principal pattern related to each measured waveform. *PP-scores* were utilized for statistical hypothesis testing. Excellent reliability was demonstrated for waveform features determined using this protocol [101].

5.2.6 Statistical Analysis

One way analysis of variance models were used to test significant group differences for WOMAC sub-scores, age, mass, body mass index (BMI), gait velocity, strength measures and knee flexion angles at heel strike, early stance maximum and mid to late stance minimum. Normality and equal variance of the *PP-scores* were determined from Kolmogorov-Smirnov and Levene's tests respectively. A two-factor (group, muscle) mixed model Analysis of Variance tested for main effects and interactions (alpha=0.05). All significant findings were post hoc tested using a Bonferroni adjusted alpha level to determine pair-wise significant differences. Statistical procedures were completed on Minitab™ Ver.15 (Minitab Inc. State College, PA, USA).

5.3 RESULTS

Group demographics are shown in Table 5.1. The proportion of women to men was greater in the asymptomatic (54%) and KL IV (45%) groups compared to the KL II and III groups. Asymptomatic individuals had greater quadriceps strength than the KL II group ($p<0.05$). No other strength differences were found among groups ($p>0.05$). No differences in age or walking velocity were found among groups and no differences in WOMAC sub-scores were found among the three KL groups ($p>0.05$), as expected due to matching. Comparable BMI was found between the KL groups and between asymptomatic individuals and the KL IV group ($p>0.05$) where the asymptomatic group

was within a healthy range and the knee OA groups were in either the overweight (KL IV) or obese categories (KL II and III). Group sagittal plane knee angles are shown in Figure 5.2. No group differences were found at heel strike, early stance maximum or mid to late stance minimum ($p>0.05$).

Table 5.1: Mean and standard deviation (SD) subject demographics, gait characteristics, knee joint strength and WOMAC scores.

	KL-Scores			
	ASYM	II	III	IV
N	35	38	33	11
# females	19	11	5	5
Age (years)	56 (6)	56 (8)	59 (8)	59 (8)
Mass (kg)	71.9 (14.0)*	93.0 (18.2)	96.0 (17.7)&	80.6 (16.8)
BMI (kg/m^2)	24.6 (3.5)*	30.5 (5.1)	31.2 (5.6)	28.4 (4.3)
Walking Velocity (m/s)	1.29 (0.12)	1.28 (0.20)	1.25 (0.16)	1.21 (0.22)
Muscle Strength (Nm/kg)				
KE45	1.48 (0.44)#	1.17 (0.41)	1.29 (0.45)	1.24 (0.51)
KF55	0.64 (0.26)	0.53 (0.20)	0.62 (0.23)	0.59 (0.27)
PF	1.08 (0.35)	0.89 (0.43)	0.94 (0.35)	0.97 (0.34)
WOMAC				
Pain	-----	6.8 (3.8)	6.7 (3.5)	6.2 (3.4)
Stiffness	-----	3.5 (1.7)	3.7 (1.6)	3.5 (1.1)
Physical Function	-----	23.0 (12.1)	20.5 (13.0)	15.7 (12.4)

Note: symbols indicate significant differences (Bonferonni corrected alpha)
* indicates ASYM < KLII and KL III, ASYM = KL IV
& indicates KLIII > KLIV
# indicates ASYM > KL II

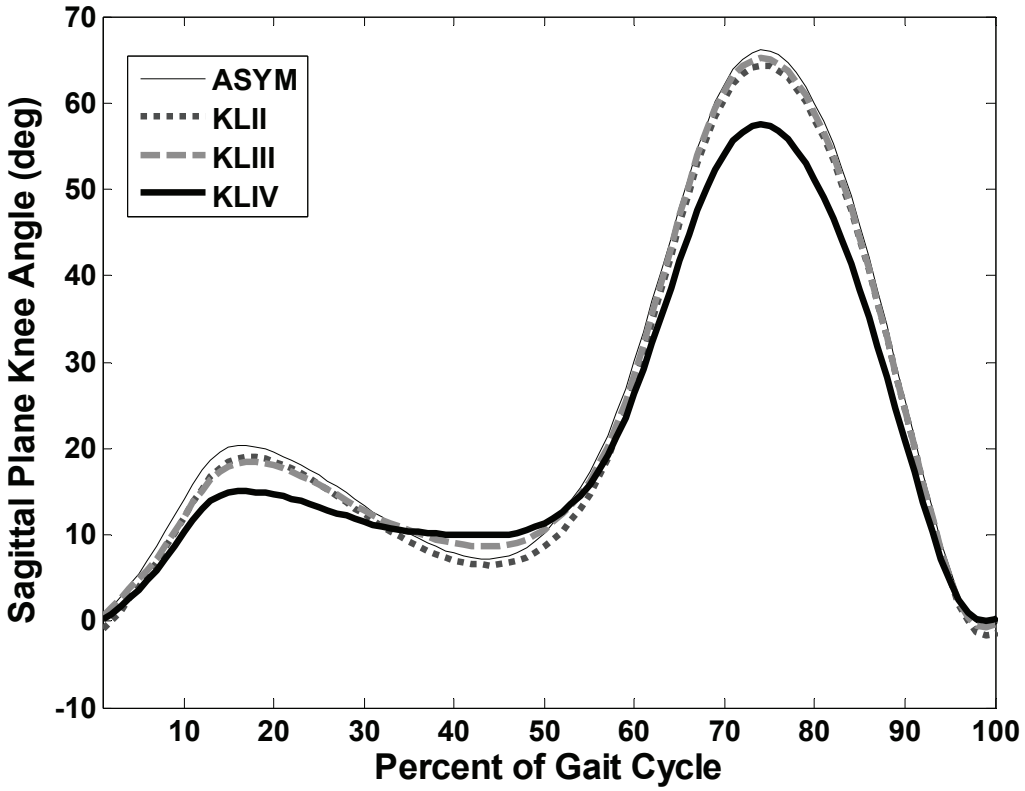

Figure 5.2: Ensemble-averaged sagittal plane knee angles for each group. Positive values indicate flexion.

The group ensemble-averaged waveforms for the gastrocnemii (Figure 5.3), quadriceps (Figure 5.4) and hamstrings (Figure 5.5) show systematic changes with increased structural severity. Three principal patterns explained over 94% of the variance in the waveform data for each muscle grouping. For each muscle group, unequal variance and non-normality existed for the *PP-scores* associated with PP1, PP2 and PP3. All data were transformed using either a natural logarithm or inverse hyperbolic sine function. A description of the salient features captured by the principal patterns and the mean *PP-scores* for each group and muscle are found in Tables 5.2 and 5.3. Post hoc results are found in Table 5.4.

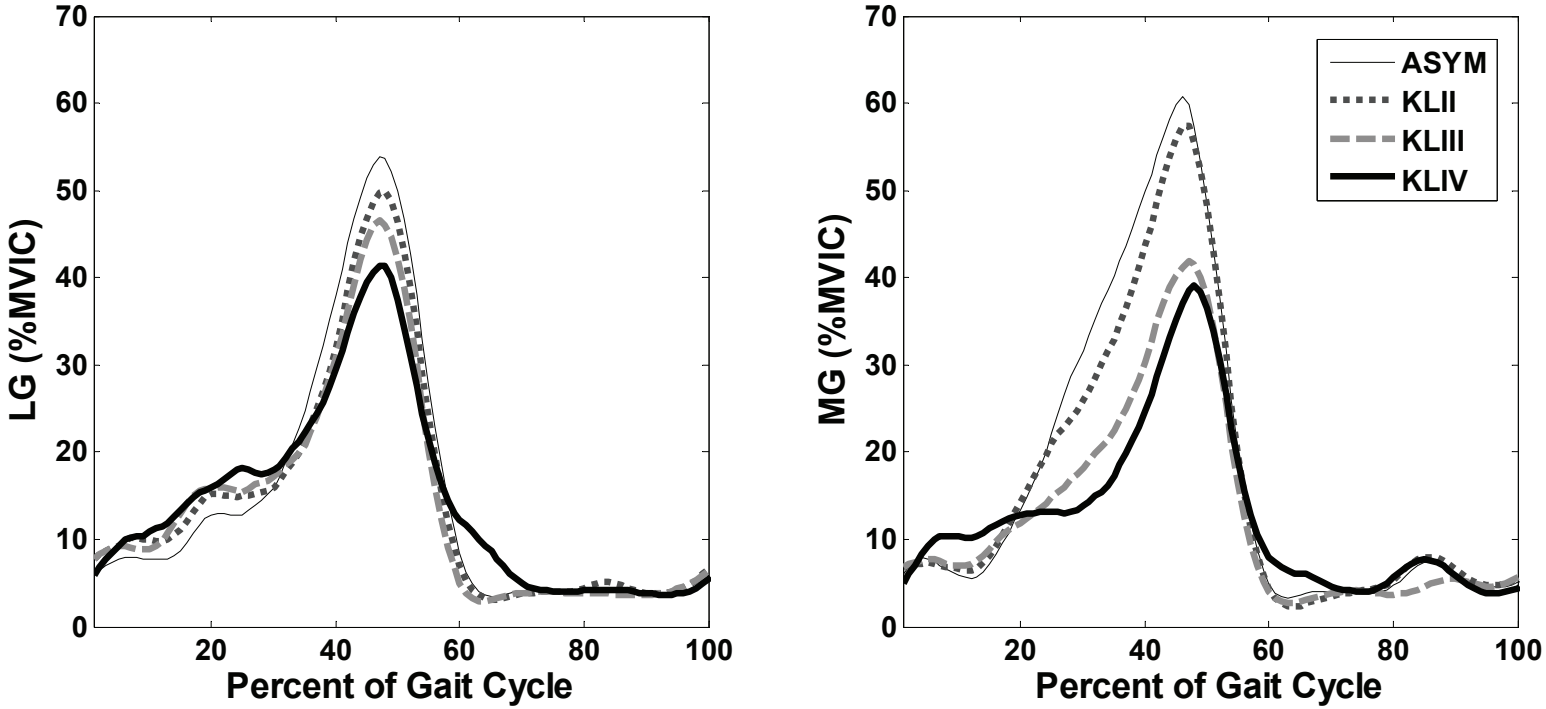

Figure 5.3: Ensemble-averaged electromyogram of lateral gastrocnemius (left panel) and medial gastrocnemius (right panel) for each group. Percent MVIC is on the y-axis and percent of gait cycle on the x-axis.

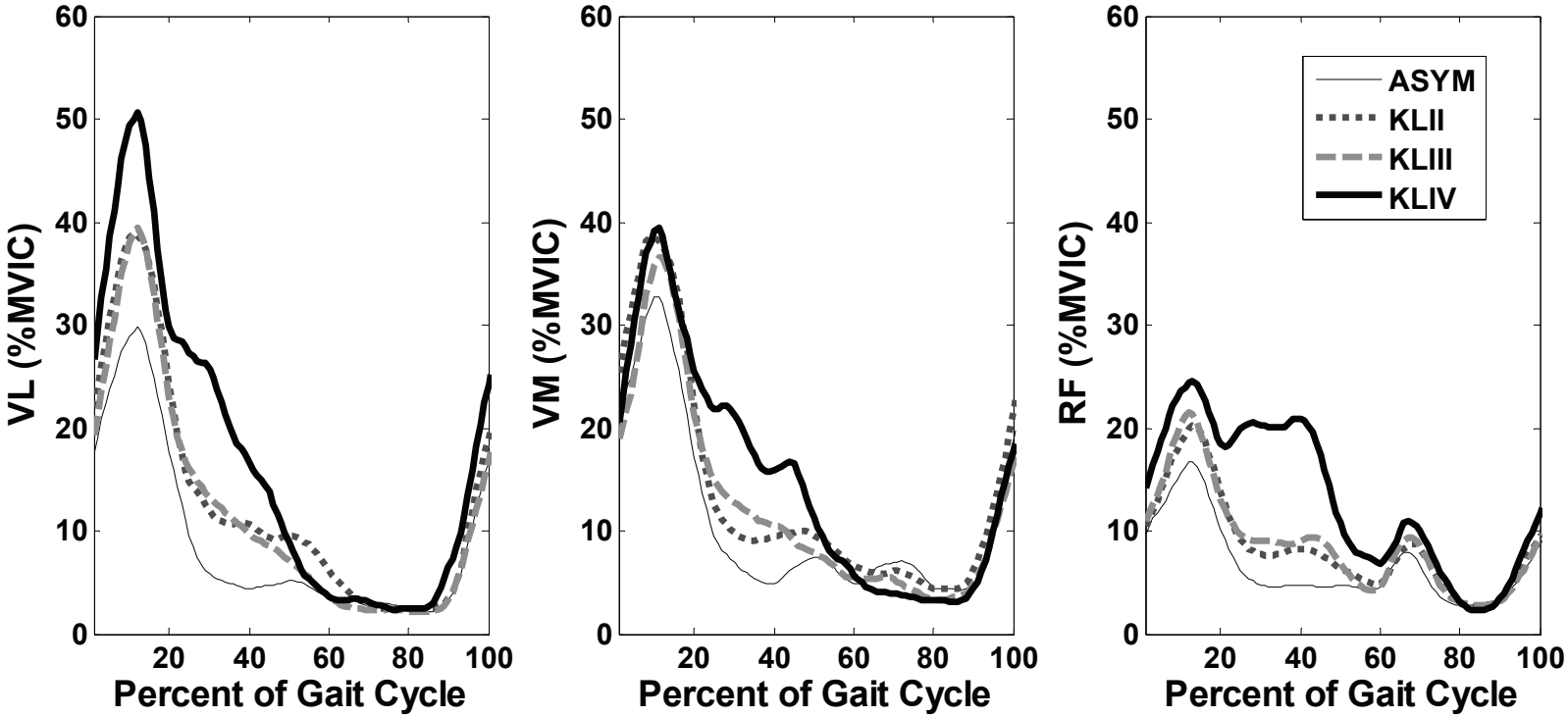

Figure 5.4: Ensemble-averaged electromyogram of vastus lateralis (left panel), vastus medialis (middle panel) and rectus femoris (right panel) for each group. Percent MVIC is on the y-axis and percent of gait cycle on the x-axis.

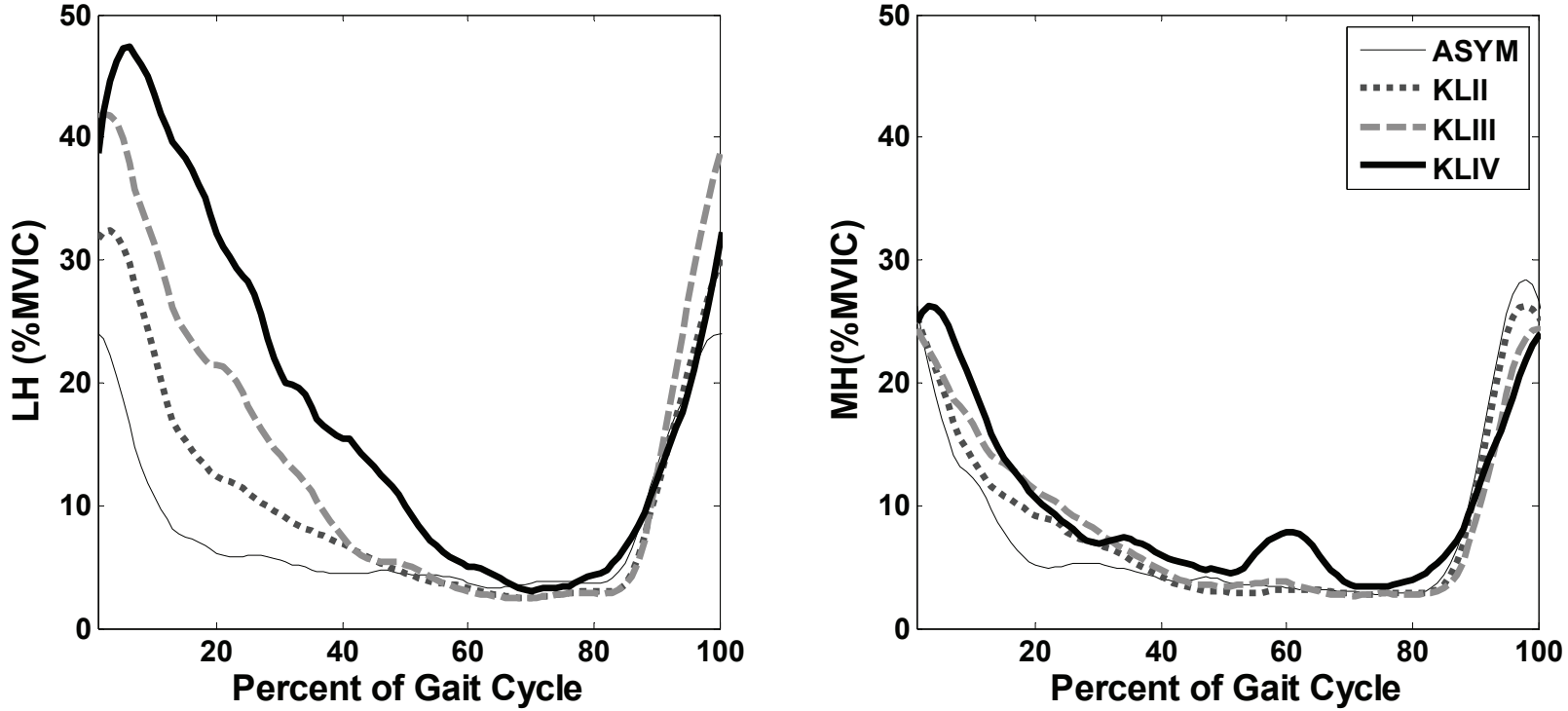

Figure 5.5: Ensemble-averaged electromyogram of lateral hamstring (left panel) and medial hamstring (right panel) for each group. Percent MVIC is on the y-axis and percent of gait cycle on the x-axis.

Table 5.2: Gastrocnemii and hamstrings principal pattern description and *PP-scores*

	Gastrocnemii			Hamstrings		
	PP1	PP2	PP3	PP1	PP2	PP3
Principal Pattern Description	Greater scores = Greater amplitude	Greater scores = Earlier activity	Greater scores = larger difference between early and late stance activity levels	Greater scores = Greater amplitude	Greater scores = higher activity during mid-stance and late swing burst of activity attenuation	Greater scores = burst of activity during early stance compared to activity during mid gait cycle
Lateral						
ASYM	210.2 (84.4)	-23.9 (34.7)	6.1 (27.8)	97.4 (42.8)	-26.6 (24.6)	-11.2 (26.7)
KL II	194.4 (91.5)	-21.7 (54.6)	-6.7 (42.7)	139.6 (68.1)	-9.1 (46.0)	6.8 (26.2)
KL III	184.0 (78.3)	-11.9 (28.0)	-9.9 (33.0)	188.2 (93.0)	1.3 (53.0)	12.0 (40.7)
KL IV	176.6 (62.4)	-6.7 (31.4)	-25.7 (49.2)	223.0 (115.6)	59.3 (84.9)	13.7 (54.7)
Medial						
ASYM	248.7 (99.9)	25.3 (42.1)	12.1 (40.8)	102.5 (37.9)	-35.3 (24.2)	-13.7 (20.8)
KL II	229.6 (75.7)	10.4 (51.6)	8.1 (34.7)	108.7 (45.9)	-22.5 (32.4)	-8.7 (23.5)
KL III	170.2 (81.4)	-0.7 (39.3)	-2.8 (34.9)	110.5 (60.8)	-8.2 (48.1)	-2.2 (16.9)
KL IV	155.5 (51.7)	-16.1 (44.9)	-17.5 (46.3)	119.3 (57.0)	-6.6 (37.0)	2.3 (35.3)

Three principal patterns captured 95% of the gastrocnemii waveform variance. A progressive trend in *PP-score* alterations with increasing structural severity was found for all muscle activation features (Table 5.2, Figure 5.3). Significant group by muscle interactions were found for the *PP1-scores* and *PP2-scores* ($p<0.05$). Significant group and muscle main effects were found for *PP3-scores* ($p<0.05$). In general, MG had more significant differences than LG with increasing structural severity (Table 5.4). For MG and LG, waveform differences were not found between the asymptomatic and KL II groups or between the KL III and KL IV groups. The KL III and KL IV groups had lower overall MG amplitude (PP1) and a delayed increase in MG activation (PP2) than the asymptomatic and KL II groups.

Three principal patterns captured 94% of the quadriceps waveform variance. Six of nine quadriceps *PP-scores* showed a progressive trend in alterations with increasing structural severity (Table 5.3). Two VL and one VM feature did not follow this trend. Significant muscle and group main effects were found for all *PP-scores* associated with the quadriceps ($p<0.05$) (Table 5.4). In general, all knee OA groups had greater overall amplitudes (PP1) and greater mid-stance activity compared to early stance (PP2) than the asymptomatic group where the KL IV group had the highest activity levels throughout the gait cycle (PP1, PP2). Differences in mid-stance activity compared to late stance (PP3) were found among all three OA groups.

Table 5.3: Quadriceps principal pattern description and *PP-scores*

	Quadriceps		
	PP1	PP2	PP3
Principal Pattern Description	Greater scores = Greater amplitude	Greater scores = larger difference between early and mid-late stance activity levels	Greater scores = higher activity during late stance compared to mid-stance and swing phase
VL			
ASYM	124.1 (60.4)	17.5 (17.4)	0.3 (19.3)
KL II	169.8 (102.7)	4.2 (40.8)	-3.5 (30.9)
KL III	162.5 (96.5)	5.1 (37.2)	-15.0 (17.3)
KL IV	222.7 (169.9)	-9.6 (48.1)	-30.7 (45.7)
VM			
ASYM	137.9 (89.6)	15.1 (21.1)	12.3 (26.2)
KL II	171.7 (111.4)	10.6 (44.3)	9.8 (38.4)
KL III	156.3 (91.8)	-2.0 (36.6)	-5.7 (22.9)
KL IV	182.0 (118.8)	-24.3 (45.2)	-14.4 (27.3)
RF			
ASYM	75.5 (36.7)	-3.6 (14.4)	8.7 (9.5)
KL II	94.5 (46.7)	-13.8 (27.9)	4.5 (12.5)
KL III	98.7 (45.4)	-16.1 (30.0)	3.6 (12.1)
KL IV	137.7 (51.6)	-54.6 (66.4)	-6.9 (14.0)

Ninety-four percent of hamstring waveform variance was captured by three principal patterns. A progressive trend in *PP-score* alterations, associated with increasing structural severity was also found for all muscle activation features, greater differences were noted for LH than MH (Table 5.2). A significant group by muscle interaction was found for the *PP1-scores* ($p<0.05$). Muscle and group main effects were found for the *PP2-scores* and *PP3-scores* ($p<0.05$) (Table 5.4). All knee OA groups had greater LH amplitudes (PP1), more prolonged hamstrings activity during stance (PP2) and a burst of hamstrings activity during early stance (PP3) compared to the asymptomatic group. For the knee OA group, LH had an overall increase in the magnitude feature (PP1) for the two groups with the greater structural impairment (KL III and KL IV) compared to the KL II group. Subsequently, a significantly higher LH than MH activation magnitude was found for the KL III and IV groups. Only the prolonged activity feature (PP2) was different between the KL III and IV groups.

