The Effect of Knee Joint Effusion on Gait Mechanics and Muscle Activation Characteristics in Moderate Knee Osteoarthritis

by

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Allah, thank you for the countless blessings & everlasting guidance.

This thesis is dedicated to my parents,
Amal Sunjuq & Hisham Saleh,
for always believing in me.

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ABSTRACT

Knee osteoarthritis (OA) is one of the most prevalent joint diseases, and knee effusion, as a manifestation of synovitis, is associated with knee OA clinical outcomes and disease progression. Thesis objectives were i) to determine whether an association between maximum suprapatellar recess (SPR) depth, and knee gait mechanics, muscle torques and activation amplitudes exists, and ii) to compare gait mechanics and knee joint muscle activations between individuals with and without effusion based on a cut-off value of ≥ 4 mm depth of the SPR. 50 participants were recruited, and knee joint motion was calculated from skin markers and moments calculated through inverse dynamics. Electromyography (EMG) of knee muscles was recorded using standardized procedures. No correlations were found between biomechanics and EMG data and SPR depth, however based on the 4 mm cut-off value, significant EMG alterations were found, which could be attributed to the sensitivity of the cut-off value.

LIST OF ABBREVIATIONS USED

ΔKFA1 – Difference between IC to peak knee flexion angle during stance

ΔKFA2 – Difference between early stance maximum to late stance minimum for sagittal angle

ACL – Anterior Cruciate Ligament

ACR – American College of Rheumatology

ADLs – Activities of Daily Living

ASIS – Anterior Superior Iliac Spine

BMI – Body Mass Index

CI – Confidence Interval

EMG – Electromyography

EULAR – European League Against Rheumatism

FFT – Fast Fourier Transform

GRF – Ground Reaction Forces

IC – Initial Contact

ICF – International Classification of Functioning Disability and Health

ISB – International Society of Biomechanics

KAM – Knee Adduction Moment

KL – Kellgren-Lawrence

KOOS – Knee Injury and Osteoarthritis Outcome Score

LG – Lateral Gastrocnemius

LH – Lateral Hamstrings

MG – Medial Gastrocnemius

MH – Medial Hamstrings

MOA – Moderate knee OA

MRI – Magnetic Resonance Imaging

MSK – Musculoskeletal

MVIC – Maximum Voluntary Isometric Contraction

NPRS – Numerical Pain Rating Scale

NSHA – Nova Scotia Health Authority

OA – Osteoarthritis

OARSI – Osteoarthritis Research Society International

PKAM – Peak Knee Adduction Moment

REB – Research Ethics Board

SD – Standard Deviation

SENIAM – Surface EMG for the non-invasive assessment of muscles

SPR – Supra-patellar Recess

TJA – Total Joint Arthroplasty

US – Ultrasound

VL – Vastus Laterlis

VM – Vastus Medialis

WHO – World Health Organization

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CHAPTER 1 INTRODUCTION

1.1 Introduction

Osteoarthritis (OA) is defined as a disorder that involves moveable joints that are characterized by cell stress and extracellular matrix degradation that triggers the activation of maladaptive responses in the joint which include pro-inflammatory pathways of innate immunity (1). The most commonly affected joint is the knee joint, with the medial tibial-femoral compartment mostly affected (2). The previous established hallmark of the pathophysiology of OA include the change and breakdown of articular cartilage, however the Osteoarthritis Research Society International (OARSI) established OA as a molecular derangement that is followed by anatomic or physiologic derangements. All these manifestations of the disease are characterized by cartilage degradation, bone remodelling, osteophyte formation, joint inflammation and loss of normal joint function (1).

In addition, OA has been recently classified as a whole joint disease as it not only affects articular cartilage, but the integrity of multiple joint structures, including bone, synovium, ligaments, muscles and other fibrocartilaginous structures. The discovery of non-cartilaginous changes arose from the curiosity of understanding the source of pain, as articular cartilage is avascular and aneural (3). In addition to that, the discovery of certain inflammatory mediators, such as cytokines and prostaglandins, established the beginning of an inflammatory theory. In OA, the synovial membrane becomes a source of these pro-inflammatory mediators (3). Thus, any changes occurring in the synovial membrane, such as inflammation, can induce the production of factors that degrade cartilage and decrease the factors that protect cartilage (3). This inflammatory response manifests itself in the joint as the presence of effusion synovitis and/or thickening of the synovium, and is a common clinical feature in individuals with knee OA (4), with almost 55% having moderate to large effusions (5). These discoveries have caused a shift from thinking of OA as a passive, degenerative condition to recognizing it as an active disease process of the joint, that can be modified by mechanical and biochemical interventions (6).

Not only does OA affect the individual on a personal basis, but it also has a great economic burden on society. It is the most common cause of disability and costs are

expected to rise at an alarming rate as the burden of OA increases on the health care system and workforce productivity (7). Canada has one of the longest wait times for a total joint arthroplasty (TJA) for OA (8), highlighting the fact that many individuals diagnosed with OA have been left waiting for their end-stage treatment. By understanding the functional status of an individual, rehabilitative interventions could be developed and monitored for the restoration of function.

The World Health Organization's (WHO) International Classification of Functioning Disability and Health (ICF) provides a standardized health status framework that comprehensively describes the functional status of an individual suffering from a disease or disability (9). In the context of knee OA, impairments to body and physiological functions of the knee joint include bone, cartilage, synovium (6,10) and neuromuscular system (11). These impairments associated with the OA population lead to activity limitations (12,13) and some have been reported to play an important role in the progression of the disease (2,14,15). Therefore, through studying the effect these impairments have on each other, knowledge can be obtained in order to promote quality of life during functional human movement.

Human movement is a complex dynamic process and requires highly coordinated mechanical interactions between bones, muscles, ligaments and other joints within the musculoskeletal system (16). Gait analysis has been used as a useful model to indirectly assess the *in vivo* loading environment and functional changes associated with knee joint pathology during functional activities, such as walking (17). Under normal walking conditions, loading stresses are more medially distributed in the tibia-femoral joint (18,19), however in medial-compartment knee OA, compressive loading in the medial tibia-femoral joint is increased beyond normal physiological limits (20). This frontal plane loading has been quantified via the adduction moment, which has been a measure of the medial to lateral joint load distribution (21,22), and those with knee OA have been reported to walk with higher magnitudes of knee adduction moment (22–25). Other findings based on gait analysis for knee OA report less range of motion, mainly in the sagittal plane. The reduction in sagittal knee flexion is often coupled with a reduction in knee flexion moment during loading response (26–28) and has been referred to as "dynamic joint stiffness (28,29)." In addition, neuromuscular adaptations in response to

knee OA have been reported and hence can influence joint stability and loading. The quadriceps and hamstrings generally exhibited higher and more prolonged activation levels during the stance phase of gait for individuals with knee OA (30–33), whereas gastrocnemii activation have been reported to be altered (30,34,35).

Despite knowing the effects of knee OA on the biomechanical and neuromuscular environment of the knee, little is known on how the biochemical process of knee OA impacts the biomechanical and neuromuscular environment of the knee joint. Both components of the disease, biomechanical and biochemical, have been reported to relate to patient symptom severity and progression of knee OA (2,14,15), and hence can have important implications on the disease process. The biochemical environment of the knee is usually characterized by increased levels of inflammatory biomarkers (36,37), which has been associated with synovitis, specifically effusion (38). Limited studies have investigated the effects of both components on each other and have reported inconsistent findings (39–42). Most of the previous research done on knee joint effusion mainly represented acute effusion models, where healthy knees were experimentally infused with saline. Initial research on acute effusions focused on its effect on quadriceps muscles, where they reported quadriceps inhibition patterns and altered gait mechanics (39,43–46). Other studies investigating the effect of infused-knee effusion during jogging and drop landing on healthy individuals reported more extended knee angles during stance and also reduced quadriceps electromyography (EMG) (40,47). The studies that represented acute effusion models did not investigate and represent pathological knee conditions with effusions, such as OA. However, recently a walking study was performed on individuals with moderate knee OA and clinically-detected effusion through the brush test reported contrary findings in regards to quadriceps EMG, where individuals with effusion walked with increased quadriceps muscle activations (42). Findings of Torry et al., (2001; 2005) and Palemieri et al., (2004) supported an acute effusion model causing inhibition of the quadriceps muscles, whereas findings of Rutherford et al., (2013) supported altered knee muscle activations associated with chronic effusion models, which may not cause quadriceps avoidance gait patterns as supposed by others (48,49). It could also be speculated that those differences between acute and chronic effusion models could be attributed to the cellular mechanisms associated with latter, not present in the former. It

has already been established that biochemical differences exist between OA knees with and without effusion (38), however limited information on whether biomechanical and neuromuscular differences exist between OA knees with and without effusion. Therefore, understanding the different factors associated with inflammation could help identify subsets of knee OA patients that can be targeted towards improving diagnosis and intervention.

Fluid is most commonly found in the suprapatellar recess or the lateral or medial parapatellar regions of the knee (4), with 76% of effusions found in the suprapatellar recess of the knee joint (50). Effusion-synovitis can be quantified by measuring the size of effusion present in the joint (4), and can be detected through various methods, including ultrasound (US). Ultrasound is a non-invasive imaging modality used to report objective inflammatory findings in OA (51), and although it has been found to have lower specificity and sensitivity compared to magnetic resonance imaging (MRI) (52), it has been shown to provide valid, reliable comparable assessments of synovial disease to those provided by MRI (14,52). Recent ultrasound research support other imaging and clinical evidence that synovitis is a common feature of OA (4), and that US-detected effusion is an independent predictor of joint replacements, radiographic and patient symptom severity (14,15). The European League Against Rheumatism (EULAR) established standard guidelines on the sonographic evaluation of effusion in the knee, where an effusion depth ≥4 mm is considered the cut-off value for detection of effusion (14).

Therefore, for this thesis, US will be used to detect effusion in the supra-patellar recess to understand the influence of knee effusion-synovitis on the biomechanical and muscular environment of the knee joint. To this time, there is no clear understanding on the effect of knee effusion on individuals with moderate knee OA, despite multiple studies reporting effusion-synovitis as an independent predictor of disease progression (14,15,53) and multiple studies reporting gait biomechanics and muscle activation patterns as independent predictors of progression (21,26,54). How knee effusion is related to the deterioration of knee OA is not fully understood yet the inflammatory mediators and enzymes are believed to inhibit the production and re-modelling of cartilage, thus degrading cartilage even further (37). It has also been reported that individuals with knee effusion, whether acute or chronic, demonstrate altered mechanics and neuromuscular

activations, but only one study explored the effect of these alterations on OA knee joint function (42). Therefore, understanding whether a relationship exists between knee joint mechanics and effusion in a sample of individuals with moderate knee osteoarthritis, is the main focus of this thesis. This could possibly bring us to a closer understanding of why effusion is considered an independent predictor of disease progression and could provide a more holistic understanding of knee OA.

1.2 Specific Objectives

The thesis objective will be divided into two sub-objectives:

1. Determine whether an association between maximum suprapatellar recess (SPR) depth, as a measure of knee effusion, and sagittal plane knee motion, sagittal and frontal plane net external moments and knee joint muscle torques, and activation amplitudes exists during gait in individuals with moderate medial compartment knee OA.

The following alternative hypotheses will be tested:

1. There will be a positive linear association between SPR depth and sagittal knee flexion motion during stance, and a negative linear association between SPR depth and sagittal extension motion during stance.

2. There will be a positive linear association between SPR depth and net external sagittal knee flexion moment throughout the stance phase, and a negative linear association between SPR depth and net external sagittal knee extension moment throughout the stance.

3. There will be a positive linear association between SPR depth and peak knee adduction moment (PKAM) throughout stance.

4. There will be a positive linear association between SPR depth and quadriceps and hamstrings muscle activation amplitudes, and no association between SPR depth and gastrocnemius muscle activation amplitudes during stance.

5. There will be a positive linear association between SPR depth and both knee flexor and extensor strength values.

2. Compare sagittal plane knee motion, net external sagittal and frontal plane moments and knee joint muscle activation amplitudes between individuals with and without effusion based on a cut-off value of ≥ 4 mm depth of the SPR in individuals with moderate knee OA.

The following alternative hypotheses will be tested:

1. There will be higher sagittal knee flexion motion and lower knee extension motion through stance phase in those with knee effusion of ≥4 mm in the SPR.

2. There will be higher net external sagittal flexion and lower sagittal extension moments throughout stance phase in those with knee effusion of ≥4 mm in the SPR.

3. There will be a higher frontal plane moment, peak knee adduction moment (PKAM), in those with knee effusion of ≥4 mm in the SPR.

4. There will be increased and more prolonged quadriceps and hamstrings activation levels, and no differences in medial and lateral gastrocnemius activations in those with knee effusion of ≥4 mm in the SPR.

5. There will be no difference in knee flexion and extension strength values between groups.

CHAPTER 2 REVIEW OF RELEVANT LITERATURE

2.1 Introduction on OA

Knee osteoarthritis (OA) is the most common joint disease and is a major cause of pain and disability (2). It has been characterized as a whole joint disease that affects the integrity of multiple knee joint structures, including the mechanical and biochemical environments of the knee. The mechanical environment describes the loading environment and the structures that contribute to the loading and mechanics of the joint. Whereas, the biochemical environment is usually characterized by increased levels of inflammatory biomarkers (55), which has been associated with synovitis, specifically effusion (38). Most of the previous research conducted studied the effects knee OA has on the mechanical environment of the knee. However, little is known on whether the biochemical process of knee OA impacts the mechanical environment of the knee joint, especially since both components of the disease have been related to the progression of knee OA (14,15).

2.2 Burden of OA

2.2.1 Economic Burden

Osteoarthritis is an important community healthcare burden and with increased longevity, reduced physical activity and lack of access to timely health care, the burden of OA is expected to rise (7). Adults diagnosed with OA are twice as likely more than those without OA to have at least one other chronic health condition, which is a major barrier to receiving appropriate care and leads to progression of the disease (7). Findings from *The Impact of Arthritis in Canada: Today and Over the Next 30 Years* show that in the next 30 years, the burden of arthritis is expected to have significant implications on healthcare and costs on Canadians (7). More than 4.4 million Canadians are living with OA, and within 10 years more than 10 million (one in four) Canadians are expected to suffer from OA. There will be a new diagnosis of OA every 60 seconds, with almost 30% of the working population (one in three workers) facing difficulty during work due to OA (7). OA is already reported to have devastating effects on employment, community mobility, leisure and social activities in middle-aged and older adults (7). The yearly cost of arthritis in Canada is estimated to be $33 billion (8), mostly burdening Canadians of

working age. Costs are expected to rise at an alarming rate as the burden of OA will increase on the health care system and workforce productivity (7). Joint replacements are on the rise and also expected to increase, and in Canada's 10-year plan to strengthen health care, joint replacements were one of the five priority areas identified to wait time reductions (8); indicating that many individuals have been left to wait for their end-stage treatment.

2.2.2 Physical Burden

People with knee OA often show characteristic patterns of decline in functioning concerning mobility and activities of daily living (ADLs) involving lower extremities (56). Understanding the functional status of an individual serves importance in the development and monitoring of rehabilitative interventions for restoration of function. From this perspective, the World Health Organization's (WHO) International Classification of Functioning Disability and Health (ICF) provided a globally-agreed health framework that described an individual's functional status in a comprehensive view (57).

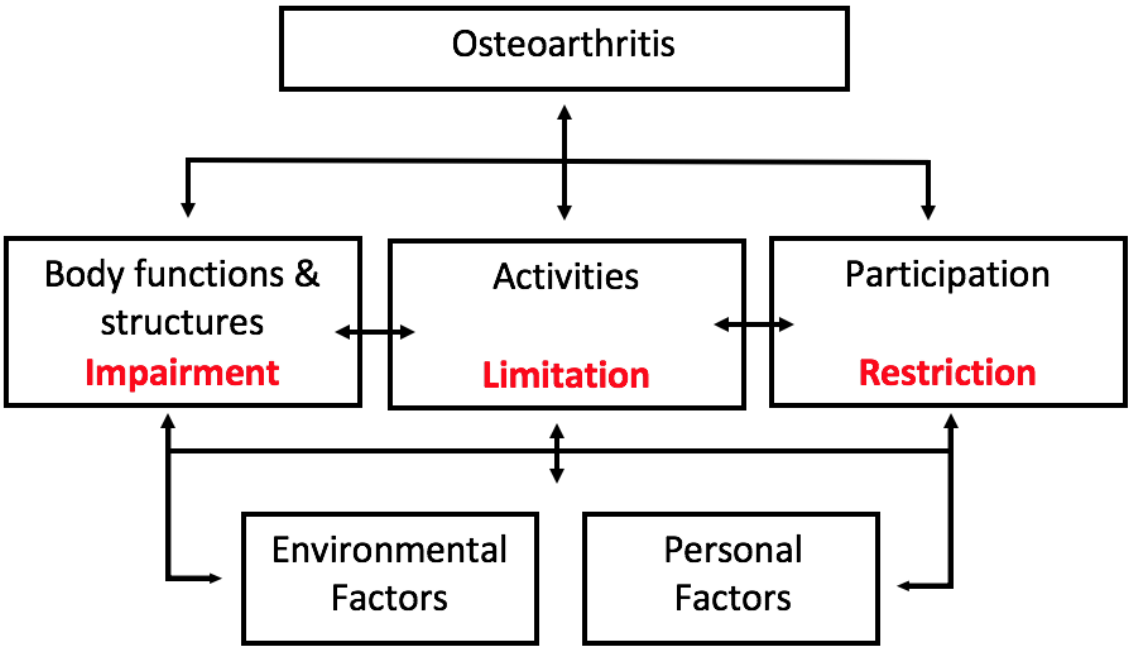


Figure 2. 1: The World Health Organization's International Classification of Functioning Disability and Health Framework (World Health Organization, 2001), and has been modified to reflect knee OA.

The ICF model can be used when investigating diseases and disabilities by providing a multi-dimensional view for classification of the disease (58) and is composed of three main components, i) body function & structural impairments ii) activity limitations iii) participation restriction together with contextual factors that include i) personal and ii) environmental factors. The functional aspect in ICF is classified into activity and participation components. The health-related part of the ICF model classifies OA into two components; 1) body structures that include categories like cartilage, bone and soft tissues and 2) body function that include categories like pain and mobility in the joints (58). Additional impairments to the physiological functions of the knee joint include the synovium (6,10) and neuromuscular system (11). The ICF also addresses the contextual factors of an individual that can be affected by the functional and health-related components of the disease (56,58). In OA, it has been established that a discrepancy exists between objective measures related to structural changes associated with OA and patient reported measurement outcomes (58,59). Impairments to the synovium, synovitis, has been seen to explain some of the discrepancies reported in individuals with symptom and radiographic severity in OA (4), specifically US-detected effusion synovitis. Since structural and physiological impairments affect joint function and can lead to activity limitations, the ICF model provides an overview for understanding how the joint functions in response to knee OA, particularly synovitis effusion for this thesis. The main purpose of this thesis is to understand the relationship between joint impairments and activity limitations, specifically walking as it is the most common activity of daily living as well as one that produces cyclical patterns of loading (54).

The next section will provide an overview on the studies that investigated the mechanical (kinematic and kinetic) environment of the knee joint in response to different levels of knee OA severity.

2.3. The Knee Joint

Current research has mainly focused on the effects of passive osteoligamentous impairments in the presence of knee OA, which has helped expand the scope on knee joint function and muscle activations on healthy and diseased joints. While important, it has diverted focus from other important mechanisms involved in knee joint function. Little is known on their impact on joint function and stability, especially in those with

knee OA, since it's an essential component of neuromuscular control, which allows engagement in everyday activities (60). Therefore, this section will provide a literature review on the anatomy and impact of healthy and osteoarthritic knee articular pressures and capsules on the knee and its structures.

2.3.1 Healthy Knee Joint

2.3.1.1 Anatomy

The knee joint is a modified hinge joint in the lower extremity, composed of three articulations located in the same capsule, the medial and lateral tibiofemoral joint and patellofemoral joint (61,62). As a modified hinge joint, it allows great range of motion around the sagittal plane in the coronal axis, and accessory motions in the transverse and coronal planes (62). In addition to the knee's role in providing mobility, it also serves an important role in providing stability during static and dynamic situations (61,62). The knee joint is composed of multiple joint structures, including bones, cartilage, ligaments, synovium and other fibrocartilaginous structures (3), that serve the joint's overall mobility and stability needs. This stability framework is highlighted in Panjabi's stability model, where the stabilizing system of joint function is influenced mainly by the coordination of three subsystems that include the passive, active and neural subsystems (63).

Of the passive structures, there is not much literature on the role that synovial fluid and the corresponding intra-articular pressures play in providing stability. Therefore, the next section will discuss the effect intra-articular pressures and synovial fluid have on maintaining a healthy knee joint.

2.3.1.2 Intra-Articular Pressures

Observations from previous literature agree that resting intra-articular pressures in healthy knees are slightly sub-atmospheric, approximating around -4 mm Hg (64). When the joints are moving and muscles are contracting, the intra-articular pressure has been seen to decrease even further by more than 100 mm Hg during isometric quadriceps contractions (65), however Gaffney et al. (1995) found no changes with isometric exercises for smaller joints, like the wrist, elbow and ankle. The most likely explanation to the decrease in intra-articular pressures are attributed to patellar motion during knee isometric exercises, which is a factor not present in other smaller joints (66). This

explanation supports the stabilizing factor associated with decreased pressures, as the simple movement of one joint surface over the other draws tissues towards each other (66,67).

2.3.1.3 Synovial Fluid

In addition to the knee's intra-articular pressures in providing stability, the knee joint's capsule also protects and adds stability to the knee. The joint capsule that encloses the tibiofemoral and patellofemoral joints extends anteriorly above the patella to attach along the edge of a shallow fossa (62). This capsular attachment forms a deep recess above the patella, called the suprapatellar recess (SPR). Due to the SPR's location between the quadriceps femoris muscle tendon and femur, it helps reduce friction between these two structures (62). In addition to the SPR, there are various other recesses formed in order to lubricate the joint and reduce friction between surfaces (61,62). During normal knee motions of knee flexion and extension, synovial fluid moves from recess to recess for lubrications purposes, promoting the mobility needs of the joint. (62). Although there are no standardized values for all physiological recesses present in the knee, there have been inconsistent studies that reported physiological values of SPR, where some have reported SPR depth to range from 1-4 mm in depth (68), while others reported it to be less than 2 mm in depth on a longitudinal US scan (4,69).

Similar to other joints in the body, the knee joint is subject to injuries and disease processes. The knee however is predisposed to more injuries compared to other joints since it supports the body weight while providing mobility, and also joins two of the longest levers in the body (62). Thus, when normal function is disrupted, the knee becomes subject to abnormal stresses that eventually lead to degenerative changes to the rest of the knee structures. Hence, the next section will discuss the anatomy of an osteoarthritic joint and its effect on surrounding joint structures.

2.3.2 Osteoarthritic Knee Joint

2.3.2.1 Anatomy

In previous years, OA was established simply as a "wear and tear" condition of cartilage, which was based on the preceding theory that chondrocytes had no ability to repair cartilage due to their non-vascularized and non-innervated nature (36). The

development in molecular biology in 1990's began to change this theory, where discovery of certain inflammatory mediators, such as cytokines and prostaglandins (36) established the beginning of an inflammatory theory as well. Although most of the striking pathological changes are found in articular cartilage, OA is not a disease of any single tissue, rather a disease of the entire synovial joint, the synovial joint (70). This concept is analogous to heart disease, where a primary issue in either the endocardium, epicardium or myocardium may lead to congestive heart failure (70). Similarly, any problem in any of the knee joint's components, such as cartilage, subchondral bone, synovium, periarticular muscles or supporting ligaments, could lead to joint failure. Panjabi's model, as described in *section 2.3.1.1.* is vital in OA, where damage to the passive subsystem due to degeneration of knee joint structures and joint deformity, triggers the neurological subsystem to cause compensatory changes in the active, muscular subsystem.

2.3.2.2 Intra-Articular Cartilage

The synovial membrane is believed to be the source of inflammation during the osteoarthritic disease process (3), and is usually manifested by joint effusion, which is a common clinical finding in those with knee OA (5). In the presence of effusion in OA, the stabilizing influence is seen to be lost (66), as intra-articular pressures increase to supra-atmospheric levels (49,71). Gaffney and colleagues (1995) found resting intra-articular pressures greater than atmospheric pressures in rheumatoid joints. It's also been reported that isometric muscle contractions actually lead to substantial increases in intra-articular pressures (71,72). This increase in pressure is suggested to be explained by the extrinsic compression of the closed articular space, and is associated with rheumatoid knees and older adults that have less compliant articular capsules (73). The increase in pressure has been associated with quadriceps inhibition and also seen to depend on whether effusion is acute or chronic. Acute effusion models mainly represented acute traumatic conditions or experimentally-infused effusions into healthy knee joints, whereas chronic effusions represented effusions present in chronic conditions, such as OA. Merry et al. (1991) has investigated differences related to intra-articular pressures and quadriceps inhibition between acute and chronic effusions present, with resting mean intra-articular pressures significantly lower (2.0 mm Hg) and greater quadriceps inhibition seen in those with acute effusions compared to those with chronic effusions (19.6 mm Hg) (49). These

pressure differences have been seen to be related to decreased quadriceps muscle tone in those with acute effusions, as they exhibited greater quadriceps inhibition compared to those with chronic effusions (49). Additionally, the chronically effused joint capsule demonstrated higher elasticity, allowing generation of higher joint pressures (49). Even though the differences in joint health could also be a contributor to the differences seen between both effusion models, these differences provide an insight on the role effusion plays during acute and chronic situations.

2.3.2.3 Synovial Fluid

The changes seen in intra-articular pressures are assumed to occur as a result of inflammation of the synovium. How inflammation of the synovium, synovitis, develops seems to not be clear, however a few hypotheses have been formulated. The most accepted hypothesis states that synovitis occurs due to the falling fragments of cartilage into the synovium during the degradation process of cartilage (36). The body views these fragments as foreign bodies, initiating an inflammatory response in the synovium. This inflammatory response produces inflammatory mediators that activate chondrocytes and synovial cells into synthesizing inflammatory cytokines, further increasing the degradation process (36). Synovitis, hence, is hypothesized to cause a vicious perpetuating cycle of cartilage degeneration. This inflammatory response manifests itself in the joint as the presence of effusion synovitis and/or thickening of synovium, and is a common clinical feature in individuals with knee OA (4). Excessive synovial fluid is most commonly found in the suprapatellar recess or lateral or medial parapatellar regions of the knee (4), with 76% of effusions found in the suprapatellar recess of the knee joint (50). According to the European League Against Rheumatism (EULAR) guidelines, an effusion depth ≥ 4 mm is considered the cut-off value for detection of effusion (14). Similarly, Martino et al. (1992) considered thickness values of SPR depth greater than 3-4 mm to be pathological features, supporting EULAR's findings. Hong et al. (2010) however found that 4 mm decreases the detection rate of knee effusion by 50% and that 4 mm is too high, since more than 10 ml of fluid has to be in the joint in order for it be detected sonographically; and suggested that 2 mm would be a more reasonable cut-off value (69). Despite Hong et al.'s (2010) findings, it was concluded that the exact amount

of effusion that was deemed clinically significant is still unknown (69) and more studies are needed to establish the most appropriate cut-off value for detection of effusion.

