LOWER EXTREMITY MUSCLE CONTRIBUTIONS TO ACL LOADING IN HEALTHY AND ACL-RECONSTRUCTED FEMALES

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DEDICATION

This dissertation is dedicated to my father, Jack Peel, and my brother, Rhett Peel. Without the sacrifices my father made as a single father to provide a great life for my brother and I, I would not have a dissertation to dedicate. I am forever grateful to you, dad. My brother's pursuit to service of our country as a Naval seaman continues to be one of my biggest inspirations. Thank you, Rhett, for your service and commitment to protect our country, all while still thinking of me and offering support throughout my doctoral work. Thank you both for your unconditional love, your encouragement, and for the kick in the pants when I needed it throughout this dissertation process. I hope this achievement is something you both can be proud of. From the bottom of my heart, thank you.

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ABSTRACT

Females are 16 times greater to sustain a second ACL injury compared to their healthy female counterparts. Many of these females return to play their respective sport after an ACL-reconstruction (ACL-R). However, one variable hypothesized to be associated with injury that cannot be avoided is muscular fatigue. Little is known about the influence fatigue has on lower extremity mechanics of ACL-R females. The purpose of this dissertation was to determine how fatigue and surgical intervention of the ACL influenced lower extremity mechanics as well as how is to determine how individual lower extremity muscles contributed to healthy and ACL-R females. Chapter 3 discusses how lower extremity mechanics changed in healthy and ACL-R females pre- and post-fatigue. Chapter 4 examines how overall ACL loading (F_{ACL}) was influenced in healthy and ACL-R females pre- and post-fatigue. Finally, Chapter 5 discusses how fatigue and ACL-R affected individual muscle contribution to F_{ACL}.

Chapter 3 showed that ACL-reconstruction and fatigue is influential on specific hip and knee mechanics in recreationally active females. ACL-R female displayed altered hip mechanics that may place them at a higher risk of ACL re-injury, especially after muscular fatigue has been induced, compared to healthy females. Chapter 4 found that fatigue or surgical intervention did not influence F_{ACL}. Finally, Chapter 5 showed that fatigue or surgical intervention did not influence individual muscle contributions to F_{ACL}.

Future research should focus on the effects fatigue did have on hip mechanics in ACL-R females as a way to improve injury prevention as well as rehabilitation protocols. Future research should also focus on improving the limitations of this dissertation.

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NOMENCLATURE

ACL	Anterior cruciate ligament
ACL-R	Anterior cruciate ligament reconstruction
AM	Anteromedial bundle
BTB	Bone-Patellar Tendon-Bone autograft
BW	Body weight
cm	Centimeter
deg/s	Degrees per second
dof	Degree of freedom
EMG	Electromyography
F_{ACL}	Overall ACL loading
GRF	Ground reaction force
IAA	Induced acceleration analysis
IKDC	International Knee Documentation Committee
JRF	Joint reaction force
KOOS	Knee injury and Osteoarthritis Outcome Score
LEFS	Lower Extremity Functional Scale
mm	Millimeter
ms	Millisecond
N	Newton
Nm	Newton-meter
PL	Posterolateral bundle
ROM	Range of motion

SPM	Statistical parameter mapping
ST-G	Semitendinosus-Gracilis hamstring autograft
TSK-11	Tampa Scale for Kinesiophobia
yrs	Years old

Chapter 1: Development of the Problem

Background and Rationale

Anterior cruciate ligament (ACL) injuries are extremely prevalent, costly, and result in long term consequences, such as early onset knee osteoarthritis. Approximately 200,000 ACL injuries occur every year in the United States (1). Up to 30% of these athletes will sustain a second ACL injury within 24 months of the original injury (2). Numerous studies have reported that females are two to eight times more likely to sustain an ACL injury compared to their male counterparts (1, 3-6). This is influenced by both anatomical factors, such as females having larger Q-angles, smaller ACL length and circumference, and increased hormonal fluctuations throughout the month, and biomechanical factors like landing with a more erect posture or cutting with larger knee abduction angles (7, 8). As such, gaining new perspective into the mechanisms behind the high ACL injury rates for females is critical.

It is well known that the primary role of the ACL is to prevent excessive anterior tibial translation. It has also been theorized that co-activation of the hamstrings and quadriceps help protect the ACL. Recruitment of the hamstrings help reduce ACL loading via counteracting excessive quadriceps force (9, 10). However, it is reasonable to assume that additional muscles beyond the quadriceps and hamstrings influence ACL loading. While muscles that cross the knee joint do, to various degrees, play a role in ACL loading, muscles that do not span the knee joint cannot be overlooked. It is known that muscles can accelerate joints that they do not directly span due to the phenomenon known as “dynamic coupling” (11), which in turn would also influence loading of the ACL. Previous research has also shown that non-knee spanning muscles, such as the gluteus maximus, gluteus medius, and the soleus do influence tibiofemoral shear force as well as frontal and transverse plane knee moments during an unanticipated sidestep cut

(12). However, loading of the ACL was not calculated in this study. While the movement patterns that often lead to ACL injuries are established (e.g. unanticipated cutting, single leg landing, change of direction, sudden deceleration), it is important to understand what muscles are contributing to the overloading of the ACL during these movements. It is also critical to understand how the contributions of these muscles may alter after surgical intervention of the ACL, known as ACL reconstruction (ACL-R).

Approximately 100,000 to 150,000 of all ACL injuries occurring in the United States each year will undergo an ACL-R (13). The cost for ACL-R and subsequent physical therapy exceeds $2 billion annually (14-16). The primary goal of conducting an ACL-R is to return individuals back to an active lifestyle by regaining stability after an ACL injury (17). While ACL-R returns most athletes back to play, kinematic and kinetic changes to the reconstructed knee still exist compared to the contralateral knee or control knees. These include changes in knee joint kinematics and kinetics, decreased muscular strength, altered muscular activity, loss of proprioception, and changes in coordinative variability of the knee joint (18-25). These altered mechanics are responsible for why 17% of athletes do not return to play after ACL-R, and why 10% to 30% of athletes who do return to play after an ACL-R will sustain a second ACL injury (26-30). Unfortunately, females are four times more likely to experience a second ACL injury after the initial ACL-R compared to their male counterparts (31). As such, great effort has been placed on decreasing this high reinjury rate.

Because up to 83% of ACL-R athletes return to their pre-injury sport (32), coaches and clinicians strive to implement rehabilitative programs that will put the athlete in the best position to avoid a secondary ACL injury. However, regardless if an athlete is healthy or ACL-R, fatigue is one factor that cannot be avoided. Fatigue is a complex system. It is thought that when an

individual becomes fatigued, the fatigued musculature is not able to absorb energy as well as non-fatigued musculature (33). This in turn leads to decreases in neuromuscular control, decreased proprioception of the knee, and altered lower extremity mechanics, thus potentially overloading the ACL and causing injury (34-39). Few studies have observed the effects fatigue has on healthy females during tasks, such as landing and cutting (34, 35, 38, 40-45). Even fewer studies exist that report the influence of fatigue on ACL-R females compared to a healthy group (46, 47). However, these few studies do suggest that altered neuromuscular control potentially exists in ACL-R females after a fatigue protocol (46, 47). Therefore, it is possible that lower extremity muscles would exhibit altered loading patterns on the ACL in a fatigued state for these two populations.

Musculoskeletal modeling provides a way to measure physiological parameters, such as (i.e., muscle force, joint contact force, ligamentous force, etc.) that are difficult to measure *in vivo* (48-50) during athletic movements such as cutting and various landing tasks (51-54). Through the use of musculoskeletal modeling, studies have observed how individual muscles contribute to tibiofemoral contact forces, tibiofemoral shear force, and frontal and transverse knee moments in healthy individuals (12, 55, 56). Yet, no study has observed how individual muscles contribute to ACL loading in ACL-reconstructed (ACL-R) individuals. It is established that knee mechanics, such as sagittal and frontal knee moments, are different between healthy and ACL-R individuals (57). It has also been shown that vasti muscle activation is lower in ACL-R limbs compared to their noninvolved limb (58). However, it is currently unknown how lower extremity muscles influence loading of the ACL after a surgical repair, and how these muscles may be influenced by fatigue once an athlete has returned to sport. Understanding specifically which muscles most influence ACL loading in healthy and in ACL-R individuals

may help clinicians, trainers, and coaches in preparing better ACL prevention and rehabilitation protocols for their athletes, as well gain insight to how muscle contribution may change after ACL reconstruction.

Statement of the Problem

While much research has been conducted regarding healthy and ACL-R females once they return to sport, high rates of primary and secondary ACL injuries still occur. Neuromuscular control is a major component that has been shown to reduce ACL injuries, when implemented properly in prevention protocols. Studies have shown that muscles, such as the quadriceps, hamstrings, gastrocnemius, soleus, and hip abductors, both directly and indirectly influence knee joint moments and forces. These muscles also influence ACL loading by the strength and timing of their contractions. While it can be hypothesized of how much these muscles contribute to ACL loading, no study to date has observed the effects of individual muscle contribution to ACL loading. By understanding how the lower extremity musculature influences ACL loading in healthy and ACL-R females in fatigued and non-fatigued states, new insight regarding neuromuscular control can be gained with the hope of building better prevention and rehabilitation protocols.

Statement of Purpose

The purpose of this dissertation was to determine how individual lower extremity muscles contribute to ACL loading in a pre-fatigued versus post-fatigue state in healthy and ACL-R females. We accomplished this purpose with two specific aims. Specific aim 1 was to observe the lower extremity joint kinematics and kinetics pre and post a fatigue protocol in healthy and ACL-R females. Specific aim 2 was to observe individual muscle contribution to ACL loading pre and post a fatigue protocol in healthy and ACL-R females. Lower extremity

kinematics and kinetics were collected, and estimated muscle forces were calculated to determine differences between the two populations and how fatigue may have influenced muscle contribution to ACL loading.