Table 5.4: Post Hoc results for significant group and muscle main effects and interactions.

	Quadriceps	Hamstrings	Gastrocnemii
PP1-scores	ASYM<KLII=KLIII<KLIV VL=VM>RF	LH-ASYM<KLII<KLIII=KLIV MH-no group differences ASYM LH=MH KLII LH=MH KLIII LH>MH KLIV LH>MH	MG-ASYM=KLII>KLIII=KLIV LG-no group differences ASYM LG=MG KLII LG=MG KLIII LG=MG KLIV LG=MG
PP2-scores	ASYM>KLII=KLIII>KLIV VL=VM>RF	ASYM<KLII=KLIII<KLIV LH>MH	MG-ASYM=KLII, >KLIII, >KLIV MG-KLII=KLIII=KLIV LG-no group differences ASYM LG<MG KLII LG<MG KLIIILG=MG KLIV LG=MG
PP3-scores	ASYM=KLII>KLIII>KLIV VM=RF>VL	ASYM<KLII=KLIII=KLIV LH>MH	ASYM=KLII, >KLIII, >KLIV KLII=KLIII, >KLIV KLIII=KLIV MG>LG

Note; (>) indicates *PP-scores* were significantly less than the preceding *PP-scores*. (<) indicates *PP-scores* were significantly greater than the preceding *PP-scores*. (=) indicates *PP-scores* were equal between the two *PP-score* groups. (, >) only applied to gastrocnemii PP2 and PP3 and indicates *PP-scores* were less than the *PP-scores* of the first group identified (i.e. most left-positioned group).

5.4 DISCUSSION

A range of structural severities existed in this knee OA sample, but participants were homogeneous with respect to their classification of moderate OA based on function, symptoms and clinical management. Despite this homogeneity, distinct and systematic differences in knee joint muscle activation patterns were found. Strong evidence of an association between structural severity and muscle activation patterns during gait existed. Out of 21 principal patterns that identified key waveform features for each muscle grouping (Table 5.2 and Table 5.3), 18 *PP-scores* showed a trend for a progressive increase or decrease with increased KL-score.

Homogeneity of the OA groups was confirmed through several measures. Across the three knee OA groups; comparable pain and stiffness, as assessed using the WOMAC osteoarthritis index were reported with total WOMAC scores similar to previous work on individuals classified as having moderate knee OA [161]. Furthermore, walking velocity and sagittal plane knee angles were similar across all the groups. The only differences between the asymptomatic group and the OA groups were related to body mass and higher quadriceps muscle strength as indicated in Table 5.1. No trends were apparent between muscle strength and KL-scores. Collectively these findings indicate that the key difference among OA subgroups was their level of structural impairment.

GASTROCNEMII

All six gastrocnemii waveform features changed in a progressive manner with increasing structural severity as illustrated by the *PP-scores* in Table 5.2. Similarities between asymptomatic and KL II groups for all MG and LG muscle activation patterns support that definite osteophytes and minimal joint space narrowing, characteristic of the KL II score, were not associated with altered gastrocnemii activation. In contrast, both the KL III and KL IV groups had lower overall MG amplitudes (PP1) and phase-shifted MG activity (PP2) compared to asymptomatic individuals. Hence, moderate to severe structural changes in particular the inclusion of KL III associated structural impairments (i.e. moderate osteophytes, definite joint space narrowing, sclerosis and possible

deformities of bone contour) were related to MG activation pattern changes. Decreased MG activity has been inconsistently reported in the literature, where in individuals with moderate knee OA, both decreased overall amplitude [102] or no differences [214] have been found. The current findings support that amplitude was associated with structural severity thus inconsistencies in previous studies could be attributed to the different distribution of structural severities in their moderate OA group.

Medial gastrocnemius increased activity earlier in stance than LG (PP2) in asymptomatic individuals and individuals with KL II scores, consistent with previous work on individuals with moderate knee OA [102,214,216]. This asynchrony between MG and LG was not found for the KL III and KL IV groups. This corroborates the temporal synchrony previously found in those classified with severe knee OA based on clinical symptoms and function [216]. In that study, the average KL-score for the severe group was III. These results provide evidence of a relationship between MG/LG temporal synchrony and structural severity characteristic of KL III and KL IV. While decreases and phase-shifted gastrocnemii activity have been reported for slower walking velocities [232], alterations in the present study or previous studies [214,216] cannot be explained by walking velocity. Furthermore, plantar flexor strength was similar among groups, thus pointing to structural severity, as a potential mechanism for the changes to the neuromuscular system reflected in the pattern differences.

A trend towards increased early stance compared to late stance gastrocnemii activity with increased severity was found (negative *PP3-scores*). The increased MG activity found during early stance in the current study partially corroborates the higher vastus medialis-medial gastrocnemius co-contraction index (CCI) found during early stance in individuals with medial compartment knee OA [103,154,203,212]. Medial joint laxity was attributed to this higher CCI during the loading phase, but how much increased MG activity accounted for this alteration in the CCI was not known [154,203]. Increased LG activity during early stance was also previously found for individuals with knee OA [212]. The current findings support that early stance increases in gastrocnemii activity were related to structural severity. Together, gastrocnemii activation characteristics were altered in those with moderate and severe structural impairments associated with medial

compartment knee OA, but changes were not systematic across the phases of gait or between the MG and LG.

QUADRICEPS

Quadriceps activation patterns were different in the OA groups compared with the asymptomatic group, with the waveforms clearly showing a distinct pattern for the KL IV group compared to all other groups (Figure 5.4). Less clear were the differences between the other two OA groups as indicated in Table 5.4, with no medial to lateral differential recruitment. Only subtle changes in late stance activity (PP3) were found between the KLII and KLIII groups with major alterations found for the KL IV group. The structural severity results cannot be compared directly to previous studies given the heterogeneity of structural severity and symptoms in these studies [102,103,214,216,284]. The study by Astephen *et al*., [13] is the only study in which direct comparisons can be made. A similarly defined moderate OA population was examined, but no relationships between any muscle activation features and structural severity assessed by a VAS of radiograph severity existed. The present study provides evidence that the systematic changes in muscle activation features are related to the structural changes captured by the KL score.

Knee joint muscle forces, particularly the quadriceps, contribute to the control of external moments in the sagittal and frontal plane during the stance phase of gait [229]. Proprioceptive deficits [22,135,228] found in individuals with knee OA and medial compartment laxity[154,203] found in individuals with medial compartment OA indicate that greater challenges for the neuromuscular system to maintain knee stability during gait exist since the structural (passive) and neural subsystems are altered. This supports the greater overall quadriceps amplitude found for individuals with moderate knee OA in the current study. Furthermore, the KL IV group was characterized by marked joint space narrowing, large osteophytes, severe sclerosis and bone attrition suggesting a significant alteration in joint stability and function, explaining the large alteration in quadriceps activation patterns.

This finding was in complete contrast to the reduced VL activity previously reported in individuals with severe knee OA (KL IV) compared to asymptomatic and

moderate OA (KLII and KLIII) groups [284]. Increased passive stability associated with increased osteophytosis was discussed as a potential mechanism for these null findings [284]. While Zeni *et al*., [284] categorized their groups based on KL-scores, level of symptoms and physical function were not described. Furthermore, gait velocity was progressively slower for each knee OA severity group. Given slower walking speeds were associated with decreased quadriceps amplitudes in asymptomatic controls [278], walking velocity differences also provide an explanation for their findings.

In the present study, higher overall quadriceps activity could reflect a response aimed to maintain a level of function similar to individuals with lesser structural severity (Table 5.1). While we cannot specifically determine how the structural impairments, characteristic of the KLIV score altered joint function, this group did have the highest overall quadriceps activation amplitude. This provides evidence that structural severity more so than severity classification based on a combination of factors [216] can explain overall quadriceps activation amplitude increases when self-selected walking velocities are comparable.

Examining the other waveform features (PP2 and PP3) illustrated that differences were not systematic throughout the gait cycle but were specific to gait cycle phases. The increase in mid-stance amplitudes (PP2) was not stepwise with increases in KL scores, although the KLIV group had the greatest increase, which was primarily driven by the RF activity as illustrated by the RF *PP2-score* in Table 5.3. This indicated that an increased demand was placed on the quadriceps during mid-stance, when the leg was in single support. This selective increase was not reported for a moderate knee OA group [102,214] however, elevated mid-stance amplitudes were found between individuals with moderate and severe knee OA [216]. The present findings provided evidence that structural severity was related to this differential increase in mid-stance quadriceps activation amplitude.

Finally, lower mid-stance quadriceps activity compared to late stance (PP3) activity was found in the asymptomatic individuals and the KL II group. This difference progressively decreased for the KL III and KL IV groups. The activation pattern has been found for individuals with moderate knee OA compared to an asymptomatic group [102,214] and for individuals with severe knee OA compared to moderate knee OA and asymptomatic groups [216] (Chapter 4). This reduction in quadriceps activity during late

stance found in the KL III and KL IV group can explain the reduced knee extensor moments associated with knee OA presented in the literature [20,86,123].

Collectively, quadriceps activations were altered in those with greater structural impairments but changes were not systematic across the phases of gait, were not different based on laterality nor were they progressive among structural severity levels.

HAMSTRINGS

All six hamstrings *PP-scores* changed in a progressive manner with increasing structural severity, with the significant interaction for the overall amplitude (PP1). Specifically, LH activity was related to structural severity, thus providing a possible explanation for findings in previous studies [102,161,214,216] where greater LH amplitudes in individuals with knee OA were found compared to asymptomatic individuals. In contrast, MH overall activity was not significantly altered, supporting previous findings where no MH differences have been found between asymptomatic individuals and individuals with moderate knee OA [102,214,284]. In individuals with severe knee OA, MH amplitude results were more varied despite structural severities comparable to those in the current study [103,216,284] . These inconsistencies suggest that MH activation alterations can be influenced by factors other than structural severity such as symptoms, functional status or muscle strength.

Our results support our hypotheses that moderate to severe structural changes were associated with LH and MH amplitude differences (PP1) and provide an explanation for similar findings in previous literature [86,102,161,214]. Increased hamstring co-activation has been estimated to increase control of knee stability [219]. A mechanical explanation exists for this increased activity related to structural severity. Medial compartment articular cartilage degeneration will cause compartment narrowing. This can result in increased tensile strain on lateral tibio-femoral joint structures given the adduction moment found during stance [15]. Lateral hamstrings have been shown to respond to this strain in experimental studies [32,129] providing a mechanism for increasing overall LH activity with increasing KL-score.

Previous studies have also found MH and LH temporally dependent activation differences to occur in individuals with moderate knee OA compared to an asymptomatic cohort [102,214]. In the current study, these interactions were not found. In both hamstrings, prolonged activation during mid-stance (PP2) and a burst of activity during early stance (PP3) were found in individuals with knee OA compared to the asymptomatic group. The KL IV group had the most prolonged hamstrings activity (PP2). Previously, individuals with severe knee OA based on structural severity, symptoms and function, were reported to have more prolonged LH than MH activity [216]. Consistent with the overall amplitude increase, higher hamstrings activity during mid-stance specifically, could reflect a response to increased stability demands during single leg stance.

A burst of activity following heel contact (PP3) has not been shown in other studies that included heterogeneous structural impairments, different self-selected walking velocities and different symptoms [102,214,216]. Shiavi *et al*.,[231] found that peak MH activity occurred during the early stance loading phase when asymptomatic individuals walk slower, but the comparable walking velocities among groups does not support this explanation. Non-weight bearing proprioception can be impaired in individuals with knee OA [22,135,228] but passive movement detection was not found to be related to structural severity [135]. Swing to stance transitions may be affected by impaired proprioception and provide a mechanism for PP3 findings that were not sensitive to level of structural severity. The altered temporal activation findings support that knee OA and structural severity characterized by KL IV, can influence hamstring activation dynamics between late swing, heel strike and mid-stance.

Collectively, hamstrings amplitude and temporal activation patterns were altered with medial compartment knee OA with some features related to structural severity. Different medial and lateral hamstring amplitudes occurred in individuals with moderate to severe structural severity. Concurrent with temporal activation differences, data support that muscle activation changes were not systematic across KL groups or phases of gait.

The current study relied on the KL radiographic scale to determine structural severity. While more sensitive non-invasive methods for detecting structural impairments exist [63,122,134], distinct KL-score groupings were identified. The known KL-score ceiling

effect was not considered problematic given the moderate OA classification of our group and early changes could presumably be present in the asymptomatic group as discussed below. Potential for error in classification exists given that radiographic procedures and joint positioning can alter the perception of joint space narrowing [166,205], which was why KL-scores were used. Despite the potential for error in classification, the differences in activation patterns in Figures 5.3 - 5.5 clearly illustrate a progressive change throughout the gait cycle associated with an increased KL-score. The quantitative data showed that these differences were large enough to reach statistical significance. What must be considered is that only conclusions based on those changes that are captured by the KL scoring can be made.

The main limitation with the present study was the cross-sectional, comparative design as causality between structural severity and altered muscle activation patterns could not be definitively determined. Causality could be established through longitudinal or experimental studies; however, the latter would not be feasible in human participants. The strength of the current study is grouping homogeneity, in particular the three OA groups, for variables known to alter joint mechanics and muscle activation. Few significant differences were found for group characteristics (Table 5.1), and no obvious systematic relationship with the severity results existed. While impairments to other joint structures not detected using the KL-score (i.e. meniscus) can influence gait mechanics and muscle activation independently of those captured by the KL grading scheme, these were assumed minimal as participants were excluded with knee injury other than a strain or sprain or with surgical interventions other than lavage.

A second limitation is that we did not have radiographs for the asymptomatic participants and thus the asymptomatic group could have structural joint changes. However, based on the reported KL II prevalence for asymptomatic individuals of similar ages (3-9%) [148] and our inclusion criteria, the prevalence of KL II scores in this sample was thought to be minimal. If asymptomatic individuals with KL II scores were included, this increased variability would reduce our ability to detect significant differences, hence the differences found are conservative estimates.

Despite the study limitations, these data provide convincing evidence to support that an association exists between structural severity and systematic alterations to knee

joint muscle activation patterns during gait. These results confirm the association among subsystems as conceptualized by the Panjabi model [189].

5.5 Conclusion

Specific knee joint muscle amplitude and temporal activation characteristics recorded during gait were associated with knee OA presence and increasing structural severity. LH and quadriceps overall amplitudes were increased and MG overall amplitudes were decreased with increases in OA structural changes determined using KL-scores. Amplitude differences between phases of the gait cycle were also found for the quadriceps and gastrocnemii. Significant activation imbalances of features throughout the gait cycle were found between the lateral:medial gastrocnemii and hamstrings for individuals with KL III and KL IV scores. This study provides evidence that most knee joint muscle activation patterns during gait are altered in a progressive manner with increasing level of structural severity.

CHAPTER 6

KNEE EFFUSION AFFECTS KNEE MECHANICS AND MUSCLE ACTIVITY DURING GAIT IN INDIVIDUALS WITH KNEE OSTEOARTHRITIS

6.1 INTRODUCTION

Knee osteoarthritis (OA) is a major contributor to chronic morbidity in older adults causing significant activity limitations [81]. Individuals with knee OA report pain [285], stiffness [102], giving way [71] and reduced tolerance to weight-bearing activities [285]. Gait analysis has served as a good model to understand activity limitations [11] where altered knee joint biomechanics [15,123,176] and muscle activation differences [16,44,102,161,212] are found in comparison to asymptomatic cohorts. Furthermore, knee OA severity [16,103,216,284] and structural severity (Chapter 5) are also associated with altered knee joint muscle activation patterns during gait.

Various explanations have been offered as to why muscle activation patterns are altered during gait in those with medial compartment knee OA. Mechanical factors include tibial adduction features during stance [7,86,161], medial compartment laxity [154,203], osteophytosis [284], muscle strength [102,103,212], gait velocity[16,214], and alterations to reduce compressive medial joint loading [16,102]. As well, explanations related to OA symptoms including pain [13], instability [154] and stiffness [102] have been provided. Several studies report proprioception deficits in knee OA [22,135,228], greater dynamic knee stiffness [61] during gait and knee effusion [169], a factor that was shown to influence quadriceps and hamstrings activation amplitudes in healthy individuals during gait [251]. The effect of knee effusion, found in individuals with moderate knee OA, on knee joint muscle activation patterns and gait mechanics was the focus of this study.

Effusions have been found in over half of the individuals being treated for knee OA [49,169] and can provide a mechanism for knee OA progression [17,49]. Knee effusion can occur secondary to intra-articular pathologies [66,120,169,206,209]. Two recent reviews discuss effusion to reflect impaired physiological function of the knee joint synovium as a result of ligament injury, loose bodies, cartilage degeneration or meniscal damage [26,217].

Most of what is known about knee joint effusion and muscle activation is based on experimental investigations of the quadriceps muscles [6,97,187,241,245]. Static, experimental acute effusion models showed that the quadriceps force generating capacity was consistently reduced and is independent of pain stimulus. This reduction has been attributed primarily to a neurophysiological inhibition mechanism [97,187,241]. The effect of

an acute effusion on other muscles crossing the knee joint such as the hamstrings and gastrocnemii has not been studied.

Given these effects, knee effusion has the potential to influence quadriceps muscle activation during gait [251]. Currently, only one study has examined whether an acute knee joint effusion altered gait mechanics and levels of muscle activation in healthy individuals [251]. Authors reported a reduction in mean quadriceps and increased mean hamstrings activation during early to mid-stance, altered sagittal plane motion, and reduced net external knee flexion and extension peak moments. Based on this combination of findings they concluded that individuals with an acute knee effusion develop a quadriceps avoidance gait [251].

The effect of effusion, characteristic of arthritis, on quadriceps inhibition during static testing was more variable. Evidence both supported and refuted that inhibition was associated with effusion [66,120,170]. The central activation ratios of individuals with knee OA, were shown to be within 5 % of asymptomatic individuals [72,155,212] where individuals with knee OA prior to total knee replacement surgery were within 10% [174]. While knee effusion status was not presented, individuals could have had effusion and yet, levels of maximal voluntary quadriceps activation were comparable to an asymptomatic cohort. Whether the results of the acute effusion studies reflect the role of effusion to alter muscle activation characteristics, gait mechanics or muscle strength in individuals with combined knee OA and joint effusion has yet to be established.

A reduction in muscle activity because of effusion can negatively influence normal knee function while walking such as compromising knee joint stability and impact load attenuation. If muscle activity is increased, greater joint loading [7,160,229] and metabolic demand [78,171] during gait would be expected. Reduced knee flexion angles and net external knee flexion moments in early stance, as shown for healthy individuals with an acute effusion[251], may alter impact load attenuation. It is currently unknown if knee joint muscle activation and gait biomechanics are altered when individuals with knee OA and knee joint effusion walk.

Assessing knee effusion is an important component of knee OA evaluation [47,106]. Imaging techniques exist, including ultrasonography [49,113,149] and magnetic resonance imaging [106,169,209,223], that quantify the amount of effusion. Less sophisticated tests have

also been developed. The bulge sign/test[47,162], also referred to as the stroke test [243] has been shown to be a reliable [47,243] method of assessing knee joint effusion. In addition, Hauzeur *et al*., [85] found moderate agreement between a clinical evaluation, which included the bulge sign and ultrasonography evaluation for knee effusion/no effusion. Together these studies support the use of the bulge sign as a reliable and valid method for identifying whether knee effusion is present or absent in individuals with knee OA.

Given that acute knee effusions in healthy individuals alter gait mechanics and muscle activation levels, it is plausible that knee effusion is associated with altered knee mechanics and muscle activation patterns in individuals with knee OA. Therefore, the objective of this study was to determine whether knee joint effusion in those with moderate knee OA was associated with altered sagittal plane knee joint mechanics and knee joint muscle activation patterns during walking. Three null hypotheses were examined, i) sagittal plane knee angle and moments of force characteristics are not different ii) knee joint muscle amplitude and temporal activation patterns are not different and iii) lateral and medial knee joint muscle activation patterns are not different within each muscle grouping (gastrocnemii, quadriceps, hamstrings). All hypotheses will be tested between individuals with knee OA that have knee effusion and do not have knee effusion.

6.2 METHODOLOGY

6.2.1 Participants

Participants with unilateral symptomatic knee OA (n=40) were recruited from the caseload of one high volume orthopedic surgeon (2006-2010). All participants were required to meet a functional status criterion, consistent with a moderate OA classification, based on self-report indicating their ability to reciprocally ascend and descend 10 stairs, safely walk one city block, and jog five meters [102]. Participants were not scheduled for total knee arthroplasty at the time of testing. A clinical diagnosis of knee OA was made using the American College of Rheumatology guidelines [3]. Standard anterior-posterior and lateral radiographs were scored using the Kellgren Lawrence

ordinal radiographic scale [125]. Individuals with lateral compartment joint space narrowing greater than medial compartment joint space narrowing [224] were excluded. All participants were required to have no fracture or previous lower extremity injury other than a sprain or strain (i.e. no anterior cruciate ligament injuries). Participants were excluded if cardiovascular/respiratory disease, neurological disorders, or musculoskeletal disorders other than their knee OA were reported that affected their ability to safely complete the data collection protocol (i.e. stroke, Parkinson's disease, myocardial infarct, arrhythmias). Written informed consent was obtained in accordance with the Institutional Research Ethics Board.

6.2.2 Procedures

The Western Ontario McMaster Osteoarthritis Index (WOMAC-LK3.1) was completed by all participants and height and mass were recorded upon arrival to the lab. The most symptomatic knee was examined and prepared for testing. Current level of knee pain was quantified using a verbal scale (0 indicating no pain, 10 indicating extreme pain). Knee effusion was assessed by an experienced orthopaedic physiotherapist using the bulge test/sign [47,162,243]. The bulge sign has been shown to be highly reliable (R_c=0.97) [47] for detecting effusion/no effusion and substantial agreement between raters to detect grade of effusion was found (Cohens Kappa = 0.61) [243]. Participants were assigned to the effusion or no effusion group based on the outcomes of this test. Active flexion and extension range of motion was measured for both knees with a standard goniometer. This testing was completed prior to preparation for gait analysis.