In summary, changes seen in passive structures in the knee joint between healthy and effused knees suggest a change in stabilizing forces, where effused knees are a common finding in those with knee OA and have a negative effect on intra-articular pressures. The change in stability in the joint could possibly explain some of the mechanical and neuromuscular compensations seen in those with knee OA and effusion. Therefore, the next section will provide an overview on the studies that investigated the mechanical (kinematic and kinetic) and neuromuscular environments of the knee joint in response to different severity levels of knee OA.

2.4 Joint Function During Gait in OA

Measurements performed under dynamic loading, such as walking, have been done in order to assess biomechanical function of the knee joint. Modern gait analysis has enabled the understanding of mechanisms for knee OA progression by measuring biomechanical and electromyography (EMG) responses to the disease process (32,74,75). It has been used to help identify important kinetic and kinematic factors at different levels of knee OA severity. Mechanical changes such as knee angles and moments (25,26,75–77) and muscular changes of lower extremity (25,31,32,40–42,77–79) have been previously reported to be associated with increased severity of OA and with the presence of effusion synovitis.

2.4.1 Joint Mechanics

2.4.1.1 Knee Kinematics

In knee OA literature, the most commonly identified changes are sagittal plane kinematics, while frontal and transverse plane are usually smaller changes and less commonly-reported, as can be products of kinematic crosstalk (80). Not all studies reported consistent findings in regards to sagittal plane angles, where some reported greater knee flexion angles (25,77), some reported greater knee extension angles (2), while others reported no differences between asymptomatic and OA groups (27,81). In addition, one of the most common symptoms in OA, pain, has been previously reported to be associated inversely with the dynamic range of sagittal plane motion (82). This is

consistent with movement avoidance patterns in an attempt to minimize pain experienced (83). Another study supporting this notion found increases in knee range of motion and walking speeds after pain relief in people with knee OA (84).

Knee frontal angle changes have also been reported in the literature, where individuals with knee OA generally have increased knee varus during stance phase (75,85,86) and valgus during swing phase (75). Increases in varus angles during stance would be an expected mechanical response in individuals with medial knee OA as the medial compartment is narrowed and lateral compartment is opened in various degrees (75). However, in cases of excessive varus angles, another possible explanation could be an experimental error produced by unintentional placement of skin markers on the internally rotated thigh (75). Increase in valgus angles during swing could be attributed to increase in lateral soft tissue pretension or to internal rotation of the limb (75).

In summary, although kinematic assessments describe motion and are important to note, especially in situations where joint pathology exists, it does not provide information regarding the forces that cause the motion. Therefore, kinetic assessments are also required in order to get a more holistic understanding of normal and abnormal joint function during gait. Kinetic assessments study the forces that generate movement and quantifies these forces in different planes of motion. The next section will provide a summary of the literature on main kinetic changes observed in individuals with medial knee OA.

2.4.1.2 Knee Kinetics

A main and critical kinetic biomechanical indicator of OA has been the external knee adduction moment (KAM), and has been reported in the literature as a peak value of approximately 10-20% of stance phase. Load distribution of the knee during walking is determined by calculation of KAM (21), which reflects medial to lateral joint load distribution. A higher KAM would indicate higher loads in the medial compared to lateral compartment of the knee and is usually associated with a varus deformity (21,87) and increased medial joint space narrowing (21). Peak KAM (PKAM) have been found to be good indicators of rate of progression (2,21,22,88,89) and clinical outcomes in knee OA in patients with medial compartment knee OA. Astephen et al., (2008) investigated biomechanical responses of asymptomatic, moderate and severe knee OA and reported

that joint loading changes did not significantly discriminate severe from moderate groups, and was suggested that knee joint loading mostly affected earlier stages of the disease, indicating clinical significance aimed at decreasing joint loading implications at early clinical levels (26). Others have found that the adduction moment at baseline predicted radiographic progression of the disease (21) and that it correlated with disease severity in tibiofemoral knee OA (90)(84). Sharma et al., (1998) suggested that the magnitude of the adduction moment could influence structural progression in the medial compartment, and lead to a more varus alignment, which has been reported to increase risk of progression in knee OA (91). Another main factor that could explain increased peak knee adduction moments includes pain associated with OA, where individuals with higher pain scores were found to walk with higher magnitudes of PKAM (92). This however is not a consistent finding, where some have found no biomechanical alterations associated with pain (93), while others found increased PKAM following pain relief (84).

Other important kinetic changes observed in the OA population include sagittal moment differences. Net external sagittal plane moment has been shown to differ between asymptomatic, moderate and severe OA groups. Some studies have shown that individuals with knee OA walk with reduced early stance flexion moments, while others reported increases in knee flexion moments (94,95). This increase has not only been related to OA changes, but related to faster gait speeds (23,26,96). In addition, external knee extension moment has been reported to be reduced at terminal stance (54,94,95). Greater knee flexion and reduced knee extension moments could be due to elevated co-contractions of knee muscles in order to compensate for decreased joint stability (95), excessive frontal plane laxity (97) or a response to flexion deformities such as flexion contractures (94). In these cases, when knee joint remains in a flexed position, the direction of the ground reaction force would shift posterior from the joint center of rotation, lengthening and increasing the knee flexion moment and reducing the knee extension moment (Debbi et al., 2015).

In summary, these findings highlight the importance of understanding underlying mechanisms that are causing some individuals with knee OA to walk differently than others also with knee OA, especially during stance phase. These differences could potentially alter the loading environment of the knee joint and lead to faster progression

of the disease. The study of gait mechanics of a joint solely does not take into account the muscles that provide moments of force in order to produce motion. Therefore, the next section will provide a review on neuromuscular alterations that have been reported in response to OA.

2.4.2 Neuromuscular Activations

Muscles play an important role in knee joint function during walking as dynamic stabilizers (99), and it is important to understand activation differences that may be present in individuals with compromised knee function or stability. Although the main impairments associated with knee OA include passive structures associated with knee joint structures and joint deformity, the active neuromuscular system is triggered to maintain joint stability during gait, as conceptualized through Panjabi's joint stability model (63). The measurement of muscle activations during walking in knee OA is done by recording of electrical activity from muscles under investigation using electromyogram (EMG). Electromyograph amplitude differences are then calculated either by use of peak or mean values during different phases of the gait cycle or by interpretation of activation patterns (32). Recent studies have investigated EMG differences, where larger differences have been reported with increased severity of OA (31,35,100). Some individuals with knee OA seem to activate their muscles efficiently in order to counter-balance the external knee adduction moment during walking, whereas others have adopted less efficient activation strategies by co-contracting, which may increase overall joint loading (11,33).

2.4.2.1 Hamstrings

Hamstring activation characteristics have been reported to be sensitive to severity changes associated with medial knee OA, despite similar walking velocities and strength values (31). Higher lateral hamstring activity has been reported in those with knee OA compared to asymptomatic controls (30,31,100). Similar findings by Schmitt and Rudolph (2007) found increased activation of lateral hamstrings and gastrocnemius before foot contact, as well as increased co-contraction of hamstrings and quadriceps during weight-acceptance (33). These findings are consistent and demonstrate the muscles' attempt to produce an internal moment to counter-balance and minimize

external moments generated during walking. Astephen et al., (2008) found that increased medial and lateral hamstring activations could distinguish severe OA from healthy individuals. Differential activation levels between lateral (LH) and medial hamstrings (MH) have also been reported, where higher LH activity compared to MH was significantly reported in the severe group (31), but not the moderate OA group. This differential LH versus MH activity has also been previously noted in moderate OA groups as well (30,101). The asymmetric recruitment pattern between hamstring muscles has been seen as a way to unload the medial compartment in individuals with knee OA due to the nature of this medial compartment dominated disease (31). Despite the reported alterations seen in LH, MH contribution to disease severity has varied among studies, where some report no differences (33) while others report higher MH amplitudes in severe OA groups compared to asymptomatic and moderate OA (100). Additionally, factors other than knee OA severity have been seen to affect hamstring activations, such as the presence of pain, where higher activation magnitudes in the lateral hamstrings and medial gastrocnemius during walking in those with moderate knee OA have been associated with higher pain scores (32).

2.4.2.2 Quadriceps

The quadriceps muscles have also shown distinct patterns with increased severity of OA, where structural characteristics, such as marked joint space narrowing and large osteophytes, associated with a KL grade of 4 was found to have overall greater and more prolonged quadriceps activation throughout the gait cycle (31,35). The increased combination of the quadriceps has implications for increased joint loading in the tibiofemoral and patellofemoral compartments (35), and hence can overload the joint further during walking. Zeni et al., (2010) found no differences in peak and average vastus lateralis (VL) activity during self-selected speed between individuals with different KL grades. Despite no differences observed, walking velocities were slower for more severe groups (102), and therefore velocity could serve as a confounding variable that affected interpretation of the results. A study conducted by Rutherford et al., (2011) found higher VL amplitudes with similar walking speeds during mid-stance in individuals with greater severity of OA compared to moderate OA groups, that had minimal functional limitations and were not eligible to a total joint replacement. In addition, differences have

been reported between vastus lateralis (VL) and medialis (VM), with VL having greater activity (30). This greater VL activation has been thought of as way to unload the medial compartment along with greater LH activity as discussed previously by providing a counter abduction moment during stance (30). However, greater VL activity compared to VM has not been a consistent finding, where some studies have shown a concurrent increase in both VL and VM (100,103) or have found no differences (101).

2.4.2.2 Gastrocnemius

Activation differences for the gastrocnemius have been seen to also be altered in response to knee OA. Generally, gastrocnemius amplitudes have been reported to be decreased, as opposed to the quadriceps and hamstrings where higher and more prolonged activations were reported. Rutherford et al. (2013) investigated whether alterations in knee joint muscle activation patterns were related to severity in knee OA during walking. Phase-shifted and lower MG activity were reported for those with greater structural severity of KL grades ≥3 compared to moderate and asymptomatic controls. This was seen as a way to increase early stance active stiffness and reduce medial contact joint forces especially during late stance. In addition, the temporal synchrony between the medial and lateral gastrocnemii has been a consistent finding in previous literature with increased structural severity (30,31). The diminishment of the phase shift for severe OA groups has been suggested to be associated with disease severity and lower walking velocities (30,34), as severe OA groups tend to walk at slower velocities compared to asymptomatic and moderate OA groups (104). The gastrocnemius has also been reported to be involved in co-contraction with the hamstrings and quadriceps on the medial side of the knee during early stance compared to age-matched controls (97).

Although researchers mainly focused on understanding the mechanical loading environment of the knee, recent discoveries regarding the biochemical aspects of knee OA, specifically synovitis, have been reported to cause cartilage degeneration (36,37) and affect progression of the disease (15,53,105). Despite the reported implications of synovitis on joint health, little is known regarding the effect of synovitis on the mechanical environment of the knee. Therefore, the next section will provide an overview on the detection of effusion, it's relationship with OA severity, and its effect on the mechanical (kinematic and kinetic) and neuromuscular environments of the knee joint.

2.5 Joint Effusion and OA

Knee effusion is a common symptom in those with knee OA, with almost 55% having moderate to large effusions (5). By having a more in depth understanding of effusion, how it's detected, and the factors associated with structural progression of the disease, it can bring us to a closer understanding of the relationship between the biochemical and biomechanical components of OA.

2.5.1 Joint Effusion Detection

There are several detection methods of synovitis that have been used in order to detect and monitor the effect of effusion synovitis on OA. This section will discuss the different methods of effusion synovitis detection and what the missing gaps are in the literature regarding these detection methods.

2.5.1.1 Imaging Testing of Effusion

Synovitis can be quantified by measuring synovial thickness and/or the size of effusion present in the joint (4). It can be detected through the use of magnetic resonance imaging (MRI), B-Mode and Doppler ultrasound (US) (4,15,51,53). MRI has been previously reported as a valid tool to detect effusion and synovitis, and allows for assessment of soft tissue structures, cartilage and bone lesions (105,106). One of the major advantages of MRI is that it allows the manipulations of contrasts to highlight different structures and tissue types (52). Despite the MRI being regarded as the most advanced non-invasive imaging modality for evaluation of even minimal effusions and other joint structures (52), it has several economic and technical limitations to routine assessments of MR imaging of the osteoarthritic joint (106). MRI detection of synovial thickness is usually improved with contrast by enabling differentiation from effusion (107), which requires intravenous access, carries small risks of sensitivity reactions and can be associated with rare side effects (108).

Another imaging modality that reports objective inflammatory findings in OA is the ultrasound (US) (51). Although US has been found to have lower specificity and sensitivity compared to MRI (52), it has been shown to provide valid, reliable comparable assessments of synovial disease to those provided by MRI (14,52). Recent ultrasound research support other imaging and clinical evidence that synovitis is a common feature of OA, that is characterized by the presence of synovium hypertrophy and effusion (4).

The use of ultrasound has many advantages as it is non-invasive, portable, relatively inexpensive, lacks ionizing radiation and can be reproducible making it an appropriate modality to use during monitoring of treatment (109). Effusion is defined on the US as an "abnormal hypoechoic (grey) or anechoic (black) intraarticular material that is displaceable and compressible (4,110), whereas synovium hypertrophy is defined sonographically as an "abnormal hypoechoic intra-articular tissue that is non-displaceable and poorly compressible (4). A European study of 600 patients with knee OA concluded that gray scale synovitis detected by ultrasound correlated significantly with clinical symptoms of increased pain and swelling (14). This diagnostic ability of the ultrasound can be of great importance in OA patients or OA research (4). For the purpose of this thesis, effusion will be detected through the use of a grey-scale US by a registered sonographer. Therefore, US imaging guidelines regarding effusion detection will be discussed in detail.

According to the European League Against Rheumatism (EULAR) guidelines, an effusion depth ≥ 4 mm is considered the cut-off value for the detection of effusion (14), as shown in Figure 2.2.

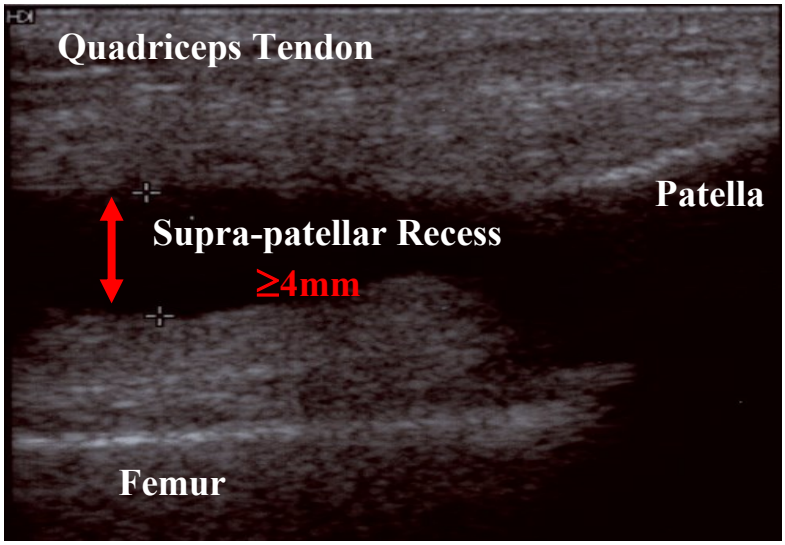


Figure 2. 2: Illustration of ultrasound scan with effusion present, demonstrated as an anechoic region.

Fluid is most commonly found in the suprapatellar recess or the lateral or medial parapatellar regions of the knee (4), with 76% of effusions found in the suprapatellar recess of the knee joint (50). EULAR guidelines recommend examining the knee joint in either an extended or 30° flexed position for musculoskeletal ultrasound imaging (109). Recent studies examined the most appropriate knee position that provided the greatest sensitivity for detecting effusion sonographically, and found that 30° of knee flexion provided the greatest sensitivity for detecting effusion sonographically in the suprapatellar recess compared to full extension and 90° of knee flexion (111). Another study conducted by Hong et al., (2010) found that the pattern of fluid distribution in the knee changes with knee flexion, where fluid was shifted more medially as the fluid volume increased (69). Therefore, fluid movement should be considered when evaluating ultrasound-detected effusion in a flexed knee position and can be accounted for by measuring of effusion in three (medial, mid, and lateral) locations of the recess (69). Other guidelines include the isometric contraction of the quadriceps during ultrasound measurements which has been seen to increase the sensitivity of detecting synovial fluid in the suprapatellar recess in osteoarthritic knees (112,113) as it helps to push fluid into the suprapatellar recess (4).

2.5.1.2 Clinical Testing of Effusion

In addition to imaging modalities, routine clinical assessments of knee effusion are also an integral part of clinical practice, where a range of clinical tests have been used to determine presence of effusion (5). Some of these clinical assessments include palpation of the knee (114), visible inspection of effusion (115) and clinical tests that include the brush test (5). Cibere et al, (2008) investigated the reliability of knee inflammation in individuals with OA, where effusion was assessed by bulge sign, balloon test and patellar tap, and it was found that the bulge sign was most reliable with a reliability coefficient (R_c) of 0.97. Sturgill et al., (2009) also reported similar results to Cibere et al., (2008), where the brush test was a reliable test to assess knee joint effusion between therapists with a kappa value of 0.75 (116).

Although the brush test has been reported in the literature to be the most reliable compared to other clinical tests for detection of effusion (116,117), agreement between clinical tests and other imaging modalities (US) has not been comprehensively

established, especially in the population of OA. Only one study investigated the agreement between the brush test and US, where moderate agreement was reported with a kappa value of 0.58.

In summary, there are various methods to detecting effusion, whether through imaging modalities or clinically through clinical tests, like the brush test. Ultrasound's portability, feasibility and non-invasiveness gives it an advantage over the MRI, especially if follow-up assessments are required for monitoring of therapy. Some physiotherapy clinics might not afford to use a US/MRI, therefore clinical tests are an essential component in detecting effusions and any abnormalities in the joints. Although the most reliable clinical test has been reported to be the brush test compared other clinical tests, research is lacking in investigating the agreement between the brush test and an imaging modality, like the US. Knowledge regarding the agreement between both methods, and the factors that affect this relationship, can be vital in clinical settings and can affect clinical practice.

There is evidence from imaging studies to suggest synovitis is involved with knee OA progression (118). The next section will discuss what is known about effusion and its implications on the progression of OA structurally and clinically. Structural progression of the disease refers to radiographic progression of OA, whereas clinical progression refers to surgical progression into joint replacements.

2.5.2 Effusion and Progression of OA

2.5.2.1 Structural Progression

Individuals with symptomatic knee OA are known to have intra-articular structural pathology, such as cartilage loss, meniscal damage, bone marrow lesions and synovitis (119). Although abnormalities within a single tissue cannot be treated yet, understanding which pathologic feature triggers the onset and progression of OA can help inform preventative efforts. While cartilage and meniscal damage may not be clearly reversed, treatments for management of inflammation are available (119).

Several studies have investigated the link between presence of inflammatory effusion or synovitis and radiographic structural severity (14,120). A study investigating the prevalence of inflammation in OA individuals using US reported high correlation

between high radiographic grades (KL score >3) and inflammatory signs; with increased probability of US-detected joint effusion (14). Another study that observed knee OA MRI features over a 24-month period reported worsening of inflammatory markers of the disease by the presence of effusion-synovitis in individuals with both radiographic and symptomatic OA (120), indicating the prospective role of inflammation in progression of the disease. The identification of non-cartilaginous changes could therefore have an essential role in the onset and progression of OA (120).

2.5.2.2 Clinical Progression

Joint replacements are on the rise and have a great impact on the rising economic burden, and despite its high prevalence, research examining the prognostic indicators for future knee arthroplasty has been limited (15,121). Understanding predictors of joint replacements will help in prioritising research, examining reversible risk factors, and evaluating disease-modifying treatments in OA population (15). Several time predictors to joint arthroplasty have been identified, such as age, baseline WOMAC scores, patient willingness, followed by level of education (7). However, the inflammatory component of the disease as a predictor of TJA was previously not identified, mainly due to absence of modern imaging techniques such as US to evaluate the presence of synovitis. Emerging evidence suggests that sonographic diagnosis of knee effusion is an important prognostic factor to the disease process (4,15). A prospective multicenter European study of 531 patients diagnosed with knee OA was the first study that found that those with knee effusion ≥4 mm in size were 2.6 times more likely to require a total joint replacement within 4 years ($p<0.0001$) (15). Additionally, Riddle et al., (2012) was the first study to associate clinically identified knee effusion via the brush test with increased risk of arthroplasty by 58%.

In summary, synovitis, particularly effusion synovitis has been reported to lead to the progression of the disease structurally and clinically. The exact mechanism to how and why effusion is related to disease progression is still not fully understood. The inflammatory mediators are believed to inhibit the production and re-modelling of cartilage (37), hence causing a continuous cycle of cartilage degradation. It has also been reported that individuals with knee effusion, whether acute or chronic, demonstrate altered mechanics and neuromuscular activations, but no studies have explored whether

these alterations could lead to progression of the condition. Therefore, understanding whether effusion is causing the knee joint to move differently, causing further alterations in addition to the OA adaptations reported, is the main focus of this thesis. This could possibly bring us to a closer understanding of why effusion is considered an independent predictor of disease progression. Therefore, the next section will summarize the existing literature on effusion and knee joint function.

2.5.3 Effusion and Joint Function during Gait

Despite knowing the effects of knee OA on the biomechanical and neuromuscular environment of the knee, little is known on how the biochemical process of knee OA impacts the biomechanical and neuromuscular environment of the knee joint. There have been very few studies done to try to link these components together and understand how the biochemical component affects the mechanical environment of the knee, but some results have been inconsistent.

Most of the previous studies that have investigated the effect of knee effusion were acute and experimental by the use of a simulated effusion model to study knee function in healthy individuals. Torry et al., (2000) was one of the first studies to investigate the effect of infused-knee effusion on walking in healthy individuals by the injection of saline to the knee joint capsule. It was reported that effusion had caused individuals to walk with a more flexed position at the hip and knee joints throughout the stance phase (39). In addition, EMG of hamstrings muscle activity was increased and quadriceps activity reduced with effusion, where the vastus medialis was significantly inhibited at 20 cm, with larger volumes of effusion required to produce similar inhibition results in vastus lateralis and rectus femoris (39). The marked reduction in VM activity has been previously noted with the least amount of fluid (46) and has been suggested to be the first muscle to experience notable atrophy following joint injury (43). Another study conducted by Torry et al., (2005) studied the effect of 20 mL of infused knee effusion on jogging and found no differences in sagittal plane mechanics, but decreased VL and VM EMG activity (40). Other findings report more decreased knee flexion angles during stance with lower quadriceps EMG during jogging following a simulated knee effusion of 60 mL (60). This could be suggestive that higher levels of effusion would be needed in order to elicit motion kinematic changes. Palmieri et al., (2007) found similar

findings during a drop landing in healthy subjects with infused effusion, where they landed with a more extended knee position and reduced quadriceps EMG (41). This increased extension during landing or heel strike could have detrimental effects of joint loading, causing large forces to be transferred through the knee (41). The observed decrease in knee flexion angles has been linked to quadriceps inhibition following effusion.

Similar to findings of Torry et al. (2000), Rutherford et al., (2012) found greater knee flexion angles during stance in individuals with knee OA and clinically-detected effusion through the brush test (42). However, Rutherford et al., (2012) reported contrary findings in regard to quadriceps EMG, where individuals with moderate knee OA and effusion walked with higher quadriceps and hamstring muscle activities; suggesting effusion is causing additional altered joint mechanics associated with knee OA (42). In some of the early studies, it was observed that individuals with 55 to 60 mL of fluid infused in their knee joints were unable to fully extend their knees from a position of 10° flexion (122), supporting Rutherford et al's (2012) and Torry et al's (2000) findings of increased flexion angles during stance. The quadriceps findings of Merry et al. (1991) and Torry et al., (2001) support an acute effusion model affecting quadriceps action, whereas findings of Rutherford et al., (2012) suggest altered knee muscle activations associated with chronic effusion models, which may not cause quadriceps avoidance gait patterns as supposed by others. In addition to the chronicity of effusions present that is driving these changes, differences in the condition of the knee, healthy vs. OA, should be considered when comparing acute and chronic effusion models, as joint cellular alterations could be present in the latter, not the former

In summary, the previous findings support the hypothesis that knee effusion shares a role in the development of knee OA, since it has been associated with increased structural and clinical severity of knee OA. This is suggestive that effusion is causing changes in the joint, and hence understanding which changes are mostly driving the joint to degrade even further could guide intervention plans in order to minimize the burden of knee OA. Therefore, understanding the extent of influence effusion can have on lower extremity gait function can enable clinicians to understand, assess and treat various gait abnormalities associated with OA.

CHAPTER 3 GENERAL METHODOLOGY

This study was funded by the Nova Scotia Health Research Foundation (Grant # MED EST 2014-9605). Recruitment, instrument selection and analysis procedures were approved by the Nova Scotia Health Authority (NSHA) Research Ethics Board (REB) (ROMEO # 1017467). Data collection and recruitment began in 2015 and proceeded until April 2018. The author took the role of research assistant to coordinate and schedule participants and assist with the laboratory and participant set-up and assist with data collection and processing pertaining to this thesis.

3.1 Participant Recruitment

3.1.1 Participants with Moderate Knee Osteoarthritis (MOA)

Participants with MOA were recruited from Dr. William Stanish at the Orthopaedic and Sports Medicine Clinic of Nova Scotia, Dr. Nathan Urquhart at Dartmouth General Hospital and Dr. Ivan Wong at QEII Health Science Center. Individuals with moderate knee OA were diagnosed using the American College of Rheumatology (ACR) guidelines. The ACR guidelines include knee pain, in addition to crepitus on active motion of the knee, osteophyte formation, morning stiffness ≤ 30 minutes and age ≥ 50 years. Standard anterior-posterior standing radiographs were obtained for each participant (acquired within one year of testing). Kellgren Lawrence (KL) grades for radiographic evidence of knee OA were assigned to all participants (123), and were assessed by a single, experienced reader as previously recommended (124). Individuals with greater lateral compartment joint space narrowing than medial compartment were excluded. The doctors introduced the walking study to suitable candidates and then were given a consent letter for the transfer of their contact information. Participants were then contacted and screened through telephone using a standardized script in order to determine final eligibility to the study. Participants had to be:

- 50 years of age or older
- Diagnosed with unilateral symptomatic medial knee OA
- Not eligible for a total joint replacement, as that it is indicative of severe stages of OA.
- No lower limb surgery within the past year

- No other musculoskeletal pathologies or injuries within the past year
- No respiratory conditions that interfere with day-to-day activities (controlled asthma is OK)
- No neurological and cardiovascular diseases (Controlled high blood pressure is OK)
- Able to meet a functional status consistent with moderate OA classification (Hubley-Kozey et al., 2006) based on self-report, which include:
    i. ability to jog 5 meters
    ii. walk more than a city block
    iii. climb stairs in a reciprocal fashion

In addition, individuals were excluded if they had an anterior cruciate ligament (ACL) injury. If participants were eligible, details of visit and scheduling of a data collection appointment were scheduled.