Research Hypotheses

Previous research suggests that ACL-R individuals have altered lower extremity mechanics during athletic movements, such as landing, compared to healthy individuals or the ACL-R individual's uninvolved limb (59-63). Therefore, it was hypothesized that hip, knee, and ankle kinematics and kinetics would be different between healthy and ACL-R females. It was further hypothesized that hip, knee, and ankle kinematics and kinetics would be different pre and post-fatigue in both healthy and ACL-R individuals.

As this was a novel and exploratory approach to understanding how lower extremity muscles contribute to ACL loading, not enough information currently exists to state a directed hypothesis regarding how fatigue will influence individual muscle contributions to ACL loading pre and post-fatigue in healthy and ACL-R females. However, it has been shown in previous research that fatigue may affect quadriceps and hamstrings muscle activity in ACL-R individuals, which could influence the contributions of lower extremity muscles on ACL loading (64-66). Therefore, it was hypothesized that individual lower extremity muscle contributions to overall ACL loading would be different between pre and post-fatigue conditions. Further, it was hypothesized that individual lower extremity muscle contributions to ACL loading would be different between the healthy and ACL-R females post-fatigue.

Independent Variables

- Fatigue state – pre-fatigue, post-fatigue
- Group – healthy, ACL-R

Dependent Variables

- Chapter 3:
    - Hip flexion/extension angle
    - Hip abduction/adduction angle
    - Hip internal/external rotation angle
    - Knee flexion/extension angle
    - Knee abduction/adduction angle
    - Knee internal/external rotation angle
    - Ankle dorsiflexion/plantarflexion angle
    - Ankle inversion/eversion angle
    - Hip flexion/extension moment
    - Hip abduction/adduction moment
    - Hip internal/external rotation moment
    - Knee flexion/extension moment
    - Knee abduction/adduction moment
    - Knee internal/external rotation moment
    - Ankle dorsiflexion/plantarflexion moment
    - Ankle inversion/eversion moment
- Chapter 4:
    - Overall ACL loading (F_{ACL})

- Chapter 5:
    - Individual muscle contribution to F_{ACL}

Limitations of the Study

- Participants were fatigued using a general fatigue protocol with a reactive task in order to represent a game-like scenario. Fatigue experienced in real games is multifactorial and varies across sports.
- The use of musculoskeletal modeling only provided estimates of muscle properties based on experimental data.
- There was a mixture of all graft types within the proposed study's participant pool. These participants came from different orthopedic surgeon groups as well as different physical therapy clinics.
- Participants in the proposed study came from various sports backgrounds.

Delimitations of the Study

- Participants were between the ages of 18 to 35 years old.
- Participants were restricted to females only.
- Participants determined to be in the healthy group that has had any lower extremity injuries which required surgery were excluded.
- Any participant who experienced a lower extremity injury within the past six months were excluded.
- Any participant who experienced pain on the days of testing were excluded.
- Any ACL-R participant who was less than 1-year post-surgery were excluded.

Assumptions of the Study

- Participants were truthful when filling out their health history forms regarding lower extremity injury history and weekly activity levels.
- Participants were truthful when completing the Lower Extremity Functional Scale, Knee injury and Osteoarthritis Outcome Score, International Knee Documentation Committee, Tampa Scale for Kinesiophobia, and the musculoskeletal health questionnaire.
- Participants gave maximal effort during the fatiguing protocol.
- Standardized laboratory shoes did not affect ankle or foot mechanics during testing.
- The twelve-camera infrared motion capture system (Vicon Motion Analysis, Inc., Centennial, CO, USA) and force platforms (BP600600, Advanced Mechanical Technology, Inc., Watertown, MA, USA) were accurately calibrated for each data collection throughout the study.

Significance of the Study

The potential for this study to add new insight into fatigue and its relationship to healthy and ACL-R females was vast. Information gained from these data confirmed and corroborate the existing literature supporting fatigue's influence on ACL injuries, and opened a new pipeline of research into what is causing the high rates of ACL injuries seen in healthy and ACL-R females. This gives invaluable information to coaches and clinicians to better protect their female athletes. Therefore, understanding how lower extremity musculature contributes to ACL loading in healthy and ACL-R females pre and post fatigue is paramount.

Operational Definition of Terms

- Noncontact ACL injury: an injury to the ACL that occurs in the absence of direct contact to the knee from another player. These injuries often occur during unanticipated athletic movements, such as cutting, single-leg landing, or rapid deceleration.
- ACL Loading: increased elongation of the ACL, thus increasing tensile forces and strain placed upon the ACL.
- Fatigue: defined as a decrease in the muscles ability to produce force after an exercise bout.
- Recreationally active: defined as a participant completing a physical training session at least 3 days per week for a minimum of 30 minutes per session, with one session being a dynamic training session.
- Joint Moments: tendency of a force to rotate an object about an axis of rotation. In this study, joint moments will be defined as internally applied moments that are the net rotational effect of muscle forces about a joint to resist an external load. Joint moments were expressed in the joint coordinate system.
- Initial contact: defined as the instance where vertical ground reaction forces exceed 10 Newtons on the force plate.
- The convention for joint kinematics and kinetics will follow the right-handed Cartesian segmental coordinate systems (x-y-z).
    - Hip: flexion (+)/extension (-), adduction (+)/abduction (-), internal rotation (+)/external rotation (-)
    - Knee: flexion (-)/extension (+), adduction (+)/abduction (-), internal rotation (+)/external rotation (-)

- Ankle: dorsiflexion (+)/plantarflexion (-), inversion (+)/eversion (-)

Chapter 2: Review of the Literature

Introduction

The tibiofemoral joint contains four ligaments critical for stability and mobility during movement. Specifically, the ACL is of great importance due to its role in resisting anterior tibial translation as well as tibial internal rotation (67, 68). Unfortunately, the ACL is highly susceptible to injury, especially during athletic activities. Because of this, the ACL has been widely researched over many decades. Although much research has been conducted regarding the ACL, injury rates are still elevated. Through various studies, it has been well established that females are two to eight times more likely to experience an ACL injury compared to their male counterparts (1, 3-6). As such, improving ACL injury prevention protocols for females is of utmost importance.

Most ACL injuries result in a subsequent ACL-R. Many of these ACL-R individuals will eventually return to sport. However, up to 30% of ACL-R athletes will sustain a second ACL injury. Research has shown that altered kinematics and kinetics exist in ACL-R females (26, 69-71). These altered mechanics after ACL-R may place these individuals at a higher risk of experiencing a second ACL injury. Various ACL injury risk factors exist, however, one factor that is grossly understudied is fatigue. Fatigue is a complex mechanism. Contradicting studies exist reporting on fatigue's relationship with ACL injury risk (34-36, 43, 72, 73). These contradictory results show how unclear the effect fatigue has on ACL injury risk. It is theorized that when individual becomes fatigued, the fatigued musculature is not able to absorb energy as well as non-fatigued musculature (74). Lower extremity musculature is highly influential on ACL loading. Fatigue may affect the contributions that these muscles have to ACL loading, particularly in females that have an ACL-R. Thus, ACL injury risk may be elevated due to

altered musculature contributions to ACL loading in a fatigued state both in healthy and ACL-R females.

The purpose of this dissertation was to determine how individual lower extremity muscles contribute to ACL loading in healthy and ACL-reconstructed females between a non-fatigued and a fatigued state. This chapter reviews current literature discussing ACL anatomy, biomechanical factors associated with ACL loading, ACL injuries, and ACL reconstruction, fatigue and its effects on cutting and landing mechanics, and musculoskeletal modeling and its relation to estimated lower extremity muscle contributions.

ACL Overview

ACL Anatomy

The ACL has been referred to as the most important ligament of the four primary ligaments of the knee joint (75-77). When discussing injuries involving the ACL, it is important to first understand the anatomy of the ACL itself, as well as its articulations on the femur and the tibia. The ACL is a thick, dense band of connective tissue that is classified as extrasynovial even though it is located intraarticularly of the knee joint (77). This connective tissue is made of a highly organized collagen matrix, with approximately 90% as type I collagen fibers and the remaining ~10% as type III collagen fibers (78-80). Thus, the ACL is a strong, relatively flexible ligament.

Named after its tibial attachment, the ACL attaches anteriorly to the tibial intercondylar eminence (81). It then extends up and backwards to attach on the posteromedial aspect of the lateral femoral condyle (81). While the ACL is commonly thought of as one, singular ligament, many studies agree the ACL contains two predominate bundles: the anteromedial bundle (AM) and the posterolateral bundle (PL) (76, 82-86). The AM originates on the anteroproximal aspect

of the femoral condyle and inserts on the anteromedial aspect of the tibia, while the PL originates at the posterodistal aspect of the femoral condyle and inserts on the posterolateral aspect of the tibia (87). Overall, the ACL is approximately 22 to 41 mm in length, with a mean length of 32 mm (87-89). Its width is approximately 7 to 12 mm, with a mean width of 11 mm (87, 88). It is most likely, however, that these measurements reflect the AM bundle of the ACL (90). More recently, studies have shown that the AM bundle is bigger than the PL bundle, and that both bundles are larger in males compared to females (76, 86). While many studies support a two-bundle model, Odensten and Gillquist (91) reported no evidence to support the presence of the AM and PL. Conversely, other studies have argued that in fact three tissue bundles exists within the ACL: the AM, PL, and the intermedial bundle (87, 92). Despite these contradicting studies, the two-bundle ACL is the most widely accepted model in understanding ACL functionality (88).