Standard procedures previously reported for surface electromyography [102] were used to measure muscle activity during gait, consistent with current guidelines as suggested by the International Society of Electrophysiology and Kinesiology and SENIAM (Surface EMG for the Non-Invasive Assessment of Muscles) [226]. Skin preparation included light shaving and abrading with 70% alcohol wipes. Surface electrodes were placed in a bipolar configuration (Ag/AgCl, 10 mm diameter, 20 mm interelectrode distance) over the lateral (LG) and medial gastrocnemius (MG), vastus medialis (VM) and lateralis (VL), rectus femoris (RF), semitendinosis/membranosis

(MH) and biceps femoris (LH). Muscle palpation and a series of isometric contractions for specific muscle groups [127] were used for signal validation and gain adjustment. Signals were amplified using an AMT-8 (Bortec, Inc., Calgary, Alberta, Canada), eight-channel EMG system (Input Impedance: ~10GΩ, CMRR:115dB at 60 Hz, Band-pass (10-1000 Hz)).

Infrared emitting diode (IRED) skin surface markers were affixed to the lateral aspect of the lower extremity. Triangular sets of IRED markers were secured to the pelvis, femur, tibia and foot. Single IRED markers were placed on the lateral malleolus, lateral epicondyle and greater trochanter of the femur and lateral aspect of the shoulder. After a standing calibration trial, the digitization of eight virtual points on predefined anatomical landmarks was completed, including right and left anterior superior iliac spines, medial epicondyle of the femur, fibular head, tibial tuberosity, medial malleolus, base of the second metatarsal and center of the posterior calcaneous [144].

6.2.3 Data Acquisition

Three-dimensional lower extremity motion during gait was recorded at 100Hz using two optoelectronic motion analysis sensors (Optotrak 3020™, Northern Digital Inc., Waterloo, ON, Canada). Three-dimensional ground reaction forces were collected from a single force plate (AMTI™, Advanced Mechanical Technology Incorporation, Newton, MA, USA) that was aligned to the global coordinates of the motion capture system. Skin surface markers, electrodes, pre-amps and lead wires were secured with adhesive tape and nylon stocking.

After three familiarization trials, participants were instructed to complete at least five walking trials at a consistent self-selected velocity (+/- 10%) along a six-meter walkway. Following the walking trials, baseline muscle activity was recorded during supine lying. For amplitude normalization, participants completed at least one practice and two standardized three-second maximal voluntary isometric contraction (MVIC) trials of i) knee extension at 45^{o}, ii) knee extension at 15^{o} , iii) knee flexion at 55^{o} , iv) knee flexion at 15^{o}, v) knee extension-hip flexion at 45^{o} vi) prone knee flexion at 55^{o}, vii) sitting plantarflexion viii) standing unilateral plantar flexion [102,215] (See Appendix A.1).

Torque output during exercises one to four and seven was collected using a Cybex™ Isokinetic dynamometer (Lumex, NY, USA). A 60-second rest period separated each contraction, and standardized verbal encouragement was given [155]. All force plate, EMG and torque signals were analog to digitally converted at 1000Hz or 2000Hz[#] (16bit, +/- 2V) using the analogue data capture feature of the Optotrak™ system and stored for processing.

6.2.4 Data Processing

Raw electromyographic signals were processed through custom MatLab™ Ver 7.1 programs (The Mathworks Inc., Natick, Massachusetts, USA). All signals were corrected for bias and converted to micro-volts, full wave rectified, low-pass filtered (Butterworth, 4th order, Fc-6Hz) and amplitude normalized to the highest 100ms window from the MVIC trials [102]. Isometric torque values were corrected for gravity and the maximum torque for a 500ms window was identified for each exercise. The average of the two trials was recorded as the maximal torque in Newton-meters and normalized to body mass (Nm/kg).

Technical and local anatomical bone embedded coordinate systems for the pelvis, thigh, tibia and foot were derived from the IRED markers and digitized points [39,50]. Joint angles were specified through Euler rotations using standard convention [79]. Net external sagittal plane knee moments were calculated using an inverse dynamics model which combined ground reaction force and moment data, limb kinematics, limb anthropometrics and inertial properties [255] and normalized to body mass (Nm/kg). Electromyograms, sagittal plane knee angles and net external moments were time normalized to 100% of the gait cycle. For the majority of subjects, an ensemble average (for each muscle) was calculated from at least five walking trials. Four trials were used in one individual.

[#] The sampling rate was changed in September 2008. Refer to Appendix C for details pertaining to sampling rate differences and EMG analysis

6.2.5 Analysis

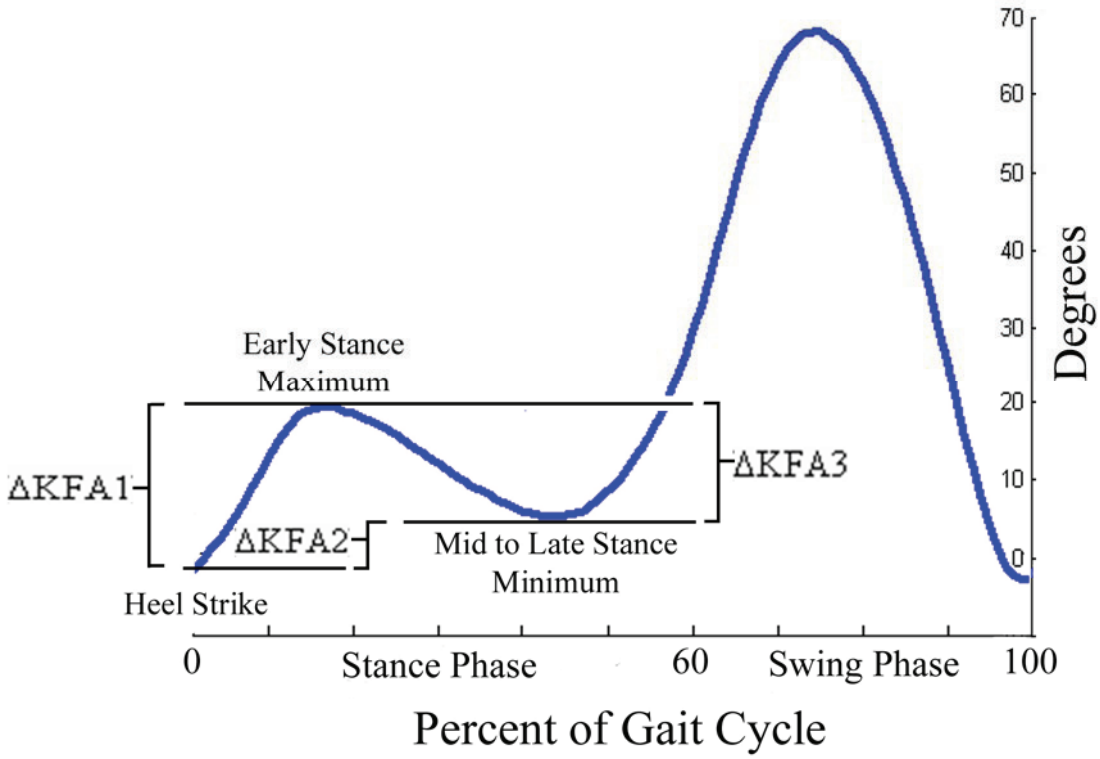

Figure 6.1: Variables used in the analysis of the sagittal plane knee angles.

WOMAC scores were tabulated. Discrete sagittal plane knee angles were determined i) at heel strike, ii) early stance maximum and iii) mid to late stance minimum. From these three angles, three difference measures were determined i) between heel strike and early stance maximum (ΔKFA1), ii), heel strike and mid to late stance minimum (ΔKFA2), and iii) early stance maximum and mid to late stance minimum (ΔKFA3) (Figure 6.1). From the sagittal plane knee moment waveforms, peak flexion and late stance extension values were identified.

Principal component analysis (PCA) was used to capture amplitude and temporal electromyographic waveform features using custom MatLab™ Ver.7.1 programs (The Mathworks Inc., Natick, Massachusetts, USA). This multivariate statistical technique has been previously described in detail [102,214]. Briefly, three separate analyses were performed, one for each muscle grouping (quadriceps (VL, VM, RF), hamstrings (LH, MH) and gastrocnemii (LG, MG)). For each muscle grouping a matrix of the original

waveform data (example for quadriceps 120 (40 subjects x 3 muscles) X 101 matrix was factored to yield a set of uncorrelated eigenvectors called principal patterns. A percent trace was calculated to determine how much variability was contained in each principal pattern. Principal patterns (PP1, PP2 etc.) that together explained greater than 90% of the variability in the original waveforms were retained for further analysis. Principal pattern scores (*PP-Scores*) were computed to provide a weighting coefficient for how each principal pattern related to each measured waveform. *PP-scores* were utilized for statistical hypothesis testing.

6.2.5 Statistical Analysis

Independent student t-tests were used to test for significant differences in pain, WOMAC, age, mass, height, body mass index (BMI), stride characteristics, strength and measures of sagittal plane knee joint angles (discrete and difference measures) and moments between the effusion and no effusion groups. A paired t-test was used to test for significant differences in active range of motion difference measures between affected and unaffected knees. Differences in Kellgren-Lawrence radiographic scores between groups were determined using a Mann-Whitney U-test. Normality and equal variance of the *PP-scores* were determined from Kolmogorov-Smirnov and Levene's tests, respectively. A two-factor mixed model ANOVA tested for significant group (between) and muscle (within) main effects and interactions (alpha=0.05). Post-hoc testing was employed for determining pair-wise significant findings using Bonferonni adjusted alpha levels. Statistical procedures were completed in Minitab™ Ver.16 (Minitab Inc. State College, PA, USA).

6.3 RESULTS

No significant differences were found ($p>0.05$) between the effusion and no effusion groups for characteristics in Table 6.1 with the exception of active knee range of motion (goniometer measure). Active knee flexion was reduced 7^o and 5^o for the affected OA knee, compared to the unaffected knee, in individuals with and without knee effusion

respectively ($p<0.05$). For individuals with effusion, active knee extension was reduced 4^o when compared to the unaffected knee ($p<0.05$).

Table 6.1: Mean and standard deviation (SD) subject demographics, gait characteristics, knee joint strength and range of motion characteristics and WOMAC scores.

	No Effusion	Effusion	P-Value
N	20	20	
# males	16	14	
Age (years)	54 (8)	58 (7)	0.115
Mass (kg)	91.7 (17.3)	91.1 (20.4)	0.926
BMI (kg/m^2)	29.7 (5.0)	30.6 (5.8)	0.600
Pain (# / 10)	1.3 (1.8)	1.4 (1.8)	0.896
Gait Velocity (m/s)	1.27 (0.18)	1.28 (0.12)	0.769
Stride Length (m)	1.43 (0.17)	1.42 (0.10)	0.925
Strength (Nm)			
KE45	1.37 (0.46)	1.41 (0.39)	0.774
KE15	0.90 (0.32)	0.88 (0.28)	0.829
KF55	0.71 (0.29)	0.68 (0.22)	0.741
KF15	0.60 (0.21)	0.50 (0.15)	0.110
PF	1.15 (0.36)	1.05 (0.35)	0.364
WOMAC			
Pain	6.3 (3.0)	5.3 (2.1)	0.258
Stiffness	3.4 (1.1)	3.4 (1.6)	0.970
Physical Function	18.2 (10.3)	17.6 (7.9)	0.825
KL-scores (median)	II	II ^	0.499
Active Knee Flexion (deg)			
Affected	128 (12)	125 (8)	
Unaffected	132 (9)	132 (5)	
Diff.	5	7	
P-value	**0.024**	**0.000**	
Active Knee Extension (deg)			
Affected	0 (3)	-2 (6)	
Unaffected	1 (2)	2 (3)	
Diff.	1	4	
P-value	0.081	**0.005**	

^ Radiographs were not available for four subjects at the time of scoring
Bolded p-values are significant at $p<0.05$.

Table 6.2: Mean and standard deviation (SD) absolute angles and difference values for sagittal plane knee motion and moments of force.

Measure	No Effusion	Effusion	Diff.	P-Value
Absolute Angles (degrees of knee flexion)				
Heel Strike	-5.3 (6.4)	-4.9 (5.9)	0.4	0.872
Early Stance Maximum	13.5 (7.8)	16.9 (6.5)	3.4	0.143
Mid to Late Stance Minimum	2.9 (4.6)	8.6 (7.5)	5.7	**0.007**
Motion (degrees)				
Heel strike to Early Stance Maximum (ΔKFA1)	18.7 (6.0)	21.8 (7.0)	3.1	0.142
Heel strike to Mid to Late Stance Minimum (ΔKFA2)	8.2 (4.5)	13.5 (6.7)	5.3	**0.005**
Early Stance Maximum to Mid to Late Stance Minimum (ΔKFA3)	10.6 (7.2)	8.3 (5.6)	2.2	0.283
Moments of Force (Nm/kg)				
Peak Flexion	0.27 (0.3)	0.29 (0.2)	0.02	0.884
Peak Late Stance Extension	-0.35 (0.19)	-0.22 (0.22)	0.13	0.070

Bolded p-values are significant at $p<0.05$

Sagittal plane knee motion and net external moment of force waveforms are shown (Figure 6.2). Discrete measures extracted from these waveforms are found in Table 6.2. While no significant differences were found for angles at heel strike or early stance maximum, the difference between heel strike and the mid to late stance minimum (ΔKFA2) was higher ($p<0.05$) in individuals with effusion. This was explained by a greater mid to late stance minimum angle for the effusion group ($p<0.05$). The late stance peak net external extension moment was increased 37% (0.13 Nm/kg) in individuals with effusion, although this was not significant ($p=0.07$).

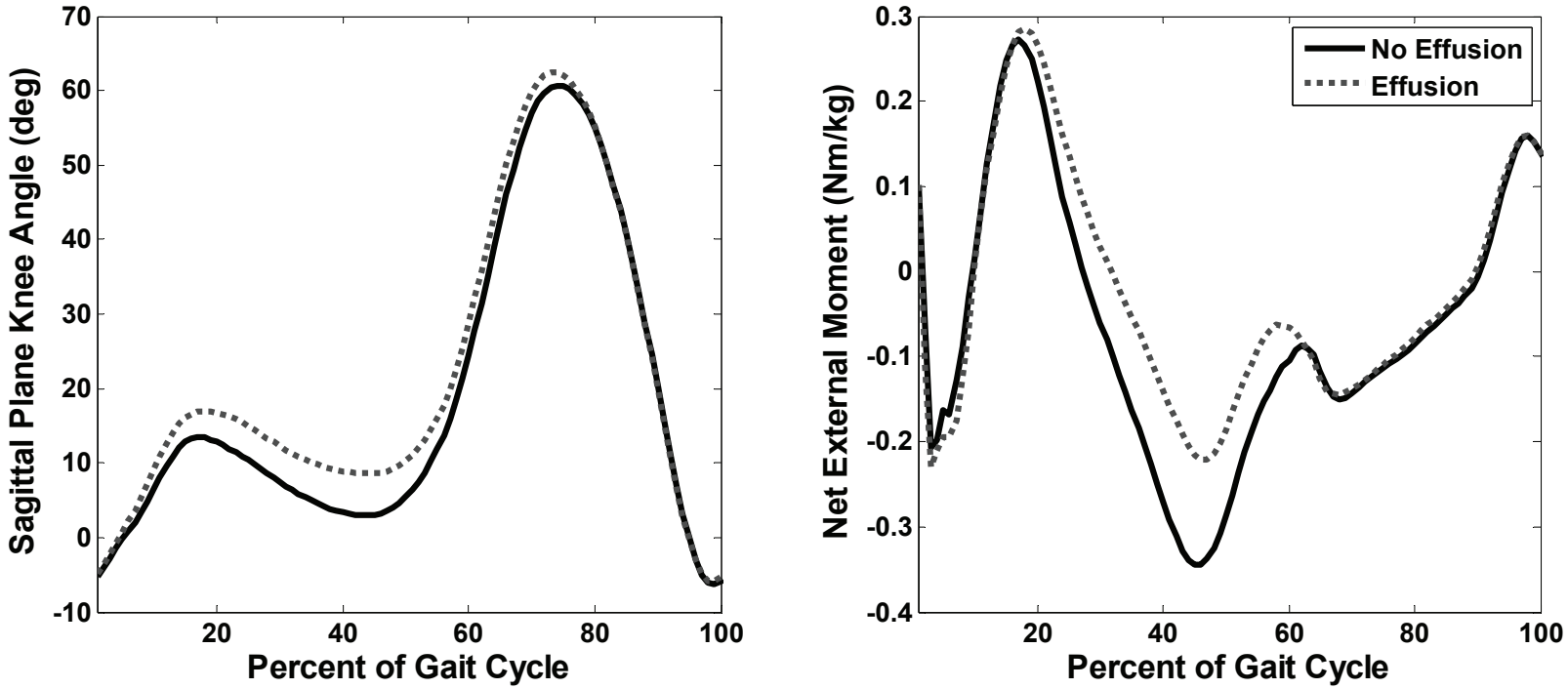

Figure 6.2: Ensemble-averaged sagittal plane knee angles (left panel) and net external sagittal plane moments of force (right panel) for individuals with effusion (dotted) and without knee effusion (solid).

Ensemble average waveforms for the two groups are shown in Figures 6.3 – 6.5. Differences occurred throughout the gait cycle and were not consistent between or amongst muscles. For each muscle group, three features were identified, which together explained greater than 90% of the original waveform variability. A description of the principal pattern characteristic and the statistical results are found in Table 6.3 along with the *PP-scores*.

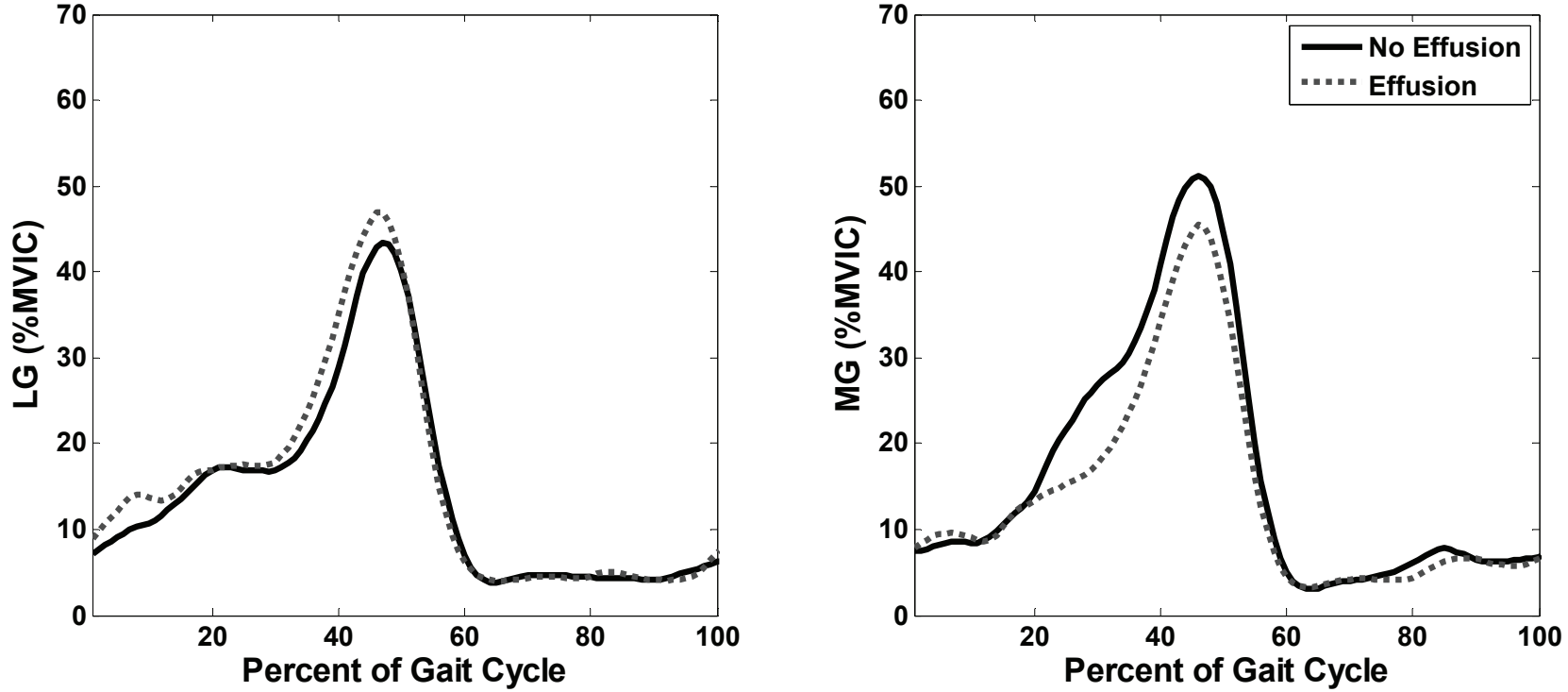

Figure 6.3: Ensemble-averaged electromyogram of lateral gastrocnemius (left panel) and medial gastrocnemius (right panel) for individuals with effusion (dotted) and without knee effusion (solid). Percent MVIC is on the y-axis and percent of gait cycle on the x-axis.