3.1.2 Sample Size

Sample size was based on an estimate from the limited literature on knee effusion and knee OA (14,15,39,42,106,125,126). The percentage of individuals with knee OA that had effusion ranged from 30% to 70%, where the sample size ranged from around 35-80. Previous work using effusion/no-effusion grouping system in individuals with moderate knee OA detected significant differences in knee sagittal plane motion, with a difference of 5.9° (Standard deviation (SD) = 5.3°) in early stance maximum (42). Another recent study detected 3° differences (SD=4°) from initial contact to peak flexion during loading response between asymptomatic and knee OA individuals.

Based on 2-sample power calculations performed on an online sample size calculator (127), with a power of 80%, a Beta (ß) of 0.20, and an alpha value of 0.05, the following has been reported:

1) Difference = 5.9°; SD = 5.3; CI = 95%; Then the sample size required = 13 in each group
2) Difference = 3°; SD = 4; CI = 95%; Then the sample size required = 28 in each group

Therefore, the number of participants that were sought after included enough to ensure at least 13-28 participants would be included in each group (effusion / no effusion).

3.2 Procedures

3.2.1 Upon Arrival

Upon arrival to the Joint Action Research (JAR) laboratory in the School of Physiotherapy at Dalhousie University, participants were introduced to the setting of the laboratory environment, equipment and general procedures before testing. Before the commencement of treadmill walking, participants were asked to provide an informed written consent to participate, and complete one questionnaire pertaining to their knee symptoms and physical abilities, the Knee Injury and Osteoarthritis Outcome Score (KOOS). Participants were instructed to change into a t-shirt and tight fitting (Spandex®) shorts and remove their footwear. Height, mass, waist, hip, thigh and shank circumferences for both lower extremities were then recorded. Current level of knee pain was quantified using the numerical pain rating scale (NPRS) from 0-10 (0 indicating no pain, 10 indicating extreme, intolerable pain) before and after the data collection.

3.2.2 Knee Joint Effusion Detection

Knee effusion was assessed clinically and sonographically. It was assessed clinically by an experienced physiotherapist using the bulge test on both knees, which has been shown to be reliable for the detection of effusion (r=0.97) (117).

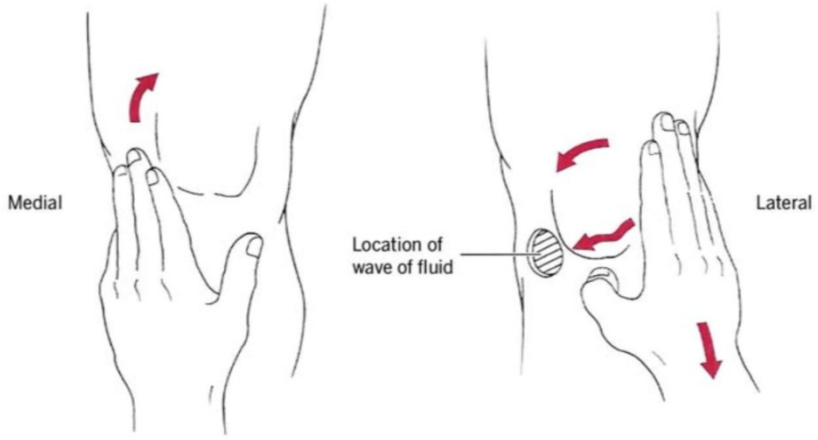


Figure 3. 1: Illustration of brush test. This illustration was published in Orthopedic Physical Assessment 4th Ed, Vol 16, David Magee, Page 726, Copyright Elsevier (2002) (161).

Following the assessment of effusion clinically, ultrasound (US) examinations were performed by a 12-year experienced musculoskeletal (MSK) sonographer, who was blinded to the results of the brush test, registered with the Canadian Association of Registered Diagnostic Ultrasound Professionals using an ATL HDI 3000 ultrasound system (Philips Medical Systems, Bothell, WA, USA) and a broad bandwidth 12-5 MHz linear array transducer. High frequency (7.5-20 MHz), linear array transducers are generally best for scanning superficial structures, such as tendons, ligaments and small joints like the knee (109,128). Phantom testing of the US was completed to provide insight on the performance characteristics of the US scanner, as shown in *Appendix E,* which showed an axial and lateral resolution of 0.08 and 0.17 cm, respectively. Participants were asked to lie supine with the knees supported by a pillow at 30 degrees flexion (111,129). The angle of 30 degrees was measured using a goniometer by an experienced physiotherapist. Longitudinal scans through the suprapatellar recess (SPR) were taken at three locations (mid, medial, lateral) of the recess on both knees as seen in Figure 3.2, while quadriceps were isometrically contracted (14). The SPR was located by visualizing the quadriceps tendon, femur, and base of patella. Effusion is defined as an anechoic (black) intraarticular material, and the maximum anterior-posterior width of the effusion was measured on the longitudinal suprapatellar scan, as shown on Figure 3.2. US has been shown to provide valid and reliable comparable assessments of synovial disease to those provided by MRI or arthroscopy, or both (14). Participants were then assigned to effusion or no-effusion group based on a cut-off value of ≥ 4 mm. According to the European League Against Rheumatism (EULAR) guidelines, an effusion depth ≥ 4 mm is considered the cut-off value for the detection of effusion in the supra-patellar recess (14).

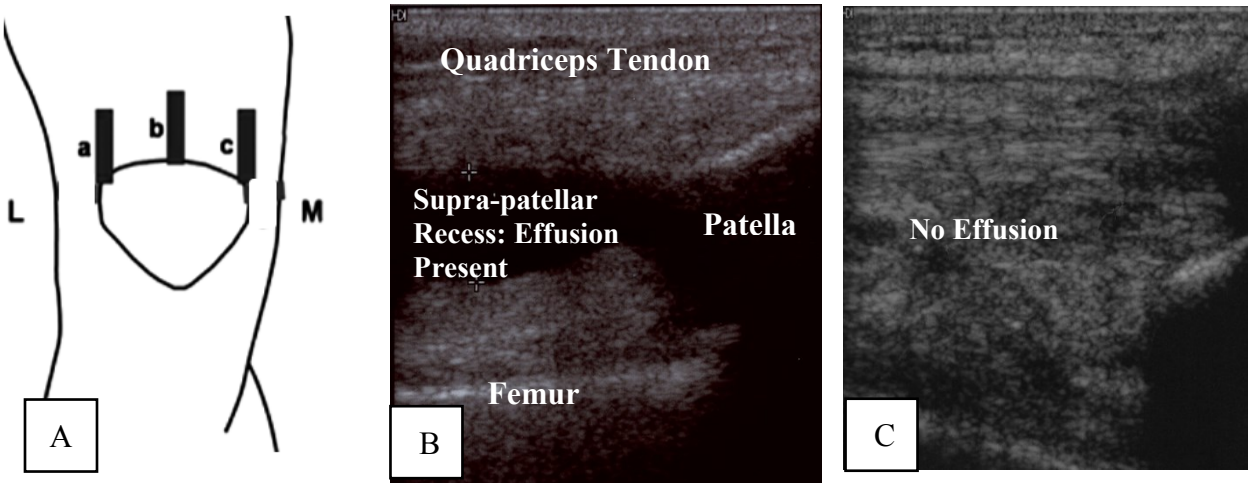


Figure 3. 2: A) Illustration of transducer orientation for the knee (a=lateral, b=mid, c=medial). B) An US scan obtained for one of the participants showing anechoic effusion in the supra-patellar recess. C) An US scan obtained showing no effusion in the supra-patellar recess.

3.2.3 Participant Preparation

Standardized skin preparation and electrode placement protocols have been previously described (30) in accordance with SENIAM (Surface EMG for the Non-Invasive Assessment of Muscles) guidelines (130). Skin preparation (light shave and abrade with 70% alcohol wipes) and placement of surface electrodes (3M^{TM} Red Dot^{TM}, Ag/AgCl, 10 mm diameter, 0.72cm^2 SA, 20mm IED) in a bipolar configuration to record EMG signals for vastus medialis (VL), vastus lateralis (VL), medial (MH) and lateral hamstring (LH), medial (MG) and lateral gastrocnemius (LG) was done. Table 3.1 provides the standardized electrode placements for each muscle (130). Muscle palpation and manual muscle tests were performed to validate electrode placement to ensure signal quality, minimize crosstalk (131) and for selecting appropriate gain adjustments. Lead wires with pre-amplification (500x) of EMG signals were connected to the electrode pairs for each muscle, and a ground electrode was placed on the anterior tibia shaft. EMG signals were further amplified and recorded at 2000Hz using an AMT-8 (Bortec, Inc., Calgary, Alberta, Canada) EMG system with gains of 100-5000x (Input impedance of ~10 GΩ, CMRR:115 dB at 60 Hz, Band-pass 10-1000Hz) in order to maximize the signal without reaching signal saturation.

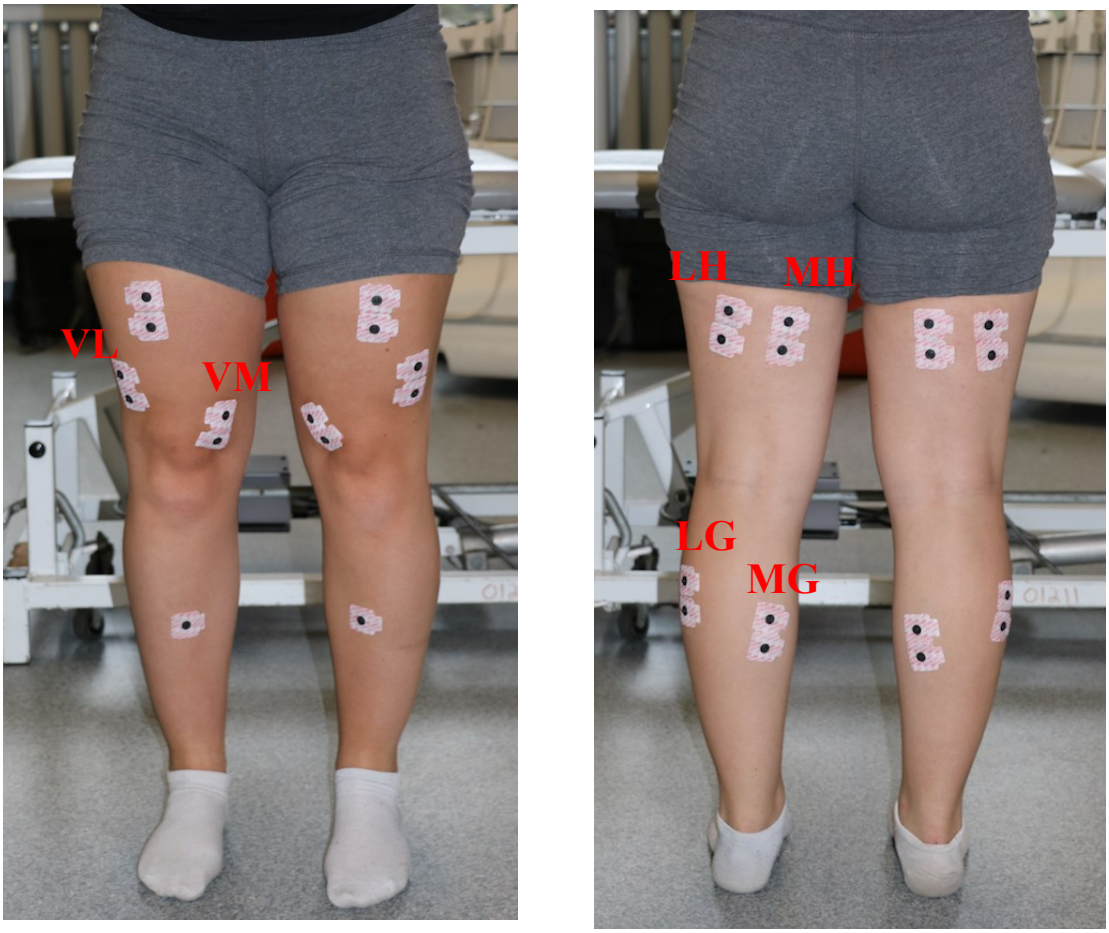


Figure 3. 3: Illustration of electrode placements according to SENIAM guidelines (130) for Vastus Medialis (VM) and Lateralis (VL), Medial (MH) and Lateral Hamstrings (LH), and Medial (MG) and Lateral Gastrocnemius (LG).

Table 3. 1: SENIAM guidelines of standardized electrode placement for lower limb. References: (130)

Muscle	Electrode Placements	Orientation
Vastus Lateralis (VL)	2/3 of the distance from anterior superior iliac spine (ASIS) to lateral side of patella.	Direction of muscle fiber orientation.
Vastus Medialis (VM)	80% of distance between ASIS and medial knee joint space.	Direction of muscle fiber orientation.
Lateral Hamstrings (LH)	50% of distance between ischial tuberosity and lateral epicondyle of tibia.	In direction of lead line.
Medial Hamstrings (MH)	50% of distance between ischial tuberosity and medial epicondyle of tibia.	In direction of lead line.
Lateral Gastrocnemius (LG)	30% of distance from lateral knee joint line to calcaneal tubercle	In direction of lead line.
Medial Gastrocnemius (MG)	35% of distance from medial knee joint line to calcaneal tubercle.	In direction of the lead line.

Participants were asked to walk across a specialized pressure-sensitive walkway over-ground, called GAITRite® approximately 15-20 times at a self-selected speed. Five walking trials were collected after at least four lengths have been walked. The average speed of five walking trials was calculated and used to set treadmill speed. GAITRite® has shown to be a valid (132) and reliable tool (ICC = 0.91) for older adults (133) for assessing walking velocities. Passive, retro-reflective skin markers were then placed on

each participant bilaterally over bony anatomical landmarks (134), including C7, right and left shoulders (placed two finger widths below lateral acromial prominences), greater trochanter, lateral and medial femoral epicondyles, lateral and medial tibial epicondyles, lateral and medial malleoli, posterior heel, and 1st, 2nd and 5th metatarsal heads. Clusters of four markers were fixed on rigid bodies on the thorax, pelvis, thigh, shank and feet. An illustration of the placement of markers is shown in *Figure 3.4*.

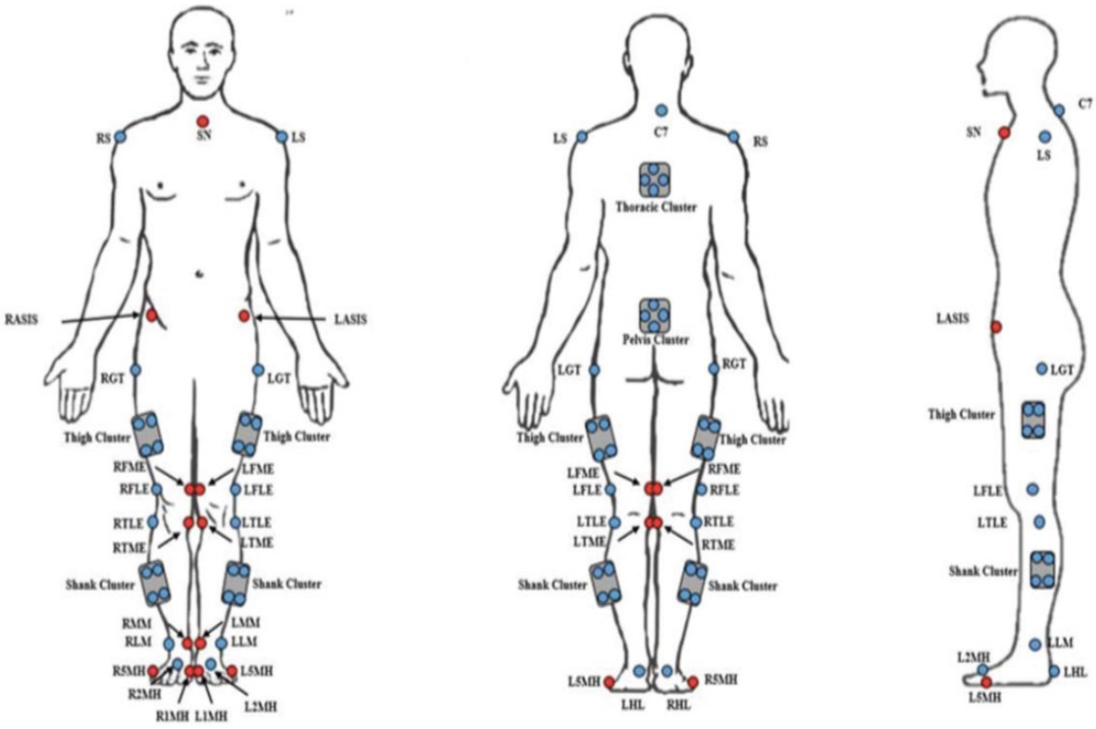


Figure 3. 4: Illustration of skin marker placement. Individual markers are illustrated by blue balls. Cluster markers are illustrated by grey squares. Virtual point markers are illustrated by the red balls.

3.2.4 Calibration

A calibration trial of 120 seconds was taken of the treadmill volume in order to align the coordinate system of each of the eight cameras to the coordinate system of the treadmill. After the placement of markers, a 2-second standing trial was collected where participants were asked to stand on the R-Mill (Motekforce Link, Culemborg, the Netherlands) dual-belt instrumented treadmill with their feet placed shoulder-width apart and facing forward. Following the standing trial, markers on the greater trochanter,

medial femoral epicondyle, lateral and medial tibial epicondyle, medial malleolus, 2nd and 5th metatarsal heads were removed. Virtual points trials were collected to define anatomical landmarks on the sternal notch, left and right anterior superior iliac spines (ASIS) using a pre-calibrated digitizer wand, as shown in Figure 3.4. Virtual points were taken to complete the joint axis definitions, as these points cannot be directly captured using the camera system installed in the lab. All skin markers and clusters were attached with adhesive tape.

3.2.5 Warm-up and Walking Trials

Prior to walking, participants were loosely harnessed to the ceiling using a rope and upper torso harness, situated to not impede the walking process. They were instructed to walk barefoot on the treadmill and keep each foot on each of the force plates. After a 5 minute familiarization period (135), a 20 second recording was completed. The walking speed set on the treadmill was pre-determined by GAITRite™ (CIR Systems, Inc., Franklin, NJ). Eight Qualisys® OQUS 500 (Qualisys®, Gothenburg, Sweden) motion analysis cameras captured marker motion during walking at a frame rate of 100 Hz. Three-dimensional ground reaction forces (GRF) and moments were sampled at 2000 Hz from the two force plates installed under each belt of the treadmill. All analog signals (force plate and electromyography) were acquired, analog-to-digital converted (16 bit, +/- 5V) and synchronized using Qualisys Track Manager V2.10.

3.2.6 Maximum Voluntary Isometric Strength Testing

Following the walking trials, all markers and clusters were removed from participant with the exception of the EMG electrodes, which were kept for the strength testing. Participants completed a 1-second resting (subject bias) trial in supine position, which was then followed by maximum voluntary isometric contractions (MVIC) for EMG normalization purposes (35,135), where participants were asked to complete a series of three exercises. Two knee (flexion and extension) strength tests were conducted on the Human Norm Isokinetic dynamometer (Computer Sports Medicine Inc., USA), with the knee angle at 45° and hip at 90° flexion. An isometric strap was placed at the distal tibia, and stabilizing straps were placed on the tested thigh and around the hip. The

dynamometer and knee joint axis of rotations were aligned. The third exercise, which was a unilateral standing calf raise was used as an additional exercise to test LG and MG (136). After at least one practice trial, two, three-second maximal isometric contractions were completed for each exercise. At least 40-seconds of rest were given between both trials, and at least 10-seconds separated the three exercises. Strong, standardized verbal encouragement were given to ensure consistent maximal contractions (78). Raw voltage signals were converted to torque (Nm) and corrected for the effect of gravity. Gravity correction were done by weighing the participant's limb. By this, the HUMAC Norm computed the MaxGET (Maximum Gravity Effected Torque), which was used along with limb position and direction of motion to adjust the torque values for the effects of gravity. During extension, the limb was resisted by gravity, whereas during flexion the limb was assisted by gravity. The following equations show the computation of the reported torques:

- When limb is resisted by gravity: Reported Torque = Measured Torque + (MaxGET*Cosine(Angle))
- When limb is assisted by gravity: Reported Torque = Measured Torque – (MaxGet*Cosine(Angle))

EMG data was simultaneously recorded during the MVICs and stored for offline processing.

3.3 Processing

All data was processed using a custom MatLab™ R2016a (The Mathworks Inc., Masssachusetts, USA) script (JAR v3). Heel strike and toe-off was determined based on a threshold value set at 30 N for the vertical GRF and used to time normalize the motion and EMG data to percent of the gait cycle (initial contact to the next ipsilateral initial contact) and net external moments to percent stance (initial contact to toe off of the ipsilateral leg).

3.3.1 Kinematics Processing

The three-dimensional motion capture used a Cartesian coordinate system (137), as recommended by the International Society of Biomechanics (ISB) in reporting

kinematic data (138). This coordinate system for the rigid body clusters (pelvis, thigh, shank and foot) was derived from skin markers, rigid clusters and virtual points (139). All lower extremity motion data were low-pass filtered (recursive Butterworth 4th order) at 6Hz. A flexion/extension, adduction/abduction, internal/external rotations sequence was used for Cardan/Euler rotations (23,135) to calculate joint angles, where the flexion, adduction and internal rotation motion around the knee was described as positive angles. Joint angles were described as the distal segment moving around a fixed proximal segment (23,135).

3.3.2 Kinetics Processing

The three-dimensional GRF was calculated using a calibration matrix of six sensors located on each force plate (Motekforce Link, Culemborg, the Netherlands) that are embedded under the two belts of the treadmill and aligned with the global coordinates of the motion capture system. Ground reaction forces were low-pass filtered (recursive Butterworth 4th order) at 30 Hz and processed. External joint moments were derived from Newton-Euler equations through inverse dynamics by using GRF, kinematics, subject anthropometrics and inertial properties (140). Moments were low-pass filtered (Butterworth 4th order recursive) at 10 Hz and normalized to body mass (Nm/kg) to standardize the known effect of mass on external moments (76). The normalized net external moments were expressed similar to the orientation of the kinematic assessment of the lower extremity.

3.3.3 Electromyography (EMG) Processing

All signals were visually inspected for any movement artifacts, dynamic range saturation or 60 Hz noise. In addition, to verify power spectrum of each EMG signal, Fast fourier transform (FFT) was completed on each participant. EMG signals were corrected for subject bias and gains, converted to microvolts, band-pass filtered using a 4th order Butterworth filter (Fc: 10-500 Hz), and full-wave rectified. Signals were then low pass filtered (Butterworth Fc:6 Hz, 4th order recursive). A 100-ms moving average window algorithm was used to identify the maximal amplitude of each isometric contraction throughout the three seconds (30). Gait electromyograms were amplitude normalized to this value. Muscle strength was also determined using these MVIC exercises. A 500ms

moving average window algorithm determined the maximum torque across the 3 second contraction. The average of both trials was calculated and chosen as the maximal torque generated by each participant for each muscle.

3.3.4 Data Analysis

The most symptomatic lower extremity was studied in individuals with moderate knee OA. Discrete variable analysis has been previously used in OA literature for the interpretation of joint kinetics and kinematics (24,42,141). Discrete metrics from knee sagittal angles include i) peak knee flexion angle during stance ii) peak knee flexion during swing iii) late stance minimum. From these, difference measures were calculated: i) between initial contact and early stance maximum (ΔKFA1) ii) between early stance maximum and late stance minimum (ΔKFA2). Discrete knee sagittal moments include i) early to mid-stance maximum ii) late stance minimum. From these, difference measures include i) between early to mid-stance maximum to early swing minimum (ΔKFM1). Discrete knee frontal moments include i) initial peak knee adduction moment (PKAM). Discrete metrics for each muscle was also calculated, which will include i) peak activation ii) mean activation during stance phase.

Table 3. 2: Equations used to calculate discrete metrics for sagittal angles and moments.

Discrete Metric	Equation
PKAM	Initial frontal peak knee adduction moment
ΔKFA1	Early stance maximum – IC
ΔKFA2	Early stance maximum – late stance minimum
ΔKFM1	Early to midstance maximum – late stance minimum

3.4 Statistical Analysis

Normality and equal variance tests were performed on all data using the Kolmogorov-Smirnov and Levenes test respectively.

For objective 1a: a linear and non-linear regression analysis was used to determine which discrete gait variables and knee strength measures are correlated to increased depth (mm) of the suprapatellar recess.

For objective 1b: two-sample unpaired t-tests were used to understand whether differences exist between effusion and non-effusion groups in sagittal plane knee joint angles, sagittal and frontal external moments. A two factor (Group x Muscle) Analysis of Variance Model was used to test Group and muscle main effects and interactions between effusion and non-effusion groups and between muscles within a muscle group (i.e. Medial and lateral hamstrings). In addition, two-sample unpaired t-tests were used to test for significant differences in pain, WOMAC, age, body mass index (BMI), stride characteristics, and strength. The distribution of KL radiographic grades was computed across effusion and non-effusion OA groups. Significance was determined by alpha $\leq$ 0.05. All statistical analyses were completed in Minitab V.16 (Minitab™ Inc. State College, PA, USA).

CHAPTER 4 ASSOCIATION BETWEEN SUPRAPATELLAR RECESS DEPTH AND GAIT MECHANICS AND NEUROMUSCULAR ACTIVATIONS DURING WALKING IN INDIVIDUALS WITH KNEE OA

4.1 Introduction

The knee joint is the most commonly affected joint in inflammatory joint conditions (142), such as osteoarthritis (OA). The established hallmark of the pathophysiology of OA includes the change and breakdown of articular cartilage, adjacent soft tissue and subchondral bone structures that lead to pain and disability associated with structural severity (143). However, recent evidence has shown that OA is a "whole joint disease" that affects the integrity of multiple joint structures, which include the cartilage, bone, synovium, ligaments and other fibrocartilaginous structures (3). In addition to that, with the development in molecular biology, inflammatory mediators were discovered in the synovial membrane (3), which can lead to inflammation of the synovium, synovitis. These discoveries caused a shift of thinking from viewing OA as a passive degenerative disease to recognizing it as an active inflammatory disease, that can be modified by mechanical and biochemical interventions.

Knee synovitis can be quantified by measuring the size of effusion present in the knee joint, which can be detected by imaging modalities, like the ultrasound (US) (4). Ultrasound is a non-invasive imaging modality used to report objective inflammatory findings in OA (51), and although it has been found to have lower specificity and sensitivity compared to MRI (52), it has been shown to provide valid and reliable assessments of synovial disease as those provided by the MRI (14,52). Most of the previous studies using US have only described the effect of knee effusion based on categorical variables through the European League Against Rheumatism (EULAR) sonographic imaging guidelines based on a cut-off value of ≥4 mm of the supra-patellar recess (SPR). Despite that, it is still not clear whether the quantitative evaluation of knee effusion in the SPR has any effect on joint function.