ACL Function

The AM and the PL are believed to have different functions during knee flexion and knee extension. Many studies have described that the AM lengthens and tightens as the knee flexes, while the PL lengthens and tightens as the knee extends (87, 92, 93). However, it is important to note that these studies utilized cadavers in an unloaded condition. Therefore, the function of the AM and PL in an unloaded condition may not be truly reflective of how it responds to weight-bearing activities in living individuals. During a loaded anterior drawer test, Butler et al. (94) found that the overall ACL's primary function was to resist anterior tibial translation. They observed that the ACL resisted 87% of anterior tibial translation at 30° of knee flexion and 85% of anterior tibial translation at 90° of knee flexion (94). Li et al. (95) utilized *in vivo* weight-bearing lunges to examine how the AM and PL would respond during a loaded condition. They

found that the AM bundle remained relatively constant in length from full extension to 90° of knee flexion, while the PL significantly decreased ~14% in length with increasing knee flexion beyond 60° (95). Kawaguchi et al. (96) also described the functionality of the ACL fibers in resisting anterior tibial displacement at 0° to 90° of knee flexion concomitantly with 10° or 15° of tibial internal rotation. They found that the overall central midsubstance of the ACL resisted 82% to 90% of anterior tibial translation. More specifically, the AM resisted 66% to 84% and the PL resisted 16% to 9% of anterior tibial translation from 0° to 90° of knee flexion (96). Interestingly, all fibers shared some responsibility in resisting tibial internal rotation, thus no clear loading pattern was determined (96). These data corroborate other studies that have stated the ACL's primary function is to resist anterior tibial translation, with a secondary function of resisting tibial internal rotation (87, 97).

Not only is the ACL responsible for resisting anterior tibial translation and tibial internal rotation, it is also an important component in overall knee stability and proprioception of the knee joint. The ACL plays a critical role in the body's perception of knee joint position and movement during all activities. Previous research has shown that mechanoreceptors, which are responsible for proprioception, exist within the ACL (98-100). These mechanoreceptors include Ruffini endings, Pacinian corpuscles, and Golgi tendon organs. Pacinian corpuscles are sensitive to rapid changes in accelerations and the Ruffini endings and Golgi tendon organs provide the central nervous system with information regarding knee joint position (101).

When the ACL is stretched, these mechanoreceptors become excited and send afferent impulses to the central nervous system. Consequentially, muscles surrounding the knee joint will contract to regulate dynamic stability and muscular stiffness in an effort to prevent ligament injury (102, 103). This protective mechanism was first studied using electromyography signals

from the quadriceps and hamstrings in healthy and ACL-deficient individuals (104). Solomonow et al. (104) found that by directly stressing the ACL, quadriceps muscle activity moderately decreased, but hamstring muscle activity increased in order to stabilize and protect the ACL. Later, Johannson et al. (103) used feline models to show that stretching the ACL induced afferent signal changes within the biceps femoris, semitendinosus, lateral gastrocnemius, and soleus. Thus, damage to the mechanoreceptors within the ACL would alter or inhibit the protective mechanisms of the surrounding musculature, leading to detriments in overall stability and functionality of the knee joint.

ACL Loading

ACL injuries occur when the ligament experiences excessive strain and tensile forces (i.e. load) (105). When the load on the ACL has surpassed the threshold of load the ACL can withstand, and injury occurs via a partial or full rupture. Both direct *in vivo* and experimental biomechanical models have been used to determine the loading that occurs on the ACL during unloaded and loaded conditions. Three impactful cadaver studies have reported the ultimate load the ACL can withstand before rupture (106-108). Noyes and Grood (106) saw that in younger cadavers (i.e. 16 to 26 yrs) the ultimate load was 1730 ± 660 N while in older cadavers (i.e. 48 to 86 yrs) it decreased to 734 ± 266 N. Woo et al. (107) had three age groups and showed younger cadavers (i.e. 22 to 35 yrs) had an ultimate load of 2160 ± 157 N, middle aged cadavers (i.e. 40 to 50 yrs) had 1503 ± 83 N of load, and older cadavers (i.e. 60 to 97 yrs) had 658 ± 129 N of load. It is important to note that the differences in magnitude between these two studies can be accounted for by 1) differences in methodology, and 2) the split of three age groups compared to only two. While these studies used age as their group split criteria, they did not account for the differences in gender. Chandrashekar et al. (108) used eight male and nine female (average age:

37 yrs) to observe how ultimate load was different between genders. Males had an ultimate load of 1818 ± 699 N while females had 1266 ± 527 N, indicating that males can withstand a greater ACL load before failure compared to females.

As previously discussed, the ACL's primary role is to prevent anterior tibial translation, which is a sagittal plane movement. Thus, it could be hypothesized that sagittal plane loading alone would be enough to rupture an ACL during athletic movements. Interestingly, this is not the case. McLean et al. (109) demonstrated that sagittal plane ACL loading alone was not enough to rupture the ACL. They performed 5000 random perturbations via musculoskeletal modeling and used peak anterior drawer force as their metric for ACL load. They found that none of their trials exceeded the 2000 N threshold they set based on previous cadaveric findings (107, 109). Therefore, ACL ruptures are more likely to be multi-planar in nature.

Many groups have studied the multi-planar nature of ACL injuries in both cadavers and computer simulations (54, 75, 110-113). Markolf et al.(75) directly measured ACL loading during four different conditions: 1) anterior tibial shear force plus internal/external tibial torque, 2) anterior tibial shear force plus adduction/abduction moment, 3) internal tibial torque plus adduction/abduction moment, and 4) external tibial torque plus adduction/abduction moment. They found that the highest ACL loads existed in the presence of anterior tibial shear force plus internal tibial torque near extension as well as anterior tibial shear force plus knee abduction moment at more than 10° of knee flexion (75). However, video analyses have shown that ACL injuries often occur with a combination of internal or external rotation torque coupled with knee abduction, not anterior tibial translation (114). Therefore, it is becoming more widely accepted that a combination of knee abduction with internal tibial torque results in the highest ACL loads

(110-113). While knee abduction and internal rotation both independently increase ACL load, the combination of the two often results in the highest ACL load magnitude.

It is well established that the ACL is highly influenced by both muscles spanning and non-spanning of the knee joint (10, 52, 104, 115-119). The primary muscle groups influencing the ACL are the quadriceps femoris (i.e. quadriceps) and the hamstrings. The quadriceps consists of four distinct layers of muscles with the rectus femoris being the most superficial layer, the vastus lateralis and vastus medius forming the intermedial layer, and the vastus intermedius forming the deepest layer (120). These four layers converge into one common tendon, known as the quadriceps tendon, and spans across the patella and inserts on the tibial tuberosity via the patella tendon (120). The primary role of the quadriceps is to extend the knee joint (121). In order to pull the knee into extension, the quadriceps must contract and pull the tibia anteriorly. The antagonists to the quadriceps are the hamstrings. The hamstrings are comprised of three muscles: biceps femoris on the lateral side, and the semitendinosus and semimembranosus on the medial side. The semitendinosus and semimembranosus insert on the posteriomedial side of the tibia, while the biceps femoris inserts on the posterolateral side of the tibia (122, 123). The primary role of the hamstrings is to flex the knee joint by pulling the tibia posteriorly.

Cadaveric studies have been used to describe the quadriceps and hamstrings function and their relationship to ACL loading. Early studies have established that isolated quadriceps loading increases ACL loading via increased anterior tibial translation (116, 117, 124-127). Arms et al. (124) recorded that significant ACL strain occurred with isometric quadriceps loading from 0° to 45° of knee flexion. Yasuda and Sasaki (127) later corroborated these data and showed that anterior drawer forces caused by quadriceps contraction were highest from 0° to 45° of knee flexion. In knee flexion beyond 45°, the quadriceps no longer added significant loading to the

ACL (128). Li et al. (10) applied a 200 N isolated quadriceps load to cadaveric knees and made them undergo passive knee flexion. They found that anterior tibial translation and tibial internal rotation increased as knee flexion increased from 0° to 30° of knee flexion. Beyond 30° of knee flexion, these translations and rotation movements decreased (10). They also reported that *in situ* ACL forces during the isolated quadriceps loading were 27.8 ± 9.3 N at full knee extension, peaked at 44.9 ± 13.8N at 15° knee flexion, and were reduced to 10 N beyond 60° of knee flexion (10).

While the quadriceps work to pull the tibia anteriorly, causing anterior tibial translation and loading of the ACL, the hamstrings work as antagonists to the quadriceps. Renstrom et al. (128) was one of the first groups to report that the hamstrings work to unload the ACL. While they showed reductions in ACL strain during cadaveric simulated isometric hamstring contractions, these findings were not significant from 0° to 60° of knee flexion. Other studies, such as Li et al. (10), found reductions in anterior tibial translation and internal tibial rotation by 18% and 30%, respectively, at 30° of knee flexion when applying an 80 N hamstring load in combination with a 200 N quadriceps load to cadaver knees. ACL load was also reduced by 30%, 43%, and 44% at 15°, 30°, and 60° of knee flexion, respectively (10). They concluded that the hamstrings significantly helped to reduce ACL loads between 15° and 60° of knee flexion (10). Markolf et al. (118) later supported these findings and concluded the hamstrings had a great mechanical advantage in controlling anterior tibial shear force up to 90° of knee flexion, thus helping control ACL loading. More recently, Weinhandl et al. (53) observed the hamstrings relationship to ACL loading from a different perspective. They utilized a strength reduction protocol to reduce the strength of the hamstrings following an anticipated cutting task. After strength reduction, the participants were asked to complete the same anticipated cutting task.

They found that by reducing the strength and effectiveness of the hamstrings, overall peak ACL loading increased by 36% (53). Most of this increase was attributed to a 44% increase in sagittal plane ACL loading (53).

Through musculoskeletal modeling, Pandy and Shelburne (129) were able to describe the relationship between the ACL load, quadriceps force, and knee flexion angle was accounted for by the geometry of the knee extensor mechanism and how the orientation of the ACL changes throughout knee joint range of motion (ROM). They also stated that while hamstring co-contraction concomitant with quadriceps co-contraction was effective in reducing ACL loading at almost all knee flexion angles, it was not effective near full knee extension (129). This is due to the insertion angle the hamstrings becoming very small as the knee reaches full extension. This becomes a mechanically disadvantageous position for the hamstrings, thus inhibiting them from producing a large posterior force to counteract the anterior force of the quadriceps (129).