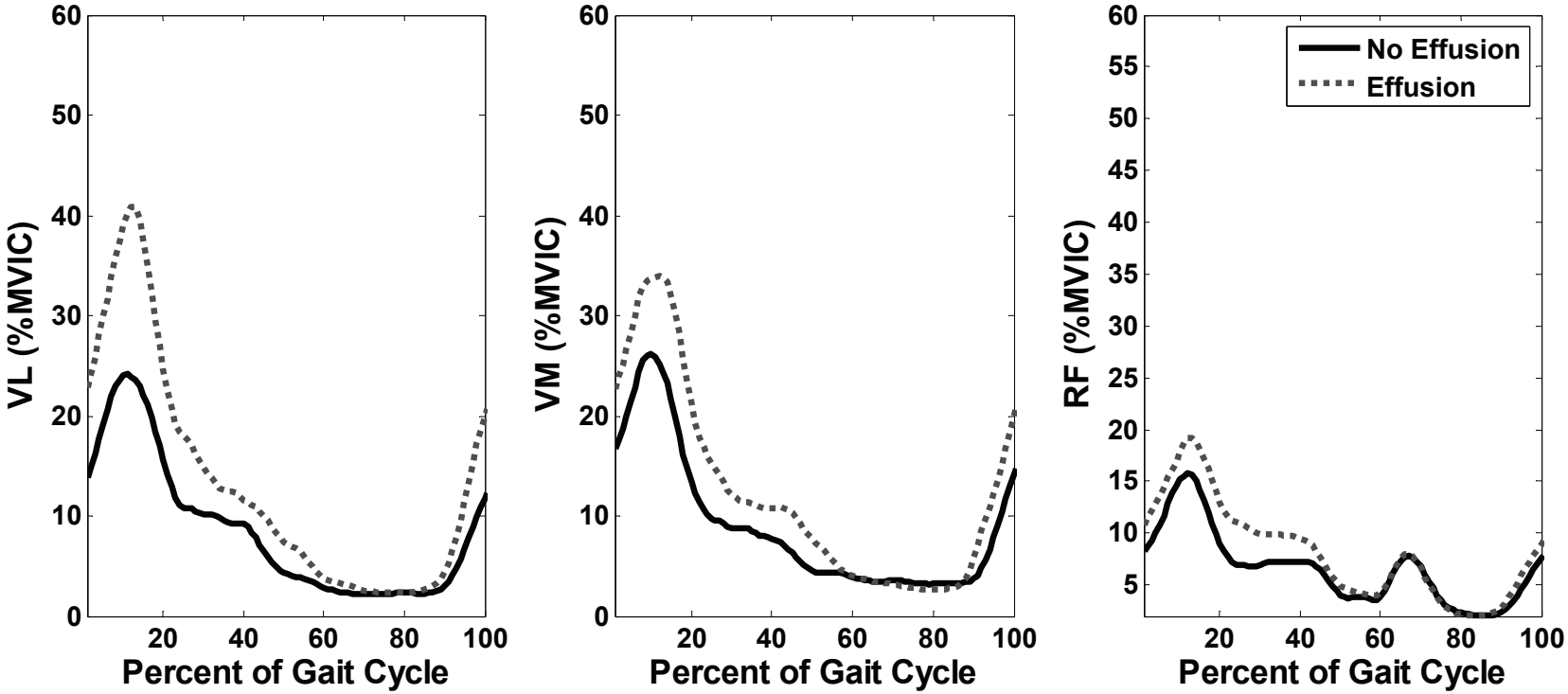

Figure 6.4: Ensemble-averaged electromyogram of vastus lateralis (left panel), vastus medialis (middle panel) and rectus femoris (right panel) for individuals with effusion (dotted) and without knee effusion (solid). Percent MVIC is on the y-axis and percent of gait cycle on the x-axis.

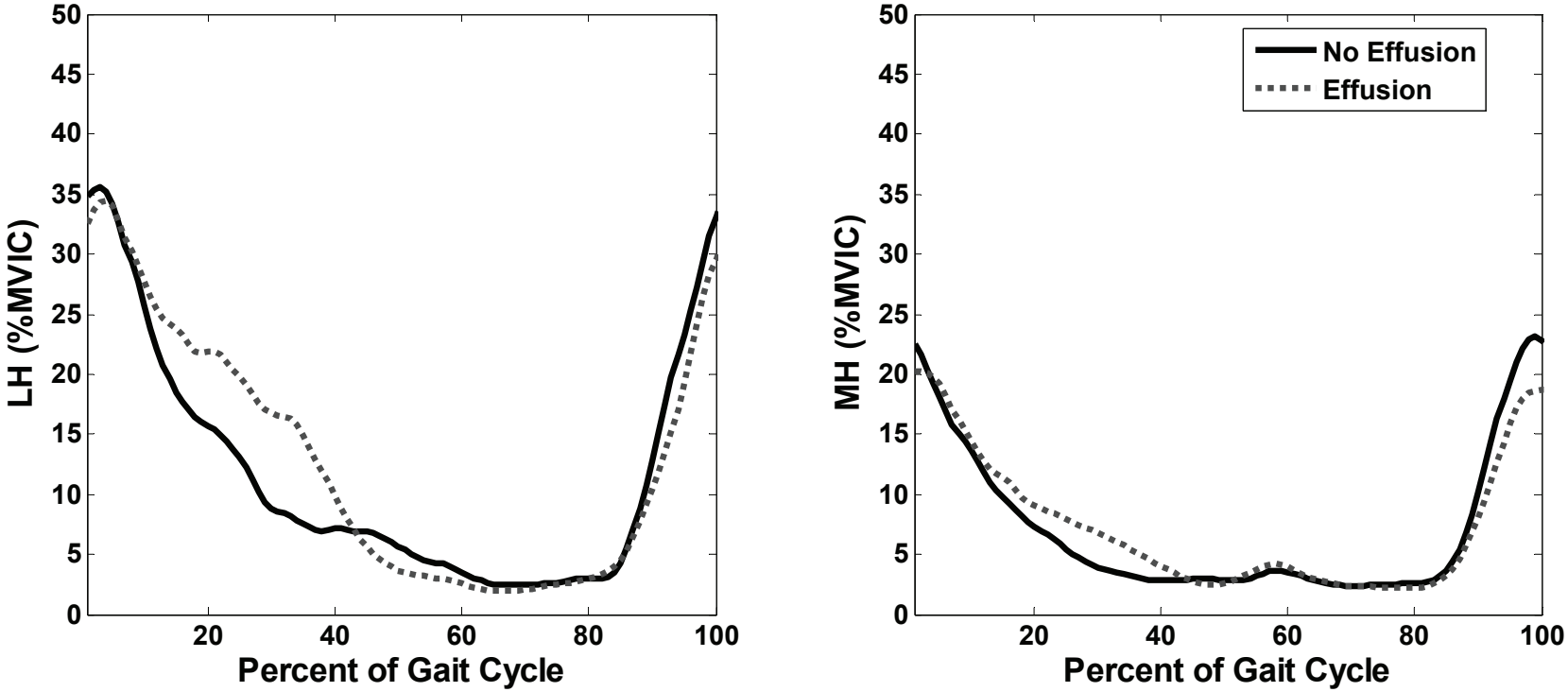

Figure 6.5: Ensemble-averaged electromyogram of lateral hamstring (left panel) and medial hamstring (right panel) for individuals with effusion (dotted) and without knee effusion (solid). Percent MVIC is on the y-axis and percent of gait cycle on the x-axis.

Three principal patterns captured over 95% of the gastrocnemii waveform variability. No significant group differences ($p>0.05$) were identified for each of the three patterns. A significant muscle main effect for the phase shift pattern was found ($p<0.05$) where MG had greater scores than LG indicating an earlier increase in activation for MG compared to LG.

Ninety-six percent of the quadriceps waveform variability was accounted for by three principal patterns. Unequal variance and non-normality were apparent in the *PP-scores* and therefore the data were transformed. Significant group and muscle main effects ($p<0.05$) were found for the transformed *PP1-scores* as indicated in Table 6.3. Greater *PP1-scores* were found for individuals in the effusion group, indicating a higher overall amplitude as illustrated in Figure 6.4.

Three principal patterns captured over 95% of the hamstrings waveform variability. Unequal variance and non-normality were apparent in the *PP1* and *PP2-scores* and again, data were transformed. A significant muscle main effect ($p<0.05$) was found for the transformed *PP1-scores* (overall magnitude) and *PP2-scores* (prolonged stance phase activity) where, LH had greater amplitudes and prolonged activation compared to MH (Table 6.3 and Figure 6.5). *PP2-scores* were greater in individuals with effusion compared to those without effusion ($p=0.056$).

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Table 6.3: Principal pattern description, principal pattern scores and P-values for *PP-score* main effects and interactions

	Principal Pattern Description	Group	Muscle	Group x Muscle	Principal Pattern Scores					
					No Effusion			Effusion		
Gastrocnemii					**LG**		**MG**	**LG**		**MG**
PP1 - scores	Greater scores = Greater amplitude	0.617	0.368	0.083	179.5 (63.4)		217.8 (100.0)	195.0 (74.2)		182.7 (61.3)
PP2 - scores	Greater scores = Earlier activity	0.830	**0.002**	0.114	-17.4 (29.2)		9.2 (44.6)	-6.7 (27.1)		2.5 (29.7)
PP3 - scores	Greater scores = larger difference between early and late stance activity levels	0.860	0.359	0.568	-0.81 (44.0)		1.1 (49.5)	-1.9 (35.7)		-6.3 (29.3)
Quadriceps					**VL**	**VM**	**RF**	**VL**	**VM**	**RF**
PP1 - scores	Greater scores = Greater amplitude	**0.045**	**0.000**	0.131	109.8 (52.3)	113.2 (62.9)	73.0 (37.3)	175.5 (97.0)	157.9 (95.6)	92.8 (45.2)
PP2 - scores	Greater scores = larger difference between early and mid-late stance activity levels	0.996	**0.000**	0.095	-1.0 (27.4)	7.4 (22.6)	-10.2 (22.7)	4.2 (40.7)	7.3 (47.0)	-14.7 (23.5)
PP3 - scores	Greater scores = higher activity during late stance compared to mid-stance and swing phase	0.600	**0.000**	0.183	-2.1 (22.4)	1.3 (25.4)	2.5 (11.7)	-10.0 (17.1)	-1.1 (26.0)	2.9 (10.6)
Hamstrings					**LH**		**MH**	**LH**		**MH**
PP1 - scores	Greater scores = Greater amplitude	0.821	**0.000**	0.552	157.2 (87.3)		94.0 (42.7)	166.7 (84.2)		93.4 (40.7)
PP2 - scores	Greater scores = higher activity during mid-stance and late swing burst of activity attenuation	0.056	**0.045**	0.507	-13.8 (45.1)		-24.5 (28.3)	18.5 (57.3)		-8.4 (25.6)
PP3 - scores	Greater scores = burst of activity during early stance compared to lower activity during mid gait cycle	0.739	0.080	0.615	1.4 (26.7)		-6.2 (19.7)	1.8 (26.6)		-2.5 (12.3)

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6.4 DISCUSSION

The current findings showed that individuals with moderate knee OA and effusion walked with altered knee joint motion, moments of force and knee joint muscle activation characteristics but only specific features were significantly different. Individuals with effusion walked in more flexion during mid to late stance. Greater overall quadriceps activity, and prolonged hamstrings activity during mid-stance stance were found. These results occurred despite similarities in strength, WOMAC scores and pain scores during data collection, subject anthropometrics, KL–scores and walking velocity.

Consistent with the results of Torry *et al*., [251], a study of acute knee effusions in healthy participants, the effusion group in the present study walked in a more flexed knee position during mid to late stance (Figure 6.2). Also consistent with Torry *et al*., [251], late stance sagittal plane knee extension moments were reduced for the effusion group (37%), although the latter difference was not statistically significant. The sagittal plane peak moment during early stance was not different between the two OA groups in the current study, a finding that was not consistent with Torry *et al*., [251]. They reported a decreased early stance flexion moment even for the lowest level of effusion ($20cm^3$) in healthy participants compared to the no effusion condition [251]. This decrease in knee flexion moment was thought to reflect a quadriceps avoidance gait and was confirmed by a reduction in quadriceps activation amplitudes. Their findings were consistent with quadriceps inhibition reported during static, experimental acute effusion studies [97,241]. Torry *et al*., [251] reported that increasing levels of effusion did not generate a pain response, but there was no report on walking velocity between the conditions. Early stance sagittal plane knee moments [144] and quadriceps activity amplitudes [231] can be reduced by decreased walking velocity, making it difficult to ascertain the effect of knee joint effusion alone. In the current study, pain and walking velocity did not differ between the two OA groups, nor did the peak early stance sagittal plane knee moments or early stance knee flexion angles. Our findings of higher quadriceps amplitudes in the effusion group do not support the inhibition mechanism to account for alterations to early stance gait mechanics proposed by Torry *et al*., [251].

Higher quadriceps activity was found in individuals with effusion despite comparable strength, mass, gait velocity, symptoms and KL-scores between groups. This finding contrasts the results of Torry *et al*., [251], where quadriceps activity with an acute effusion was significantly reduced during the first 50% of stance. Acute knee joint effusion has been consistently shown to create quadriceps arthrogenic muscle inhibition, thought to prevent increases in intra-articular pressure that can result from uninhibited quadriceps activity [170]; supporting the quadriceps avoidance theory reported by Torry *et al*., [251]. In contrast, the inhibitory influence on quadriceps muscle strength is more variable in non-acute effusion studies [66,120,170], suggesting that alterations in quadriceps activation seen in the current study are possibly related to altered joint mechanics.

Knee joint muscle forces, particularly the quadriceps, contribute to the control of external moments in the sagittal and frontal plane during the stance phase of gait [229]. It is estimated that hamstrings co-activation during stance assists to maintain knee joint stability [219]. Cho *et al*., [45] found that joint effusion impairs knee joint proprioceptive function in individuals with OA. Greater non-weightbearing, compared to weightbearing proprioceptive deficits were found [45]. Thus, effusion may impair the body's ability to sense and respond to mechanics associated with swing phase to heel strike transitions. Proprioceptive deficits provide an explanation for the higher quadriceps activity found during late swing and early stance. Furthermore, Simkin *et al*., [234] provided a theoretical rational, based on available evidence, to support that effusions reduce the stabilizing features of sub-atmospheric intra-articular pressure in synovial joints. This may also influence proprioception and explain findings of Cho *et al*., [45]. In combination, these effects would increase the requirement of the neuromuscular system, particularly the quadriceps, to maintain knee stability.

This elevated quadriceps activity also continued into mid-stance, where prolonged hamstrings activation was found (Figure 6.5). This was identified by PP2, partially corroborating the findings of Torry *et al.,* [251] for acute effusion. Higher quadriceps activity and hamstrings co-activation in individuals with effusion during mid-stance can be partially explained as a response to increased joint stability demands associated with the greater flexed knee position. The reasons for this knee flexed position are not completely clear, but higher intra-articular knee pressures were reported when the knee

joint was extended in comparison to mid-range knee flexion angles of approximately 20-40 degrees [152,272]. Attempts to minimize this higher intra-articular knee pressures provides a possible explanation for why individuals with effusion adopted a knee flexed position during mid to late stance in the current study and in response to an acute effusion [251]. *In vitro* studies showed that joint stiffness for both varus/valgus bending and tibial torsion was increased as the knee joint was extended [165]. The increased knee flexed position has the potential to minimize the stabilization characteristics that ligamentous structures provide [165]. In combination with the increased knee extension moment, these alterations will increase the requirement of the neuromuscular system to maintain joint stability.

Higher levels of muscle co-activity, while contributing to joint stability can however lead to altered joint loading [7,160,229], metabolic cost [78,171], and potentially increased intra-articular pressures [170] and muscular fatigue. It is estimated that healthy older adults take between 6000 and 8500 steps in a day where individuals with disabilities and chronic illnesses can take up to 5500 steps in a day [252]. Increases in muscle activation during walking might have implications for cumulative joint loading, as has been discussed in the context of gait biomechanics [163].

In contrast to the alterations in quadriceps and hamstrings activation, the gastrocnemii were not affected by effusion in this cohort. The reduced medial gastrocnemius amplitude, phase shifted activity and early to late stance gastrocnemii amplitude differences have been previously reported and related to knee OA severity [102,214,216] (Chapter 5). So while, sagittal plane knee mechanics were altered (Table 6.2) amplitude or temporal activation characteristics of the gastrocnemius muscles were not. Thus, mid to late stance knee joint mechanics and effusion have minimal effect on gastrocnemii activation during gait in those with OA.

Diminutive inhibition was reported to occur with effusions in individuals with arthritis [120,170], however the possibility still exists that a maximal effort contraction during the normalization exercises was not achieved in the effusion group because of inhibition. Lower activity during MVIC exercises could explain the overall higher quadriceps activity in individuals with effusion. While plausible, a number of reasons challenge this explanation. For these standardized exercises, comparable quadriceps strength was found (Table 6.1) between the effusion and no effusion groups. Maximal levels of activity for

normalization were obtained from exercises that positioned the leg differently from earlier studies on inhibition [66] and pain levels were not increased during testing and were similar between groups. Furthermore, while acknowledging the limitations of reporting raw EMG amplitudes, these values were similar between the two groups for the MVIC exercises (not shown). This was consistent with a number of studies that have assessed the ability of individuals with knee OA to volitionally generate maximum knee extensor force using burst superimposition testing [72,155,174,212]. The central activation ratios of individuals with knee OA, were shown to be within 5 % of asymptomatic individuals [72,155,212]. While knee effusion was not discussed, levels of maximal voluntary quadriceps activation were minimally affected by knee OA. Therefore, quadriceps inhibition associated with effusion during the MVIC was not likely the main mechanism for the increased quadriceps activity during gait.

The bulge sign provided a dichotomous evaluation of knee effusion and previous work demonstrated reliability of this test and moderate agreement with ultrasonography [47,85,243]. However, there is the potential for false negative tests. Individuals classified as not having effusion may have had a small or conversely a very large effusion not detectable using the bulge sign. The current findings would thus be considered a conservative estimate of the difference. Using an instrument, such as ultrasonography, with improved sensitivity and specificity could determine whether a dose response exists.

As with any cross-sectional comparative study, there are limitations with drawing conclusions regarding a causal effect of the independent variable. Future longitudinal studies or studies where effusion is evoked or aspirated may provide further insight. Strength of the present study however is the homogeneity between the two groups for variables known to alter joint mechanics and muscle activation including muscle strength, symptoms (pain), walking velocity and structural impairments. The similarity in structural impairments was particularly important since effusion was more prevalent in those with higher KL grades [139] and muscle activation pattern differences have been related to knee OA severity difference [15,103,216] (Chapter 5). Furthermore, while impairments to other joint structures not detected using the KL-score [26,209,217] (i.e. meniscus) could be present, possibly influencing gait mechanics and muscle activation independently of knee effusion, the exclusion criteria minimized that potential.

In summary, this was the first study to examine the relationship between knee joint effusion in individuals with moderate knee OA and alterations in gait mechanics and muscle activation patterns. It was not possible to confirm the duration of effusion, but radiographic evidence suggests long-standing knee OA and hence the assumption was that effusion was not the result of a single episode. The findings for the muscle activation effects differed from the acute effusion models. While the latter has more experimental control, the differences suggested that the acute effusion model does not necessarily provide an accurate picture of the alterations found in those with knee OA. Greater muscle activity found in the quadriceps and hamstrings for the effusion group, although thought to maintain joint stability, can have implications for increased joint loading and metabolic demand during walking. Knee effusion reduction may be a viable option to improve the biomechanical environment of the knee during gait in individuals with moderate knee OA.

6.5 Conclusion

In conclusion, sagittal plane knee mechanics and muscle activation patterns were altered in individuals with knee OA and knee joint effusion. The knee was generally more flexed during stance with significantly less extension motion and a reduced extension moment during mid to late stance. Higher quadriceps and prolonged hamstrings activity during mid-stance were found with no effect on gastrocnemii. Alterations occurred despite homogeneity between groups with respect to age, mass, lower extremity muscle strength, walking velocity, WOMAC scores, symptoms and KL-scores. These alterations to joint mechanics and muscle activations can have consequences for effective joint stability maintenance and long-term joint function in individuals with moderate knee OA.

CHAPTER 7

CONCLUSION

7.1 SUMMARY AND CONCLUSION

The aim of this dissertation was to improve our understanding of how muscle activation patterns during gait were altered across the knee OA severity spectrum and to examine how factors related to the OA process were associated with these alterations. While knee OA has been associated with impaired function, in particular walking, the forces acting on the knee joint during walking have also been considered in knee OA development and progression. This reciprocal relationship was captured in the ICF framework (Figure 1.1). While this framework is all encompassing from impairment to participation restrictions, this dissertation focused on the anatomical and physiological impairment and activity components to better understand that relationship. Part of the rationale for this approach was that symptoms and joint impairments are not well correlated and it has recently been recognized that these two entities should be considered separately to better understand the OA process [145]. Furthermore symptoms are based primarily on self-reports with few objective metrics to aid in clinical decision-making for the management of knee OA. Thus, the goal of this research was to contribute to the development of gait-based metrics that can facilitate knee OA diagnosis and monitor knee OA progression.

Kinematic and kinetic data during walking have been extensively studied in knee OA. The present study exploited the interrelationship between the passive osteoligamentous sub-system, active muscular subsystem and neural subsystem as described by Panjabi [189] for the control of knee stability during gait. While joint impairments associated with knee OA primarily occur to the osteoligamentous structures, the subsystem framework by Panjabi [189] illustrates that other systems are affected. Using this framework, the neuromuscular system was monitored through surface electromyography to determine the influence of OA severity, structural severity and effusion on muscle activation patterns during gait in individuals with knee OA. Three separate but related studies were conducted to address the three objectives of this dissertation. The objectives and key findings are described below.

7.1.1 Objective One – Knee Osteoarthritis Severity and Gait Velocity

The first objective (Chapter 4) determined whether alterations in knee joint muscle activation patterns exist between asymptomatic individuals, individuals with moderate knee OA and those with severe knee OA who had similar average self-selected walking velocities. Walking velocity decreases are generally thought to be part of the knee OA process. There was ambiguity associated with whether changes in muscle activation patterns across knee OA classifications merely reflected changes in walking velocity. Studying this cohort of individuals with varying knee OA severity (based on a radiographic, functional and clinical management based criteria that walked at similar self-selected walking velocities) helped to confirm that some of the differences previously reported were not just the result of walking velocity. The alterations found for the gastrocnemii, quadriceps, and hamstrings largely corroborate previous work in which walking velocities differed between groups. Key muscle activation findings are summarized below.

GASTROCNEMII

- MG activity occurred earlier in stance compared to LG (Phase shift) in asymptomatic individuals and those with moderate knee OA where this difference was not found for individuals with severe knee OA.
- The difference between early and late stance gastrocnemii amplitude was reduced in individuals with severe knee OA.

QUADRICEPS

- Greater VL, VM and RF amplitudes were found in individuals with moderate and severe knee OA compared to asymptomatic individuals.
- Progressive increase in VL, VM, and RF mid-stance amplitudes compared to early stance were found with increasing level of knee OA severity.

- Greater VL, VM and RF activity during mid-stance compared late stance was found in individuals with severe knee OA.

HAMSTRINGS

- LH amplitude was greater in individuals with moderate and severe knee OA compared to asymptomatic individuals and greater than MH amplitude in individuals with severe knee OA only.
- Prolonged LH amplitudes were found during stance compared to MH amplitudes in individuals with severe knee OA.
- Prolonged LH amplitudes were found during stance in individuals with severe knee OA compared to asymptomatic individuals and those with moderate knee OA.
- No differences in MH activation patterns were found between the three groups.

For this objective, the specific null hypotheses for each muscle grouping were rejected illustrating that knee joint muscle activation differences existed among asymptomatic individuals and individuals with varying knee OA severities while walking at the same velocity. This provided evidence to show that muscle activation alterations could not be explained by differences in self-selected walking velocity alone.

Regarding hypothesis one, overall amplitudes of LH and quadriceps differed among the asymptomatic and the OA severity groups, however temporal pattern differences were found among groups for all three muscle groupings. Regarding hypothesis two, the gastrocnemii and hamstrings had differences in lateral and medial muscle site activation patterns.