Gait analyses have been used for decades to understand the implications of knee OA on joint function during the most common functional task humans perform; walking. To date, few studies have investigated the impact of knee effusion on knee function capture

during walking. To the authors knowledge, no studies have evaluated whether effusion detected using US is related to altered joint function during walking in individuals with knee OA. The importance in this understanding lies in the fact that both US detected effusion and specific gait features are predictive of knee OA progression, yet whether a relationship between these two entities exists remains to be determined. Therefore, the main aim of this chapter is to understand whether a relationship exists between knee joint mechanics and effusion in a sample of individuals with moderate knee OA.

4.2 Methodology

4.2.1 Participant Recruitment

As presented in Chapter 3, Fifty participants were recruited who were diagnosed with unilateral symptomatic medial knee osteoarthritis after consultation with an orthopaedic surgeon and were excluded if they were eligible for a total knee replacement. They were diagnosed according to the American College of Rheumatology (ACR) clinical guidelines, which include knee pain, crepitus on active knee motion, morning stiffness ≤ 30 minutes and age ≥ 50 years (114). Kellgren-Lawrence (KL) grades for radiographic evidence of knee OA were assessed by a single, experienced reader (124) and each participant was assigned a KL grade. Additionally, a functional classification was used to determine moderate OA severity (30). Participants were not eligible if they had other musculoskeletal, neurological and cardiovascular conditions that affected their gait during activities of daily living.

4.2.2 Procedures

All participants completed The Knee Injury and Osteoarthritis Outcome Score (KOOS) and height, weight and circumferential measurements of the waist, hip, thigh and shank of both lower extremities were recorded. Current knee pain scores through the numerical pain rating score (NPRS) were also taken before and after the data collection.

4.2.3 Knee Joint Effusion Detection

A 12-year experienced sonographer registered with Sonography Canada took ultrasound (US) scans of the supra-patellar recess at three locations (mid, medial, lateral) using an ATL HDI 3000 US system (Philips Medical Systems, Bothell, WA, USA) and a broad bandwidth 12-5 MHz linear array transducer. Scans were taken while the knees

were supported by a pillow at 30 degrees knee flexion (111) while the quadriceps were isometrically contracted (14). The detection of the SPR was done by the visual locating it between the quadriceps tendon, femur bone, and base of the patella.

4.2.4 Data Acquisition

Standardized skin preparation (Shaving and abrasion with 70% alcohol wipes) and electrode placement protocols were done in accordance to SENIAM guidelines (130), as previously described in the methodology section of Chapter 3. Electrodes (3M^{TM} Red Dot^{TM}, Ag/AgCl, 10 mm diameter, 0.72cm^2 SA, 20mm IED) were placed in a bipolar configuration to record electromyography (EMG) signals for vastus medialis (VL), vastus lateralis (VL), medial (MH) and lateral hamstring (LH), medial (MG) and lateral gastrocnemius (LG), and recorded at 2000 Hz using Qualisys Track Manager 2.10 (Qualisys, Sweden). Passive, retro-reflective skin markers and clusters were placed bilaterally on bony anatomical landmarks and rigid body segments and secured with adhesive tape. Motion marker data was tracked using eight Qualisys ® OQUS 500 motion analysis cameras at 100 Hz, while participants walked on a dual-belt instrumented treadmill (R-Mill, Motek Forcelink, Netherlands) at a self-selected speed pre-determined by GaitRITE™ walkway. One 20-second trial was recorded after a 5 minute familiarization period (135). Three-dimensional ground reaction forces (GRF) and moments were sampled at 2000 Hz from the two force plates installed under each belt of the treadmill and synchronized with marker trajectories through Qualisys Track Manager V2.10.

Following the walking trials, a resting muscle activation trial was recorded in supine. Maximum voluntary isometric contractions (MVIC) using a Humac Norm Isokinetic Dynamometer (Computer Sports Medicine Inc., USA) were then completed for EMG normalization purposes (35). Knee flexion and extension strength testing were done on the dynamometer with the knees at 45° flexion, where the dynamometer and knee joint axis of rotations were aligned. To test MG and LG, a unilateral standing calf raise was done (31). Three-second maximal isometric contractions were completed following at least one practice trial. A 40-second rest period was given between contractions, and standardized verbal encouragement was given to ensure consistent maximal contractions (78).

4.2.5 Data Processing

Custom programs written in MatLab™ R2016a (The Mathworks Inc., Masssachusetts, USA) were used to process data. Motion data was low-pass filtered (recursive Butterworth 4th order) at 6Hz, and joint angles were calculated using a 6-degree of freedom model through Cardan/Euler rotations (23,135). Ground reaction force data was low-pass filtered (recursive Butterworth 4th order) at 30 Hz. Net external moments were calculated using inverse dynamics (140), which were low-pass filtered (Butterworth 4th order recursive) at 10 Hz and normalized to body mass (Nm/kg) to standardize the known effect of mass on external moments (144). Raw EMG signals were corrected for subject bias and gains, converted to microvolts, band-pass filtered using a 4th order Butterworth filter (Fc: 10-500 Hz), and full-wave rectified (126). Signals were then low-pass filtered (Butterworth Fc:6 Hz, 4th order recursive), and a 100-ms moving average window algorithm was used to identify maximum amplitude for each isometric contraction throughout the three seconds in order to normalize to gait EMGs (30). All waveforms were time normalized to 100% gait cycle (initial contact to subsequent ipsilateral initial contact), whereas moment waveforms were time normalized to 100% stance phase. Heel strike and toe-off were determined a 30N vertical GRF threshold.

4.3 Statistics

Difference measures were calculated between initial contact (IC) to peak knee flexion angle during stance (ΔKFA1) and between early stance maximum to late stance minimum for sagittal motion data (ΔKFA2). For knee net external moments, difference measures between early-to-mid stance maximum to late stance minimum (ΔKFM1) were calculated for sagittal moments, and peak knee adduction moment was calculated for knee frontal moment, as shown in **Error! Reference source not found.**. Discrete metrics or each muscle were also calculated, which included peak activation and mean activation during stance phase. In addition, difference measures between the lateral and medial hamstrings were calculated during the stance phase, as it has been previously associated with increased structural severity (32,35). Normality and equal variance tests were performed on all data using the Kolmogorov-Smirnov and Levene's test (α=0.05), respectively. A regression (linear, quadratic, cubic) analysis was done in Minitab to determine which discrete gait variables are correlated to increased depth (mm) of the

suprapatellar recess. Visual inspection of scatter plots was performed in order to detect outliers in the data.

4.4 Results

A total of 50 participants were recruited for this study, and participant characteristics of the study sample are presented in Table 4.1.

Table 4. 1: Mean ± Standard deviation values of subject demographics and radiographic grades

	Mean ± Standard Deviation
N	50
% Females	42%
Age (years)	61 ± 5.9
BMI (kg/m^2)	27.4 ± 4.7
Mass (kg)	85.3 ± 17.8
Walking velocity (m/s)	1.1± 0.1
Pre-walking pain (#/10)	1.7 ± 1.6
Post-walking pain (#/10)	2.0 ± 1.9
Strength KF (Nm)	71.1 ± 27.4
Strength KE (Nm)	113.2 ± 44.5
KOOS Pain	66.8 ± 16.6
KOOS QoL	45.2 ± 16.3
KOOS ADL	73.6 ± 16.8
Kellgren-Lawrence (KL) Grades*	KL 0 (3)
	KL I (18)
	KL II (19)
	KL III (6)

*Radiographic KL grades were not available for 4 participants

Table 4. 2: Mean ± Standard deviation values of biomechanical discrete variables

Biomechanical Discrete variables	Mean ± Standard Deviation
PKAM (Nm/kg)	0.4 ± 0.1
ΔKFA1 (degrees)	11.6 ± 3.8
ΔKFA2 (degrees)	9.3 ± 3.8
ΔKFM1 (Nm/kg)	0.6 ± 0.2

Outliers were visually detected however were not removed, since the outliers were not due to incorrectly entered or measured data and did not seem to affect the assumptions or change the results. Results of all regression analyses showed that the depth of the SPR assessed by ultrasonography had non-significant correlations with all biomechanical and neuromuscular factors ($p>0.05$). See Appendix A for scatter plots of all data. Maximum SPR depth had a significant curvilinear quadratic association with knee flexor and extensor strength values ($p<0.05$), where very high and low depth values of the SPR were associated with high strength values.

Table 4. 3: R-values, R-squared and p-values of the linear regression analysis for all variables.

Linear Regression Analysis

Variable	**r**	**R-squared**	**P-value**
PKAM (Nm/kg)	0.06	0.4%	0.675
ΔKFM1 (Nm/kg)	0.07	0.5%	0.633
Sagittal Angle IC (°)	0.00	0.0%	0.975
ΔKFA1 (°)	-0.03	0.1%	0.811
ΔKFA2 (°)	0.15	2.3%	0.291
Peak Stance Flexion Angle (°)	0.03	0.1%	0.864
Average Stance VM (%MVIC)	-0.23	5.1%	0.115
Average Stance VL (%MVIC)	0.16	2.7%	0.255
Average Stance MH (%MVIC)	0.00	0.0%	0.925
Average Stance LH (%MVIC)	0.21	4.3%	0.148
Average Stance MG (%MVIC)	-0.03	0.1%	0.866
Average Stance LG (%MVIC)	0.15	2.2%	0.300
LH – MH Stance (%MVIC)	-0.24	5.6%	0.099
VM peak (%MVIC)	0.26	6.9%	0.064
VL peak (%MVIC)	0.17	2.8%	0.246
MH peak (%MVIC)	0.00	0.0%	0.910
LH peak (%MVIC)	0.19	3.6%	0.187
MG peak (%MVIC)	0.15	2.2%	0.306
LG peak (%MVIC)	0.04	0.2%	0.780
Flexion Strength (Nm)	-0.03	0.1%	0.843
Extension Strength (Nm)	-0.06	0.4%	0.662

Table 4. 4: R-squared and p-values of the non-linear (Quadratic) regression analysis for all variables.

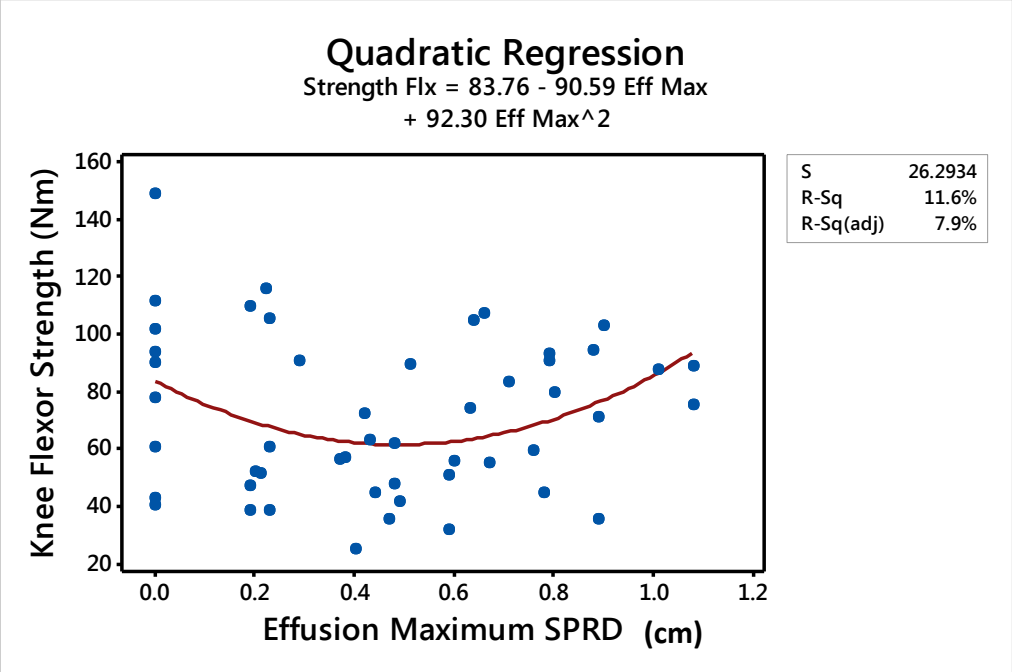
Non-Linear (Quadratic) Regression Analysis

Variable	R-squared	P-value
PKAM (Nm/kg)	0.7%	0.852
ΔKFM1 (Nm/kg)	5.6%	0.258
Sagittal Angle IC (°)	1.4%	0.724
ΔKFA1 (°)	2.6%	0.535
ΔKFA2 (°)	7.8%	0.146
Peak Stance Flexion Angle (°)	0.1%	0.981
Average Stance VM (%MVIC)	9.3%	0.101
Average Stance VL (%MVIC)	4.1%	0.377
Average Stance MH (%MVIC)	0.2%	0.959
Average Stance LH (%MVIC)	4.4%	0.348
Average Stance MG (%MVIC)	0.1%	0.986
Average Stance LG (%MVIC)	2.4%	0.566
LH – MH Stance (%MVIC)	5.9%	0.242
VM peak (%MVIC)	9.1%	0.105
VL peak (%MVIC)	3.6%	0.424
MH peak (%MVIC)	0.4%	0.903
LH peak (%MVIC)	4.6%	0.333
MG peak (%MVIC)	2.2%	0.588
LG peak (%MVIC)	0.2%	0.952
Flexion Strength (Nm)	11.6%	**0.017**
Extension Strength (Nm)	12.6%	**0.014**

Table 4. 5: R-squared and p-values of the non-linear (Cubic) regression analysis for all variables.

Non-Linear (Cubic) Regression Analysis

Variable	R-squared	P-value
PKAM (Nm/kg)	0.7%	0.957
ΔKFM1 (Nm/kg)	5.6%	0.441
Sagittal Angle IC (°)	5.1%	0.483
ΔKFA1 (°)	3.2%	0.678
ΔKFA2 (°)	7.9%	0.283
Peak Stance Flexion Angle (°)	2.0%	0.819
Average Stance VM (%MVIC)	9.4%	0.206
Average Stance VL (%MVIC)	7.4%	0.314
Average Stance MH (%MVIC)	0.5%	0.971
Average Stance LH (%MVIC)	4.4%	0.551
Average Stance MG (%MVIC)	0.3%	0.988
Average Stance LG (%MVIC)	2.4%	0.771
LH – MH (%MVIC)	5.9%	0.422
VM peak (%MVIC)	9.2%	0.213
VL peak (%MVIC)	5.2%	0.481
MH peak (%MVIC)	0.6%	0.961
LH peak (%MVIC)	5.0%	0.499
MG peak (%MVIC)	2.5%	0.754
LG peak (%MVIC)	0.3%	0.988
Flexion Strength (Nm)	1.3%	0.359
Extension Strength (Nm)	17.9%	0.090



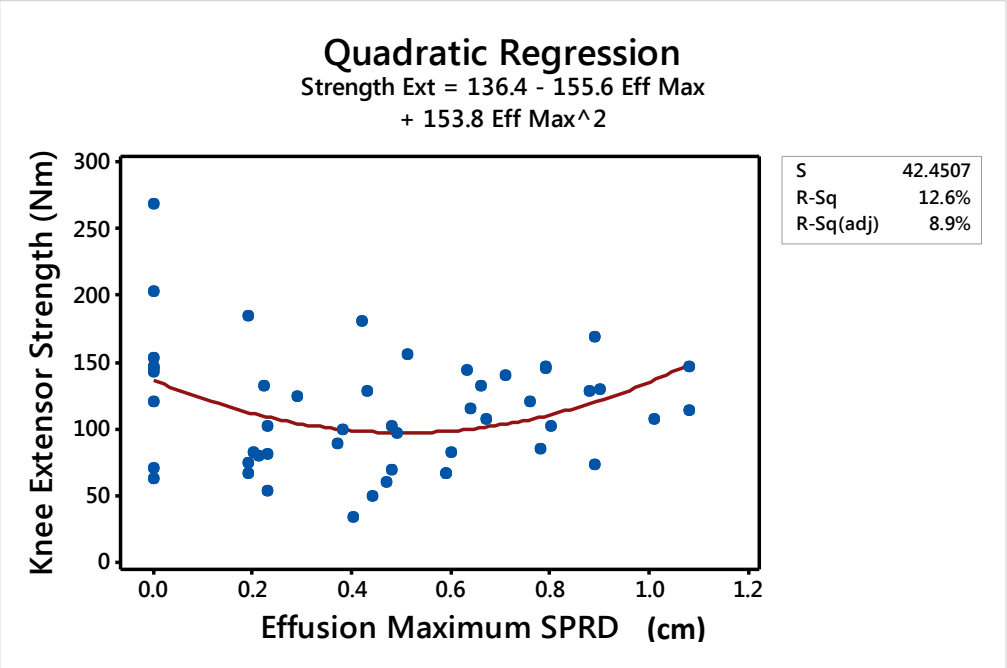


Figure 4. 1 A curvilinear relationship between maximum supra-patellar recess depth and knee flexor and extensor strength values.

4.5 Discussion

The inflammatory component of OA, effusion synovitis, along with many other mechanical and neuromuscular factors have been previously linked to increased structural severity of knee OA (14,15,17). Despite that, no studies to our knowledge have investigated the association between the amount of effusion with biomechanical and neuromuscular factors of knee joint function during walking, making this the first study to do so.

Previous studies have investigated the effect of experimentally-infused knee effusion on gait parameters and muscle activations during functional activities and walking (39–41,43,145). These studies reported altered knee biomechanics and muscle activation levels although inconsistencies have existed. Some have found increased flexion angles during stance phase of walking (39), increased knee extension angles during stance of a single-legged drop landing (145), while no differences were found in sagittal knee kinematics during walking (40). Although inconsistent findings have been reported on knee biomechanics, consistent findings have been reported in regards to decreased and inhibited quadriceps activity (39,40,145). This inhibition is seen to be a result of arthrogenic muscle inhibition as an adaptive protective mechanism due to capsular distention associated with acute effusion (39,43). Similarly, the hamstrings have been consistently found to have higher activation levels as a stabilizing mechanism of the knee joint by balancing the knee agonists and antagonists during walking (39).

Although these changes do signify that effusion is leading to changes in the mechanical environment of the knee joint, they might not fully represent the effusion present during chronic degenerative conditions, like OA. These previous experimental studies represented acute effusion models, which may not cause similar changes in the joint as found in chronic effusion models. Previous research have found the joint's response to effusion to differ between acute and chronic effusion models (42,48,49). In chronic effusion models, increased knee flexion angles during stance were reported along with increased quadriceps and hamstrings muscular activation levels during walking (42). Despite similarities in biomechanics, muscular inhibition was not noted in either muscle groups, which is consistent with previous reports on chronic effusions (48,49).

In spite of these previous findings, no biomechanical and neuromuscular factors during gait were significantly associated with suprapatellar recess (SPR) depth in this moderate OA sample, suggesting that effusion and gait mechanics are independent from each other. The only significant correlation was found in knee extensor and flexor strength values, where a curvilinear association was found between increased effusion depth and isometric strength values. Although the percent variation explained was low at 12.6% and 11.6% for extensor and flexor strength, respectively, the findings suggest that little and high effusion levels are associated with greater strength values, while moderate effusion depth is associated with lower strength values. These findings could indicate that moderate amounts of effusion are more likely associated with strength deficits, whereas lower and higher amounts are not associated with strength deficits thought to be related to inhibition when underlying articular pathologies are present; which are not entirely consistent with chronic effusion models associated with OA (42,48,49).

The exact mechanism of the current findings is not fully understood, however could be attributed to the fact that the sample under investigation had both acute and chronic effusions. Since the sample under investigation included individuals with moderate knee OA, it was presumed that they represented chronic effusion models due to the chronicity of the disease. However, this was never established, nor investigated in order to confirm the chronicity of the effusion present, and thus could also include individuals with acute or subacute effusions. Presumably those with little to moderate amounts of effusion could be more acute than those with larger amounts of effusion. And thus, those with large amounts would have higher strength values compared to those with subacute effusions, while those in the acute/subacute phase may exhibit more inhibition. Arthrogenic muscular inhibition has been reported to not occur until the level of effusion reached a certain threshold ranging from 30-60 ml (43,46,71), which explains why very little amounts of effusion did not exhibit inhibition, even though it could have represented acute/subacute effusion models. This however cannot be confirmed, since most of the previous literature on effusion-induced acute models represented volumetric measurements measured in milliliters of fluid, whereas in this study, a linear measurement in millimeters was taken sonographically of the SPR depth. However, despite differences in measurement, effusion-induced volumes have been positively

associated to sonographic linear depth (113). Despite the significant p-values, the r and r-squared values were relatively low, concluding that the association between SPR depth and knee flexor and extensor strength values to be weak. In addition, it's been reported that inflammation associated with knee OA can also occur in skeletal muscle, which could lead to decreased muscle strength (146). Strength deficits that occur in individuals with OA is a complex phenomenon and could also be related to disuse of the symptomatic limb due to higher levels of knee pain (147).

Other limitations of this chapter include the presence of those with no effusion, hence the presence of zeros could affect the correlation and significance values. In addition, since regressions are sensitive to the presence of outliers, they could have an effect on the regression. There were some outliers detected visually in some of the scatter plots, present in Appendix A, which could have affected the variance in data and the significant values. The association between SPR depth and KL grades were not performed, however, future research could include non-parametric tests to investigate the association. Finally, a strong significant correlation does not necessarily imply causation, which could imply that there are other unknown factors that are causing these significant associations. There could be other variables that do influence the response variable other than the x variable, which were not included, such as participant characteristics.

4.6 Conclusion

In summary, no previous studies have investigated the association between both components of the disease, inflammatory and mechanical, which has left a gap in OA research. This is crucial in understanding the disease process especially since there are many discordances between subjective reports and radiographic findings (108), suggesting that perhaps there are other under-reported factors that could gap these disparities. The only correlation that was significant was a curvilinear correlation between effusion depth and knee flexor and extensor strength, suggesting a relationship between inflammatory factors and strength values in knee OA. In addition, this study found that there is no direct association between the amount of effusion and the mechanical environment during walking in individuals with knee OA. Despite these results, OA-related effusion detected sonographically has been previously correlated with progression of the disease and knee pain (14,15). These significant associations reported were based

on a sonographic standardized cut-off value of 4 mm (14), which was possibly sensitive enough to draw out group differences that could be predictive of disease progression.

Therefore, the next chapter will investigate the second objective of this thesis; effect of the 4 mm cut-off on gait mechanics and neuromuscular activations during walking in those with moderate medial knee OA. This could possibly bring us to a closer understanding of why effusion is considered an independent predictor of disease progression.

CHAPTER 5 THE EFFECT OF KNEE JOINT EFFUSION ON GAIT MECHANICS AND MUSCLE ACTIVATIONS DURING WALKING IN INDIVIDUALS WITH KNEE OA

5.1 Introduction

Osteoarthritis (OA) is the most common joint disease and is a major cause of pain and disability (7), with the medial side of the knee most commonly affected (2). People with knee OA often show patterns of decline in function concerning mobility (56), severely affecting the quality of life of those suffering from it. Gait analysis has been used to model and assess the mechanical environment of the knee associated with walking in individuals with knee OA (17), where biomechanical and neuromuscular alterations have been reported when compared to people with healthy knee joints. Alterations in gait include higher magnitudes of knee adduction moment (22,23,25), less range in the sagittal plane and moment (26,27), and increased and more prolonged muscular activations (30–33). Additionally, there are gait alterations in mechanics and muscular activations that have been reported to be sensitive to severity changes associated with medial knee OA, despite similarities in subject characteristics. Biomechanical changes include higher knee adduction moments during mid-stance, decreased stance phase knee flexion angles and decreased early stance knee extension moments (23,26,74,98). Neuromuscular activations associated with increased structural severity include increased and prolonged quadriceps, higher lateral hamstrings activation levels, and diminished phase shift between medial and lateral gastrocnemius (30,31,93).

Despite the known effects of knee OA on the biomechanical environment of the knee during different OA severity levels, little is known on how the biochemical environment of the knee affects the biomechanical and neuromuscular environment, specifically since recent findings have associated the presence of effusion with increased structural and symptom severity (14,15). In the presence of OA, the biochemical environment of the knee is characterized by increased levels of inflammatory biomarkers in the synovium (3,36,37), manifested in the knee joint as effusion (38). The effect of knee effusion on joint function has been understood mainly through acute effusion models; reporting altered joint biomechanics and quadriceps inhibition (39–41).

However, only one study has looked at knee mechanics and muscle activation during walking in individuals with knee OA, who have been thought to have effusions of a chronic nature (42). Higher levels of quadriceps activation and altered biomechanics have been found that negated the inhibition theory associated with acute effusion models (42). These findings report that individuals with knee effusion, whether acute or chronic, demonstrate altered mechanics and muscle activations while walking, highlighting the rationale of this study.

Knee synovitis can be assessed directly through histological evaluations and by serum markers (148), or indirectly by imaging modalities through magnetic resonance imaging (MRI) and ultrasound (US) (4), or by a "hands on" clinical evaluation (5). Synovial histology and serum biomarkers have been considered to be invasive approaches compared to other detection methods (3). Although the MRI is considered to be the most advanced non-invasive imaging modality for detecting the presence of even minimally effusions (52), it has technical and economic limitations to routine assessments of the osteoarthritic joint (106). Ultrasound is another non-invasive imaging modality used to report objective inflammatory findings in OA (51), which has been shown to provide valid and reliable assessments of synovial disease as those provided by the MRI (14,52). The European League Against Rhematism (EULAR) established standard guidelines on the sonographic evaluation of effusion in the knee, where an effusion depth ≥4 mm is considered the cut-off value for detection of effusion (14).

Therefore, the main purpose of this chapter is to compare sagittal knee motion, net external sagittal and frontal moments and knee joint muscular activations between individuals with and without effusion based on a 4 mm cut-off value. It is hypothesized that those with effusion will have increased sagittal flexion motion and moments and reduced knee extensor motion and moments, as well as increased frontal plane moments, and higher quadriceps and hamstrings activations.

5.2 Methodology

5.2.1 Participant Recruitment

Fifty participants diagnosed with unilateral moderate medial knee OA were recruited for this study according to the American College of Rheumatology (ACR) guidelines through orthopaedic surgeons. The ACR guidelines include knee pain,

crepitus on active knee motion, morning stiffness ≤ 30 minutes and age ≥ 50 years (114). Kellgren Lawrence (KL) grades for radiographic evidence of knee OA were assessed by a single, experienced reader (124) and each participant was assigned a KL grade. For eligibility of this study, participants have to be:

- 50 years of age or older
- Diagnosed with unilateral symptomatic medial knee OA
- Not eligible for a total joint replacement, as that it is indicative of severe stages of OA.
- No lower limb surgery within the past year
- No other musculoskeletal pathologies or injuries within the past year, and no cardiorespiratory and neurological diseases that interfere with day-to-day activities
- Able to meet a functional status consistent with moderate OA classification (Hubley-Kozey et al., 2006) based on self-report, which include:
    iv. ability to jog 5 meters
    v. walk more than a city block
    vi. climb stairs in a reciprocal fashion

In addition, individuals were excluded if they had an anterior cruciate ligament (ACL) injury, and if they had lateral compartment OA > medial compartment OA.