While the quadriceps and hamstrings are the primary influencers of ACL loading, research has shown that other muscles, such as the gastrocnemius, soleus, and potentially hip musculature may be secondary influencers of ACL loading (52, 117, 119, 130-133). Lass et al. (133) was one of the first groups to recognize the potential the gastrocnemius had in influencing ACL loading. They saw increased gastrocnemius muscle activity in participants with ACL-deficient knees compared to controls. This finding led the group to conclude that the gastrocnemius acts as a functional stabilizer in ACL-deficient knees by preventing anterior tibial translation, which would reduce the load on the ACL if it were present (133). Durselen et al. (117) later supported the findings of Lass with the use of cadavers.

These studies, however, contradict the findings of more recent studies. O'Connor (134) was one of the first to hypothesize that the gastrocnemius is actually an ACL antagonist and pulls

the tibia anteriorly during contraction due its origin attachments sites. Fleming et al. (131) used transcutaneous electrical muscle stimulation in six healthy participants. They observed that isolated contractions of the gastrocnemius increased ACL strain, and the co-contraction of both the quadriceps and gastrocnemius increased ACL strain greater than either muscle individually at 5° and 15° of knee flexion (131). Later, a cadaveric study showed that at all knee flexion angles, the gastrocnemius generates force on the tibia that causes it to translate anteriorly, with the greatest anterior translation occurring at 50° knee flexion (130). Musculoskeletal modeling has also been used to support these studies (52, 119).

While the gastrocnemius has been shown to have antagonistic characteristics in regards to ACL loading, increasing evidence shows the non-knee spanning soleus acts as an ACL protector (52, 119, 130). The soleus originates on the posterior tibia and inserts on the posterior calcaneus. When the foot is planted, the soleus acts to resist anterior tibial translation about the ankle (130). Thus, it has been hypothesized that it could have these same resisting effects about the knee. Elias et al. (130) observed that across the entirety of knee flexion ROM, the soleus acted to translate the tibia posteriorly. Through musculoskeletal modeling, it has been shown during landing that the soleus has the capacity to produce a posterior force between 28% to 32% of the hamstrings posterior force, indicating the co-contraction between the soleus and hamstrings is important in protecting the ACL (52).

Though the evidence is only speculative, hip musculature is thought to have some connection to ACL loading. Few studies have suggested that improper hip kinematics and kinetics are associated concomitant with improper knee kinematics and kinetics, and can lead to increased ACL loading (2, 132, 135). Khayambashi et al. (136) was the first to show that hip

muscle strength can be used as a predictor for ACL injuries. In order to concretely state that hip musculature influences ACL loading, more research is warranted.

Musculature, both spanning and non-spanning of the knee joint, plays a critical role in ACL loading. Studies via musculoskeletal modeling have shown that the quadriceps, hamstrings, and gastrocnemius play a role in loading of the ACL in the sagittal plane (53, 54, 137). However, these studies only determine how much loading the ACL experienced in the sagittal, frontal, and transverse planes. The exact quantification of how much the lower extremity musculature contributes to ACL loading is currently unknown. It is also unknown, outside of the quadriceps, hamstrings, and gastrocnemius, how other muscles, such as the glutes, hip abductors, and soleus, contribute to loading of the ACL. By determining how major lower extremity muscles contribute to ACL loading, new innovations in ACL prevention and rehabilitation programs could emerge.

ACL Injury Overview

ACL Injury Prevalence

ACL injuries are one of the most common knee injuries sustained by active individuals (138). Over a 10-year period, 6,434 patients experienced 7,769 knee injuries (139). Approximately 20.3% of these knee injuries were classified as ACL injuries (139). Since the United States does not keep a database of ACL injuries, the exact number of injuries occurring each year is unknown. However, studies have approximated that 60,000 to 250,000 injuries occur every year (140, 141). Unfortunately, the incidence of ACL injuries has increased throughout the years, rising from 32.9 per 100,000 person/years to 43.5 per 100,000 person/years from 1994 to 2006 (142). Herzog et al. (143) stated the rate of ACL reconstructions has also increased 22% from 2002 to 2014. These incident rates are not beholden to just the United States. Finland has reported 60.9 people per 100,000 person/year sustains an ACL injury, while

Sweden reported 78, New Zealand reported 36.9, and Australia reported 77.4, respectively (144-147). This further indicates that ACL injuries have become a worldwide epidemic.

ACL injuries can occur at any age. However, research supports that those between the ages of 10 to 25 years old are the most at risk for injury (140, 148-151). This can most likely be attributed to the increasing number of children playing multiple sports throughout the year at higher levels and more young adults continuing to play intercollegiate and intramural sports in college (142, 151, 152). Sports that ensued the highest injury rates were basketball, football, and soccer (139, 153, 154). Interestingly, Sanders et al. (151) showed that injury rates for females peaked between the ages of 14 to 18 years old, while males peaked between 19 to 25 years old, indicating ACL injuries are more common for females in high school while it was more common in college for males. They attributed this to the decline in sport participation for females once they leave high school (151).

When observing the injury itself, ACL injuries fall under one of two categories: contact and non-contact. Contact ACL injuries involve direct contact by another player or an object to the knee, thus causing the injury (155). Non-contact ACL injuries are injuries that occur in the absence of direct contact to the knee from another player (156). These injuries often occur during unanticipated athletic movements, such as cutting, single-leg landing, or rapid deceleration. Nearly 70% of all ACL injuries are defined as non-contact (157). As such, much research has been conducted to understand the risk factors and injury mechanisms associated with ACL injuries to stop these incidence rates from increasing further.

ACL Injury Risk Factors

Risk factors for ACL injuries are classified as either internal or external risk factors. Internal factors are those that pertain to the athlete themselves, such as gender, anatomical

variables (i.e. knee geometry, limb alignment, etc.), hormones, age, fatigue, prior ACL injury, and neuromuscular and cognitive function (158). External risk factors are factors outside of the athlete, such as playing surface, footwear, environmental conditions, and type of activity (158). Briefly, gender and age have been shown to be highly influential in ACL injury risk. It is well established that females are two to eight times more likely to sustain an ACL injury compared to their male counterparts (1, 3-6). This is influenced by both anatomical factors, such as females having larger Q-angles, smaller ACL length and circumference, and increased hormonal fluctuations throughout the month, and biomechanical factors like landing with a more erect posture or cutting with larger knee abduction angles (7, 8). As discussed in the previous section, ACL injury occurrence peaks between 10 to 25 years of age. Being an athlete increases risk of injury as it has been shown that ACL injuries are more common in athletic populations compared to the general public (146, 158, 159). Anatomical variables, such as smaller intercondylar notch widths and increased posterior tibial slope are correlated with increased injury risk (140). Finally, playing on artificial turf compared to natural grass or artificial floors compared to hardwood have been associated with ACL injuries (160, 161).

Two understudied injury risk factors are player fatigue and prior ACL injury. Fatigue is a controversial injury risk factor as it is poorly understood in its relationship to ACL injury due to its complexity. However, increases in knee abduction and knee internal rotation angles as well as decreased knee flexion angle has been observed following a fatigue protocol (45, 66, 162). Alterations in quadriceps and hamstring muscle activity has also been observed post fatigue (64, 65). Both alterations in lower extremity mechanics and muscle activity appear to indicate that fatigue may place an athlete at an increased risk for ACL injury. ACL-R subsequent to an ACL injury also seems to influence ACL injury risk. After ACL-R, post-surgery consequences exist in

the form of altered knee mechanics, decreased hamstring strength, and altered knee proprioception. Unfortunately, 10% to 30% of athletes who return to play after ACL-R will sustain a second ACL injury (26, 27, 30). Therefore, understanding how fatigue and prior ACL injury affects the risk of experiencing an ACL injury is of utmost importance.

ACL Injury Mechanisms

As stated previously, much research and work has been dedicated to understanding and preventing ACL injuries. However, despite the numerous studies available regarding ACL injuries and preventative protocols, the rate at which ACL injuries occur every year is not decreasing. The exact injury mechanism of the ACL is overloading the ligament beyond its acceptable load threshold. However, different biomechanical and neuromuscular factors can lead to this overloading of the ACL, thus causing injury.

Non-contact ACL injuries occur most often during the landing phase from a jump or during the stance phase during movements that involve quick decelerations and change of directions (i.e. cutting) (140). Most ACL injuries occur within the first 40 ms to 100 ms of the landing or stance phase (163-167). There are also specific gender differences, such as females experiencing decreased hip and knee flexion angles, increased knee abduction moment, and altered muscular activity and recruitment of the lower extremity muscles during landing and cutting movements compared to males (168-173).

Regardless of gender, the most common lower extremity positioning associated with ACL injuries is known as medial knee collapse in both landing and cutting movements. Medial knee collapse occurs when there is a combination of increased hip internal rotation, knee abduction, and knee internal rotation concomitate with increased internal knee adduction moment, with the knee joint between 0° to 30° of knee flexion (8, 111, 114, 157, 174). This

disadvantageous combination of joint positioning causes the knee joint to forcefully collapse inward to the midline side of the body. While this medial knee collapse is common in both landing and cutting movements, there are other biomechanical factors associated with ACL injury during these two movements.