Given the severe OA group was receiving a total knee arthroplasty, a key difference between the two OA groups was primarily related to the "illness" component as captured by the self-report of lower physical function and their clinical status. The severe group did have higher KL-scores, but differentiating the illness effects from structural severity effects was smeared given this heterogeneity in symptoms and clinical status of the OA groups. Impairments to joint structure, including articular cartilage

degeneration, osteophytosis, bone attrition and sclerosis and impairments to physiological function, resulting in knee effusions, may lead to specific alterations in knee joint muscle activation during gait. These hypotheses were tested by objectives two (Chapter 5) and three (Chapter 6) of this dissertation.

7.1.2 Objective Two – Structural Severity

The second objective (Chapter 5) determined whether alterations in knee joint muscle activation patterns were associated with structural severity for those with a moderate knee OA classification. Sub-groups were based on Kellgren Lawrence ordinal radiographic scores. A sub-objective was to determine if all OA sub-groups differed from asymptomatic controls. Despite similarities in anthropometrics, muscle strength, gait characteristics and self-reported physical function, specific knee joint muscle activation characteristics recorded during gait were systematically altered with increasing structural severity, providing significant evidence to reject the specific null hypotheses related to this objective. Key muscle activation findings are summarized below.

GASTROCNEMII

- Overall MG amplitude was lower for individuals with greater structural impairment (KL III and KL IV) where structural severity did not affect overall LG amplitude.
- MG activity occurred earlier in stance compared to LG (Phase shift) in asymptomatic individuals and those with minimal structural impairment (KL II) where this difference was not found for individuals with greater structural impairment (KL III and KL IV).
- The difference between early and late stance gastrocnemii amplitudes were reduced in individuals with greater structural impairment (KL III and KL IV) compared to asymptomatic individuals.

QUADRICEPS

- Greater VL, VM and RF overall amplitudes and mid-stance amplitudes compared to early stance were found in individuals with minimal and moderate structural impairment (KL II and KL III) compared to asymptomatic individuals. Individuals with severe structural impairments (KL IV) had the greatest VL, VM and RF overall amplitude and mid-stance amplitudes.
- Greater VL, VM and RF activity during mid-stance compared to late stance in individuals with moderate structural impairment (KL III) was found compared to asymptomatic individuals and those with minimal structural impairment (KL II). Individuals with the greatest structural impairment (KL IV) had the highest VL, VM and RF amplitudes during mid-stance compared to late stance.

HAMSTRINGS

- LH amplitude increased with structural severity through to moderate structural impairment (KL III). Individuals with moderate and severe structural impairment (KL III and KL IV) had similar overall LH amplitudes.
- LH amplitudes were similar to MH amplitudes for asymptomatic individuals and those with minimal structural impairment (KL II). In contrast, LH amplitudes were greater than MH amplitudes in individuals with moderate and severe structural impairment (KL III and KL IV).
- Individuals with knee OA, regardless of structural severity, had more prolonged stance phase hamstrings activity (MH and LH). Individuals with the greatest structural impairment (KL IV) had the most prolonged activation.
- Isolated MH activation patterns were not affected by increases in structural severity

This study provided evidence of a strong association between structural severity and changes in both amplitude and temporal muscle activation patterns for specific muscles during gait in individuals with moderate medial compartment knee OA.

Regarding the first hypothesis, LH and quadriceps overall amplitudes were increased and MG overall amplitudes were decreased with increases in structural severity. Regarding hypothesis two, significant activation imbalances were found between the lateral:medial gastrocnemii and hamstrings for individuals with more severe structural impairment (KL III and KL IV scores). This study provides evidence that most knee joint muscle activation patterns during gait were altered in a progressive manner with increasing structural severity.

7.1.3 Objective Three – Knee Joint Effusion

In contrast to structural impairments associated with the knee OA process, knee joint effusion has been known to occur because of a wide variety of intra-articular pathologies. Effusion is thought to represent impairment to knee joint physiological function that has been related to knee OA progression. In healthy individuals, acute experimental knee effusions alters quadriceps and hamstrings activations and changes knee joint mechanics. The final objective of this dissertation (Chapter 6) was to determine whether knee joint effusion in individuals with moderate knee OA was associated with altered sagittal plane knee joint mechanics and knee joint muscle activation patterns during walking. Specific null hypotheses of this study were rejected, illustrating the association of knee joint effusion with altered gait mechanics and quadriceps and hamstring muscle activation patterns. Key muscle activation findings are summarized below.

GASTROCNEMII

- Gastrocnemii activation patterns were not affected by knee joint effusion.
- MG activity occurred earlier in stance compared to LG (Phase shift) in both groups.

QUADRICEPS

- Greater VL, VM and RF amplitudes across the entire gait cycle were found in individuals with effusion compared to those that did not have effusion.

HAMSTRINGS

- LH amplitude was greater than MH in both groups (with and without effusion). Individuals with effusion had more prolonged stance phase hamstrings activity than individuals without effusion.

This study provided evidence that knee effusion in individuals with moderate knee OA was associated with altered gait mechanics and muscle activation patterns. Regarding the first hypothesis, the knee joint was generally more flexed during stance with effusion. A significant difference in late stance knee angles was found between effusion and no effusion groups. Regarding hypothesis two, overall quadriceps amplitudes and temporal hamstrings activation features (prolonged stance phase hamstrings activation) were altered in individuals with knee OA who had knee effusions compared to a group with similar characteristics without effusion. Significant evidence to reject the final null hypothesis was not found. No lateral and medial muscle activation pattern alterations were found between individuals with and without effusion. In addition, no differences in gastrocnemii, quadriceps or hamstrings isometric strength were found. These participants had similar WOMAC scores, walking velocities and KL-scores. This suggests comparable moderate knee OA groupings.

Collectively the findings from the three studies in this dissertation provided objective *in vivo* measures to understand the reciprocal relationship between knee joint impairments and limitations in walking. This further established the role of knee OA severity to alter knee joint muscle activation patterns and provided novel findings on the association of structural severity and knee effusion to muscle activation patterns during gait. These components are important features that many criteria for the diagnosis and

classification of knee OA do not currently address. Therefore, there are direct applications for these studies as a collection of works to our understanding of gastrocnemii, quadriceps and hamstrings activation features in the context of knee OA gait. Specifically, this work documented the change in amplitude and temporal characteristics of EMG patterns during gait to better understand how specific factors contribute to these alterations.

7.2 IMPLICATIONS

Table 7.1 provides a summary of trends found for the overall **amplitude** for each muscle in each study. For a complete description of the results, refer to the Tables 4.2-4.3, 5.2-5.4 and 6.3 contained in the individual chapters.

Table 7.1: Indication of the overall amplitude effect for each muscle in each study

Objective	MG	LG	VL	VM	RF	LH	MH
1 **"OA severity"**	---	---	↑	↑	↑	↑	---
2 **"Structural Severity"**	↓	---	↑	↑	↑	↑	---
3 **"Effusion"**	---	---	↑	↑	↑	---	---

Note: arrows indicate direction of change and (---) indicates no change.

The use of principal component analysis also allowed for determining **temporally** dependent activation features. Temporally dependent activation features included both amplitude difference operator patterns and phase shifts. An indication of the whether or not temporally dependent features were found for each muscle is shown on Table 7.2.

Table 7.2: Indication of whether or not temporally dependent muscle activation features were found for each muscle, in each study.

Objective	MG	LG	VL	VM	RF	LH	MH
1 **"OA severity"**	√	√	√	√	√	√	√
2 **"Structural Severity"**	√	√	√	√	√	√	√
3 **"Effusion"**	---	---	---	---	---	√	√

Note: (√) indicates temporal features were found and (---) indicates temporal features were not found.

The dominant gastrocnemii finding was related to amplitude reduction with structural severity (Table 7.1). Temporally dependent activation features (i.e. phase shift and early to late stance amplitude differences) were found for individuals with severe knee OA (Chapter 4) and individuals with moderate to severe structural impairments (Chapter 5). This occurred more so for MG than LG. The MG electromyograms from Chapter 5 and the severe knee OA group from Chapter 4 are illustrated in Figure 7.1.

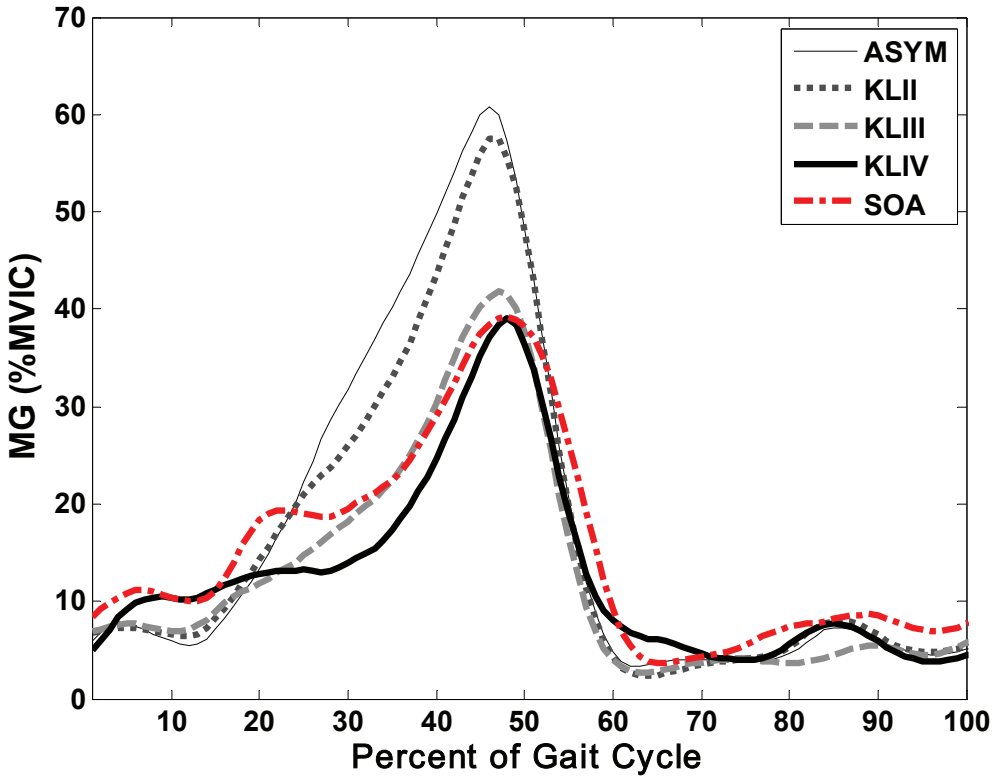

Figure 7.1: Ensemble-averaged electromyogram of the medial gastrocnemius from the group of individuals moderate knee OA included to address Objective 2 (ASYM, KL II, KL III, KL IV) and the individuals included in the severe knee OA group (SOA) to address Objective 1. Note: individuals in the SOA group had an average KL-score of III and consisted of individuals with KL III and KL IV scores only.

Individuals with severe knee OA, despite greater self-reported disability and having gait data collected within one week before their total knee replacement, walked with MG activations similar to individuals with moderate knee OA who had a corresponding KL-score (i.e. KL III and KL IV). This suggests that MG overall activation amplitudes and temporal features are related to structural severity. In contrast, overall LG amplitudes were not affected by knee OA severity, structural severity, or knee effusion. In fact, both MG and LG activation patterns were not altered in individuals with knee effusion. The phase shift (earlier MG than LG) found in Chapter 6 was consistent with the Chapters 4 and 5 for individuals with moderate knee OA and asymptomatic individuals. This occurred despite changes to the knee flexion angle and extension

moment during late stance indicating that gastrocnemii activations were not associated with alterations to sagittal plane mechanics.

Gastrocnemii activation features captured by the first three principal patterns were unique to minimal structural impairment separately from moderate/severe structural impairment (Chapter 4 and Chapter 5) and not affected by effusion (Chapter 6). Thus, gastrocnemii activation features can be useful for differentiating individuals with minimal or moderate to severe structural impairments or for evaluating treatments that target progression of structural impairment using gait analysis.

For the quadriceps, the dominant finding was higher EMG amplitudes associated with knee OA severity, structural severity and knee joint effusion (Table 7.1). Temporally dependent activation features (difference operators between early, mid and late stance) were also found for knee OA severity and structural severity, but not found with effusion for individuals with moderate knee OA (Table 7.2). This supports that while effusion can explain greater amplitudes in individuals with knee OA found in Chapter 4 and 5, effusion did not provide a mechanism for altered temporal activation features.

Generally, greater levels of mid-stance activity with increasing knee OA severity and structural severity were found. Specifically, mid-stance amplitudes with respect to early stance increased with increasing knee OA severity (Chapter 4), and in individuals this increase was progressive from asymptomatic to KL II/III to KL IV groups (Chapter 5). As well, mid-stance amplitudes with respect to late stance were the greatest in individuals with severe knee OA (Chapter 4) and those with KL IV scores (Chapter 5). The mid-stance differences between the findings of these two studies could be explained by the heterogeneity of the structural impairments in the knee OA severity groups where the severe knee OA group had a mixture of KL III and KL IV scores and the moderate knee OA group a mixture of KL I, II and III scores. In contrast, knee effusion only affected the overall quadriceps amplitude, with no differences found for early, mid and late stance difference operators.

Greater quadriceps activity has the potential for greater joint loading (tibio-femoral and patello-femoral) and increased metabolic demand. The former has the potential for increased injury risk. Knee effusion had an independent effect of increasing

overall quadriceps amplitudes. Given this, effusion presence needs to be included in gait-metric models to understand overall quadriceps activity in individuals with knee OA. While structural impairments are difficult to modify, knee joint effusions are treatable, in some cases preventable, and should be considered a component of early knee OA management.

Monitoring overall quadriceps activity could have utility in determining the impact of effusion management on gait in individuals with moderate knee OA. In addition, quadriceps activation features could be useful for identifying individuals with symptomatic knee OA and minimal structural impairments from an asymptomatic cohort or individuals with severe structural impairments from individuals with minimal to moderate structural impairments. Finally, the results of these studies support that quadriceps activation features would not be useful for monitoring structural knee OA progression from minimal to severe impairments, without, at minimum, the assessment of effusion.

For the hamstrings, the dominant finding was related to EMG amplitude increases with increasing severity and structural severity, but not for effusion (Table 7.1). Greater LH compared to MH overall amplitudes were found for individuals with severe knee OA (Chapter 4), for individuals with KL III and KL IV scores (Chapter 5) and for both groups of individuals with moderate knee OA in the effusion study (Chapter 6). This supports that a relationship existed between structural severity and medial:lateral hamstrings overall activation differences found in this series of studies. While the *PP-scores* associated with PP1 for LH were similar for the moderate knee OA classification, respective of KL-score, across the three studies in this dissertation (Table 4.3, 5.2, 6.3), MH *PP1-scores* were lower for the group of individuals with moderate knee OA in Chapter 6. This lower MH overall amplitude score could have contributed to the medial:lateral hamstring differences found in Chapter 6 despite the average KL II associated structural impairments found for the two groups.

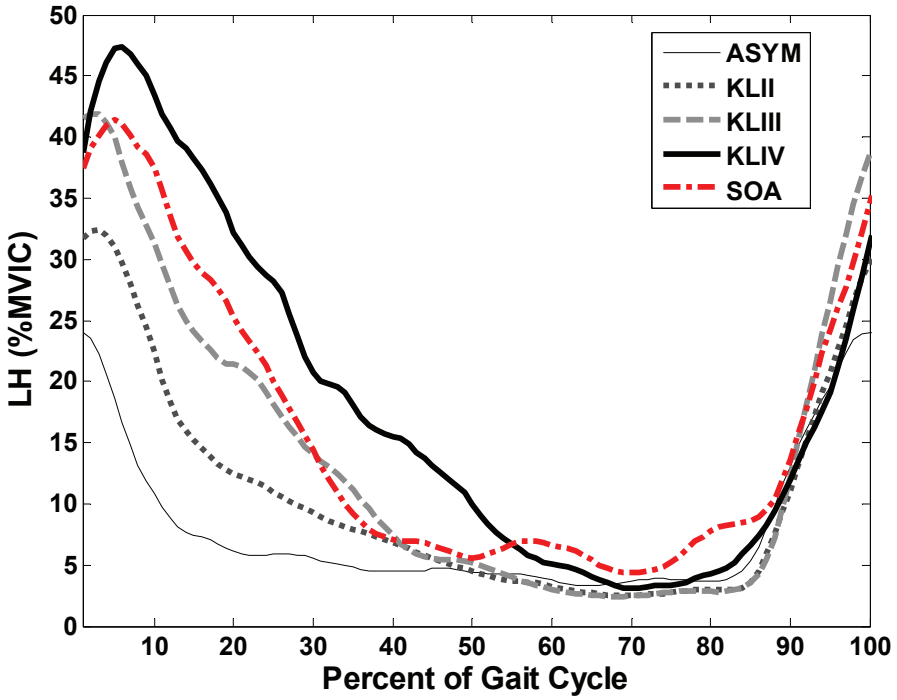

Figure 7.2: Ensemble-averaged electromyogram of the lateral hamstring from the group of individuals moderate knee OA included to address Objective 2 (ASYM, KL II, KL III, KL IV) and the individuals included in the severe knee OA group (SOA) to address Objective 1. Note: individuals in the SOA group had an average KL-score of III.

Temporally dependent activation features were also found for all objectives (Table 7.2). This indicated that prolonged activity during mid-stance existed with increasing knee OA severity, structural severity and knee joint effusion. This occurred more so for LH than MH in individuals with severe knee OA (Chapter 4), and equally between the hamstrings for increasing structural severity and knee joint effusion. The LH electromyograms from Chapter 5 and the severe knee OA group from Chapter 4 are illustrated in Figure 7.2 to demonstrate activation features that occurred in LH during gait. Note the amplitude similarities (overall amplitudes) between KL III and severe knee OA groups and the pattern similarities (burst of activity during early stance) between the KLIV and severe knee OA groups. Much like MG shown in Figure 7.1, LH activation patterns were related to structural severity, where differences in the amplitude and shape of the severe knee OA LH waveform could be explained by the heterogeneity of structural impairment in that group.

Hamstrings assist to maintain knee stability. Fatigue and injury would theoretically lead to abnormal loading and impaired gait mechanics, limited activity tolerance and ultimately, reduced joint longevity. Therefore, treatments designed to control knee stability should be investigated (i.e. bracing [202]), as should treatments to maintain muscle contractile characteristics such strength and endurance in an attempt to reduce the demand on LH during gait. Hamstrings activation features could be useful for identifying individuals with symptomatic knee OA and minimal structural impairments from an asymptomatic cohort. In addition, these activation features would be useful for monitoring OA progression from minimal through to severe structural impairment.

Knee OA is associated with significant ambulatory disability. The International Classification of Function provided the basis for understanding functioning and disability in individuals with knee OA. Central to this dissertation was developing an understanding of the reciprocal relationship between joint impairments, characteristic of the knee OA process, and activity limitations, in this case walking. Using a modification of Panjabi's subsystem model of joint function [189], the interactive relationship between impairments to joint structure and function and activity limitations was investigated using surface electromyography of the knee joint musculature during gait.

Collectively, these studies provide original data on the relationship between knee joint muscle activation patterns during gait and the knee OA process. While causality cannot be determined because of their cross-sectional design, these findings clearly demonstrate that relationships were specific to muscles and were not simply characterized by EMG amplitude changes alone. The dynamics of gastrocnemii, quadriceps and hamstrings activation during the gait cycle were also important to consider. To date, studies have shown that knee joint muscle activation is altered, but few studies tested the association with specific factors to determine their role in knee OA progression. The present study provides a solid foundation for understanding how muscle activation patterns are altered and a framework for developing gait-based metrics that can facilitate knee OA diagnosis and monitor knee OA progression.

7.3 LIMITATIONS AND FUTURE DIRECTIONS

Over the past 6-8 years, there has been a gradual increase in research aimed at understanding knee joint muscle activation characteristics during gait in individuals with knee OA. This dissertation provided foundational knowledge on how the gastrocnemii, quadriceps and hamstrings muscle activation patterns were altered during walking and how these alterations were associated with factors related to the knee OA process. Together with previous work, a framework to utilize knee joint muscle activity patterns to understand knee OA progression is beginning to emerge. While strong relationships were established, in particular for structural severity and muscle activation alterations, there are key limitations that exist for interpreting the findings of this dissertation. These are addressed below.

7.3.1 Limitations

1) As with any cross-sectional comparative design, this study was limited with respect to determining cause and effect. However, the inclusion and exclusion criteria for each study resulted in relatively homogeneous samples with the exception of the specific factor examined. Thus, while causality cannot be determined, relatively strong associations were established providing solid evidence of the relationships between specific OA-related variables and altered muscle activation patterns during walking. Designing an experiment to establish causality *in vivo* for some of the factors examined (i.e structural severity) would be difficult, and longitudinal studies require significant time. Given the control of variables (i.e. gait velocity) that could alter these relationships, the results do advance our understanding.

2) Sample sizes have been problematic in many cross-sectional studies; however, the sample size in the present studies is comparable or larger than most studies of this nature. Specifically, identifying a large sample size of high functioning individuals with severe knee OA (Chapter 4) and individuals with moderate knee

OA (high function and conservative management) with a KL IV score (Chapter 5) was difficult. Hence these groups had smaller sample sizes in comparison to the other groups in the analysis. Given the criteria utilized to classify the severity of knee OA in the current dissertation, these groups were unique but it was not feasible to recruit large numbers of individuals that fit these criteria given the time frame over which the data in the present study were collected. Despite this smaller sample, significant findings were found and the expectation would be that increasing the number would increase statistical power.

3) Knee radiographs of asymptomatic individuals were not completed and this was a feasibility issue. It was possible that some of the asymptomatic participants could have had knee OA associated structural impairments. The prevalence of KL II level structural impairment was estimated to be between 3-9% for the asymptomatic age group identified in this dissertation [148]. For Chapter 4 and 5, the possibility exists that a small percentage of the asymptomatic group could have structural impairments characteristic of a KL II score, although the inclusion and exclusion criteria minimized this potential. The addition of asymptomatic individuals with KL II scores would increase group variability thus reducing the ability to detect significant differences. If this were the case, a greater number of muscle activation features than currently identified could have been different between the asymptomatic group and the moderate OA groups in Chapter 4 and 5. Therefore, the differences found were a conservative estimate.

4) Structural severity was identified using the Kellgren Lawrence radiographic scale. Radiographic measures were limited to identify impairments of non-contractile soft-tissue elements (i.e. capsule, meniscus, ligaments). For this dissertation, it was assumed that impairments to these structures would be randomly distributed across groups and that no large impairments were present based on the exclusion criteria. As discussed in limitation 3), if individuals did have significant impairments to non-contractile soft-tissue elements, this would have increased group variability and reduced the ability to detect significant differences. While

the KL-score was used as a gross approximation of structural severity, the differences found in this dissertation supported that specific alterations to muscle activity were associated to changes in joint structure captured by the KL-score criteria.