5.2.2 Procedures

The Knee Injury and Osteoarthritis Outcome Score (KOOS) was completed by all participants, in addition to height, weight and circumferential measurements of the waist, hip, thigh and shank of both lower extremities were recorded. Current knee pain scores through the Numerical Pain Rating Scale (NPRS) were taken before and after the data collection.

5.2.3 Knee Joint Effusion Detection

Ultrasound (US) examinations were performed by a 12-year experienced musculoskeletal (MSK) sonographer, registered with Sonography Canada, using an ATL HDI 3000 US system (Philips Medical Systems, Bothell, WA, USA) and a broad bandwidth 12-5 MHz linear array transducer. Scans were taken while the knees were supported by a pillow at 30 degrees knee flexion (111) and quadriceps were isometrically

contracted (14). The detection of the SPR was done by visually locating the quadriceps tendon, femur bone, and base of patella. Participants will then be assigned to effusion or no-effusion group based on a cut-off value of ≥ 4 mm (14,68).

5.2.4 Data Acquisition

Standardized skin preparation and electrode placement protocols were done in accordance to SENIAM guidelines (130), where skin was lightly shaved and cleaned with 70% alcohol wipes. Electrodes (3M^{TM} Red Dot^{TM}, Ag/AgCl, 10 mm diameter, 0.72cm^2 SA, 20mm IED) were placed in a bipolar configuration to record electromyography (EMG) signals for vastus medialis (VL), vastus lateralis (VL), medial (MH) and lateral hamstring (LH), medial (MG) and lateral gastrocnemius (LG). Two AMT-8™ 8-channel Bortec systems were used to record surface EMG signals at 2000 Hz using Qualisys Track Manager 2.10 (Qualisys, Sweden). Passive, retro-reflective skin markers and clusters were placed bilaterally on bony anatomical landmarks and rigid body segments and secured with adhesive tape. Marker data was tracked using eight Qualisys ® OQUS 500 motion analysis cameras at 100 Hz. Participants walked on a dual-belt instrumented treadmill (R-Mill, Motek Forcelink, Netherlands) at a self-selected speed pre-determined by the average of five over-ground walking trials on GaitRITE™ walkway. One 20-second trial was recorded after a 5 minute familiarization period (135). Three-dimensional ground reaction forces (GRF) and moments were sampled at 2000 Hz from the two force plates installed under each belt of the treadmill. All analog signals (force plate and electromyography) were acquired, analog-to-digital converted (16 bit, +/-5V) and synchronized using Qualisys Track Manager V2.10.

After completion of treadmill walking, all reflective markers were removed, and participants rested supine on the plinth for a resting EMG recording. This followed by maximum voluntary isometric contractions (MVIC) using a Humac Norm Isokinetic Dynamometer® (Computer Sports Medicine Inc., USA) for EMG normalization purposes (126). Knee flexion and extension strength testing were done on the dynamometer with the knees at 45° and hip at 90° flexion, where the dynamometer and knee joint axis of rotations were aligned. The third exercise, unilateral standing calf raise, was done to test MG and LG (31). Three-second maximal isometric contractions were completed following at least one practice trial, with 40-seconds of rest given between each trial.

Strong, standardized verbal encouragement was given to ensure consistent maximal contractions (78).

5.2.5 Data Processing

All data was processed using a custom MatLab™ R2016a (The Mathworks Inc., Masssachusetts, USA) script (JAR v3.1). Three-dimensional motion capture used a Cartesian coordinate system (137), which was derived from the marker system and virtual points. All lower extremity marker motion and kinetic data was low-pass filtered (recursive Butterworth 4th order) at 6Hz. Ground reaction force data was low-pass filtered (recursive Butterworth 4th order) at 30 Hz prior to processing. Joint angles were calculated using a Cardan/Euler rotations (23,135).

Three-dimensional GRF and moments were calculated using a calibration matrix of six sensors located on each force plate (Motekforce Link, Culemborg, the Netherlands) that are embedded under the two belts of the treadmill and aligned with the global coordinates of the motion capture system. Net external joint moments were calculated through inverse dynamics (140), which were low-pass filtered (Butterworth 4th order recursive) at 10 Hz and normalized to body mass (Nm/kg) to standardize the known effect of mass on external moments (144).

All EMG signals were corrected for subject bias and gains, converted to microvolts, band-pass filtered using a 4th order Butterworth filter (Fc: 10-500 Hz), and full-wave rectified. Signals were then low-pass filtered (Butterworth Fc:6 Hz, 4th order recursive), and a 100-ms moving average window algorithm was used to identify maximum amplitude for each isometric contraction throughout the three seconds in order to normalize to gait EMGs (30). All waveforms were time normalized to 100% gait cycle (initial contact to subsequent ipsilateral initial contact), whereas moment waveforms were time normalized to 100% stance phase. Heel strike and toe-off were determined a 30N vertical GRF threshold.

5.3 Statistics

Difference measures were calculated between initial contact to peak knee flexion angle during stance (ΔKFA1) and between early stance maximum to late stance minimum for sagittal motion data (ΔKFA2) to capture stance phase ranges of motion. For net external knee moments, difference measures between early to mid-stance maximum to

late stance minimum were calculated for sagittal moments (ΔKFM1), and peak knee adduction moment (PKAM) was calculated for knee frontal moment, as shown in **Error! eference source not found.**. Discrete metrics for each muscle were also calculated, which included peak activation and mean activation during stance phase. In addition, difference measures between the lateral and medial hamstrings were calculated during the stance phase as this differential hamstring activation has been previously related to increased severity of OA (104).

Normality and equal variance tests were performed on all data using the Kolmogorov-Smirnov and Levene's test respectively. Two-sample unpaired t-tests were used to understand whether differences exist between effusion and non-effusion groups in sagittal plane knee joint angles, sagittal and frontal external moments. In addition, two-sample unpaired t-tests were used to test for significant differences in pain, KOOS, age, body mass index (BMI), stride characteristics, and knee extensor/flexor strength. The distribution of KL radiographic grades was computed across effusion and non-effusion OA groups. A two factor (Group x Muscle) mixed model Analysis of Variance Model was used to test Group and muscle main effects and interactions between effusion and non-effusion groups and between muscles within a muscle group. Bonferroni corrections were used for all multiple comparisons. Significance was determined by alpha ≤ 0.05. All statistical analyses were completed in Minitab V.16 (Minitab™ Inc. State College, PA, USA).

5.4 Results

Out of the fifty participants, 29 had effusion in the supra-patellar recess based on the 4mm cut-off sonographic value. No significant differences between groups in subject anthropometrics, questionnaire outcomes, walking velocity, pre-walking pain through the NPRS and knee strength ($p>0.05$), however individuals with effusion and knee OA reported higher post-walking pain through the NPRS ($p=0.03$). In addition, the effusion group had a greater distribution of higher KL grades than the non-effusion group.

Table 5. 1: Mean ± Standard deviation values of subject demographics, KOOS and radiographic grades

	No Effusion	Effusion	p-value
N	21	29	
% Females	52%	34%	
Age (years)	60 ± 6	63 ± 5	0.070
BMI (kg/m^2)	28.1 ± 3.7	29.9 ± 5.1	0.148
Mass (kg)	81.0 ± 16.3	88.4 ± 18.4	0.074
Gait Velocity (m/s)	1.1 ± 0.1	1.1 ± 0.1	0.720
Strength KF (Nm)	75.8 ± 31.7	67.7 ± 23.9	0.334
Strength KE (Nm)	117.8 ± 53.6	109.8 ± 37.2	0.560
Pain pre-walking (#/10)	1.5 ± 1.0	1.8 ± 1.9	0.542
Pain post-walking (#/10)	1.3 ± 1.4	2.5 ± 2.1	0.026
KL Grade*	KL 0 (2)	KL 0 (1)	
	KL I (10)	KL I (8)	
	KL II (5)	KL II (14)	
	KL III (1)	KL III (5)	
	KOOS		
Pain	66.8 ± 14.3	66.9 ± 18.9	0.990
Activities of daily living	74.0 ± 15.2	73.3 ± 18.4	0.896
Quality of life	45.6 ± 17.6	44.8 ± 15.0	0.841

*Radiographic KL grades were not available for four participants

Table 5. 2: Mean ± Standard deviation values and p-values for knee frontal and sagittal moments and sagittal motion data

Discrete Measures	Non-Effusion	Effusion	Difference	p-value
Knee Sagittal Angle				
Initial Contact (°)	0.4 (4.1)	-0.0 (5.0)	0.4	0.727
ΔKFA1 (°)	11.9 (3.1)	11.3 (4.2)	0.6	0.579
ΔKFA2 (°)	9.5 (3.2)	9.1 (4.2)	0.4	0.731
Knee Sagittal Moments				
ΔKFM1 (Nm/kg)	0.6 (0.2)	0.6 (0.2)	0	0.507
Knee Frontal Moment				
PKAM (Nm/kg)	0.4 (0.1)	0.4 (0.2)	0	0.987

Discrete metrics were extracted from the waveforms, found in Table 5.2. Ensemble average waveforms for the two groups are shown in Figures 5.1 - 5.2. No statistically significant differences were found in sagittal plane range of motion, sagittal and frontal net external moments between groups ($p>0.05$). A group ($p=0.04$) and muscle ($p<0.001$) main effect was found for the quadriceps, where the effusion group had higher average and peak quadriceps activation levels during stance and VL mean and peak values were greater than VM. A significant group by muscle interaction was found for the hamstrings muscle analysis ($p=0.038$). The effusion group had greater LH average activation compared to MH ($p<0.05$), whereas LH and MH in the non-effusion group were similar. Average LH activation was similar between groups ($p<0.05$). This was also found for MH ($p<0.05$). No group, muscle main effects or group by muscle interactions existed for the gastrocnemius muscles.

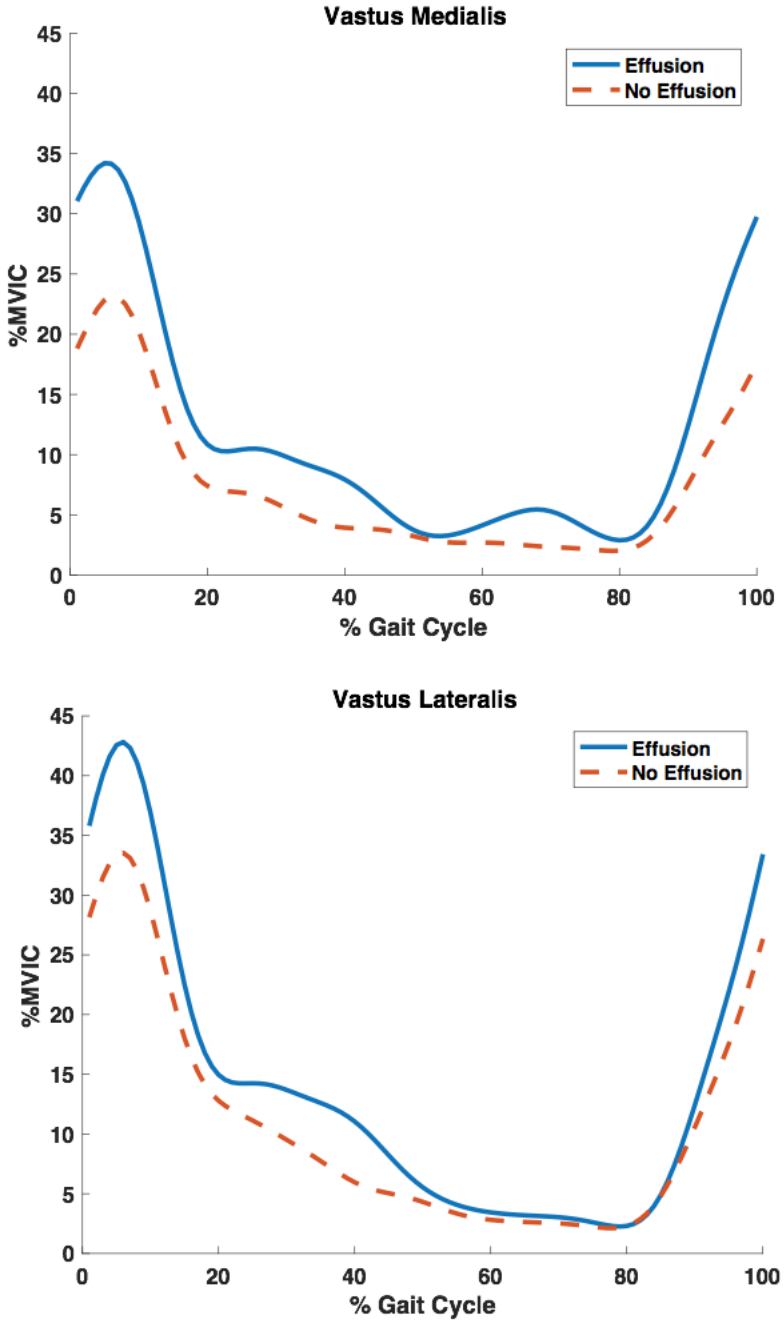


Figure 5. 1: Ensemble averaged electromyogram (EMG) waveforms of vastus medialis and lateralis for individuals with effusion and without effusion.

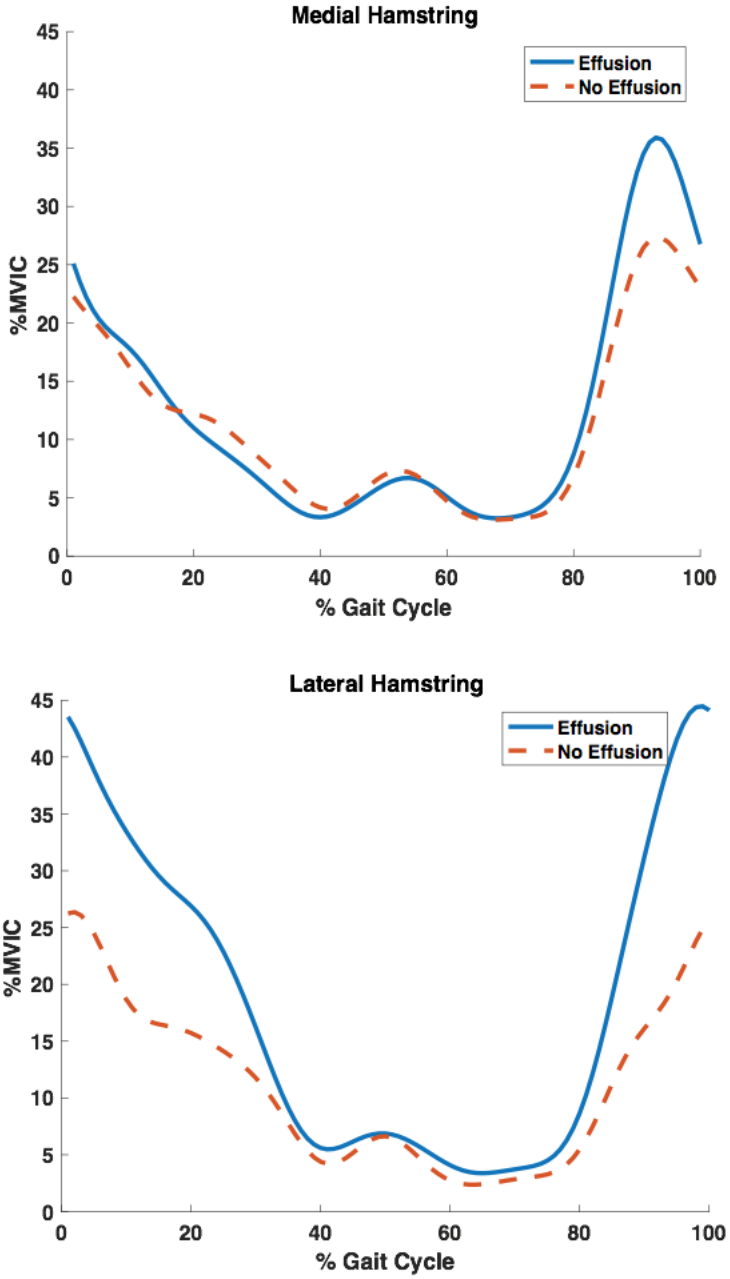


Figure 5. 2: Ensemble averaged electromyogram (EMG) waveforms of medial and lateral hamstrings for individuals with effusion and without effusion.

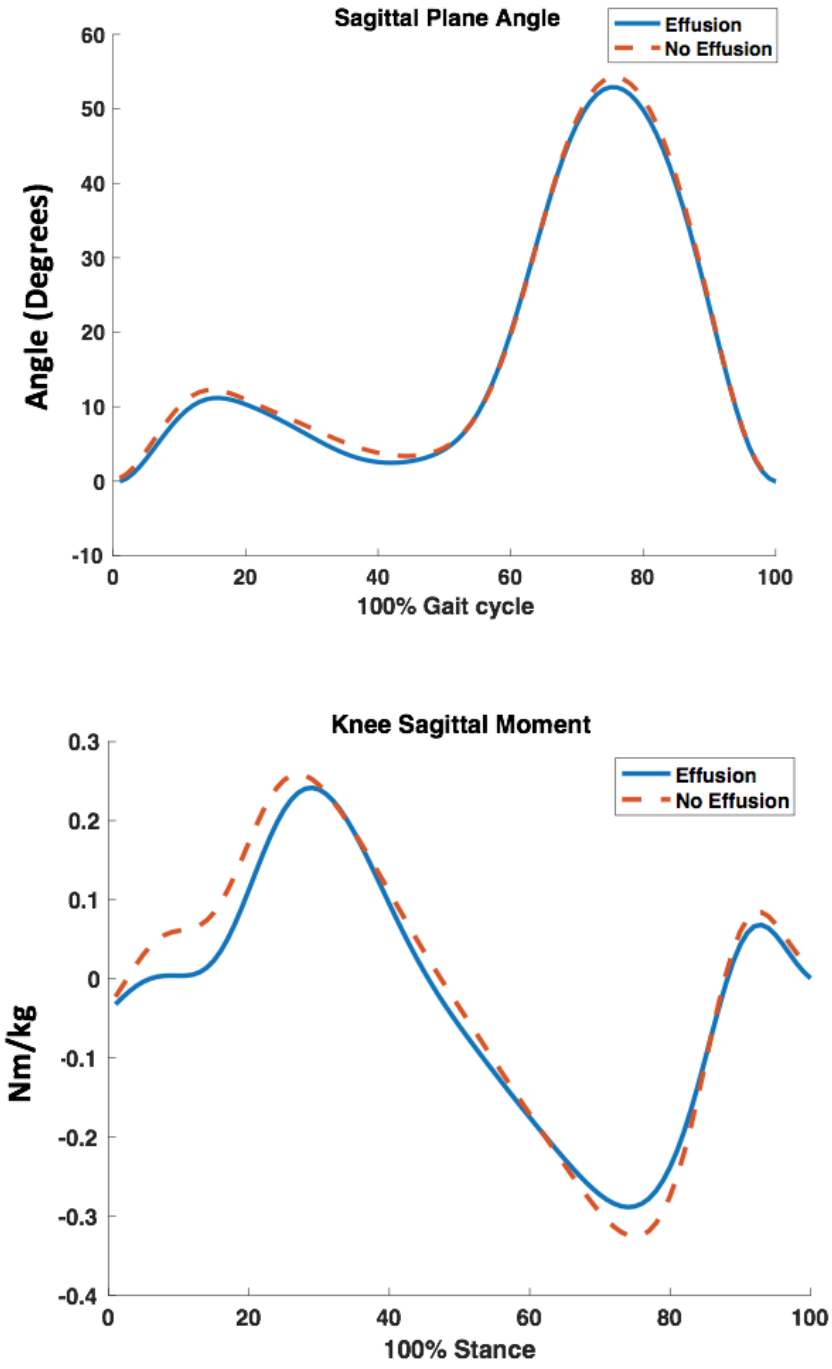
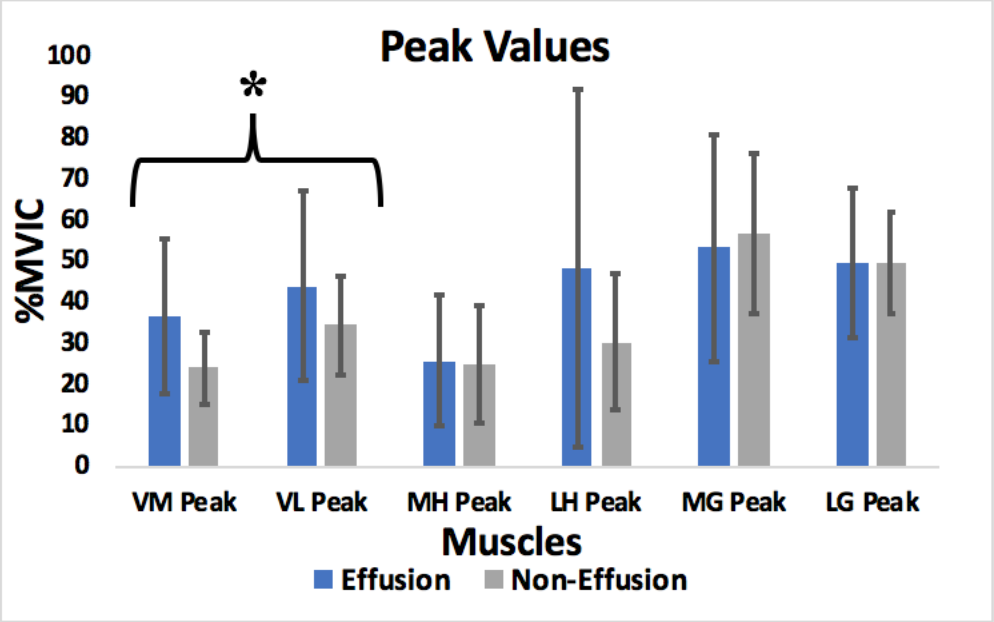


Figure 5. 3: Ensemble averaged biomechanics waveforms of knee sagittal plane motion and external moments for individuals with effusion and without effusion.



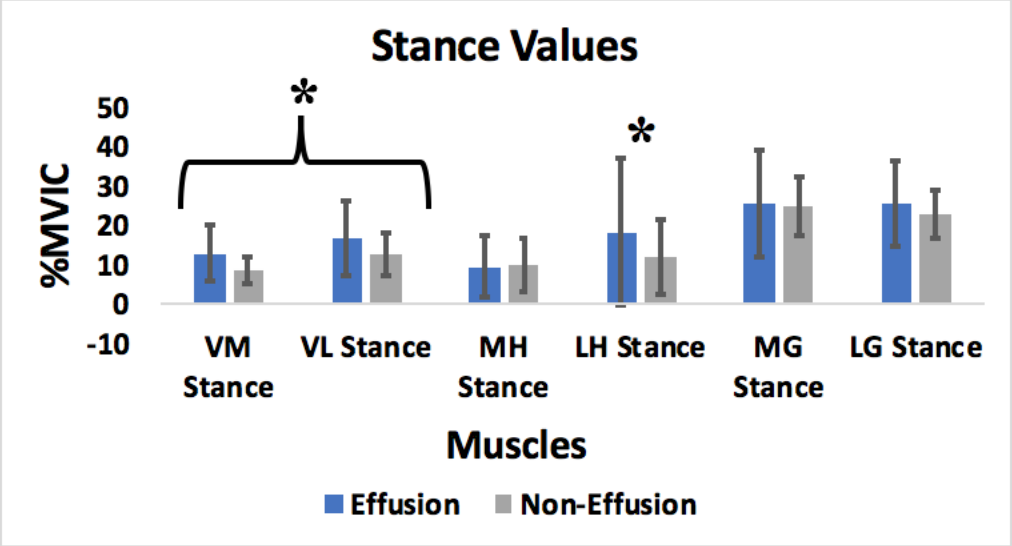


Figure 5. 4: Bar graphs of peak & stance values for all muscles with standard deviations; *: significant difference ($p<0.05$).

5.5 Discussion

The main aim of this chapter was to investigate the effect effusion has on the mechanical environment of the knee joint during walking. Increased peak and average activation levels in the quadriceps and lateral hamstrings during stance in the effusion group partially support the original hypothesis. In addition, higher PKAM, and increases in sagittal knee flexion motion and moments and decreases in knee extensor motion and moments during stance were hypothesized, however no differences in biomechanics between groups were found ($p > 0.05$).

Out of the 50 participants, 58% of those with knee OA had knee effusion based on the 4 mm cut-off value, which has been supported by previous studies where ~50% of those presenting knee OA also had effusions (15,42). Both groups included those with moderate, medial knee OA and had no significant differences in subject characteristics ($p > 0.05$). The only significant difference found between both groups was the numerical pain rating scale (NPRS) after walking ($p = 0.03$), where individuals with effusion had higher pain scores. Although the change in scores pre and post in the effusion group was only 0.7, those without effusion had a decrease in pain scores by 0.2. Although no statistical test was done on KL grades since it represents a Likert scale, the effusion group had a higher distribution of KL grades of II and III compared to the non-effusion group. Together, these results might suggest that the effusion may be of a greater severity within the moderate classification.

The findings of the current study show that individuals with medial moderate knee OA and effusion walked with altered muscle activation levels activations, including higher peak ($p = 0.03$) and average quadriceps activation levels ($p = 0.04$) during stance compared to non-effusion group. In addition, those with effusion walked with higher levels of lateral hamstrings activation compared to medial hamstrings than those with effusion ($p = 0.03$). A recent study conducted by Rutherford et al., (2012) supported these findings in regards to quadriceps, where individuals with moderate knee OA and effusion walked with higher quadriceps and hamstrings muscle activities; supporting previous findings on the chronically effused knees (42,48,49). Effusion was detected through the brush test (5,42) rather than through the ultrasound; yet despite these differences in detection, similar neuromuscular findings were reported. However, Rutherford et al.

(2012) found increases in sagittal plane knee flexion angles during stance, which associated with a lower net external extension moment in mid-to-late stance (42). Although Rutherford et al. (2012) studied a similar sample to those of this study, the difference in findings in biomechanics could be attributed to the differences in detection methods. A preliminary analysis has been done in Appendix D in order to investigate the agreement between both detection methods, the brush test and ultrasound, of effusion, which found moderate agreement between both methods (kappa = 0.51), consistent to existing literature (149).

Increased quadriceps activation during stance could reflect the stability demands of the chronically effused knee joint in the presence of knee OA (42). These differences occurred despite similarities between both groups in strength, mass, gait velocity, and questionnaire outcomes. This finding is consistent with previous studies, where greater quadriceps activation has been previously associated with increased structural severity of OA (31,35). This increase in activation could have implications on increased joint loading in the tibiofemoral and patellofemoral compartments, and hence overload the joint even further during walking. In addition, it's been reported that hamstring co-activation could be present during the stance phase in order to assist in maintaining knee joint stability (94) and increase active stiffness in the lateral compartment (35). In this study, the lateral hamstrings were found to activate at higher levels compared to the medial hamstrings in the effusion group compared to the non-effusion group. Differential activation levels between LH and MH have been previously associated with the severity level of OA, where it distinguished the severe OA group from the moderate OA group (31) and from healthy individuals (32). This is crucial as effusion has also been linked to OA severity, suggesting a possible link between gait muscular activations and knee effusion as knee OA progresses.