Landing Mechanics and ACL Injuries

Landing is an extremely common athletic movement, occurring in sports such as basketball, volleyball, football, and soccer. During landing, common injury risk mechanisms are medial knee collapse, increased joint stiffness and stiff landings, large vertical ground reaction forces, and foot placement during the landing phase (51, 157, 175-179). Many of the same injury mechanics profiles (i.e. decreased knee flexion angle, increased knee abduction angle, increased knee adduction moment) are observed in both bilateral and unilateral landings (157, 173, 180). However, unilateral landings are considered to be more dangerous than bilateral landings due to the decreased base of support and increased demand of the lower extremity musculature to absorb the impact of a unilateral landing (180). During video analyses of athletes who sustained an ACL injury, unilateral landings with medial knee collapse concomitant with a strong contraction of the rectus femoris was associated with more ACL injuries than bilateral landings (114, 181). Gender differences also exist between males and females during both bilateral and unilateral landings (173, 180, 182-185). These differences are typically similar between both types of landings.

In a comparing gender differences during landings, females have demonstrated having a more erect posture through decreased knee flexion (females: 22.8 ± 8.0°; males: 30.0 ± 7.7°; $p < 0.05$) at initial contact of the landing phase from a drop vertical landing (183). Other studies have supported these findings of decreased knee flexion in females (186, 187). However, several

studies have shown that there is no difference in knee flexion angle between males and females during bilateral landings (179, 182, 188). One potential cause of the inconsistency between studies is jump height. Previous research has shown in unilateral landings that males and females respond differently between various jump heights (189). Since the previously mentioned studies occurred at different jump heights, it appears that jump height is a cofounding factor when comparing lower extremity mechanics between males and females (189).

Females have been shown to land with increased knee abduction angles and increased knee adduction moments compared to males (182, 183, 190, 191). In a prospective study, Hewett et al. (8) found that nine females who experienced high knee abduction angles and high knee adduction moments during bilateral drop vertical jumps went on to sustain an ACL injury. These females had 8.4° higher initial contact knee abduction and 7.6° higher peak knee abduction angles compared to uninjured females (8). The injured females also had greater peak knee adduction angles (-45.3 ± 28.5 Nm) compared to the uninjured females (-18.4 ± 15.6 Nm) (8). To this date, knee adduction moment is the only confirmed predictor of ACL injury risk.

Research supports that a combination of altered sagittal and frontal plane mechanics during landings influence injury risk. Pollard et al. (192) studied 58 female soccer players while performing a drop landing task. The females were separated into a “low flexion” and a “high flexion” group. Females in the low flexion group landed with 14° less knee flexion and 23° less of hip flexion compared to the high flexion group (192). The low flexion group exhibited knee adduction moments 2.2 times higher than the high flexion group and had greater knee abduction angles compared to high flexion females (192). The low flexion group also demonstrated decreased energy absorption at the hip and knee, as well as a 35% increase in vastus lateralis

muscle activation (192). This study showed that decreases in sagittal plane mechanics negatively affected frontal plane mechanics.

Laughlin et al. (51) explored the effects of soft versus stiff unilateral landings. A soft landing was characterized as increased hip and knee joint flexion, while a stiff landing had decreased hip and knee joint flexion. At peak ACL force, hip (stiff: 22.2 ± 7.0°; soft: 29.6 ± 7.5°; $p < 0.01$) and knee (stiff: 13.9 ± 3.2°; soft: 18.0 ± 3.4°; $p < 0.01$) flexion angles were significantly less in the stiff versus soft landings (51). Vertical ground reaction force was also larger in the stiff landings (0.70 ± 0.18 BW) compared to the soft landings (0.58 ± 0.24 BW; $p = 0.04$) (51). As such, peak ACL force was higher during stiff landing (0.80 ± 0.19 BW) compared to soft landings (0.71 ± 0.28 BW; $p = 0.05$). The authors concluded that a softer landing resulted in increased knee flexion angle, thus increasing hamstring shear force, which allowed for the posterior pull on the tibia to help unload the ACL during landing (51). Decreased knee flexion during stiff landings may minimize this protective mechanism against ACL injuries. Podraza et al. (193) supported this research by showing in male athletes that landing with decreased knee flexion angle increased vertical GRFs experienced during landing, thus increasing risk of injury.

For both genders, the knee has been shown to be the primary absorber of impact during landing (183, 194). However, studies report that females have altered lower extremity energy absorption in all three joints compared to males (183, 192). Decker et al. (183) reported that females utilize their plantarflexors more for impact attenuation during landing, compared to males who utilized their hip extensors. Therefore, it is plausible that when females land with a more erect posture with increased frontal plane movement while using their ankle musculature for impact attenuation, it may put the hamstrings at a disadvantageous position to counteract the

pull of the quadriceps on the tibia, thus increasing risk of ACL injury (182, 183). However, as stated previously, unilateral landings are considered more high-risk than bilateral landings.

Foot position during bilateral landings have been theorized to influence ACL injury risk. Cortes et al. (179) examined the effects of sagittal plane foot position (forefoot, rear foot, and preferred) on hip and knee kinematics in men and women. While they found no sex effect with landing, their results stated that forefoot landing significantly decreased initial contact hip flexion, while rearfoot landing significantly decreased knee flexion angle at peak vertical ground reaction force. They also found that a self-preferred and forefoot landing positions resulted in greater knee adduction angles than rearfoot landing, thus influencing ACL injury risk (179). Foot position in the transverse (i.e. toe-in, toe-out) also affects knee mechanics during landing. Padua (195) concluded that landing with greater than 30° of toe-in or toe-out was a high-risk landing position. Previous research supports this conclusion showing that landing with excessive toe-in FPA increases peak hip adduction, knee abduction, and knee internal rotation angles and moments, as well as decreases hip flexion angle (177, 196). Currently, it is unknown how foot position will affect lower extremity mechanics during unilateral landings. However, it could be hypothesized the effects would be similar to those of bilateral landings.

Through the work of unilateral landings, it has been observed that neuromuscular control is of upmost importance during landing to control knee stability. The quadriceps and the hamstrings are the two primary lower extremity muscles associated with ACL loading. As the quadriceps contract, they pull the tibia anteriorly, thus increasing the loading on the ACL. The hamstrings act to offset and reduce the loading on the ACL by pulling the tibia posteriorly when contracted. The coactivation between these two large muscle groups contribute to the stability of the knee joint (115, 126). Lloyd et al. (197) stated the best activation pattern for stabilizing the

knee joint was when the quadriceps or hamstrings generated flexion or extension moments. They also reported the second most effective way to stabilize the knee joint was through proper coactivation of the quadriceps and the hamstrings (197). When the coactivation between these two muscles are not in sync (i.e. excessive quadriceps activation or insufficient hamstring activation), the likelier increased anterior tibial shear force and increased knee abduction angle will occur (198).

Because ACL injuries during landing happen in such a small amount of time, muscle pre-activation prior to landing is necessary for proper knee stability. Interestingly, it has been shown that females display less activation in the vastus medialis and medial hamstrings compared to the vastus lateralis and biceps femoris (199). Palmieri-Smith et al. (200) concluded that less pre-activation of the vastus medialis and medial hamstrings and more pre-activation of the vastus lateralis and biceps femoris prior to landing was associated with larger knee abduction angles. Palmieri-Smith et al. (201) extended this research to observe gender differences in quadriceps-hamstring coactivation between males and females. They reported that females had decreased coactivation between the quadriceps and hamstrings compared to males, suggesting females had less neuromuscular control and increasing knee instability upon landing (201). Other studies have corroborated these findings and have also shown that females have greater pre-activation of the rectus femoris (202), which increases anterior tibial shear force, a known indicator of ACL load (203).

Not only are the quadriceps and hamstrings critical for knee stability, but other muscles, such as the hip abductors, gastrocnemius, and soleus have shown to be influential during landing (52, 185, 193, 204). Podraza et al. (193) provided evidence to show the soleus had great potential in stabilizing the knee joint during landing. During the landing phase, the soleus produced

sizable muscle moments. This in combination of its orientation on the tibia results in a posterior pull of the tibia, thus assisting the hamstrings in unloading the ACL. Hip abductors, such as the gluteus medius, may help transfer forces from the lower extremity through the trunk during landing (194, 205). While there was no gender difference reported, gluteus medius muscle activity increased in both males and females during unilateral landings (185). Russell et al. (185) hypothesized this increase in gluteus medius activity was most likely a response to the hips trying to stabilize the trunk and pelvis during landing, thus avoiding medial knee collapse. Therefore, it is likely if hip musculature is weak, it could potentially lead to a more unstable leg during landing, which would be detrimental to the ACL. Overall, the ability to properly pre-activate lower extremity musculature potentially decreases the likelihood of landing in a high-risk position. It can also reduce the strain on the ACL, thus decreasing risk of injury (206).

Cutting Mechanics and ACL Injuries

As stated previously, landing is one of the high-risk athletic movements that can lead to ACL injury. However, cutting and change of direction movements are also detrimental to ACL injuries. Many of the same injury profiles exist between landing in cutting. Both movements can lead to increased knee abduction angle, increased knee adduction moment, as well as decreased knee flexion angle and increased knee extension moment. However, landing and cutting tasks can lead to different demands on the lower extremities, thus causing ACL injuries in different ways (207-209). Therefore, it is important to understand how ACL injuries can occur during cutting movements.

Cutting is a unique movement in that it has distinct phases within the stance phase. With landing, a person lands and either stays planted on the ground, or they land and have a subsequent jump after foot contact with the ground. With cutting, the body must always be

prepared to make a change of direction after the stance phase of the plant foot. At the initiation of the stance phase, the body must decelerate to prepare for the cut. Once the body has decelerated, the body will then redirect itself depending on which direction it has to move. Finally, after the planting and redirecting of the body, the body must accelerate itself forward in the new running direction (155). Studies show that risk of injury was highest during the early stage of the deceleration phase (~57 ms) (165, 210, 211). This time to injury is also very comparable to the time range that ACL injuries occur during landing tasks.

Injury risk can be different depending on what phase of the cutting movement is examined. Throughout the whole stance phase of a cutting movement, the knee experiences flexion, abduction, and internal rotation (5). This positioning may allow for the knee to become highly unstable and allows for the tibia to move more freely in the anterior direction. This theory is supported by the findings of Peel et al. (212) who found that females experience both increased knee adduction moment and increased anterior tibial shear force during unanticipated 45° cuts.