7.3.2 Future Directions

From this dissertation work several future research questions could form the next logical steps for this area of inquiry. The following section will highlight three key future directions.

Future Direction 1

Chapter 4 focused on understanding whether muscle activation patterns were affected by knee OA severity. The experimental continuum included asymptomatic individuals and individuals with moderate and severe knee OA. Two key differences related to structural impairment and symptoms were found between the moderate and severe knee OA groups (Table 4.1) and the resulting clinical management was vastly different between the two OA groups (conservative versus surgical treatment). To isolate the factors associated with changes in muscle activation related to structural impairment in Chapter 5, the two variables (clinical management and symptoms) were consistent among groups. While Chapter 5 furthered our understanding of the relationship between structural impairments and muscle activation patterns, the influence of symptoms on muscle activation was not specifically addressed in this dissertation. The next step for this research would be to understand whether symptoms, specifically mechanical knee pain, alter muscle activation patterns during gait. These data would add to a multidimensional gait metric model to understand key factors for knee OA development and progression and the effect of this disease, and associated illness on physical function.

Future Direction 2

In Chapter 4, all individuals scheduled for total knee replacement had structural impairments scored as KL III or IV. In fact, only 1 of the 62 individuals that met the severe knee OA criteria (Chapter 4) had a KL-score <III. In Chapter 5, systematic alterations to knee joint muscle activation patterns during gait were related to structural severity, with both amplitude and temporal gastrocnemii and hamstrings activation patterns distinctly different between structural impairments associated with KL II and KL III scores. The question is clear, "can surface EMG be utilized to triage individuals for appropriate management; identifying individuals who require a surgical stream of care from those where conservative management would be more effective?"

Surface electromyography has the advantage of being portable, in comparison to the expensive and space-occupying laboratories required for a biomechanical evaluation of gait. A future step for this research is to implement knee joint muscle surface electromyography recorded during self-selected gait, independent of radiographic measures, to inform primary care health care professionals on whether or not the individual diagnosed with knee OA should be directly referred to an orthopaedic surgeon for consultation or managed conservatively.

Future Direction 3

Objective three of this dissertation was novel. Effusions are present in over half the individuals treated with this disease. To my knowledge, knee joint effusions have not been considered in the interpretation of biomechanics and knee joint muscle activation pertaining to knee OA gait. This has occurred despite considerable evidence that effusion impairs the quadriceps and alters gait mechanics and muscle activity during gait in healthy individuals. The findings of Chapter 6 provided convincing evidence that knee effusion played a significant role in altering how the quadriceps were activated and to a lesser extent the hamstrings in individuals with knee OA during walking. Future work to ascertain the effect of altering effusion status, either through creating an experimental effusion (non-acutely) or reducing effusions already found (aspiration), on gait

mechanics and muscle activation patterns would establish the causal role of knee effusion to alter gait mechanics and muscle activation patterns. In addition, understanding whether the findings of Chapter 6 were sensitive to effusion volume and/or intra-articular pressure fluctuations would facilitate our knowledge of the mechanisms generated by effusion to alter gait. These data would be required to integrate the consideration of effusion status into gait metric models of knee OA development and progression.

7.4 Concluding Remarks

Osteoarthritis is a chronic, progressive disease that has worldwide prevalence. For decades, the knee has been recognized as the most common lower extremity joint affected with knee OA associated with significant ambulatory disability. At present, there is no cure, and minimal evidence that current management approaches, particularly those that target symptoms, are abating progression. This trend is very costly and only projected to increase in coming years. The International Classification of Function framework provided the basis for understanding functioning and disability in individuals with knee OA for this dissertation. Many individuals report activity limitations, most notably walking. In many instances, these limitations are understood through self-report measures. Self-report measures, including those focused on pain and activity limitations are used routinely to evaluate the knee OA process and treatment effectiveness. Lane *et al*., [145] suggests that this trend provides the background to understand why research and clinical work have not discovered a method to slow down the knee OA process and prevent the exponentially increasing requirement for end-stage treatment.

While knee OA symptoms are very important and can modify muscle activation characteristics and gait biomechanics, basing clinical decision making on self-reports is flawed, as this practice does not directly address the mechanisms of impairment. Hence, measures that are more objective are necessary. Central to this dissertation was developing an understanding of the reciprocal relationship between joint impairments, characteristic of the knee OA process, and activity limitations, in this case walking.

A key motivation of this dissertation was to understand progression in individuals spanning the disease spectrum with moderate knee OA or more specifically those that are

not currently surgical candidates. These individuals have the greatest potential to respond to methods of management targeting the attenuation of structural impairment progression. Thus, foundational data are needed to support the development of treatment/management approaches that aim to alter mechanisms associated with knee OA progression and not simply to treat symptoms. For the clinician, it is frustrating to know that despite this potential for improvement, current tools to evaluate the knee OA process provide little appreciation for the relationships that exist between joint impairments and walking. For the scientist, challenges are presented to quantify gait features that associate to these impairments, building a framework to understand the knee OA process and advance evaluation and management strategies that target individuals with moderate knee OA that is readily useful for clinicians and researchers alike.

Using techniques in surface electromyography, knee joint muscle activation patterns recorded during gait captured the progressive and unique nature of the knee OA process. Osteoligamentous structures are the primary tissues compromised with knee OA presence and progression. This creates the potential for increased reliance on the neuromuscular system to maintain knee joint mobility and stability during gait, as conceptualized through the Panjabi model of joint stability. The knowledge gained in the areas pertaining to knee OA severity, structural severity and knee effusion and the relationships found to knee joint muscle activation patterns have consequences for understanding knee OA. The goal of this research was to contribute to the development of gait-based metrics that can facilitate knee OA diagnosis and monitor knee OA progression. The novel relationships found in this dissertation work contributed to this goal.

In conclusion, this dissertation has provided a comprehensive, novel examination of the interrelationships that exist between knee joint muscle activation patterns and the knee OA process including impairments to joint structure and function characteristic of knee OA progression. Given the current reliance on self-report measures to understand activity limitations and evaluate the knee OA process, the assessment of knee joint muscle activation during gait provides the potential to augment these assessments with quantifiable gait metrics that are directly related to joint impairments characteristic of individuals with knee OA.

APPENDIX A

AMPLITUDE NORMALIZATION: MAXIMAL VOLUNTARY ISOMETRIC CONTRACTION EXERCISES

This appendix is divided into two parts. A summary of the manuscript titled "Maximal Voluntary Contraction Exercises: A Methodological Investigation in Knee Osteoarthritis" is included in Appendix A.1. This manuscript illustrates the value of a series of exercises used for amplitude normalization purposes and has been modified from its original format to conform to the structure of this dissertation. Secondly, Appendix A.2 illustrates, on a randomly selected sub-group of knee OA participants, the influence of exercise selection on amplitude normalization of the electromyographic waveforms for seven muscle sites during walking. The main issue addressed in this appendix is the amplitude normalization procedures used for the analysis. Amplitude normalization has received considerable attention and debate but these methods are fundamental to understanding amplitude comparisons and we included this appendix for dissertation completeness.

APPENDIX A.1

MAXIMAL VOLUNTARY CONTRACTION EXERCISES: A METHODOLOGICAL INVESTIGATION IN KNEE OSTEOARTHRITIS

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Appendix A.1 was included in this dissertation to summarize the results of the investigation titled, "Maximal Voluntary Contraction Exercises: A Methodological Investigation in Knee Osteoarthritis". The specific objectives of the investigation were to determine the relative activation amplitudes associated with an exercise series aimed to elicit maximal quadriceps, hamstrings and gastrocnemii activation, and to determine if

there were differences between participants with asymptomatic knees and a clinical population of participants with moderate knee OA. Secondly, to determine whether maximum activations occurred on the same exercise between participants with asymptomatic knees and a clinical population of participants with moderate knee OA.

METHODOLOGY

Individuals were recruited to the Dynamics of Human Motion Laboratory, Dalhousie University, Halifax, Nova Scotia for muscle strength, gait biomechanics and electromyographic studies. This analysis was conducted on 68 participants with asymptomatic knees (age=49 years, SD=9.5, body mass=75.5 kg, SD=15.3, height=1.69 m, SD=0.08, and Body Mass Index (BMI)=26.1 kg/m^2, SD=4.3) and a clinical population of 68 participants with moderate knee OA (age=56.9 years, SD=8, body mass=92.3 kg, SD=18.3, height=1.74 m, SD=0.09, and BMI=30.53kg/m^2, SD=5.3). Recruitment, EMG collection hardware and data collection procedures were consistent with those employed for this dissertation as outlined in Chapter 3.

MAXIMAL VOLUNTARY ISOMETRIC CONTRACTION DATA ACQUISITION

A series of eight standardized exercises were performed (Figure A.1). These exercises were identified from a series of pilot studies to determine exercise positions that elicited maximal activation amplitudes from the seven muscle sites. This MVIC exercise series has been previously utilized for normalization purposes [102]. For exercise familiarization, a warm-up, specific to the MVIC exercise and at least one practice contraction was completed. When participants reported satisfactory familiarization, two three-second maximal isometric contractions were completed for each exercise. Participants were instructed to provide maximal efforts on each trial. Standardized positions are shown in Figure A.1 and include i) knee extension at 45^o of knee flexion (KE45) in sitting, ii) knee extension at 15^o of knee flexion (KE15) in supine, iii) knee extension-hip flexion at 45^o of knee flexion and 90^o of hip flexion (KEHF) in sitting, iv) knee flexion at 55^o of knee flexion (KF55) in sitting, v) knee flexion at 15^o of knee

flexion (KF15) in supine, vi) knee flexion at 55^{o} of knee flexion (prone KF55) in prone, vii) sitting plantarflexion with the ankle in neutral and viii) standing unilateral plantar flexion. A Cybex™ dynamometer (Lumex, NY, USA) was employed for exercises i-vii. A minimum 60-second rest period separated each contraction, and standardized verbal encouragement was given [102]. Decisions to accept or repeat trials were based on examining the torque and/or EMG signals in real time to determine if a maximal steady state contraction was achieved and to identify artefact. Participants were provided with verbal feedback. If a steady state contraction was not achieved or a difference between trials greater than 10% was noted, the lower exercise trial was repeated. All electromyographic signals were analogue to digital converted at 1000Hz (16bit, +/- 2V) and stored for processing.

Data Processing

Electromyographic data were processed through custom MatLab™ Ver 7.1 programs (The Mathworks Inc., Natick, Massachusetts, USA). Signals were corrected for bias and converted to microvolts, full wave rectified and low-pass filtered (Butterworth, 4th order, Fc-6Hz). A 100ms moving-average window, advancing one sample at a time (99ms-overlap between two adjacent windows) identified the maximal amplitude for each muscle in both trials of all eight MVIC exercises [102].

Analysis

Maximal electromyographic amplitudes were identified from three quadricep, two gastrocnemius and two hamstring muscle sites for each exercise. The single highest amplitude, regardless of trial and exercise was utilized to represent absolute maximum activity for each muscle. Activity levels for each exercise were normalized to this maximum amplitude and were reported as a percentage of MVIC (% MVIC). For each muscle, a two-factor mixed model Analysis of Variance, for group (asymptomatic or knee OA) with repeated measures for exercise was employed to test main effects and interactions. Bonferonni adjusted post-hoc testing was utilized on all significant findings.

Significance was determined with alpha = 0.05. Frequency counts for exercises that elicited the absolute maximum activity were recorded for each muscle for each subject group.

Results and Conclusion

Mean normalized amplitudes in % MVIC for each exercise, group and muscle are shown in Table A.1. For each muscle, Table A.2 contains the number of participants that produced maximum activation for each exercise.

This study provides new information on how exercise selection influences amplitudes obtained during maximal voluntary isometric testing in those with confirmed knee OA compared to those with asymptomatic knees. Consistent with findings of Vera-Garcia *et al*., [256] on trunk musculature, no single exercise produced a maximum activation for all muscles for all individuals. Greatest activation for gastrocnemii occurred during standing plantar flexion, for vasti muscles during KE45 and KE15 and for RF during KE15. KF15 and PKF55 produced the greatest hamstrings activation, where a tendency existed for LH to be influenced by the former and MH to be influenced by the latter. Furthermore, the findings illustrate that those with asymptomatic knees and those with medial joint knee OA were not different with respect to relative activation amplitudes for the majority of exercises or for which exercise was most effective at eliciting a maximum activation. This study provides an important first step in standardizing normalization criteria for understanding levels of sub-maximal activity produced during functional tasks in individuals with knee OA.

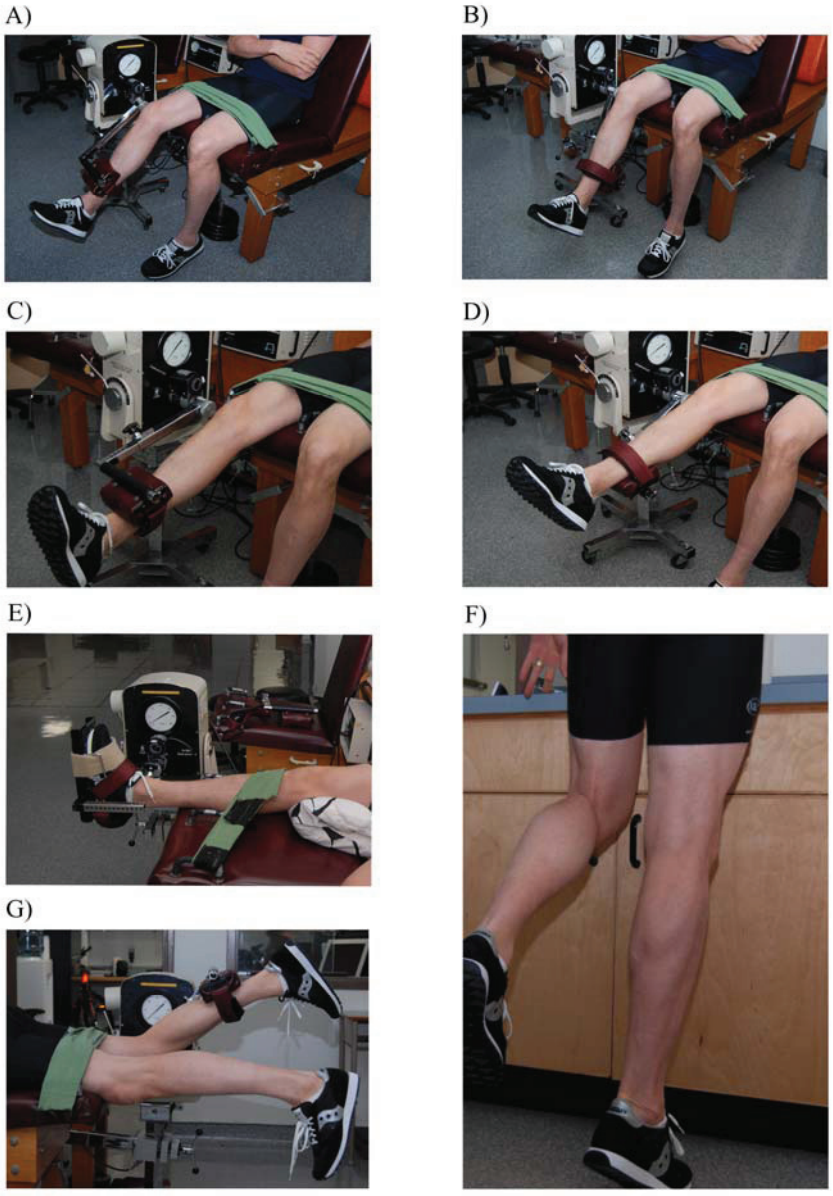

Figure A.1: Standard positions for the series of MVIC exercises. A) Knee extension at 45 degrees of knee flexion in sitting (KE45), B) Knee flexion at 55 degrees of knee flexion in sitting (KF55), C) Knee extension at 15 degrees of knee flexion in supine (KE15), D) Knee flexion at 15 degrees of knee flexion in supine (KF15), E) Plantar flexion at neutral in supine, F) Plantar flexion in standing and G) Knee flexion at 55 degrees of knee flexion in prone (PKF55). Note: combined knee extension and hip flexion was performed as per position A) (KEHF). With standard instructions, participants were asked to provide a maximal effort for a period of three seconds during each exercise. The thigh was secured with Velcro straps for all seated testing and participants were required to keep their hands crossed over their chest. For prone testing, a single pillow was placed under the hips and the thigh was strapped to the table. During seated plantarflexion, the leg was strapped to the table.

Table A.1: Relative muscle activation (in %) normalized to absolute maximum amplitudes for each exercise [Mean (standard deviation)]. Greatest relative maximal activations for each muscle are indicated in **bold** (P<0.05).

	LG		MG		VL		VM		RF		LH		MH	
	AS	OA	AS	OA	AS	OA	AS	OA	AS	OA	AS	OA	AS	OA
KE45	14.2	12.4	12.0	12.6	**84.1**	**86.0**	**80.7**	**85.2**	84.2	82.4	15.7	16.3	8.7	9.7
KE15	14.8	13.9	15.7	17.2	**86.0**	**85.6**	**86.5**	**86.0**	**89.2**	**89.4**	17.1	16.5	9.7	10.0
KEHF	32.7	36.6	29.3	30.1	42.7	56.6	44.0	57.0	82.5	82.7	19.8	15.3	21.5	15.9
KF55	63.4	70.4	57.1	61.4	9.9	11.0	14.6	12.5	9.6	9.12	69.3	59.1	73.3	70.8
KF15	59.9	64.9	62.8	68.4	11.4	13.1	14.9	15.0	8.9	8.9	**91.7**	**90.2**	81.1	83.4
PKF55	53.4	50.1	56.4	57.1	8.9	9.3	13.5	14.8	8.2	8.4	**89.6**	**86.4**	**93.5**	**93.0**
PF Sit	71.0	74.2	71.5	75.2	13.3	20.1	13.1	22.1	10.5	14.3	13.4	15.9	13.0	13.1
PF Stand	**85.6**	**88.7**	**91.9**	**93.2**	39.6	49.5	49.6	51.9	32.9	38.7	24.8	37.6	15.2	18.6

Exercises: KE45 (knee extension at 45^{o} knee flexion), KE15 (knee extension at 15^{o} knee flexion), KEHF (knee extension-hip flexion at 45^{o} knee flexion and 90^{o} hip flexion), KF55 (knee flexion at 55^{o} knee flexion), KF15 (knee flexion at 15^{o} knee flexion), PKF55 (knee flexion at 55^{o} knee flexion in prone position), PFsit (plantarflexion at neutral ankle, knee extended, hip flexed), PFstand (unilateral plantarflexion in standing).

Table A.2: MVIC exercises that produced maximum activations for each muscle. The numbers of individuals, separated by group are shown.

Exercise	Muscle													
	LG		MG		VL		VM		RF		LH		MH	
	AS	OA	AS	OA	AS	OA	AS	OA	AS	OA	AS	OA	AS	OA
KE45	0	0	0	0	28	30	23	28	17	19	0	0	0	0
KE15	0	0	0	0	33	28	35	29	32	32	0	0	0	0
KEHF	1	3	0	0	2	6	2	3	19	16	0	0	0	0
KF55	7	13	2	3	0	0	0	0	0	0	8	4	12	10
KF15	7	4	8	3	0	0	0	0	0	0	30	38	16	23
PKF55	3	2	3	1	0	0	0	0	0	0	30	24	39	35
PF sit	17	14	12	13	2	0	1	1	0	0	0	0	0	0
PF stand	33	32	43	48	3	4	7	7	0	1	0	2	1	0

Exercises: KE45 (knee extension at 45^o knee flexion), KE15 (knee extension at 15^o knee flexion), KEHF (knee extension-hip flexion at 45^o knee flexion and 90^o hip flexion), KF55 (knee flexion at 55^o knee flexion), KF15 (knee flexion at 15^o knee flexion), PKF55 (knee flexion at 55^o knee flexion in prone position), PFsit (plantarflexion at neutral ankle, knee extended, hip flexed), PFstand (unilateral plantarflexion in standing).
Muscles: LG (lateral gastrocnemius), MG (medial gastrocnemius), VL (vastus lateralis), VM (vastus medialis), RF (rectus femoris), LH (lateral hamstrings), MH (medial hamstrings)
Groups: OA (moderate knee OA), AS (asymptomatic knee)

APPENDIX A.2

The Effect of Maximal Voluntary Isometric Contraction Exercise selection on Amplitude Normalization of the Gait Electromyogram

Appendix A.2 was included in this dissertation to illustrate the effect of maximal voluntary isometric contraction exercise selection on amplitude normalization of the gastrocnemii, hamstrings and quadriceps gait electromyographic waveforms. The exercises selected for this illustration were based on those tested in Appendix A.1 and shown to generate maximum amplitudes for each respective muscle group for the majority of individuals.

Methodology and Data Processing

A sub-group of 12 individuals was randomly selected from the moderate knee OA data set. Surface electromyograms were recorded as per the methodology outlined in Chapter 3. Following the gait trials, all individuals completed a series of eight MVIC exercises, as described in Appendix A.1. All gait and MVIC signals were corrected for bias and converted to microvolts, full wave rectified and low-pass filtered (Butterworth, 4^{th} order, Fc-6Hz). Signals were time normalized to represent the gait cycle as 100%. A 100ms moving-average window, advancing one sample at a time (99ms-overlap between two adjacent windows) identified the maximal amplitude for each MVIC exercise and muscle.

Analysis

From the MVIC exercises, maximal level of activity, regardless of which exercise elicited this activity, was identified for each muscle (absolute maximum). From Table A.2, the exercises that elicited the majority of the maximum levels of activity were selected. For the quadriceps, the levels of maximal activity obtained from KE45, KE15 and KEHF were identified. Maximal levels of activity obtained from KF55, KF15 and PKF55 were identified for the hamstrings and for the gastrocnemii, maximal levels of

activity were identified from PFstand, PFsit, KF55 and KF15. Ensemble-averaged gait electromyograms of each muscle were amplitude normalized to each of their respective values and plotted.

Results and Conclusions

Exercise selection for MVIC amplitude normalization affects amplitude measures of the electromyogram in each muscle. In some cases, for instance the LH, peak amplitude differences exceeded 40% MVIC between using a single exercise and the absolute maximum. These amplitude differences are based entirely on which exercise was used during the normalization procedures. Gait electromyograms amplitude normalized to exercises that generated the greatest relative activity (Appendix A.1) as expected were of similar amplitude when compared to the absolute maximum, with the exception of RF. These results further highlight the importance of considering a series of normalization exercises for interpreting gait waveform amplitude measures. The use of an absolute maximum across a series of exercises provided the lowest normalized amplitude compared to any single exercise.