It was also found that all OA individuals, regardless of knee effusion, exhibited higher lateral-compartment muscular activations in the hamstrings and quadriceps during the stance phase. These findings are consistent with previous findings (30,31,33), which demonstrate the muscles' attempt to provide a counter abduction moment during stance, and the increased level of co-contraction may reflect the joints internal strategy to stabilize the joint (102). Although this internal compensatory strategy may improve joint

stability, it may expediate the disease process even further as it results in a more metabolically demanding gait pattern (150).

In contrast to the quadriceps, gastrocnemius activation levels during stance were not significantly different between both groups. Since it's been previously reported that there is faciliatory activity to the soleus as a result of acute effusion and quadriceps inhibition (145), it's postulated that individuals with chronic effusion and knee OA may not require gastrocnemii and soleus activation since there is no inhibition reported (42). Rutherford et al., (2012) reported similar findings in regard to the gastrocnemius, confirming the minimal effect chronic effusion has on gastrocnemius during walking in those with medial OA.

Previous studies have reported altered biomechanical responses in the presence of OA, where individuals with effusion walked with greater flexion angles during stance (39,42), in an attempt to minimize the increased intra-articular knee pressures. In the contrary, some have reported increased knee extension angles during landing from a jump (145), while others reported no differences in sagittal knee kinematics (40) supporting the findings of this study as no differences were detected. Although frontal plane loading in the knee joint, expressed through the peak knee adduction moment (PKAM), is usually higher in individuals with knee OA (22,88,89), no previous studies have investigated the effect of knee effusion on the PKAM despite the fact that effusion synovitis has been linked to OA structural progression (15). This study investigated the effect effusion had on the PKAM, and the results showed no differences in PKAM between the effusion and non-effusion groups ($p>0.05$). It has been reported that knee joint loading mainly affects earlier stages of the disease, however does not discriminate severe from moderate OA groups (26).

There are a few confounding variables that could significantly alter joint mechanics and neuromuscular activations, which include gender disparities, strength, walking velocity, and pain reporting (23,126,151). Despite the effect these variables can have, only post-walking NPRS scores were significantly different in the effusion group, while no other statistically significant differences between both groups were found, limiting their effect on the findings of this study. Pain has been previously associated with altered gait biomechanics (152) and reduced walking speeds (153) in patients with

knee OA compared to healthy controls. In addition, some findings have reported increased adduction moments after pain relief (92), while others have reported the opposite (154). Findings on the association between US inflammatory features and pain are inconsistent, where no associations (155) and positive associations have been reported (59,125). The impact of pain on gait activation levels has not been clearly established, and other factors can affect knee joint dynamics, making it hard to assess and conclude the isolated effect of pain on knee activations in a patient population. Furthermore, the effusion group exhibited a greater number of KL II and III than the non-effusion group, suggesting the presence of individuals with more structural severity of the disease in the effusion group. Marked joint space narrowing and increased KL grades have been previously associated with greater overall quadriceps activations (35), and neuromuscular alterations have been related to increased OA severity (26,100). These findings are based on the differences between the effusion and non-effusion group based on the 4 mm cut-off sonographic value of the supra-patellar recess (14). It seems that this cut-off value was sensitive enough to divide groups not solely on effusion, but also on other group differences. Conversely, some researchers are beginning to question this cut-off value, where 4 mm has been found to decrease the detection rate of effusion by 50% (69). It's been suggested that perhaps 2 mm could be a more appropriate cut-off value as more than 10 ml of fluid has to be in the joint in order for it to be detected sonographically based on the 4 mm cut-off value (69). The cut-off value could potentially affect the distribution of groups and affect findings of this study; however, no studies have established the exact amount of effusion that would be considered clinically significant.

A number of limitations need to be considered when interpreting findings of this chapter. Although the use of standardized protocols and exercises were used, and comparable strength values between groups have been found, low MVIC values could cause increased muscular activations during walking. While it is possible that the increased quadriceps and hamstrings activation is due to inhibition that was caused during MVICs, this is likely not the case due to the non-significant differences between both groups in regard to strength and due to the chronicity of the effusion present in this study. Lastly, other structural impairments in the joint were not detected by the standard radiographs, which could affect interpretation of findings, however the exclusion criteria

would have minimized that effect.

5.6 Conclusion

In summary, those with effusion and OA walked with higher quadriceps and lateral hamstrings activation levels, which may suggest that those with effusion and knee OA are more likely to walk in a manner similar to those with increased structural progression of OA. The 4 mm suprapatellar cut-off value has been reported to be an independent predictor of joint replacements, radiographic and patient-symptom severity (15). Future studies can investigate different cut-off values for the detection of effusion sonographically to establish whether biomechanical and neuromuscular subgroups exist, and whether there is agreement between different cut-off values of the ultrasound and the brush test as shown in Appendix D.

Despite significant findings in this chapter, no associations between the depth of the supra-patellar recess and knee joint biomechanics and neuromuscular activations were found in Chapter 4. The next chapter will discuss some of the factors that could have contributed to these discordant findings in order to provide us with a more comprehensive understanding of the relationship between the inflammatory and mechanical components of the disease.

CHAPTER 6 DISCUSSION

For many years, the biomechanical and biochemical components of the disease have been studied separately. This has created a gap in OA literature, especially since OA is now recognized as a "whole joint disease" that affects the mechanical and biochemical environments of the joint. The main purpose of this study was to understand whether a relationship exists between knee joint mechanics and effusion in a sample of individuals with moderate knee OA. In addition, many discrepancies exist between pain reports and radiographic joint impairments (108), suggesting that perhaps there are other underlying pathologies associated with OA that could be attributed to these discrepancies, such as joint effusion. Another rationale was to investigate the effect 4 mm of suprapatellar effusion depth could have on biomechanical and neuromuscular activations during gait, since there are no other standardized sonographic cut-off values.

6.1 Objective 1

The first objective of this thesis (Chapter 4) was to determine whether an association between maximum suprapatellar recess (SPR) depth, as a measure of knee effusion, and knee biomechanics and knee joint muscle activation amplitudes exist during gait in individuals with moderate medial compartment knee OA. No associations were found between maximum SPR depth and knee sagittal motion and net external sagittal and frontal moments, as well as quadriceps, hamstrings and gastrocnemius activations, despite previous reporting of altered gait mechanics in the presence of effusion (39,42,145). Conversely, knee flexor and extensor strength were the only variables that had a significant curvilinear correlation with maximum SPR depth, where very low and high amounts of SPR depth were associated with higher strength values.

These findings suggest that effusion level, based on SPR depth and knee motions, moments and muscle activation levels are independent from each other, except for isometric strength. Since the electromyographical (EMG) data is reported in percent of maximum voluntary isometric contractions (MVIC), strength values could have an effect on EMG data during walking, where lower strength values would lead to higher %MVIC activation levels, and vice versa (42). Despite that, no associations were found in neuromuscular activations as effusion depth increased in the supra-patellar recess. These findings suggest that perhaps there are other factors associated with the presence of knee

effusion and OA that are leading to alterations in gait patterns, rather than merely effusion. In addition, the curvilinear relationship between strength and SPR depth could be attributed to the heterogeneity of the OA sample in regard to the chronicity of effusion. Since the duration of the presence of effusion was never confirmed, perhaps the OA sample had both subacute and chronic effusions, which led to a non-linear association with effusion depth. Acute effusion-models are usually short-lived, lasting a few hours to a few days, however chronic effusions are referred to when effusion persists for an extended period of time (156). Due to the long-standing nature of OA disease, it was hypothesized those with OA would have chronic effusion, however there is a nebulous period of time between acute and chronic, subacute, which could possibly also include those with OA as well.

6.2 Objective 2

The second objective was to compare knee joint biomechanics and knee joint muscle activation amplitudes between individuals with and without effusion based on a cut-off value of ≥ 4 mm depth of the suprapatellar recess in individuals with moderate knee OA. The 4 mm depth threshold is based off EULAR guidelines for detection of effusion in OA (14). Participant characteristics in both groups were similar, however the effusion group had higher pain scores post-walking and a greater distribution of KL grades II and III. No biomechanical differences were found between groups, however muscular activation differences were found. Key neuromuscular findings are summarized below:

- Effusion group exhibited:
    - Higher peak and average quadriceps activation during stance
    - Greater lateral hamstrings compared to medial hamstrings during stance

Despite previous reports on altered gait biomechanics in the presence of effusion, the findings of this study suggest no biomechanical changes detected between the effusion and non-effusion OA groups. Though muscular activation differences have been detected and been consistent with previous findings related to the presence of effusion (42) and increased severity of OA (104). These findings were reported based on the standardized 4 mm cut-off value set by EULAR (14), which has been found to be a high cut-off value by some (69), and a sensitive and reasonable cut-off value by others (14,68, Appendix D). Therefore, more research is required to determine the most appropriate and sensitive

sonographic cut-off value to detect the smallest clinically significant changes in gait mechanics and muscular activations. This will help bring us to a closer understanding regarding the clinical significance of effusion and its implications on joint function.

6.3 Discussion

The findings of the first objective report no relationship between increased effusion depth and altered gait mechanics, whereas objective two reports knee muscle activation differences in the presence of effusion based on a 4 mm threshold value. The discordance in findings between both objectives in regard to the presence of effusion could be attributed to the sensitivity of the 4 mm cut-off value, which didn't only divide groups based on the amount of fluid in the joint, but also helped identify group differences in structural severity and pain scores. When both groups were divided based on 4 mm of effusion depth in the supra-patellar recess, those with effusion had higher pain scores and greater distributions of higher KL grades compared to those without effusion. The 4 mm cut-off value is the standardized value set by EULAR for detecting effusion sonographically (14), however the rationale behind why this value was chosen hasn't been clarified (69). Although researchers are beginning to question this cut-off value and are beginning to investigate other cut-off values, such as 2 mm, research is lacking on the amount that's clinically significant (157). Martino et al. (1992) investigated the physiological parameters of the supra-patellar recess in healthy, sedentary and active individuals using the ultrasound, and found normal supra-patellar thickness to range from 1-4 mm and considered thickness values greater than 3-4 mm to be pathological features, supporting the current cut-off value.

Effusion is considered to be one of the main manifestations of inflammation, and pain in individuals with knee OA and reflects the presence of inflammation in the joint. Additionally, effusion detected sonographically has been associated with increased radiographic severity (158), and thus it's been suggested that the presence of effusion is more correlated with structural changes occurring in the joint during the disease process rather than a specific mechanism or biomarker that is linked to pain (158). Similarly, effusion depth of 4 mm or higher has been previously reported to be associated with increased pain levels and radiographic severity (14,15), supporting our findings.

In addition, since the duration and chronicity of effusion present were never investigated nor confirmed, it cannot be guaranteed that the sample under investigation represented chronic effusions solely based on the chronicity of OA. It could be possible that the sample under investigation had either subacute or chronic effusions, which could have affected findings for objective 1 mainly. This assumption was made due to the curvilinear relationship shown in Appendix A between maximum effusion depth and strength values, where it was presumed that those with low to moderate amounts of effusion exhibited muscular inhibition and represented subacute effusion models. However, when the 4 mm cut-off value was used to divide groups based on presence of effusion, it could have accounted for that heterogeneity and divided those with low-to-moderate amounts from those with moderate-to-high amounts.

One of the main aims behind this thesis was not only to determine the effect effusion has on gait mechanics, but also to understand how it may contribute to the progression of OA. Effusion-synovitis has been associated with increased patient-symptom and radiographic severity (15), and has been reported to alter how an individual walks (39,40,42,145). The findings of objective two suggest that those with knee OA and effusion walk with altered neuromuscular activation levels that are more similar to those with greater OA severity. Individuals with greater structural severity have been reported to walk with greater quadriceps (136) and lateral hamstrings activations (33) and lower and phase-shifted medial gastrocnemius activations (30,35). In addition, greater differential activation between medial and lateral hamstrings have been found to differentiate severe OA groups from moderate (31) and healthy controls (32). Although no gastrocnemius activation differences were found between both groups, the effusion group had higher quadriceps activation levels and greater lateral hamstrings activation compared to the medial hamstrings. This increase in activation could be a compensatory mechanism in order to counteract high medial loading in the knee joint (31,33,93). These differences occurred despite similarities in strength, walking speed, age and BMI.

Although no biomechanical differences were found between both groups in objective two, the role of the muscular system is equally important in influencing joint loading (159). The causality between structural severity and alteration in the neuromuscular environment cannot be conclusive from cross-sectional designs solely,

however findings of this study are supported by existing literature supporting the association between increased structural severity and muscular activation differences in knee OA (32,35).

In summary, research on how the inflammatory component affects the mechanical component of the disease is lacking, especially in the population of knee OA, even though the inflammatory component has been reported to be associated with increased progression of the disease and altered walking patterns (15,42). The findings of this thesis support previous findings, where neuromuscular alterations exist in the presence of chronic effusion based on the 4 mm cut-off value, however SPR depth was not significantly correlated with any neuromuscular or biomechanical variable. Although these changes are responses aimed at providing neuromuscular knee joint support, they could have future implications on the joint for increased joint loading.

6.4 Limitations

The results of this study must be interpreted within the limitations of the data. The main limitation of a cross-sectional study design is that it does not allow us to draw conclusions regarding the relationship between exposure and outcome, since they are simultaneously assessed. Without longitudinal data, it's difficult to establish a true cause and effect relationship. There are several confounding variables that could have affected the findings of the data, which include age, BMI, gender, walking velocity, and strength values (96,103,126,151). In this study, similarities in these confounding variables were found between both groups, limiting their effect on the findings of this study. Individuals with effusion and knee OA had a distribution of higher KL grades and pain scores post walking, which could act as confounding variables in the interpretation of the results. In addition, using MVICs as a method for normalization has been previously questioned in regards to eliciting a maximal voluntary effort (104), however studies have found that standardized procedures and consistent feedback individuals can recruit to similar maximum percentages as healthy controls (160). The chronicity of effusions in those with knee OA was not established, and therefore could have affected findings since acute and chronic effusion models have been reported to respond differently (48,49). Lastly, the instructions provided by the sonographer regarding isometric contractions were non-standardized, which could affect amount of fluid detected. However, palpation,

maintenance of knee position and shift of fluid seen on the scan were used as signs of quadriceps isometric contractions by sonographer.

6.5 Future Directions

There are numerous future directions to take following this study, mainly due to the fact that there is limited research on the effect of chronic effusion and knee OA during gait. In this study, the use of discrete metrics was used to perform statistical testing, however there are other multivariate statistical methods to use in order to analyze gait, such as principal component analysis (PCA). The use of PCA in future could help identify pattern changes at different phases of the gait cycle, especially since pattern changes through PCA have been detected in those with effusion and knee OA (42). Alternate statistical analyses, such as an analysis of covariance (ANCOVA), could be performed in the future to help account for factors that could have confounded the results. Non-parametric testing could be performed to assess bi- and multi-variate associations with non-continuous data, like KL scores. In addition, longitudinal follow-up studies on individuals with knee OA and effusion during gait could help us understand the role effusion plays during the disease process. Also, future studies can investigate the effect of aspiration of chronic effusions on gait mechanics in the OA population in order to determine the true cause-and-effect of effusion. Other future directions could include investigation of a number of cut-off values, above and below the standardized 4 mm, to determine the most sensitive value in detecting effusion-related changes in the joint. There are various detection tests in determining the presence of effusion, like imaging modalities and clinical tests, however agreement between both is lacking. Therefore, agreement between the ultrasound and brush test, the most reliable clinical test in detecting swelling, could be more thoroughly tested (See Appendix D for preliminary assessment) and analyzed. This could help inform clinical practice, especially since many clinics might not afford to use imaging modalities like MRI and US.

6.6 Concluding Remarks

The main aim of this thesis was to understand the effect knee effusion, as a manifestation of inflammation, has on gait mechanics during gait in individuals with moderate knee OA. While findings of this study do not provide enough information to make assumptions on disease progression, it has been found that those with knee OA and

effusion walk differently than those who have knee OA and no knee effusion. Some of the neuromuscular alterations observed are similar to those reported with greater structural severity, indicating the prospective role inflammation plays in the disease process. Clearly, the biology of the joint is a fundamental component in maintaining the joint's normal function (159). A change in the mechanical environment as a result of OA could be a trigger for biological responses at the cellular level, leading to inflammation (36). Therefore, isolating the mechanisms of loading and motion on the knee joint without including the response of the biological system can lead to a gap in understanding the factors that affect OA progression.

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APPENDIX A: Correlation Scatter Plots for Chapter 4

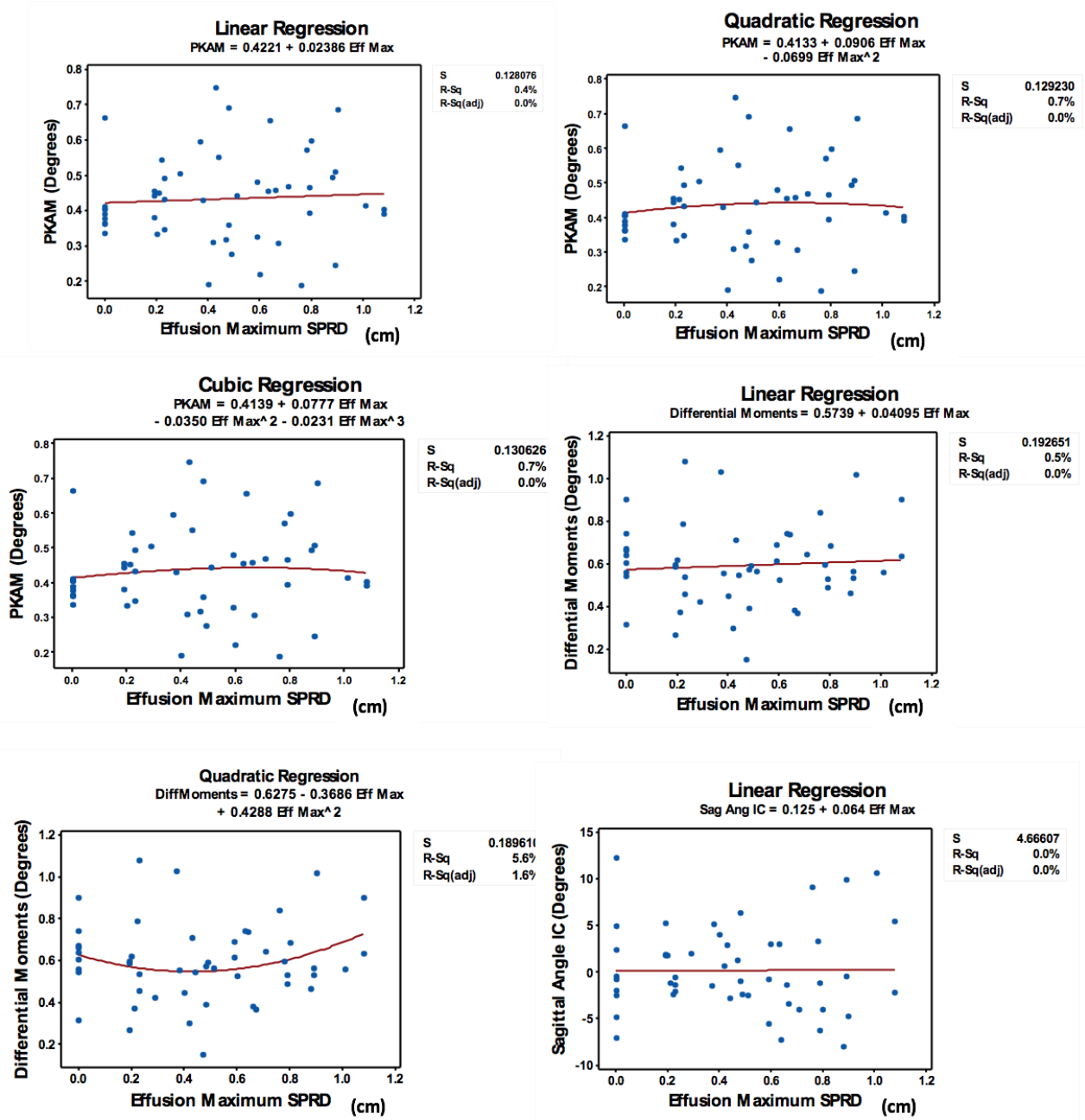


Figure A. 1: Correlation scatter plots for linear and non-linear regressions for biomechanical discrete variables.

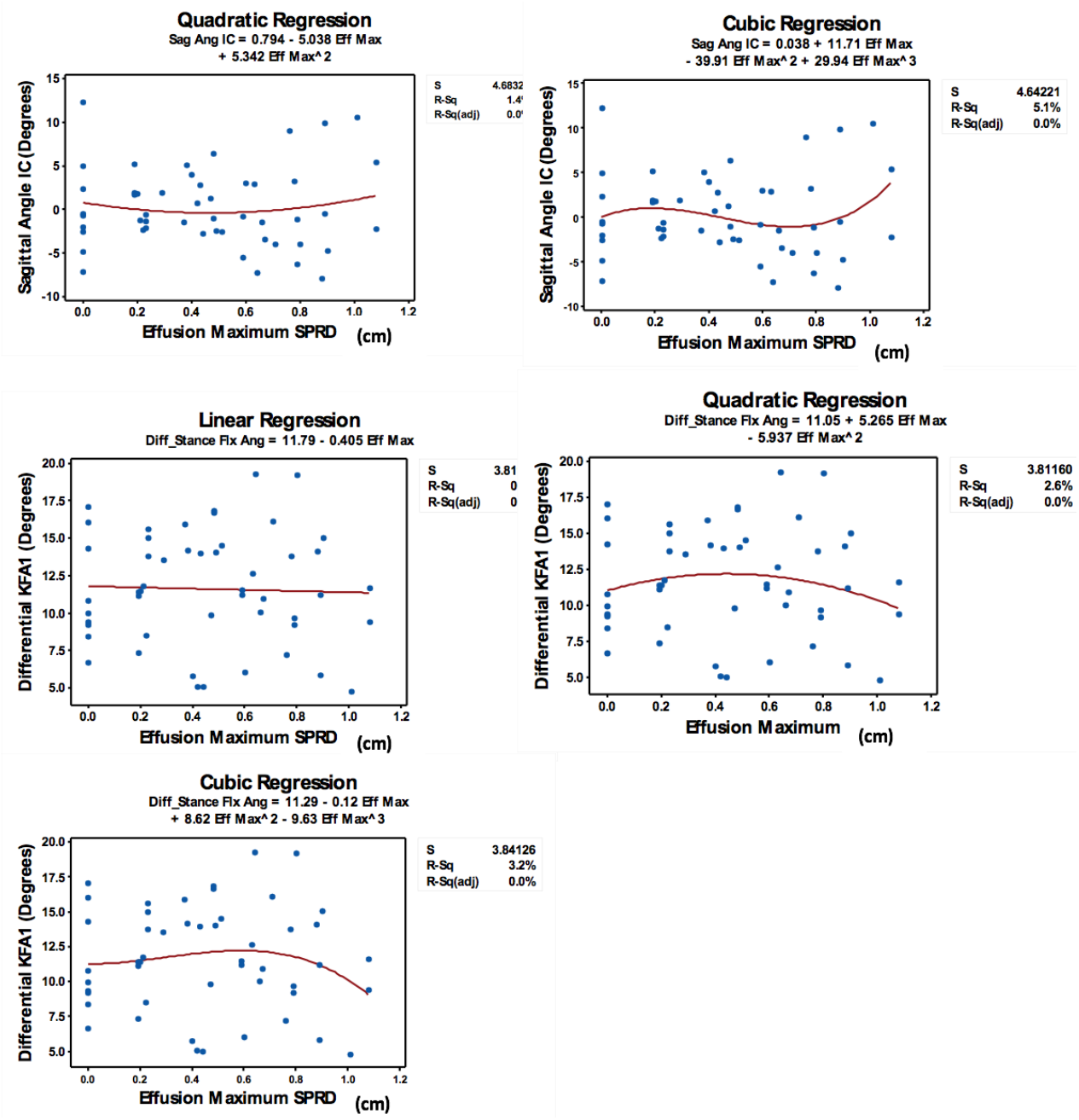


Figure A. 2: Correlation scatter plots for linear and non-linear regressions for biomechanical discrete variables.

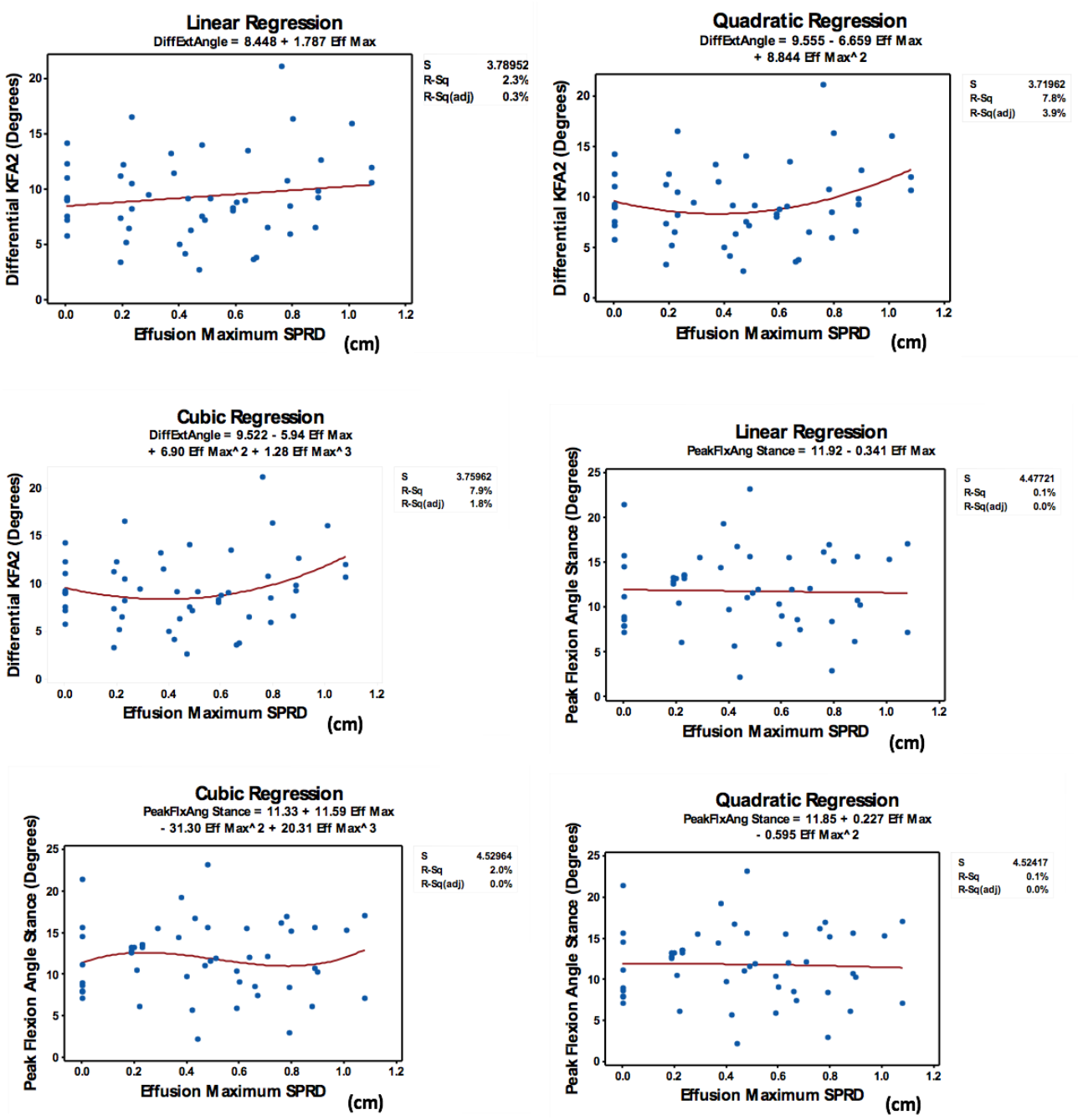


Figure A. 3: Correlation scatter plots for linear and non-linear regressions for biomechanical discrete variables.