Not surprisingly, females exhibit greater knee adduction moments compared to males during cutting tasks (213, 214). Sigward and Powers (214) found that females demonstrated knee adduction moments that were two times greater than their male counterparts. Sigward and Powers (215) found that females who had higher knee adduction moments are related to greater laterally directed GRFs during the early stage of deceleration. Inconsistent findings exist regarding gender differences in knee abduction angles during cutting. McLean et al. (216) and Malinzak et al. (217) both reported that females have greater knee abduction angles compared to males. However, Pollard et al. (218) reported no differences in knee joint kinematics. These differences could be simply due to the high variation found in both frontal and transverse plane

mechanics as well as differences in methodology. Females also exhibit greater hip internal rotation, decreased hip flexion, and increased knee extension and decreased knee flexion moments, as well as decreased hip extension moments compared to their male counterparts (168, 214, 217, 219). These kinematic and kinetic differences found in females help explain why females have an increased risk of ACL injuries.

Xie et al. (211) studied the three specific phases during cutting in female basketball players. During the decelerating phase, the body's center of mass moves laterally. This in turn causes the knee to go into abduction and flexion. It was shown that knee abduction angles were larger during the deceleration phase compared to the redirection phase (211). During the deceleration phase, the hamstrings to quadriceps co-contraction ration was also lower compared to the redirection phase (211). The authors concluded that the low hamstring activity during the deceleration phase may minimize the hamstrings ability to counteract the quadriceps anterior pull on the tibia, thus increasing risk of injury (211). Other studies also confirm that females have greater quadriceps and less hamstrings activity compared to males (172, 217). This disproportion of hamstrings to quadriceps muscle activity is similar to that seen in landing tasks. However, little is known how other muscles, such as the hip abductors, gastrocnemius, and soleus influence ACL injury risk during cutting tasks.

As stated previously, approximately 70% of ACL injuries are considered non-contact. Most of these non-contact injuries occur during athletic movements that involve landing and cutting. Gender differences clearly exist in both landing and cutting tasks, with females at a much higher risk of injury due to risker lower extremity mechanics during landing and cutting compared to males. While they are two completely different tasks that load the body differently, similar injury-causing mechanics are seen in both landing and cutting, such as decreased knee

flexion and increased knee abduction angles, increased knee adduction moment, and lower hamstring to quadriceps co-contractions. It is quite evident that neuromuscular control is important in decreasing injury prevalence. While evidence has shown that the quadriceps and hamstrings are critical muscles to ACL injury, less is known about how other lower extremity musculature, both spanning and non-spanning of the knee joint, affect ACL injury. While it is known lower extremity musculature influences ACL injury, it is currently not known to what extent each muscle contributes to the loads experienced on the ACL. Knowing these individual muscles contributes to ACL loading could offer valuable information in injury prevention and rehabilitation protocols.

ACL Reconstruction

When the ACL is injured, ACL-R is often required due to the ACL's inadequate biological healing process. Approximately 100,000 to 150,000 of all ACL injuries occurring each year will undergo a reconstructive surgery (13). The cost for ACL-R and subsequent physical therapy exceeds $2 billion annually (14-16). The primary goal of conducting an ACL-R is to return individuals back to an active lifestyle by regain stability after an ACL injury (17). Specifically in athletes, ACL-R is often necessary in sports that require multidirectional movements (i.e. cutting) (220). However, a secondary goal that can be considered is to decrease the risk of developing knee osteoarthritis as approximately 50% of individuals with an ACL injury will develop knee osteoarthritis (221, 222).

Because the primary goal of ACL-R is to return individuals as close as possible to their pre-injured state, numerous studies have been conducted on ACL-Rs and its effect on athletes and athletic performance. A recent systematic review/meta-analysis showed that 83% of athletes return to sport within 6 to 13 months after ACL-R, indicating that ACL-R does a good job of

accomplishing the primary goal of return to play (32). However, while ACL-R returns most athletes back to play, kinematic and kinetic changes to the reconstructed knee still exist compared to the contralateral knee or control knees. These changes include decreased hamstring strength, anterior knee pain, loss of proprioception, and altered coordinative variability of the knee joint (18-25). These altered mechanics are responsible for the 17% of athletes who do not return to play and why 10% to 30% of athletes who do return to play will sustain a second ACL injury after an ACL-R (26-30). To understand this phenomenon, it is important to briefly discuss surgical interventions used in ACL-R and how they may play a role in these return to play statistics.

ACL Reconstruction Operative Techniques and Grafts

Operative Techniques

There are two types of operative techniques used in ACL-R: single bundle and double bundle ACL-R. Single bundle ACL-R refers to reconstructing only the AM bundle of the ACL, while double bundle ACL-R reconstructs both the AM and the PL bundles. The single bundle ACL-R has been the gold standard for many years. However, cadaveric studies have shown that the double bundle ACL-R may provide better anterior and rotational stability compared to the single bundle because the reconstruction better reflects the native ACL anatomy better by using two separate grafts compared to the single bundle (223, 224). Thus, it appears that the double bundle technique is often used more in athletic populations, while the single bundle is more commonly used in sedentary groups. However, the double bundle ACL-R often comes with a more complicated and invasive surgery with longer operational time and higher financial costs. Systematic reviews and meta-analyses have also shown that while double bundle provides better knee stability than single bundle, clinical outcomes and risk of failure are approximately the

same between the two operative techniques (225, 226). Unfortunately, while the clinical outcomes between the double and single bundle techniques are similar, neither technique restores knee kinematics back to its preoperative state (227).

ACL Graft Types

There are three main categories of grafts that can be used in ACL-R: 1) autograft, 2) allograft, and 3) synthetic graft. Autografts (using a graft from one's own body) are more commonly used than allograft (using a cadaver graft) or synthetic graft as it has less chance of rejection from the body, better long-term graft strength, and is readily available. The two most commonly used autografts in ACL-R are bone-patellar tendon-bone (BTB) and the four-strand hamstring tendon (ST-G) (228, 229). The BTB utilizes the central third of the patellar tendon and includes a bone plug at both endpoints from the patella and the tibia, respectively. The ST-G consists of a combination of the semitendinosus and gracilis tendons.

Most research supports that there is no real difference in functional outcomes when comparing the two grafts to each other (230-235). Abdalla et al. (230) used 30 individuals with BTB and 33 individuals with ST-G to show that those who received the BTB had a greater extension torque deficit, and those that had the ST-G had a greater flexion torque deficit. Feller and Webster (236) support these findings and reveal that the extension torque deficit observed in the BTB group only existed 4 to 8 months postoperative, while the flexion torque deficit in the ST-G was only present in 8 to 24 months postoperative. These studies indicate that while there may be kinematic and kinetic differences between the two graft types, they only exist short-term, not long-term. Stanczak et al. (237) corroborated these data by following 96 individuals (48 BTB, 48 ST-G) for 12 years and showed as early as 1 year postoperative that both groups had comparable improvement with their functional results.

ACL Graft Failure Rates

Graft failure rates between the two autografts have mixed results within the literature. A previous cadaveric study reported the ST-G graft had a load resistance of 4500 N before failure, while the BTB had 2646 N and the intact ACL had 1725 N load resistance, respectively, therefore suggesting the ST-G graft may be more resistant to failure compared to the BTB (238). Contrary, Konrath et al. (19) stated that because the BTB graft has a high tensile strength, it has been considered the "gold standard" in ACL graft type. Laboute et al. (239) showed in a population of 955 athletes who had ACL-R (713 ST-G graft, 242 BTB graft), the ST-G graft had a failure rate of 6.5%, while the BTB had a 2.1% failure rate. Graft failure rate and graft laxity have been correlated to one another (240). There has also been research to support that ST-G grafts are more prone to failure due to increased laxity in the ST-G ligament and lack of bone plug reinforcement compared to the BTB (241, 242). It is important to note that while Laboute et al. (239) reported a significantly higher rate of ST-G graft failure, the number of individuals who had a ST-G was much higher than the number who had BTB, naturally skewing any results found. Conversely, many meta-analyses have reported little to no difference in graft failure rate in large sample sizes (233, 235, 243, 244).

Therefore, it appears the risk of failure is not significantly large when choosing one graft over another. However, it is important to note that there are disadvantages associated with both grafts. For example, BTB has been associated with increased patellar fractures, anterior knee pain, patellar tendon ruptures, and increased risk of knee osteoarthritis (240, 245-247). Regardless, choosing an operative technique and graft type must be made on a patient to patient basis that best fits the patient goals, whether that be return to full athletic movements or improve daily quality of life. It is important to note that while there may be no difference in functional

outcomes or failure rates between the two grafts, altered knee mechanics still exist when comparing an ACL-R using either graft to a healthy population.

ACL Reconstruction and Altered Knee Mechanics

Several studies have shown that a subsequent ACL injury after a primary ACL-R occurs in high frequency (27, 240, 248, 249). The risk of a second ACL injury is between 6% to 26% on the ipsilateral limb (operative side), while it is 2% to 20.5% on the contralateral (non-operative side) limb (27, 240, 249). The risk for a second ACL injury, however, appears to be highest during the first two years post ACL-R (2). Unfortunately, athletes are typically at the highest risk of experiencing a second ACL injury. Approximately 1 in 17 athletes with sustain a reinjury after a primary ACL-R within the first two years post ACL-R (248). This number decreases to 1 in 8.3 athletes 5 years post ACL-R (27). Reinjury after return to sport is likely multifactorial, with factors including increased asymmetry between the ACL-R leg and uninvolved leg and decreased subjective knee function.