Table A.3: Mean and standard deviation (SD) activation level (microvolts) for each exercise and the absolute maximum activity regardless of exercise.

Muscle	Exercises				
	Absolute Max	**PFStand**	**PFSit**	**KF55**	**KF15**
LG	338.4 (225.9)	289.2 (190.2)	245.7 (190.5)	252.0 (193.8)	214.8 (192.8)
MG	292.0 (190.7)	257.2 (170.4)	213.4 (184.6)	214.1 (176.6)	203.4 (177.7)
		KE45	**KE15**	**KEHF**	
VL	459.6 (365.6)	432.3 (361.9)	311.2 (202.2)	241.8 (257.8)	
VM	352.6 (276.8)	335.7 (268.6)	273.7 (214.4)	220.5 (255.2)	
RF	265.7 (184.7)	224.9 (124.7)	220.4 (163.7)	214.1 (145.2)	
		PKF55	**KF15**	**KF55**	
LH	453.1 (306.1)	429.6 (295.5)	395.6 (263.4)	257.1 (217.5)	
MH	394.2 (218.5)	359.7 (183.0)	336.8 (215.8)	305.6 (232.3)	

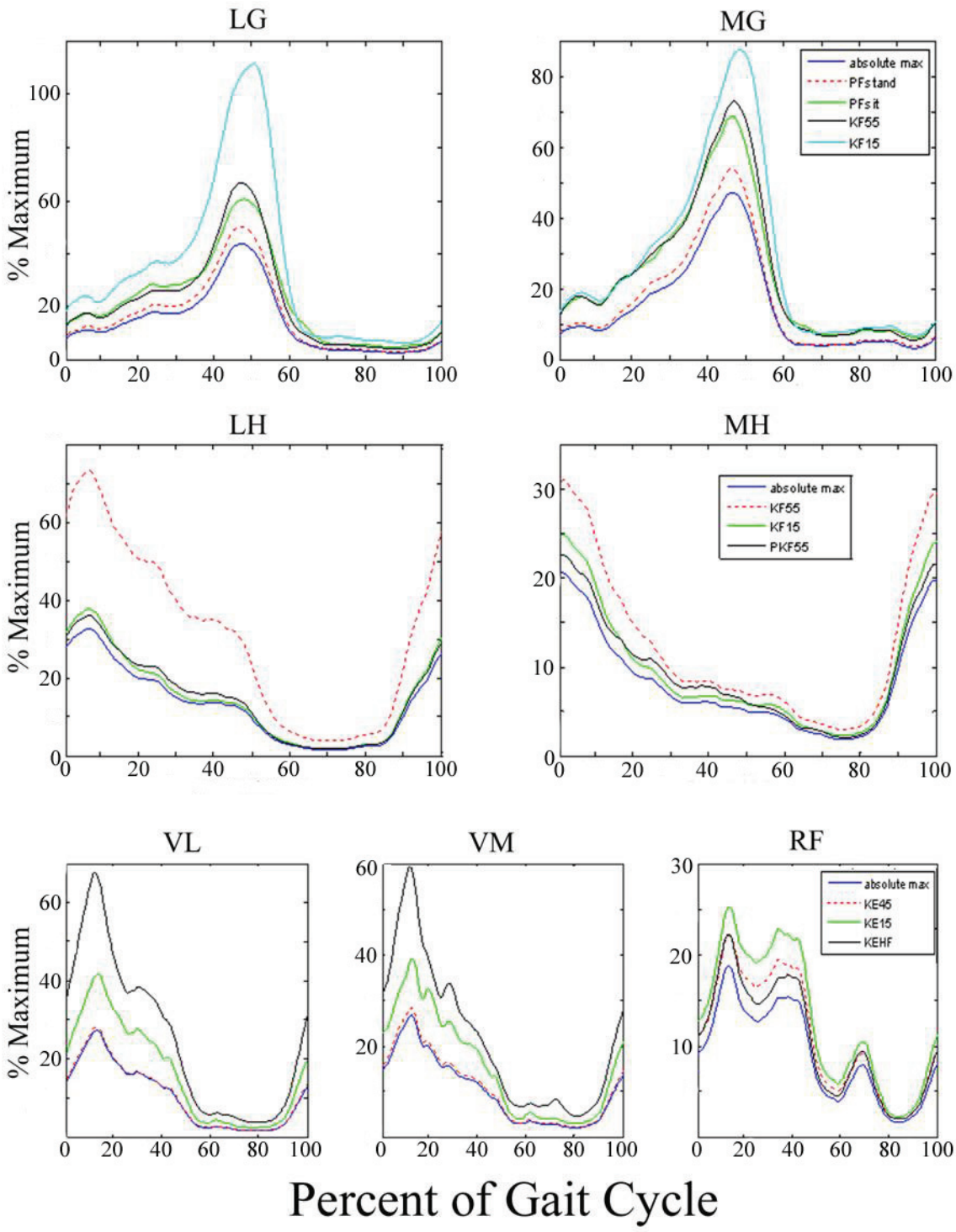

Figure A.2: Ensemble-averaged gait electromyographic waveforms of each muscle, amplitude normalized to the maximal activity of each respective exercise and absolute maximum. For each plot, the blue waveform represents the ensemble-averaged electromyogram normalized to the absolute maximum regardless of eliciting exercise.

APPENDIX B

A Summary of Principal Component Analysis Methodology for Electromyographic Waveform Analysis and Interpretation

This appendix details the key equations used for the pattern recognition procedures in this dissertation. For this dissertation, principal pattern interpretation was based on investigating individual waveforms with high and low principal pattern scores, consistent with previous work [16,102]. Appendix B was included to illustrate that the interpretation similarities between high/low principal pattern score waveforms (as used in this dissertation) were similar to using waveform reconstruction. The latter illustrates the effect of the linear combination of patterns. Finally, waveform reconstruction errors are calculated illustrating that the technique does capture the main features from the waveforms as predicted from the percent trace.

Methodology

For this appendix, the electromyographic waveforms from MG were selected from the group of individuals included to address objective one of this dissertation. Details of participant recruitment, collection procedures, group demographics and gait characteristics can be found in Chapter 3 and Chapter 4.

Principal Component Analysis

Ensemble average electromyographic waveforms from at least five trials were calculated for each subject, for each muscle [271]. Custom MatLab™ Ver.7.1 programs (The Mathworks Inc., Natick, Massachusetts, USA) performed all matrix manipulations. A matrix $[X]$ was generated from the time-normalized MG and LG waveforms (101 points) and a cross product matrix was computed $[S]$ using equation [1].

$$[S] = [X^T] * [X] \qquad [1]$$

An eigenvector decomposition of the cross product matrix $[S]$ was performed using equation [2], yielding the predominant orthonormal principal patterns (eigenvectors) and corresponding eigenvalues [43,117]. $[U]$ is a matrix of patterns (Principal Patterns (i.e. u_1=PP1, u_2=PP2 etc.) and L is a diagonal matrix of associated variances (eigenvalues).

$$[S] = [U]L[U^T] \qquad [2]$$

Waveforms from the original dataset $[X]$ were scored using equation [3]. This provides a single value that captures the projection of an individual's waveform x_r on to each principal pattern ($\overline{u}_i$) retained. These scores are referred to as *PP-Scores*.

$$PP - Score_i = [X] * [U] \qquad [3]$$

The percent trace (percent variation explained) was calculated using equation [4].

$$pct_i = \frac{L_i}{Tr(S)} * 100 \qquad [4]$$

Five waveforms with the highest and lowest *PP-Scores* were ensemble-averaged for each of the principal patterns and can be found in Figure B.2.

WAVEFORM RECONSTRUCTION

Using the mean *PP-score*$_i$ for each group, the sample ensemble average waveforms were reconstructed (x_r) using equation [5] and plotted after each iteration from i to j (where j equals the number of principal patterns retained).

$$x\_r = \sum_{i=1}^{j} PP - Score_i * \overline{u}_i \qquad [5]$$

RESULTS AND CONCLUSION

Medial gastrocnemius ensemble average electromyographic waveforms for asymptomatic individuals and individuals with knee OA are shown in Figure B.1A. Reconstructed ensemble-averaged waveforms using PP1, PP2 and PP3 are shown on Figure B.1B. Three principal patterns explained 96% (j=3) of the total waveform variability (Figure B.2). Table B.1 illustrates the *PP-scores* for each retained principal pattern and an interpretation of the high *PP-scores*. Low *PP-scores* would be interpreted as the opposite relationship. The mean of five MG waveforms corresponding to high (solid) and low (dotted) *PP-scores* are shown on Figure B.2. Figure B.3 illustrates the reconstruction of MG for asymptomatic individuals and those with moderate and severe knee OA. Table B.2 contains the root mean square differences between the original MG waveform and reconstructed waveforms for each group.

PP1 explained the most variability in the MG data set. As seen in Figure B.3, the reconstructed waveforms based on PP1 closely approximate the original waveform amplitude and general shape, more so for asymptomatic individuals and those with moderate knee OA. Greater *scores* indicate higher overall amplitude, seen both in the high and low scores (Figure B.2) and reconstruction (Figure B.3). PP1, while explaining the majority of the variability, does not capture subtle temporal activation features (phase shifts and difference operators). Adding variability accounted for by PP2 and PP3 provides a closer approximation of the original waveform as shown by the reduced mean square difference (Table B.2).

Higher *PP-scores* associated with PP2 indicate earlier activity during stance. This is illustrated in both Figure B.2E and Figure B.3. Asymptomatic individuals and those with moderate knee OA had positive *PP-scores* for PP2, shifting activation earlier in stance as shown by the addition of PP2 to variability already explained by PP1. In contrast, negative *PP-scores* were found for individuals with severe knee OA, causing a shift to later stance with the addition of PP2. Ninety four percent of the waveform variability was accounted for by PP1 and PP2 however; individuals with severe knee OA

also had large scores for PP3 indicating the importance of this pattern in this group. The addition of PP3 greatly improved the reconstruction of MG for the severe knee OA group (Figure B.3, Table B.2).

Negative *PP-scores* associated with PP3 indicate a decrease in the activation amplitude differences between early and late stance. Positive scores served to increase the difference between early and late stance activity as seen in asymptomatic individuals and individuals with moderate knee OA but this affect was minimal compared to the effect of larger negative *PP-scores* for individuals with severe knee OA (Table B.2). The addition of PP3 to the variability accounted for by PP1 and PP2 in the severe knee OA group increased the level of reconstructed activity during early stance and decreased the level of activity during propulsion, providing an improved approximation to the original waveform (Table B.2).

Smaller alterations in the reconstructed waveforms are expected after PP1, considering PP1 explains the greatest percent of waveform variability. The addition of PP2 and PP3 improved the reconstruction of the EMG data (Table B.2), and defined salient features that were unique to each group. Principal patterns are linear combinations of the original variables [43] where waveform reconstruction in this appendix illustrated the relationship between original data, principal patterns, eigenvalues and *PP-scores*. From this appendix, using either high/low scores or waveform reconstruction leads to a similar interpretation of the MG electromyogram. While not shown, interpretation similarities between these two methods were also found for the hamstrings and quadriceps.

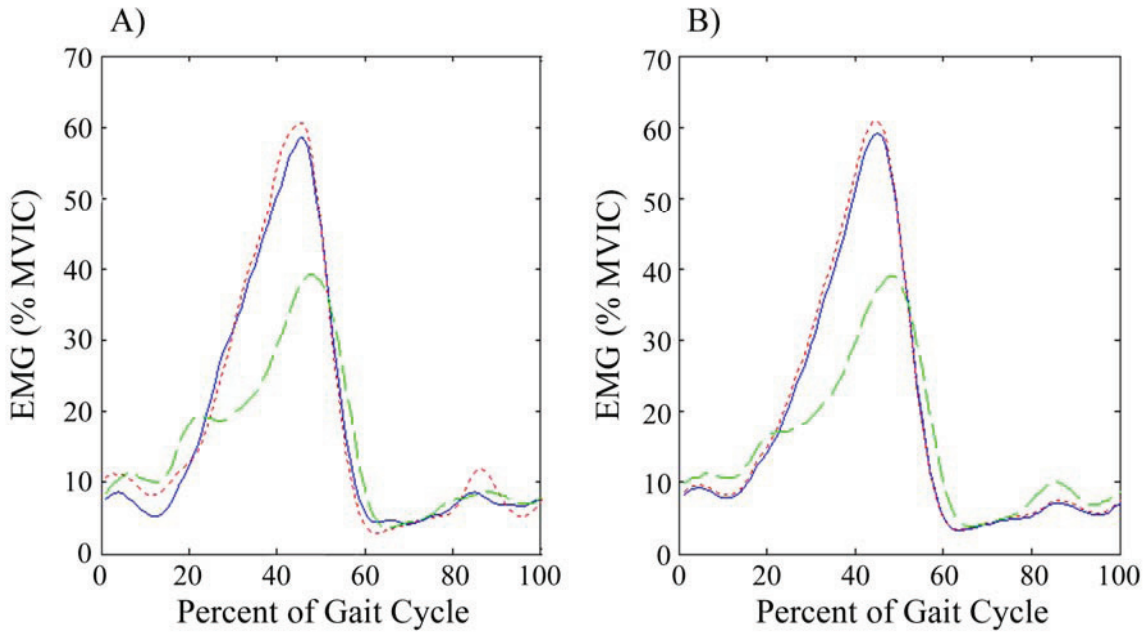

Figure B.1: A) Ensemble average medial gastrocnemius waveforms, B) Reconstructed medial gastrocnemius waveforms using PP1, PP2 and PP3. (Solid blue (ASYM), dotted red (moderate knee OA), dashed green (severe knee OA)).

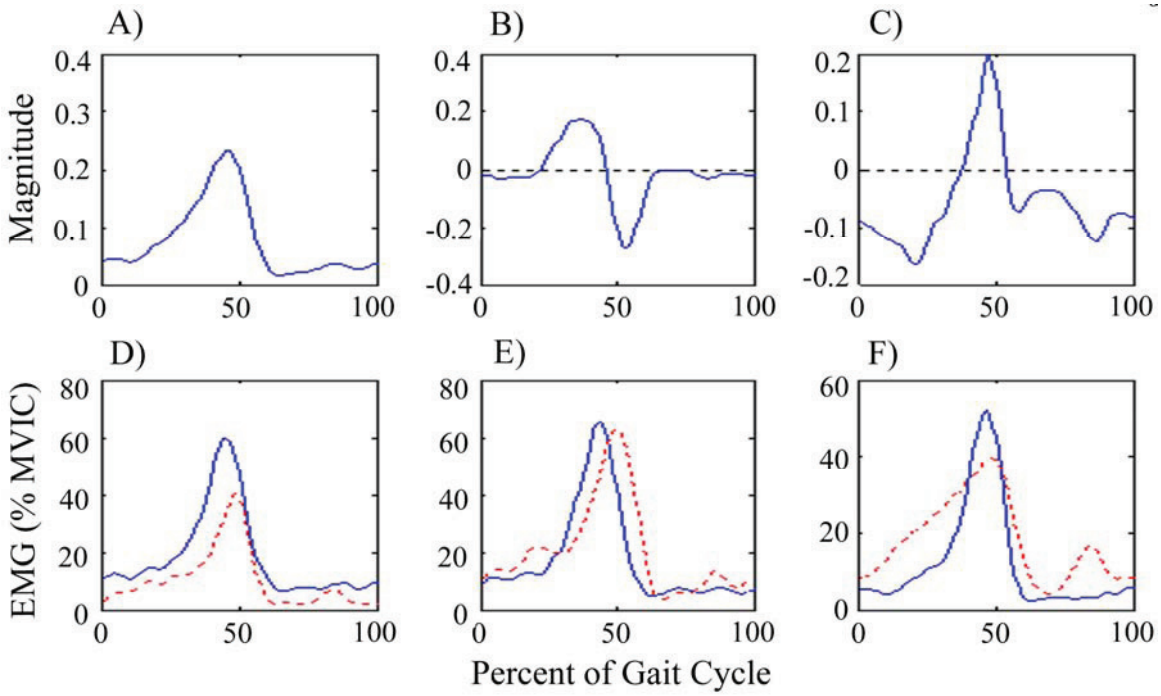

Figure B.2: Principal Patterns and waveforms associated with high and low *PP-scores*. A) PP1 – captured 90% of the waveform variance, B) PP2 – captured 4% of the waveform variance, C) PP3 – captured 2% of the waveform variance. Mean of five MG waveforms corresponding to high (solid blue) and low (dotted red) *PP-scores* for D) PP1, E) PP2, F) PP3.

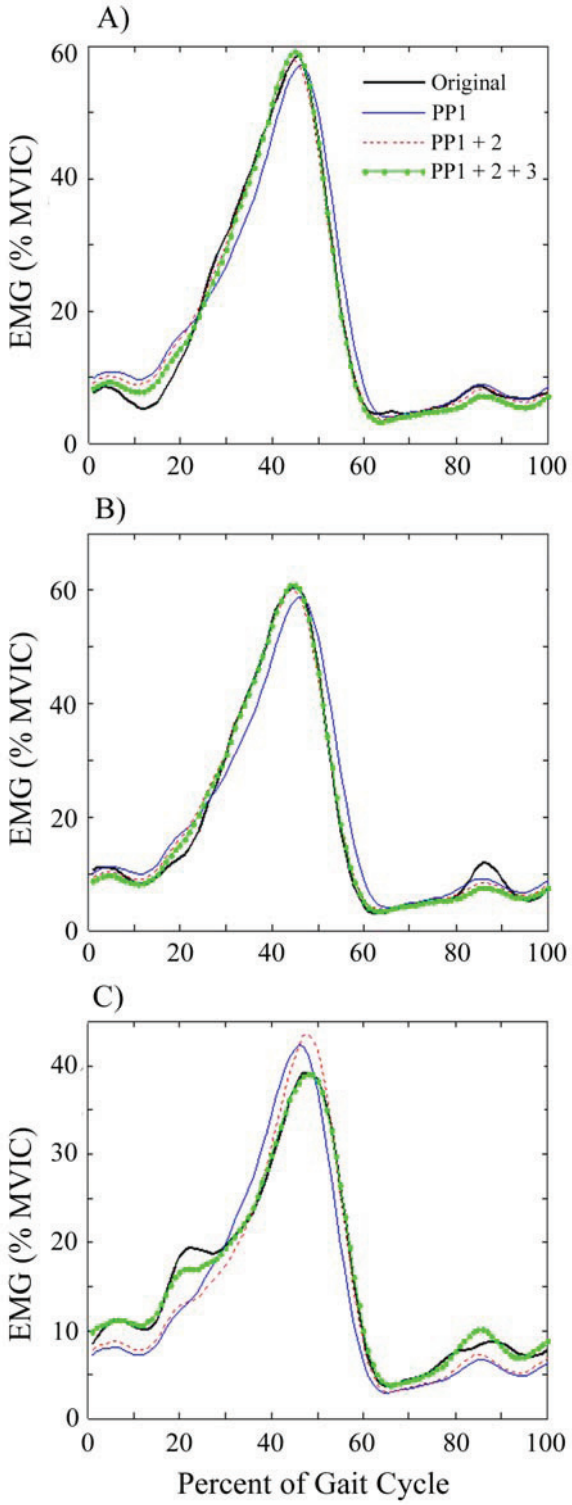

Figure B.3: Reconstruction of A) Asymptomatic B) Moderate knee OA C) Severe knee OA ensemble average medial gastrocnemius waveforms using PP1 (solid blue), with the addition of PP2 (dotted red) and with the addition of PP2 and PP3 (dash-dot green). Original ensemble average waveforms are shown in large font solid black.

Table B.1: Principal patterns, high *PP-score* interpretation and *PP-scores*.

	High *PP-Score* Interpretation	*PP-scores*		
Medial Gastrocnemius		Asymptomatic	Moderate Knee OA	Severe Knee OA
PP1	Greater Amplitude	245.0 (117.4)	253.0 (90.0)	181.6 (96.9)
PP2	Earlier Activity	28.1 (47.3)	34.2 (49.3)	-22.0 (41.0)
PP3	Larger Difference Between Early and Late Stance Activity Levels	9.0 (25.7)	6.7 (37.9)	-23.3 (24.1)

Table B.2: Root Mean Squared differences (% MVIC) between original and reconstructed medial gastrocnemius waveforms.

Group	Reconstruction		
	PP1	PP1 + PP2	PP1 + PP2 + PP3
Asymptomatic	2.5%	1.2%	1.1%
Moderate Knee OA	2.7%	1.2%	1.0%
Severe Knee OA	2.9%	2%	0.6%

APPENDIX C

SAMPLING RATE ANALYSIS: A COMPARISION OF 2000HZ AND 1000HZ ON WAVEFORM SUMMARY MEASURES

Appendix C addressed the effect of using two different sampling rates i)1000 Hz and ii) 2000 Hz for electromyographic recording on amplitude and temporal characteristics of the electromyographic waveforms. The majority of the data for this dissertation was collected at a sampling rate of 1000 Hz, however some of the data (36/272) included in the dissertation were collected using a 2000Hz sampling rate. A resultant waveform comparison of changing the sampling rate was done at the time that the change was made and minimal waveform differences were found between the two sampling rates. To demonstrate this effect, a subset of 25 participants with EMG data sampled at 2000Hz were randomly selected and compared.

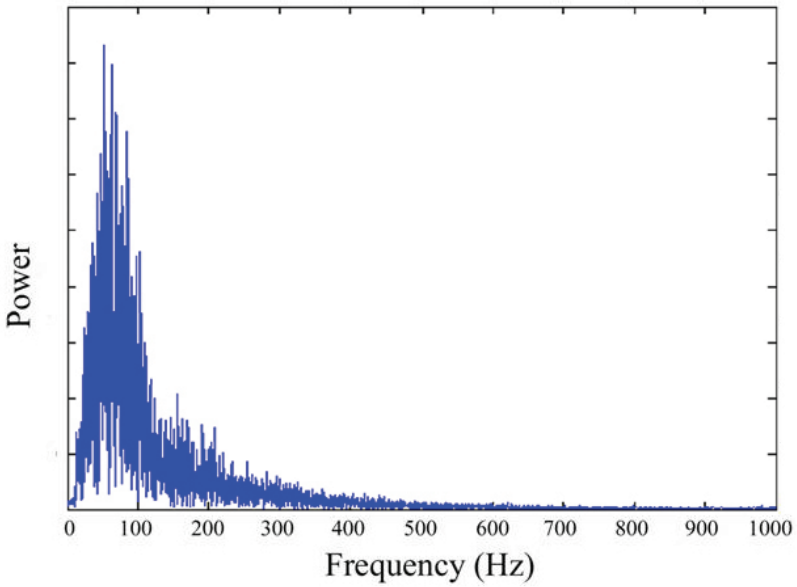

Figure C.1: Fast Fournier Transformation of EMG signal collected during three-second maximal voluntary isometric contraction at a sampling rate of 2000Hz.