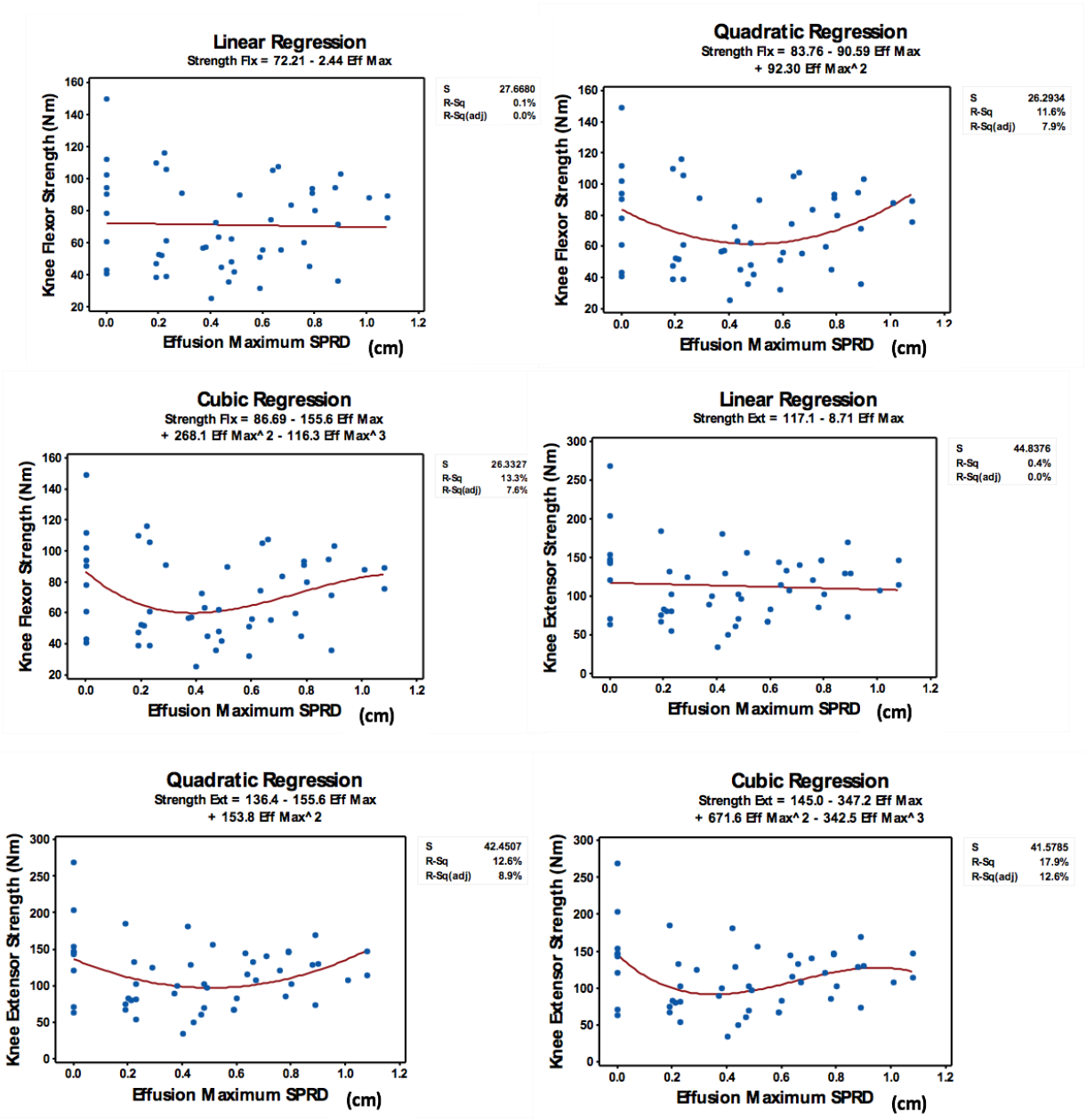


Figure A. 4: Correlation scatter plots for linear and non-linear regressions for biomechanical discrete variables.

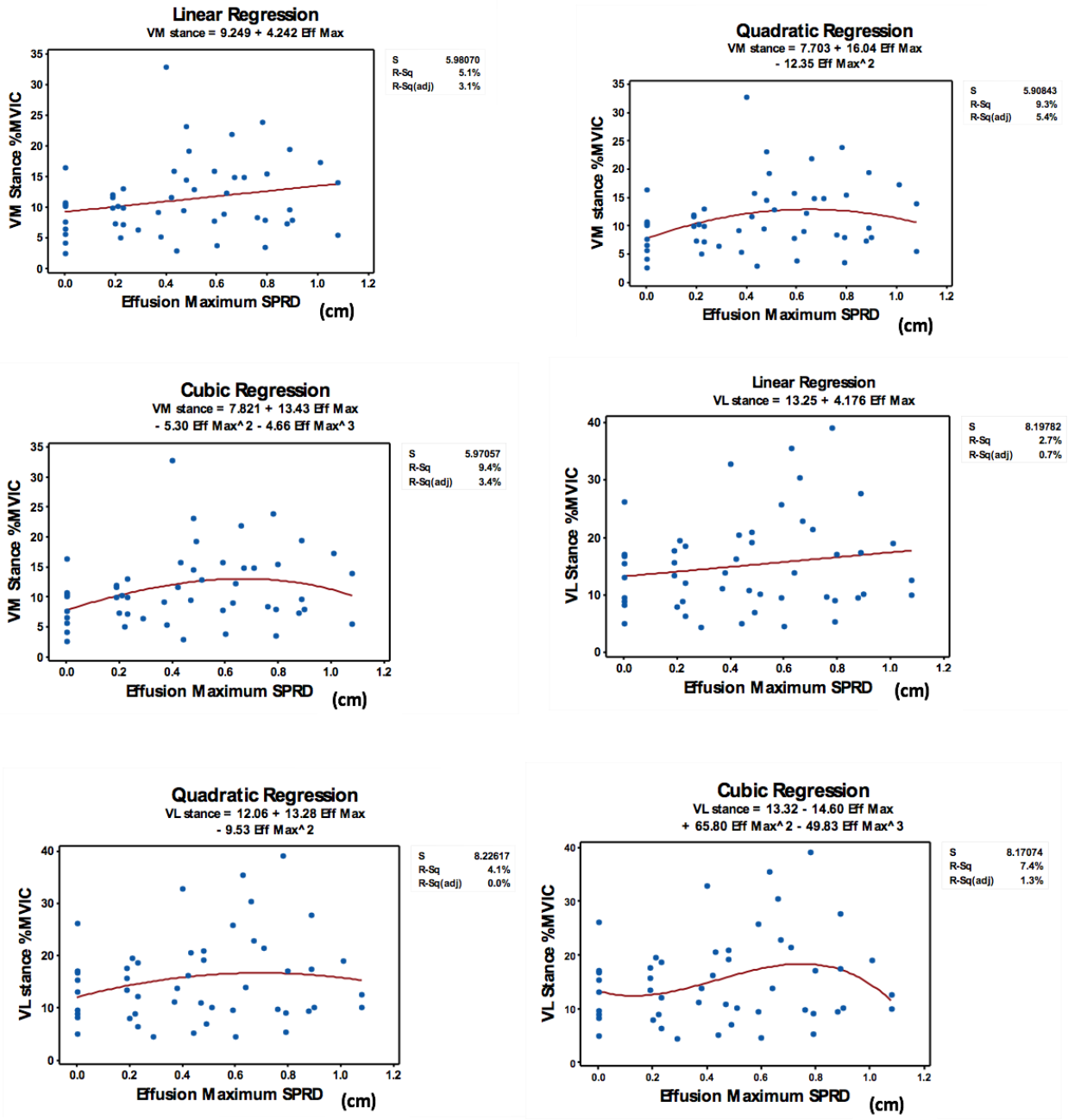


Figure A. 5: Correlation scatter plots for linear and non-linear regressions for muscular activations for all muscles.

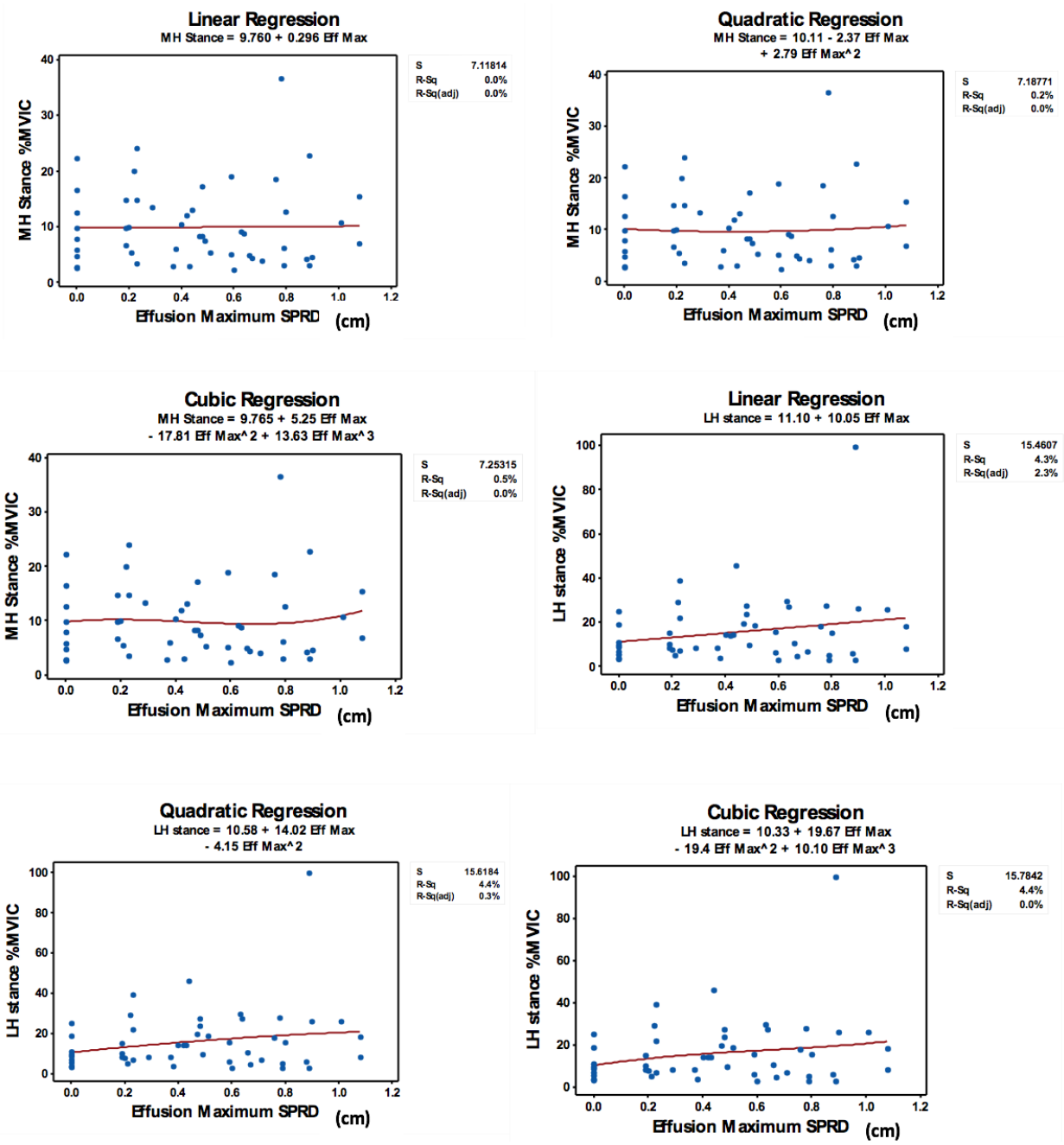


Figure A. 6: Correlation scatter plots for linear and non-linear regressions for muscular activations for all muscles.

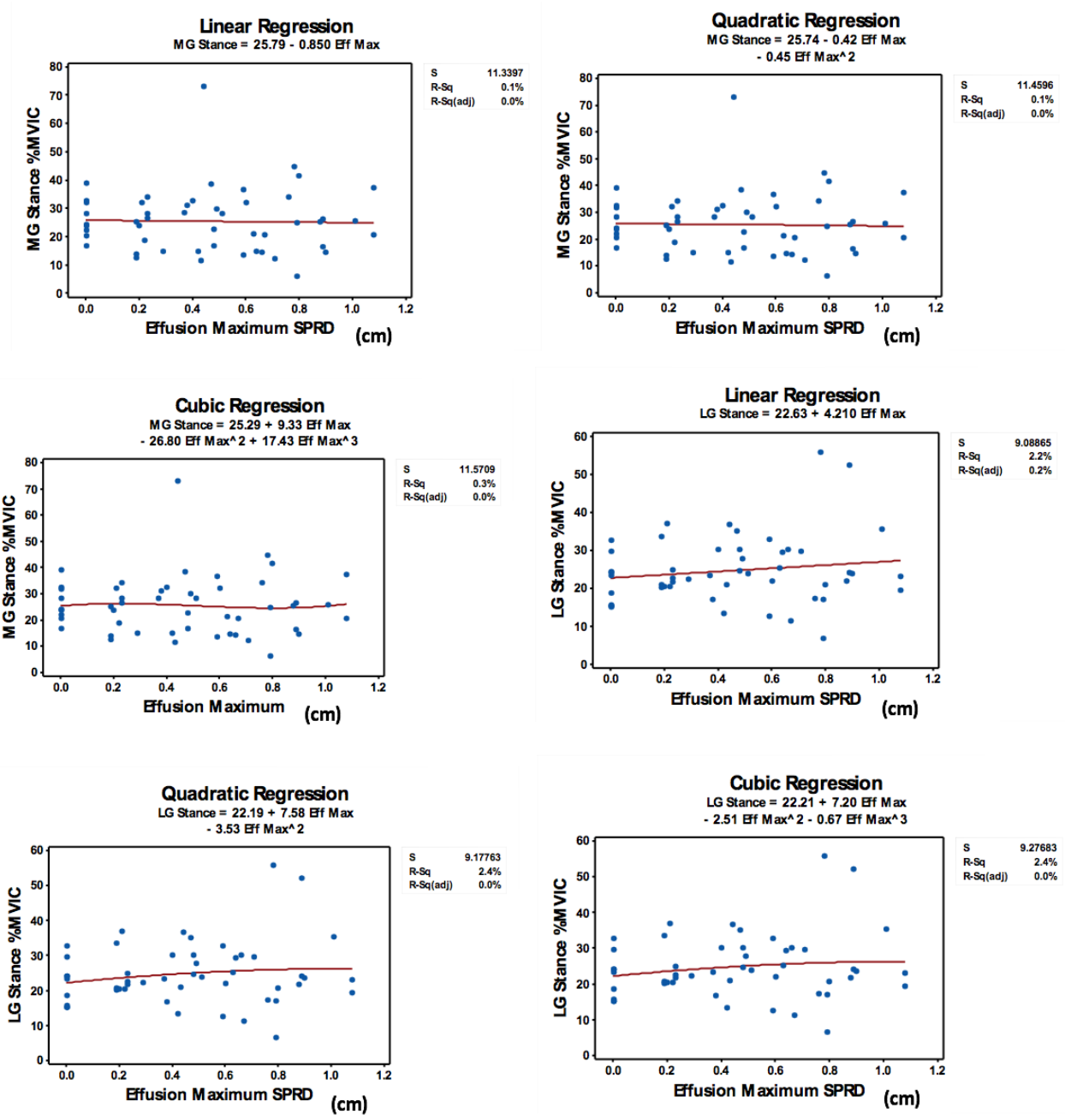


Figure A. 7: Correlation scatter plots for linear and non-linear regressions for muscular activations for all muscles.

APPENDIX B: All Graphs for Results of Chapter 5

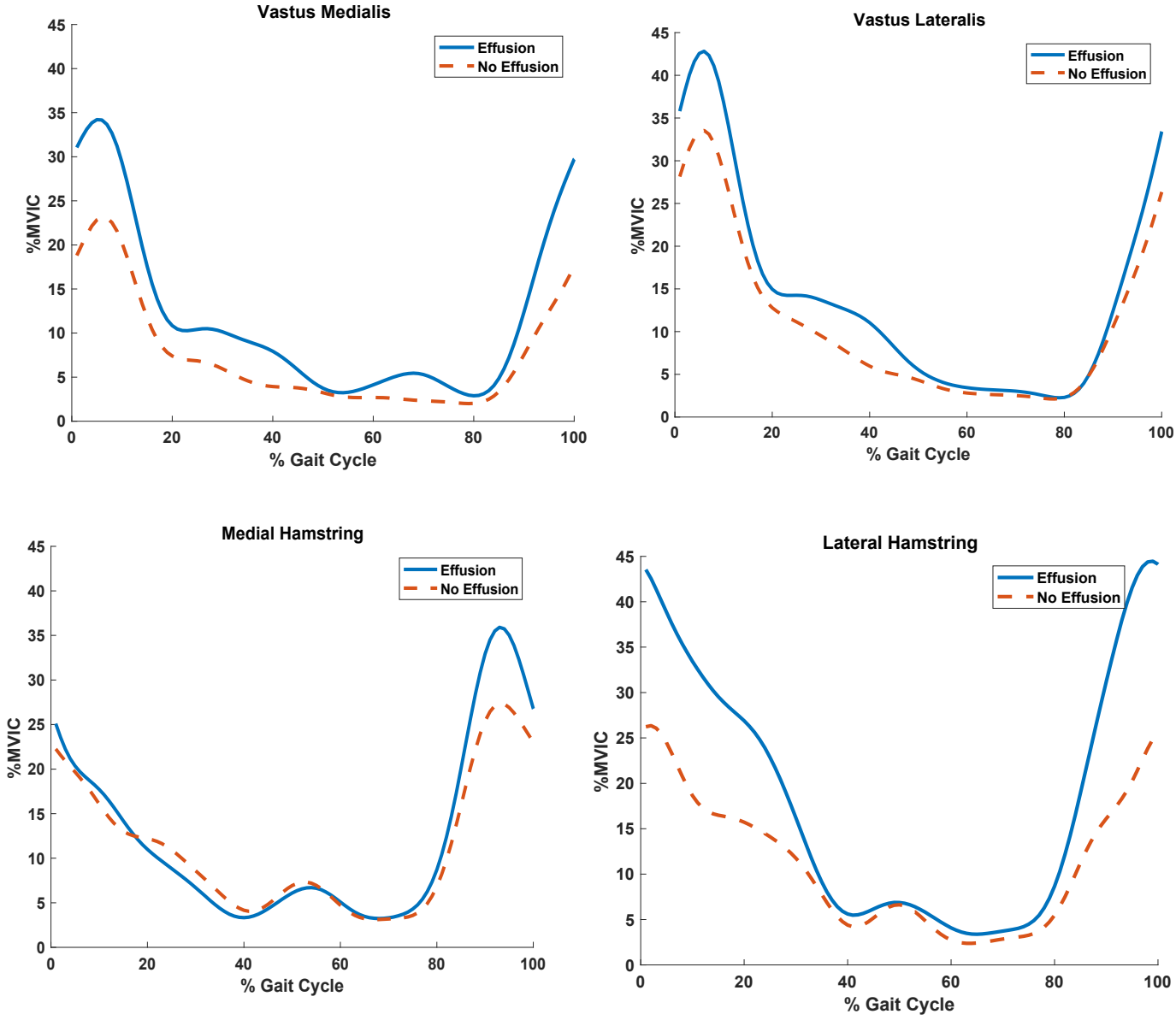


Figure B. 1*:* Ensemble-averaged electromyographic waveforms during gait normalized to %MVIC for effusion and non-effusion groups for each muscle.

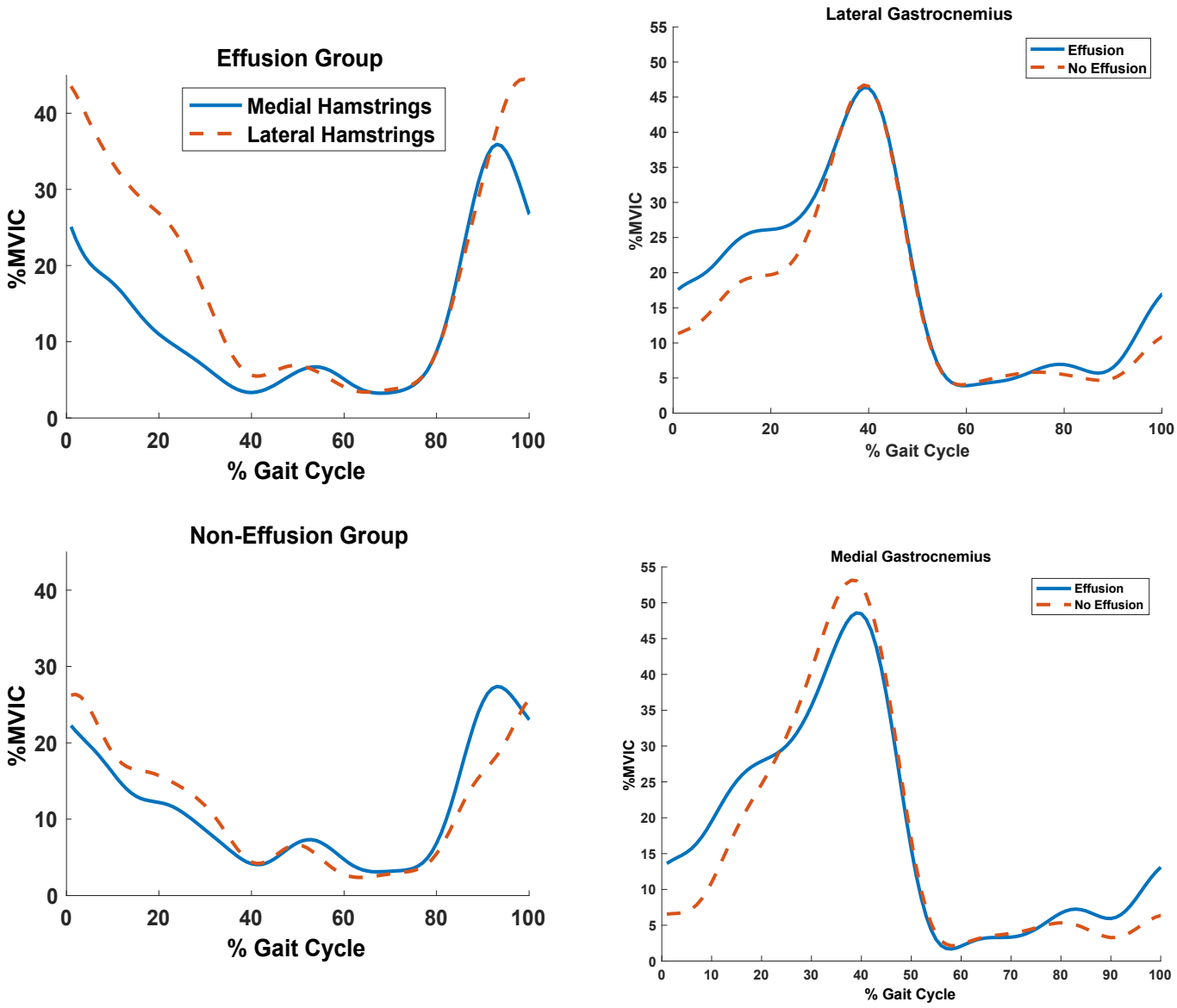


Figure B. 2: Ensemble-averaged electromyographic waveforms during gait normalized to %MVIC for effusion and non-effusion groups for the gastrocnemius (medial & lateral), and differential activation of medial & lateral hamstrings.

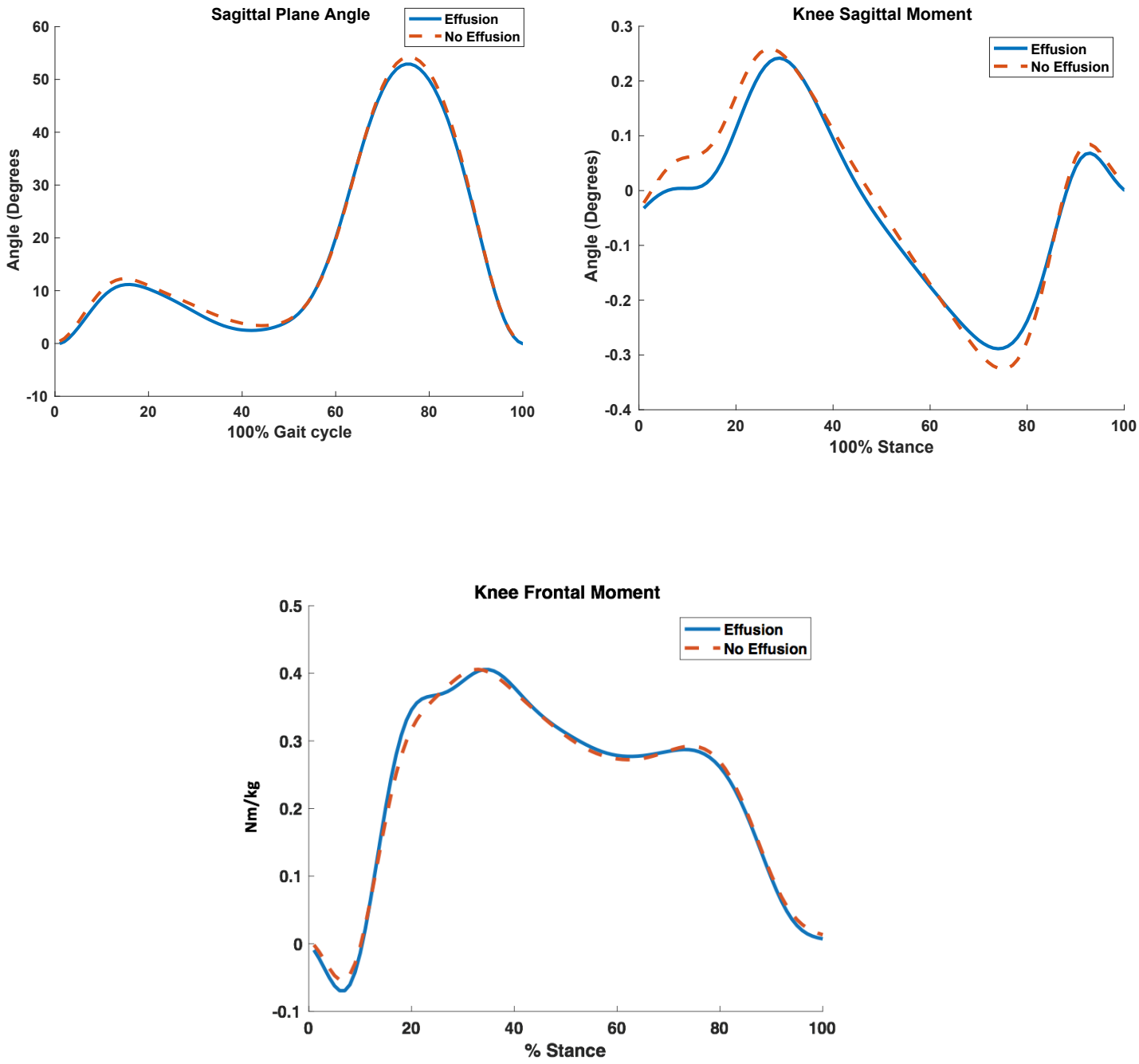


Figure B. 3: Ensemble-averaged biomechanics waveforms during gait for the effusion and non-effusion groups for knee sagittal plane angles, and sagittal and frontal knee moments.