Because of the high rate of reinjury exists after ACL-R, a great emphasis has been placed on investigating the changes in lower extremity mechanics before and after ACL-R. Research has shown that altered lower extremity mechanics can exist in ACL-R patients up to 7 years post ACL-R (69, 250). These altered lower extremity mechanics include both biomechanical and neuromuscular differences. Since athletes typically return to sports that involve various landing and cutting tasks, many studies have used these tasks to observe the mechanical differences between ACL-R and healthy controls (23, 69, 251, 252).

During unilateral landing tasks, ACL-R individuals generally exhibit increased hip adduction and internal rotation, decreased knee flexion and increased knee abduction, and increased ankle plantarflexion angles in the ACL-R leg compared to the uninvolved leg (60-63).

Deneweth et al. (253) confirmed through the use of biplane radiography that ACL-R knees demonstrated greater knee extension, external tibial rotation, and remained more anteriorly displaced throughout the landing phase of a single-leg hop test. These are comparable to the altered kinematics seen in bilateral landings (59). Meyer et al. (59) showed that the ACL-R leg during a bilateral landing had decreased peak knee flexion angle, decreased peak knee flexion moment, and increased peak knee abduction moment compared to the uninvolved limb. In both unilateral and bilateral landings, decreased power absorption by the knee joint was also observed and was compensated for by greater power absorption by the ankle (59, 254). Decker et al. (60) also reported comparable findings in that those with ACL-R performed 37% more ankle plantarflexor work and 39% less hip work during vertical drop landings. These abnormal landing joint kinematics are seen as early as 6 months post ACL-R, and are consistent between various unilateral and bilateral landing tasks (59, 61-63).

These alterations in ACL-R kinematics during landings may indicate that those with ACL-R land in a stiffer position compared to the uninvolved limb or healthy controls, which in turn may increase ACL loading and lead to a second ACL injury (51). This stiffened ACL-R landing hypothesis is also supported by EMG activity of the surrounding muscles of the knee joint. Gokeler et al. (62) saw that ACL-R legs had earlier EMG onset times of the gluteus maximus, biceps femoris, semitendinosus, semimembranosus, vastus lateralis, rectus femoris, medial gastrocnemius, lateral gastrocnemius, and soleus compared to the uninvolved limb. This possibly indicates that the ACL-R leg demonstrates an alternate landing strategy to stiffen the leg prior to landing in an effort to increase stability upon impact (62). Decker et al. (60) repeated these sentiments and stated that ACL-R individuals landed with a more erect posture, thus landing stiffer compared to controls. They also showed ACL-R individuals reached peak vertical

GRF slower than healthy individuals. This would suggest ACL-R individuals land in such a way to reduce the loading on their operative leg. However, Decker et al. (60) stated this reduction in loading could be used by individuals who had a ST-G graft during ACL-R, therefore these individuals may be avoiding loading the hamstrings.

During sidestep cutting, it has been reported that ACL-R knees exhibit increased hip flexion and knee abduction angles, as well as decreased hip extension moment, increased knee adduction moment, and increased knee internal rotation moments (69-71, 255). A case study of a single female athlete 27 months post ACL-R also reported having increased hip flexion, knee extension, and ankle dorsiflexion angles and increased hip internal rotation, knee adduction, and knee external rotation moments (71). Stearns et al. (69) concluded that females with an ACL-R had 3.8° of knee abduction angle compared to the 1.8° of knee abduction angle for the control group. They also showed that the ACL-R experienced higher peak knee adduction moments (1.33 Nm/kg) compared to controls (0.8 Nm/kg) (69).

Surprisingly, it seems that many studies report little to no significant differences in joint kinematics in the ACL-R leg during both landing and cutting tasks (70, 255, 256). Increases in knee abduction and internal rotation moments have been observed in ACL-R during cutting (70) (255). Further, Ortiz et al. (256) reported only decreases in anterior-posterior shear force and increases in gluteus maximus and rectus femoris muscle activity during drop jumps. This would suggest that most ACL-R individuals are able to return to sport and have comparable joint kinematics to healthy athletes. However, the changes in joint kinetics, especially of that in the frontal and transverse plane, could contribute to the high risk of reinjury during cutting and landing tasks.

Joint coordination and variability measurements show the capacity an individual has in choosing an optimal motor strategy that best fits the situation or task at hand (257). The larger number of motor strategies an individual has to choose from, the more flexible they are in adapting to new conditions and environments, thus increasing stability and decreasing risk of injury (257, 258). Too much or too little coordinative variability outside of the body's "optimal range" increases risk of injury (259-261). Since the ACL is an important proprioceptive tissue in the knee joint, surgical intervention can disrupt joint coordinative variability, thus not allowing individuals to return to their preinjury state (24). As such, coordinative variability differences have been observed during gait, single leg jumps, and sidestep cutting tasks between healthy and ACL-R individuals (23-25, 258, 262-265).

Interestingly, through the work of these coordinative variability studies, it has been shown that ACL-R individuals exhibit increases in variability between the hip/knee and knee/ankle joint couplings (23-25). Because the knee is in the middle of the lower extremity kinetic chain, any disruptions in the stability of the knee will affect energy transfer to the hip and ankle (266). Not only do all three joints display alternated variability, but the highest levels of variability existed in the coupling motions associated with medial knee collapse during cutting and single leg landing tasks (23). These coupling motions include increases in hip rotation/knee abduction-adduction, hip flexion-extension/knee abduction-adduction, knee abduction-adduction/knee flexion-extension, and knee abduction-adduction/knee rotation (23, 25).

It is hypothesized that these differences in coordinative variability are adaptations learned early in the rehabilitation process to avoid knee pain of the ACL-R knee (24). However, evidence suggests these learned adaptations are not short-term adaptations, but ones that potentially last a lifetime. Srinivasan et al. (25) observed variability in 33 unilateral ACL-R

individuals approximately 23 years after their initial surgery. After performing one-legged hops, they concluded they concluded that compared to healthy controls, ACL-R individuals displayed approximately 50% higher knee abduction-adduction/hip internal-external rotation variability during the take-off phase (25). They also had approximately 33% higher knee abduction-adduction/knee flexion-extension as well as greater knee abduction-adduction/hip flexion-extension variability during the landing phase (25). As a collective group, the aforementioned studies all show that ACL-R individuals have increased variability compared to healthy controls. While healthy individuals tend stay within an "optimal variability range", ACL-R individuals overshoot and go beyond this optimal variability range, thus signifying a loss of optimal joint control (25). Increased variability is thought to be associated with ACL injury because it allows for increased loads to be placed on the knee inappropriately (101, 267).

While there may not be many differences reported in joint kinematics before and after ACL-R, changes in kinetics do exist. Differences in neuromuscular control and muscle activity are most likely responsible for these kinetic variances seen in ACL-R individuals. Female athletes are four times more likely to experience a reinjury of the ACL compared to their male counterparts (31). It is plausible that understanding how alterations in neuromuscular control after ACL-R could shed light as to why these high reinjury rates exist.

Both alterations in quadriceps and hamstrings muscle activity have been shown to exist after ACL-R, and may persist years after athletes are cleared to return to sport (19, 251, 268-273). Evidence suggests quadriceps strength deficits of the ACL-R leg range from 5% to 40% and have been seen to last as long as seven years after the initial operation (274-277). Hamstrings strength deficits have been observed ranging from 9% to 27% and have been observed in athletes as long as 10 years post ACL-R (268, 274, 277, 278). Currently it is still not

well known why these deficits exist long-term after ACL-R. However, it is hypothesized that the mechanism of these deficits is different for quadriceps weakness compared to hamstrings weakness.

Research has shown that after ACL-R, deficits exist in quadriceps strength, activation, cortical drive, and alterations in quadriceps motor unit recruitment (276, 279-282). It has been hypothesized that after ACL-R, there is a loss proprioception due to reductions in afferent feedback from the ACL (101, 283). These decreases in feedback would then result in a decline in motor neuron activation, thus making it harder to recruit high-threshold motor units (284). The inability to recruit high-threshold motor units thus leads to the deficits in quadriceps strength seen after ACL-R (276). Kuenze et al. (269) reported that reductions in quadriceps strength, quadriceps activation, and cortical excitability existed in ACL-R males and females compared to a healthy control. They also showed these deficits lasted well past the time these athletes returned to sport, indicating they may influence reinjury risk.

Deficits in hamstrings strength appear to be related to the use of ST-G grafts, which are harvested from the hamstrings tendons (19, 250, 268). Magnetic resonance imaging and ultrasound both support that regrowth of the semitendinosus and gracilis occurs after harvesting the ST-G graft (285-287). However, a closer look at these studies reveals that regrowth does not necessarily occur, but that the hamstrings blend into the fascia of the medial gastrocnemius and proximal tibia (288). Because of this disruption to the insertion site of the semitendinosus and gracilis, alterations in muscle size and strength has been observed post ACL-R.

Many studies report hamstring atrophy exists post ACL-R, and that this muscle atrophy is typically a long-term affect (19, 289, 290). This atrophy also appears to affect the ability of the hamstrings to actively flex the knee. Because the semitendinosus and gracilis play a role in knee

flexion (291), knee internal rotation, and contributing to adduction moments at the knee joint, changes in the musculotendon properties of the harvest site contributes to knee flexion and internal rotation weakness (292-295). Decreases in semitendinosus and gracilis muscle volume have been moderately correlated ($\rho = 0.51$) deficits in knee flexion strength (19). Bourne et al. (268) reported that female Australian Rules Football players with a history of ACL-R had lower levels of eccentric hamstrings strength in their ACL-R leg compared to the uninvolved limb and compared to healthy players. All ACL-R players in this study had a ST-G graft during ACL-R. The ACL-R athletes were 54 N weaker in their ACL-R leg compared to their uninvolved leg, and 46 N weaker compared to healthy players. These results are similar to those found by Timmins et al. (296) who reported ACL-R male athletes were 43 N weaker in their ACL-R leg compared to their uninvolved leg.