Figure C.1 provides the frequency spectrum, derived using a Fast Fournier Transformation, of an EMG signal acquired during a maximal isometric quadriceps contraction of three seconds duration using the instrumentation described in this

dissertation. The spectrum extends from ~20 Hz to ~400Hz, with 92% of the signal power between these two frequencies consistent with previously described signal frequency spectrums acquired from surface electrodes [76,267]. As shown in Figure C.1, the majority of the signal is less than 400Hz with minimal power (~6%) between 400Hz and 1000Hz. High frequency signals between 500 and 1000 Hz could be recorded and sampling these signals at 1000Hz would result in signal aliasing, where this would not be the case if signals were sampled at 2000Hz. Based on Figure C.1, the influence of these high frequency signals are thought to be minimal. Previous work has demonstrated that minimal differences in timing and amplitude measures occur when surface EMG signals, sampled as low as 500Hz compared to higher sampling rates (1000Hz or greater) are compared [62,116] and are considered meaningless [62]. Therefore, it was hypothesized that there would be no differences in amplitude and temporal waveform characteristics between signals sampled at 2000 Hz and those down sampled at 1000Hz.

METHODOLOGY

Raw data were recorded from 25 participants with knee OA using standard procedures as outlined in Chapter 3 at a sampling rate of 2000Hz. For the gait trials, signals were windowed to demarcate the gait cycle (Chapter 3). Gait trials, MVIC trials and subject bias signals were down sampled to 1000Hz. All signals (2000Hz and 1000Hz) were corrected for subject bias and divided by the signal gain to represent the level of activity at the skin surface. All gait and normalization trials were full wave rectified and low-pass filtered (Butterworth, 6Hz cut-off frequency). Gait trial data were time normalized to a percentage of the gait cycle. A 100ms moving-average window, advancing one sample at a time (99ms-overlap between two adjacent windows) identified the maximal amplitude for each muscle from the MVIC trials. Gait trials were amplitude normalized to the respective MVIC amplitude for each muscle and sampling frequency. RMS differences were calculated across the entire gait cycle and stance phase as well as peak values during the stance phase and reported in both microvolts and % MVIC.

Results and Conclusions

RMS and peak difference values are shown on Table C.1. All gait trial differences were less than 0.28uV and less than 0.3% MVIC between the two sampling rates. As shown in Figure C.2, no observable amplitude or temporal differences existed between the electromyographic waveforms during walking sampled at 2000Hz and those down sampled to 1000Hz. The greatest voltage difference for the MVIC trials was found for MG (1.34uV) with the largest difference for an individual subject approximately 1.5% for the MG (i.e. 384.58uV and 378.86uV for the 2000 Hz and 1000Hz sampling rates respectively).

This appendix provides evidence that amplitude differences less than 1% MVIC are expected to occur between these two sampling rates using low-pass filtered, time normalized gait data. As shown in Figure C.2, these differences will have minimal effect on the interpretation of the electromyographic waveforms. Differences that have been interpreted to have either statistical or clinical importance, as shown in this dissertation, are greater than 1% MVIC. In conclusion, a 2000Hz sampling frequency is consistent with the band pass filter (10-1000Hz) of the AMT-8 (Bortec, Inc., Calgary, Alberta, Canada), eight channel EMG system. However, sampling at 1000Hz provides a representation of the electromyogram that has minimal differences compared to that obtained from 2000Hz sampling rate. Therefore including two sampling rates in the current dissertation is not expected to affect the interpretation of the electromyographic waveforms.

Table C.1: Mean and standard deviation (SD) differences between 2000Hz and 1000Hz sampling rates on electromyographic waveform summary measures.

Muscle	RMS_diff Gait Cycle		RMS_diff Stance		Peak_diff Stance		MVIC diff
	uV	%MVIC	uV	%MVIC	uV	%MVIC	uV
LG	0.14 (0.07)	0.12 (0.08)	0.18 (0.09)	0.15 (0.10)	0.23 (0.22)	0.28 (0.25)	1.24 (1.00)
MG	0.16 (0.10)	0.14 (0.09)	0.20 (0.12)	0.18 (0.11)	0.26 (0.27)	0.30 (0.25)	1.34 (1.28)
VL	0.10 (0.05)	0.06 (0.04)	0.12 (0.06)	0.07 (0.05)	0.17 (0.15)	0.11 (0.10)	0.82 (0.70)
VM	0.08 (0.07)	0.05 (0.04)	0.09 (0.08)	0.05 (0.05)	0.14 (0.17)	0.10 (0.12)	0.41 (0.39)
RF	0.05 (0.03)	0.04 (0.02)	0.06 (0.03)	0.04 (0.03)	0.06 (0.06)	0.06 (0.04)	0.50 (0.58)
LH	0.16 (0.14)	0.09 (0.08)	0.16 (0.15)	0.08 (0.09)	0.28 (0.35)	0.12 (0.12)	0.96 (0.97)
MH	0.09 (0.05)	0.04 (0.02)	0.08 (0.05)	0.04 (0.03)	0.14 (0.15)	0.07 (0.07)	0.89 (0.91)

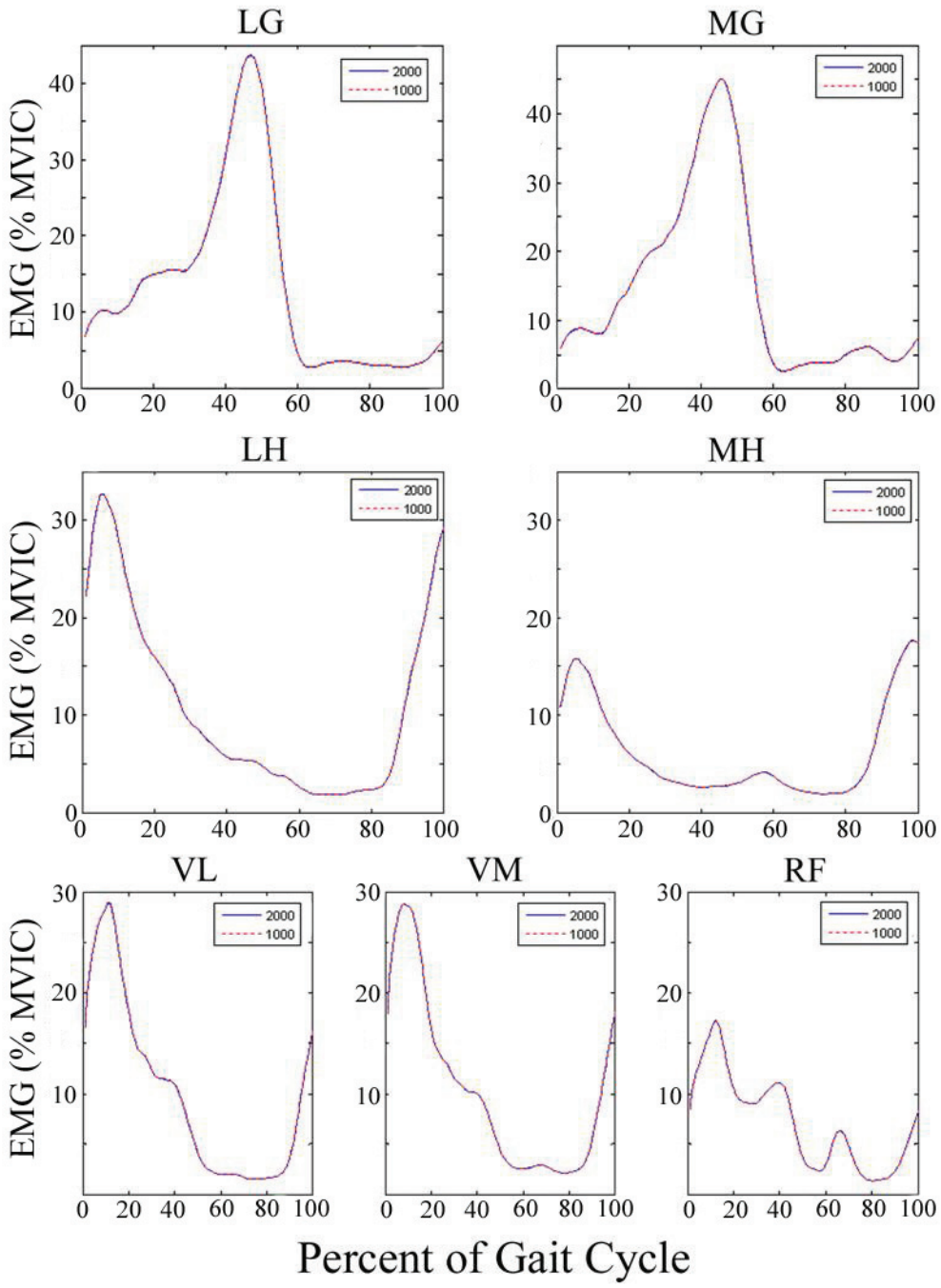

Figure C.2: Ensemble-averaged electromyographic waveforms during gait sampled at 2000Hz and those down sampled to 1000Hz for each muscle.

APPENDIX D

Electromyograms, Principal Patterns and Waveforms Associated with High and Low Principal Pattern Scores (*PP-scores*).

The information contained in Appendix D was included in this dissertation as an adjunct to the analyses completed in Chapters 4, 5 and 6. This appendix includes the individual waveforms used in the principal component analyses, the principal patterns and the mean of five waveforms to represent high and low principal pattern scores for each study separately. A figure is included for each muscle grouping. The individual waveforms are in the top panel, the three principal patterns explaining the highest percentage variance of the waveforms are depicted in the middle panels and the waveforms with the high and low scores in the lower panel. Note the similarities in principal pattern shapes regardless of the individual waveforms used in the analysis. This along with the similar high/low scores allows for comparisons of patterns across the three studies as was done in Chapter 7. It also demonstrates the stability of the patterns.

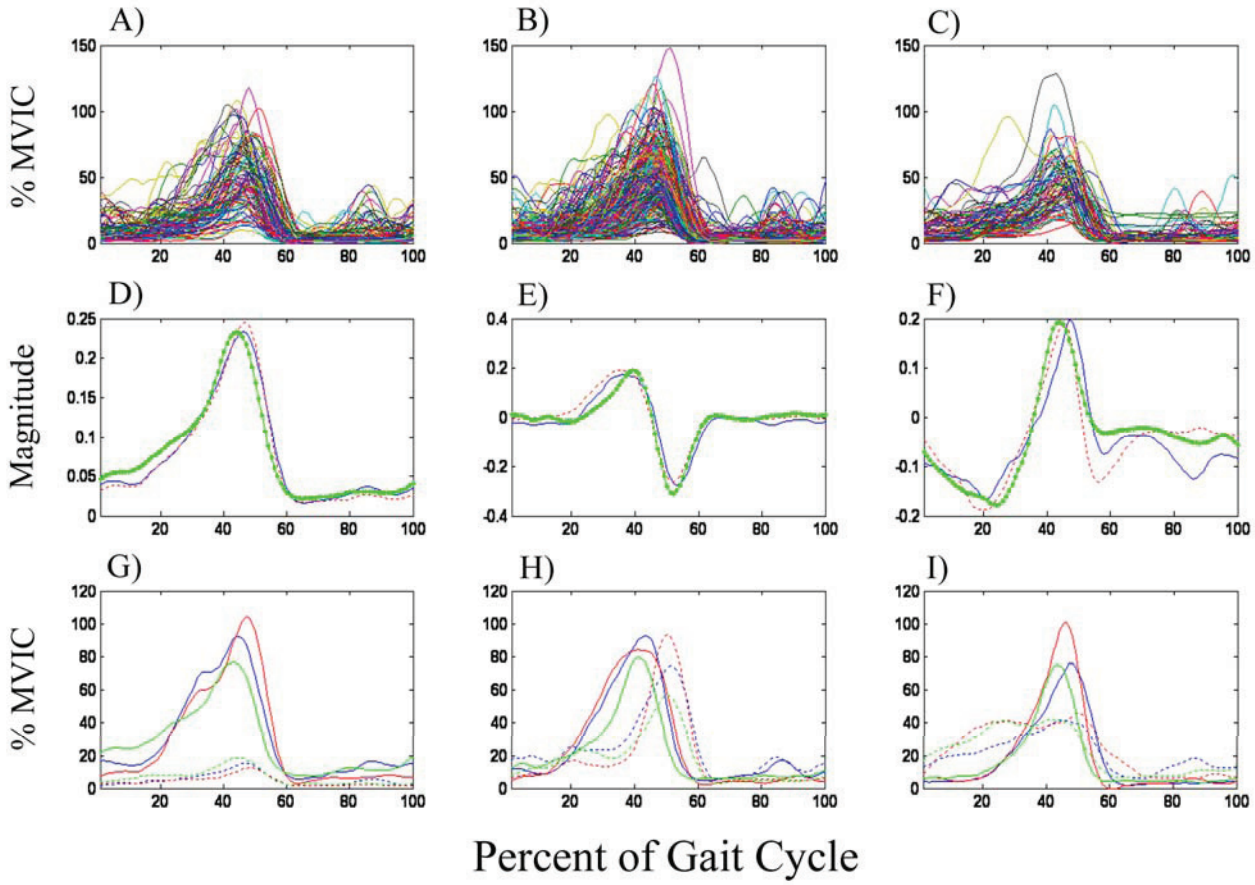

Figure D.1: Gastrocnemii electromyographic waveforms, principal patterns and the mean of five waveforms associated with high and low principal pattern scores for the studies included in Chapters 4, 5 and 6. Gastrocnemii electromyographic waveforms from Chapter 4 (n=94) (A), Chapter 5 (n=234) (B) and Chapter 6 (n=80) (C). PP1 (D), PP2 (E), PP3 (F) for each study (solid blue-Chapter 4, dashed red-Chapter 5 and dotted green-Chapter 6) and the mean of five waveforms associated with high and low principal pattern scores associated with PP1 (G), PP2 (H) and PP3 (I) where blue indicates Chapter 4, red (Chapter 5) and green (Chapter 6). Solid lines demarcate high scores and dashed lines demarcate low scores for the lower panel.

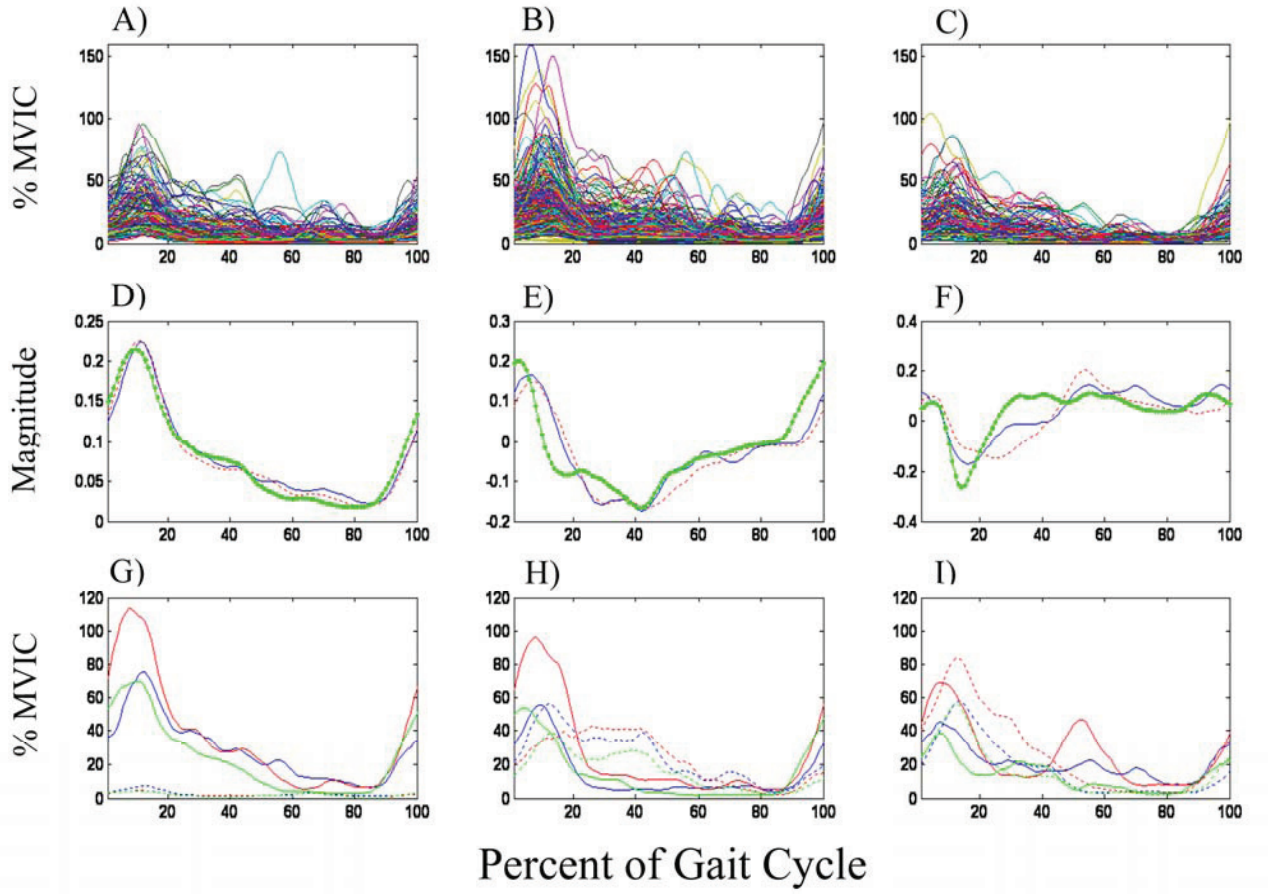

Figure D.2: Quadriceps electromyographic waveforms, principal patterns and the mean of five waveforms associated with high and low principal pattern scores for the studies included in Chapters 4, 5 and 6. Quadriceps electromyographic waveforms from Chapter 4 (n=141) (A), Chapter 5 (n=351) (B) and Chapter 6 (n=120) (C). PP1 (D), PP2 (E), PP3 (F) for each study (solid blue-Chapter 4, dashed red-Chapter 5 and dotted green-Chapter 6) and the mean of five waveforms associated with high and low principal pattern scores associated with PP1 (G), PP2 (H) and PP3 (I) where blue indicates Chapter 4, red (Chapter 5) and green (Chapter 6). Solid lines demarcate high scores and dashed lines demarcate low scores for the lower panel.

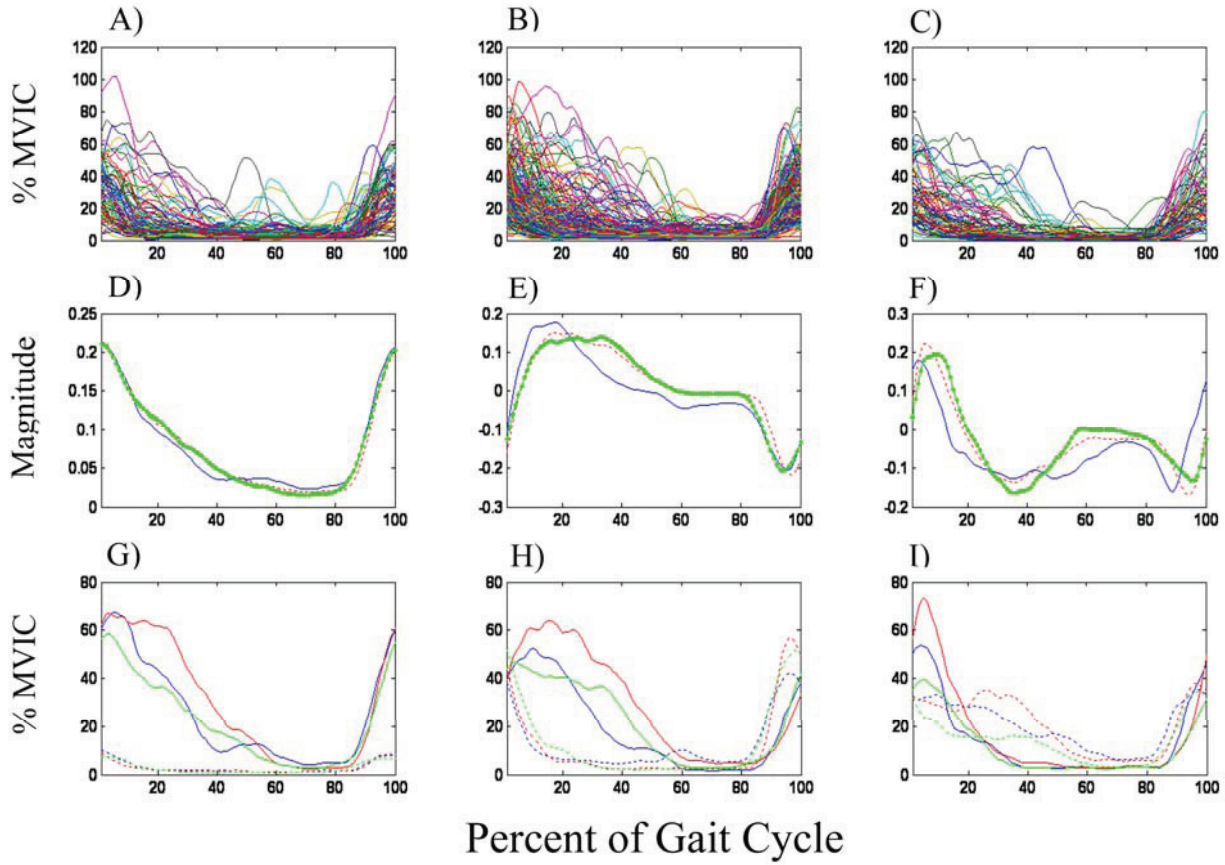

Figure D.3: Hamstrings electromyographic waveforms, principal patterns and the mean of five waveforms associated with high and low principal pattern scores for the studies included in Chapters 4, 5 and 6. Hamstrings electromyographic waveforms from Chapter 4 (n=94) (A), Chapter 5 (n=234) (B) and Chapter 6 (n=80) (C). PP1 (D), PP2 (E), PP3 (F) for each study (solid blue-Chapter 4, dashed red-Chapter 5 and dotted green-Chapter 6) and the mean of five waveforms associated with high and low principal pattern scores associated with PP1 (G), PP2 (H) and PP3 (I) where blue indicates Chapter 4, red (Chapter 5) and green (Chapter 6). Solid lines demarcate high scores and dashed lines demarcate low scores for the lower panel.

APPENDIX E

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