APPENDIX C: Inter-subject variability of processed and normalized EMG and biomechanical waveforms for all participants

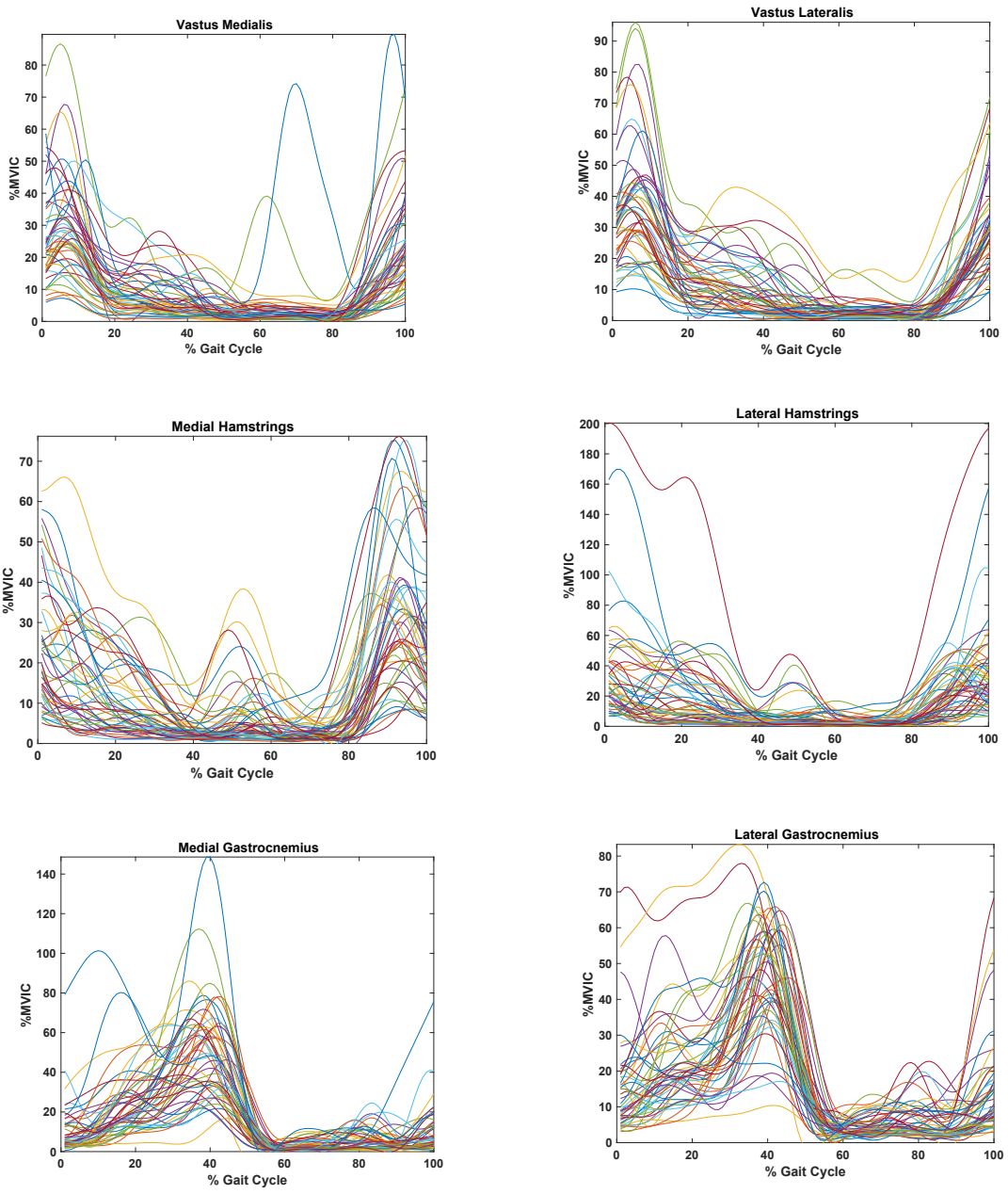


Figure C. 1: Electromyography variability plots for Quadriceps -VM & VL (first row), Hamstrings - medial & lateral (second row) and gastrocnemius - medial & lateral (third row).

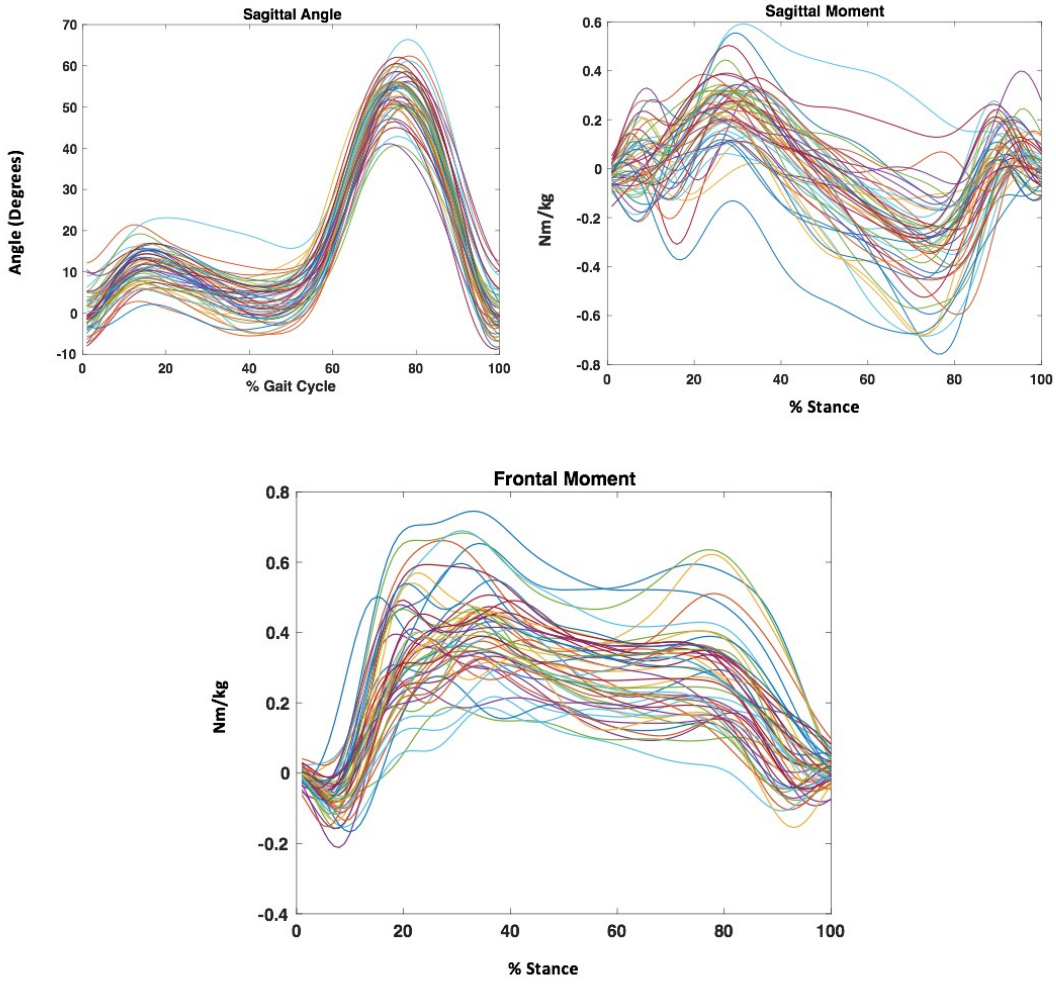


Figure C. 2: Biomechanics variability of knee sagittal plane motion, and net external sagittal and frontal plane moments.

APPENDIX D: Preliminary analysis (abstract) to assess agreement between brush test and US cut-off values

Comparison between clinical evaluation and ultrasonography in detecting knee swelling in individuals with knee osteoarthritis.

Sara Saleh, Cheryl Hubley-Kozey, William Stanish, Carol Gillis, Derek Rutherford

This abstract was presented at the Professional & Research Education Program (PREP) graduate research day held in Dalhousie University.

Introduction: Knee osteoarthritis (OA) is the most common joint disease and is a major source of pain and disability. Recent evidence has shown that OA is associated with biological inflammatory processes in the synovium, synovitis. Synovitis can be detected through the use of many imaging modalities, like the ultrasound (US), and routine clinical assessments, like the brush test.

Purpose: To investigate the agreement between the brush test and US in detecting effusion in those with knee OA.

Methods: 50 patients diagnosed with moderate medial compartment knee OA were recruited. Ultrasound examinations were performed by an experienced sonographer using an ATL HDI 3000 ultrasound system and a broad bandwidth 12-5 MHz linear array transducer. Knee effusion was measured in millimeters (mm) at three locations (mid, medial, lateral) of the supra-patellar recess (SPR). Different cut-off values of 2, 4 and 6 mm were used to determine presence of effusion. The clinical evaluation assessed the presence of effusion using the brush test by an experienced physiotherapist, and a positive finding was determined by a bulge on the medial aspect of the knee. The clinical examination was done before the US test and evaluators were blinded to each other's outcomes. Cohens' kappa (κ) values were used to assess the level of agreement between the brush test and the different cut-off values of US.

Results: The κ value between the brush test and 2, 4 and 6 mm cut-off values was 0.43, 0.58, and 0.50, respectively ($p < 0.05$). The percentage of agreement between the brush test and 2, 4 and 6 mm cut-off values of US was 74%, 80% and 74% respectively.

Table D. 1: Participant demographics and characteristics

	Mean ± SD
N	50
% Females	42%
Age (years)	61 ± 6.0
BMI (kg/m^2)	29.0 ± 4.4
Walking Velocity (m/s)	1.1 ± 0.1
Knee Flexion Strength (Nm)	71.7 ± 27.8
Knee Extension Strength (Nm)	113.8 ± 45.4

Table D. 5: Matching and % of Agreement for the different cut-off values.

	# Matched	% Agreement
2 mm	37/50	74%
4 mm	40/50	80%
6 mm	37/50	74%

Table D. 2*:* Kappa and P-values for agreement between brush test and US.

	K-value	P-value
2 mm	0.43	0.0004
4 mm	0.58	0.0000
6 mm	0.50	0.0004

Conclusion: The results of this data suggest that percentage of agreement is highest when the cut-off value of the US is set at 4 mm, with a moderate agreement between the brush test and US. Only one study investigated the agreement between the brush test and US, where moderate agreement was reported with a kappa value of 0.508 (149), similar to our findings.

There are several factors that can affect the agreement and affect the reliability of the test (149), which include:

- ✓ Clinical experience of examiner
- ✓ Amount of swelling present in the knee
  - Larger amounts increase sensitivity and specificity of test
- ✓ Patient related conditions
  - Obesity
  - Structural deformities

In summary, there are various methods to detecting effusion, whether through imaging modalities or clinically through clinical tests, like the brush test. Some physiotherapy clinics might not afford to use a US/MRI, therefore clinical tests could play an essential role in detecting swelling in the joint. Thus knowledge about the agreement between both methods could help guide clinical practice, especially since OA is reported to be a mechanical and inflammatory disease (36). So being able to assess both components of the disease in a feasible manner can significantly help improve assessment and treatment plans.

APPENDIX E: Phantom Testing of Ultrasound

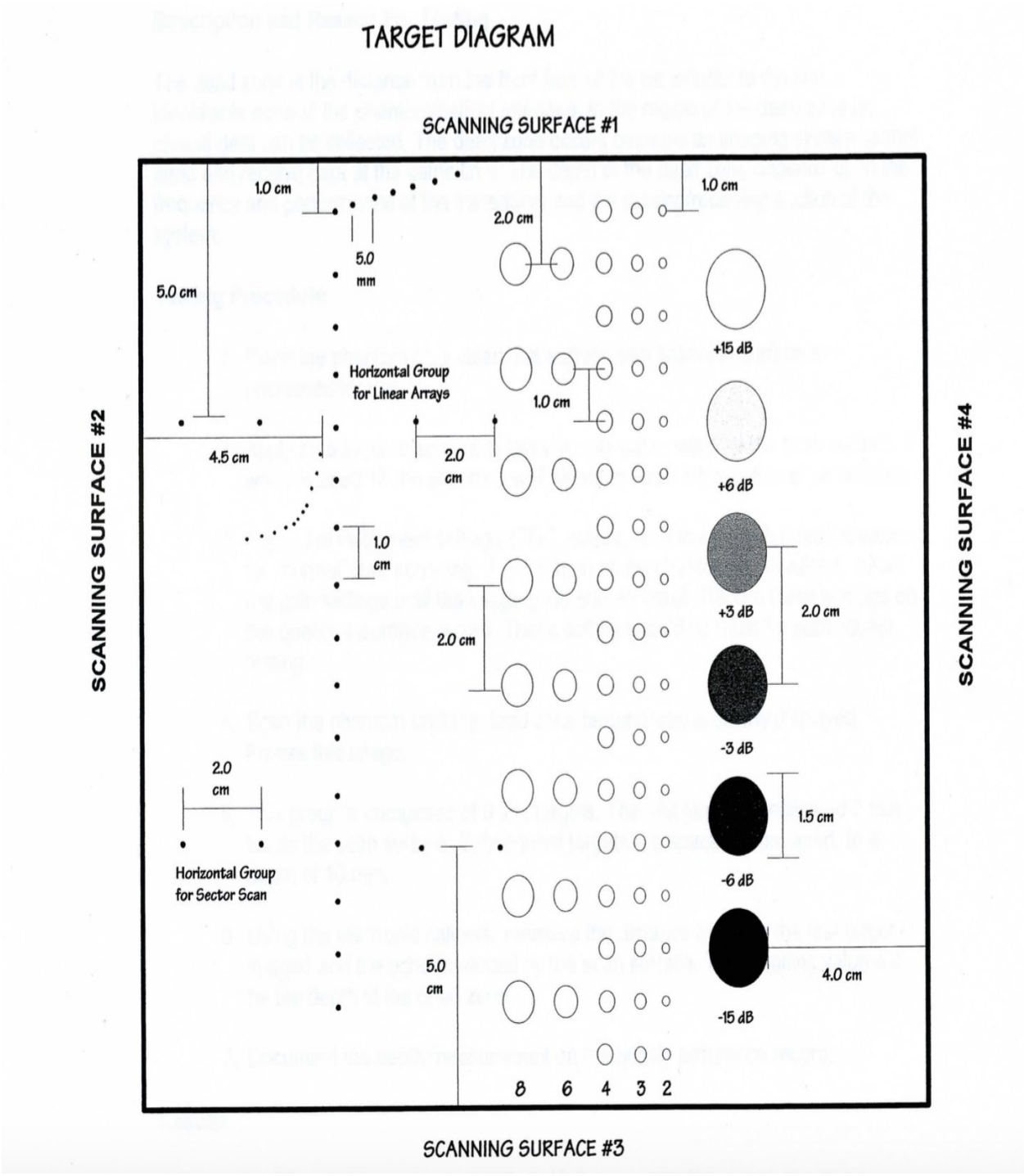


Figure E .1: Scanning surface for ultrasound phantom testing.

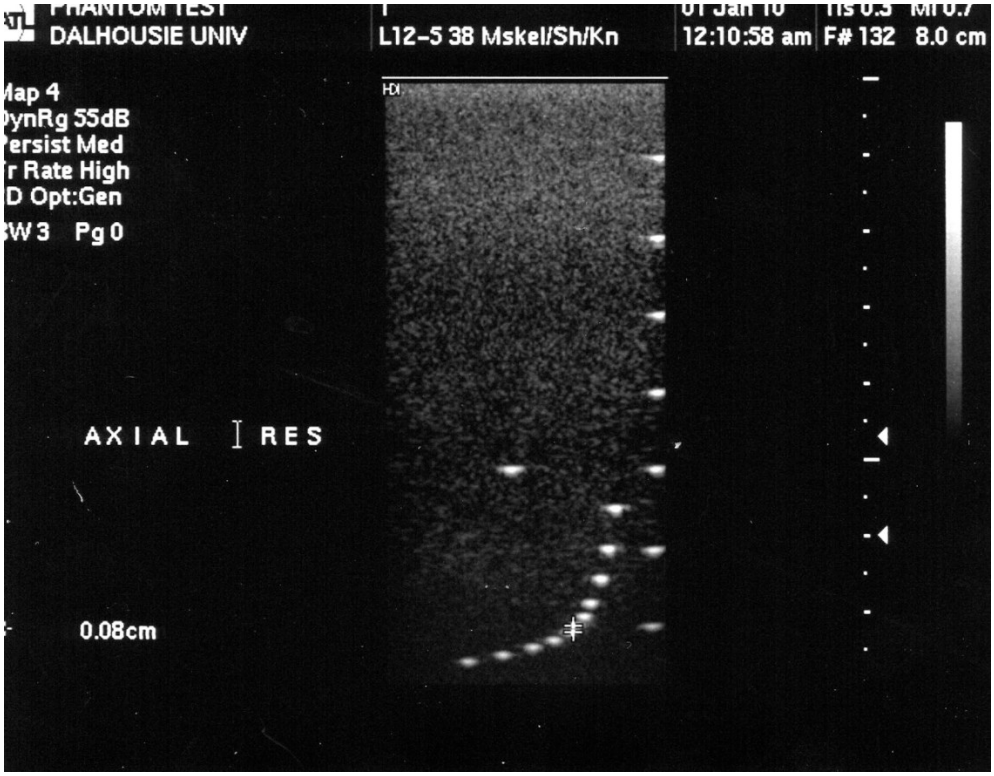
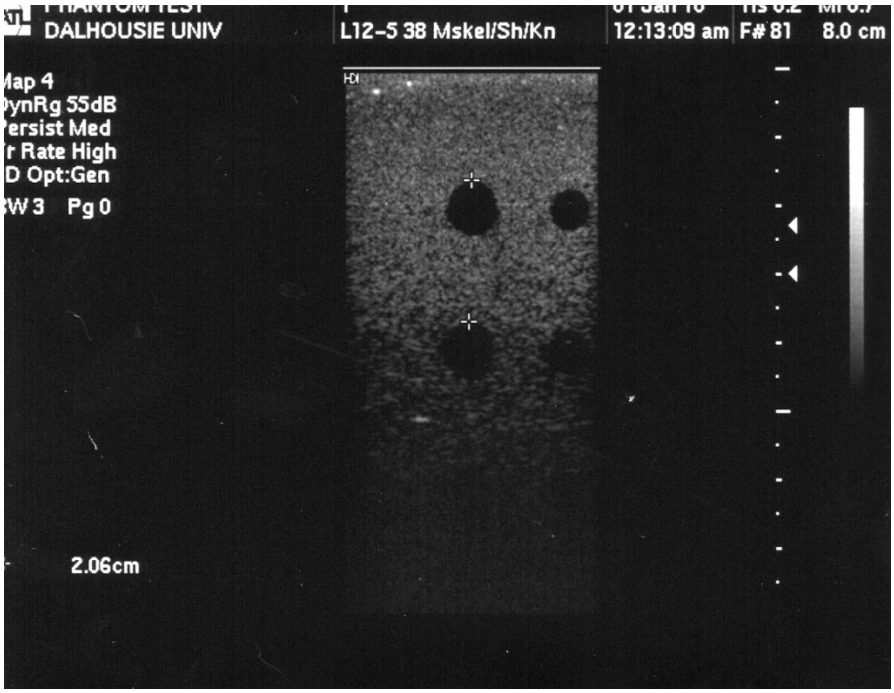


Figure E .2: Ultrasound scan of the axial resolution and hyperechoicity of the US, respectively.



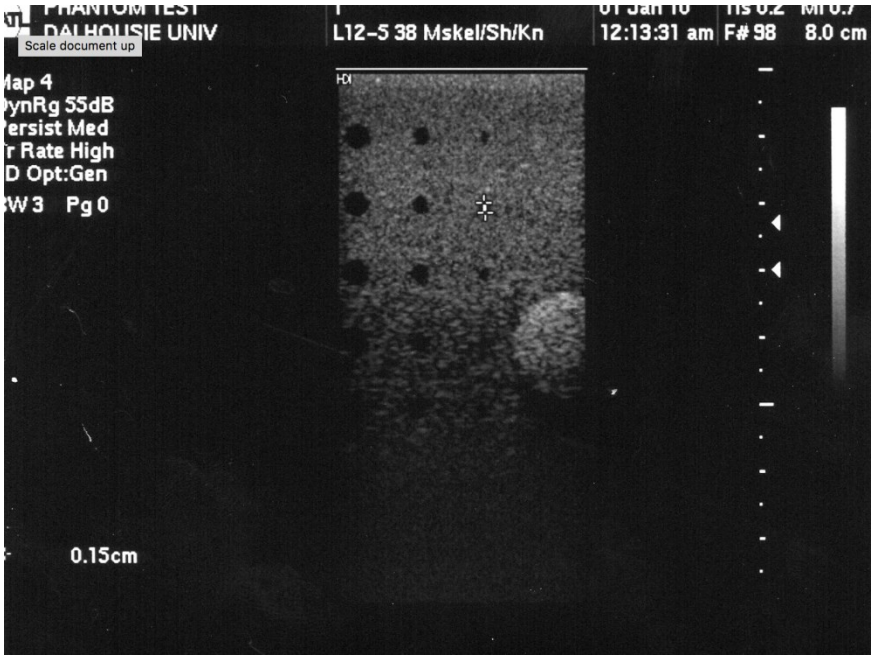
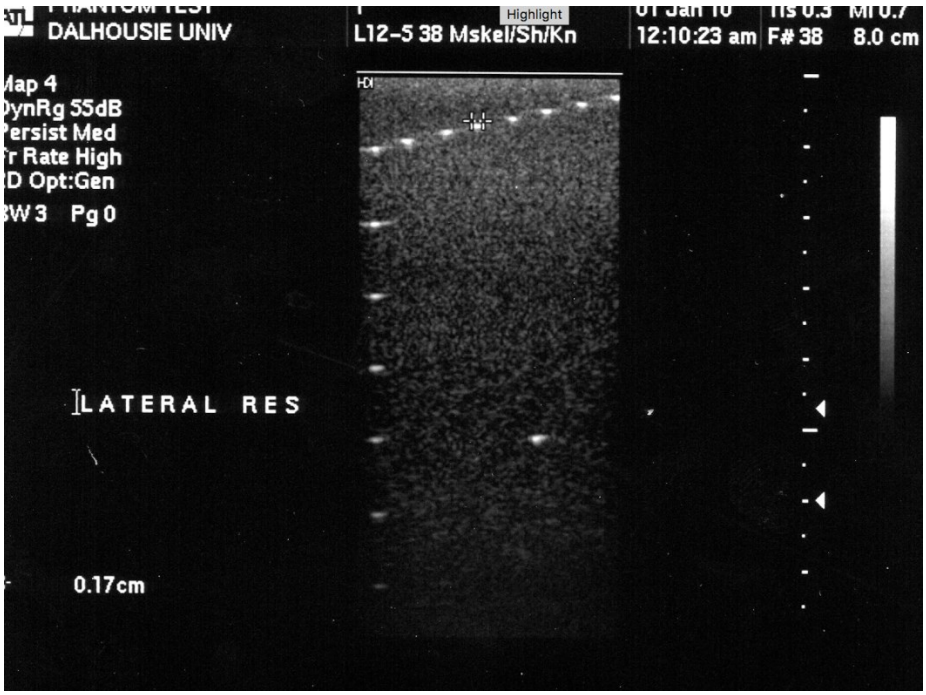


Figure E .3: Ultrasound scan of the hyperechoicity of the US, respectively.



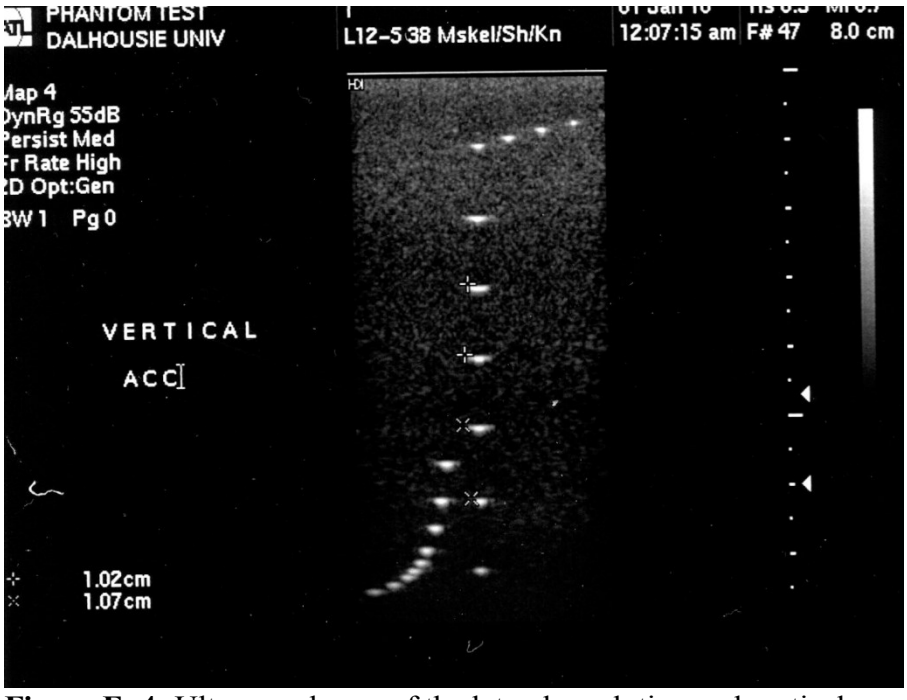


Figure E .4: Ultrasound scan of the lateral resolution and vertical accuracy of the US, respectively.