As stated by Bourne et al. (268), it is currently unclear if neuromuscular alterations are present in muscles that influence loads placed upon the ACL, such as the gastrocnemius, soleus, and hip abductors after ACL-R. Interestingly, Konrath et al. (19) reported that the combined hamstring muscles (i.e. biceps femoris, semitendinosus, and semimembranosus) and the combined medial knee muscles group (i.e. semitendinosus, semimembranosus, gracilis, vastus medialis, medial gastrocnemius, and satorius) of the ACL-R leg were 12% and 10% smaller in volume compared to the uninvolved limb of ACL-R males and females. This would suggest that other muscles besides the quadriceps and hamstrings are affected by ACL-R and would have alterations in their strength producing capabilities. This could be a potential link as to how these muscles contribute to ACL loading after ACL-R and offer new information as to why reinjury rates after ACL-R are so high. Because deficits in the quadriceps and hamstrings are still present

after athletes return to sport, understanding how return to play, specifically game fatigue would be of interest to coaches and clinicians wanting to decrease reinjury rates.

Fatigue

Fatigue Overview

Much debate surrounds the concept that fatigue may be associated with ACL injuries (34, 36, 72, 73, 297). The inconsistencies found between fatigue studies is multifactorial, including the use of different fatigue protocols, different participant populations, and different athletic tasks for assessment of biomechanical changes. Fatigue is a very complicated and complex system. Thus, despite the amount of literature that exists supporting fatigue's role in ACL injuries (34-36, 43), it has been difficult to make more than a causal link between fatigue and increased ACL injury risk due to the high variation of results between studies (298).

Epidemiology studies have reported inconsistent findings regarding ACL injuries and duration of play in various athletic groups. Two studies evaluating ACL injuries in NBA players found no significant differences between number of minutes played and injury or in quarter of the game in which an injury occurred (72, 73). However, it was shown that 40% of injuries did occur in the fourth quarter of the game (73). It is important to note that player position may be a cofounding factor in these studies, as different positions may have different fatigue demands connected to them (73). Contradictory, Hawkins et al. (297) found that the greatest potential for ACL injuries to occur in professional soccer players was the end of the second half compared to the end of the first half of a match, which has been supported by other soccer epidemiological work (299). In order to understand the relationship fatigue may have with ACL injuries, it is important to first understand what fatigue means.

Two main types of fatigue exist: psychological fatigue and physical fatigue. Psychological and physical fatigue coexist and influence one another during athletic competitions. When an athlete has a great amount of psychological stress, psychological fatigue starts to increase and the athlete experiences decreases in alertness, reaction time, and decision making (300, 301). This in turn hinders the athlete in adapting to their ever-changing environment by failing to make appropriate movement patterns, thus increasing the risk that injury may occur (302). For the purposes of this literature, fatigue will be defined as a decrease in the muscles ability to produce force after an exercise bout (303). Muscle fatigue is influenced by two factors: central fatigue and peripheral fatigue. Simply, central fatigue refers to the exercise-induced reduction of voluntary muscle activation and peripheral fatigue refers to the exercise-induced reduction of the force-generating capacities of muscles (304, 305). Central fatigue factors include altered motor neuron firing rates, decreases in muscle activity, altered muscle excitability, and inhibition of afferent feedback (306). Peripheral fatigue factors involve deficits in the excitation-contraction phenomenon due to changes in calcium release or increases in lactic acid (307). Because fatigue has been theorized to be associated with injuries, several studies have utilized fatigue protocols in various populations to gain new knowledge in fatigue's role in injuries.

Fatigue Protocols

Numerous fatigue protocols exist within the literature. Two main types of fatigue protocols exist, peripheral and general protocols. Peripheral fatigue protocols can be thought of as localized fatigue, only targeting specific muscle groups or specific limbs. Typically, the goal of these protocols is to cause either metabolic changes or muscular damage through repetitive eccentric contractions, however it is not to change neuromuscular control (298). These protocols

are usually short in duration, and usually involve isometric or isokinetic protocols to fatigue specific muscle groups, such as the quadriceps or hamstrings (298). General fatigue protocols are thought to be whole-body fatigue, with the goals of simulating realistic game like fatigue and reducing muscular activity (34). These protocols involve completing many rounds of submaximal activities, such as squatting, vertical jumping, running, agility drills, or a combination of activities. Termination criteria of a general fatigue protocol involve either individuals completing the activity until a specific time has been reached, or the individual can no longer perform the activity properly (298).

A systematic review conducted across 37 fatigue protocol studies the fatigue protocols used in these studies did not uniformly produce biomechanical or neuromuscular changes that would alter the risk of ACL injuries (298). The author states that there was a substantial amount of variation between these fatigue protocols, and therefore could not consistently produce mechanical changes (298). However, it did appear that general fatigue protocols that included some sort of reactive task saw decreases in hip and knee flexion, as well as increases in hip internal rotation and knee abduction angles (34, 36, 308, 309). A reactive task model involves unanticipated tasks, such as cutting, with the use of some sort of visual stimulus (i.e. directional computer stimulus). Using a general fatigue protocol that includes a reactive task deems most appropriate when choosing a fatigue protocol to use as it is the most realistic to a game-like situation, and it would cause not only muscle fatigue, but mental fatigue as well.

Fatigue and ACL Injuries

It is thought that when an individual becomes fatigued, the fatigued musculature is not able to absorb energy as well as non-fatigued musculature (33). This in turn leads to decreases in

neuromuscular control, decreased proprioception of the knee, and altered lower extremity mechanics, thus potentially overloading the ACL and causing injury (34-39).

Numerous studies have reported adverse changes in sagittal and transverse plane hip angles (34, 36, 309, 310) and moments (36) as well as sagittal, frontal, and transverse plane knee angles that reflect those observed during ACL injury, such as decreased hip and knee flexion, increased knee abduction, and increased hip and knee internal rotation angles (34-37, 163, 309-311). Gleeson et al. (311) saw decreases in both knee extension and flexion torques post-fatigue. However, there was a larger decrease in the flexion torque compared to the extension torque, indicating the hamstrings were most affected by fatigue compared to the quadriceps (311). It was also observed that a 44% increase in anterior tibiofemoral displacement existed after the fatiguing protocol (311). The authors stated this could potentially be due to the viscoelastic properties of the ACL and that over periods of repetitive stress could impair integrity of the ligament (311). Borotikar et al. (34) and McLean et al. (36) both reported a 3.6° and 3.8° increase in knee abduction angle, post-fatigue, respectively, while Cortes et al. (308) and Lucci et al. (309) observed a 3.0° and 3.2° decrease in knee flexion angle, respectively. While these changes are statistically significant, most of these mechanical changes are small and within a couple of degrees or Newton-meters from one another. Currently, it is unclear if these small changes in magnitude are clinically relevant.

Interestingly, some of the observed mechanical differences are not consistent between fatigue studies. For example, increased and decreased knee flexion has been reported post fatigue. Xia et al. (310) and Kernozek et al. (163) both found increases in knee flexion angle post-fatigue during a drop landing task, while Chappell et al. (37) reported decreases in knee flexion angle post-fatigue during stop-jump tasks. Xia et al. (310) stated that it was plausible that

since both they and Kernozek et al. (163) used anticipated drop landings, the body's predetermined motor program may help adjust muscle activity to cope with the impact of landing after fatigue. Other studies have confirmed that the human body changes its optimal movement strategy to perform an athletic movement between pre and post fatigue states (312).

Fatigue and ACL Reconstruction

Studies suggest that ACL-R individuals subjected to neuromuscular fatigue have decreases in performance, quality of movement, and knee stability, increases in anterior tibial translation, as well as alterations in lower extremity muscular activity, thus putting them at a high risk of ACL reinjury (46, 47, 65, 66, 313-315). ACL-R individuals already tend to display strength deficits and altered mechanics while completing athletic movements, therefore these individuals may be more susceptible to the effects of fatigue (314).

Currently, only landing studies have been utilized to compare the effects that fatigue may have on ACL-R individuals (46, 47, 64-66, 162, 314). Thomas et al. (66) compared ACL-R to healthy individuals during dynamic landing task that involved landing from a forward jump and cutting to the left or right. They reported that quadriceps strength and central activation decreased post-fatigue for both ACL-R and healthy individuals. Interestingly, the ACL-R group exhibited decreased knee flexion angle pre and post fatigue compared to the healthy group, indicating that regardless of fatigue state, ACL-R individuals landed with a stiffer lower extremity compared to healthy individuals. Both groups also displayed decreases in knee abduction angle and knee adduction moments post-fatigue compared to the pre-fatigued state. The authors state that after fatigue, both groups may not have been cutting as hard as they did before the fatigue protocol, thus allowing for a more neutral frontal plane alignment of the lower extremities (66). However, it is important to note the fatigue protocol in this study primarily

targeted the main sagittal plane muscles (i.e. quadriceps, hamstrings, and gluteus maximus). Therefore, frontal and transverse plane mechanics may not have been affected to a great degree due to lack of fatigue in frontal and transverse plane muscles. Other studies have shown altered kinematics in ACL-R individuals post-fatigue, such as increased peak trunk flexion, decreased initial contact hip flexion angle, and increased hip flexion displacement (46, 314).

Muscle strength and activity have been observed to change pre and post fatigue in ACL-R individuals. Thomas et al. (66) found a 22% decrease in quadriceps strength after fatigue in ACL-R individuals compared to healthy individuals. Despite this decrease, the ACL-R group showed similar kinematics pre and post-fatigue, leading the authors to believe potentially the ACL-R group was relying on their uninvolved limb more during the fatigue protocol than the ACL-R limb (66). Other studies have shown differences in muscle activity pre and post-fatigue in ACL-R individuals during landing. It has been observed that after fatigue, there was increased activation of vastus lateralis, biceps femoris, and gluteus maximus compared to healthy individuals (314). This increased activation of the biceps femoris and gluteus maximus was theorized to be an altered landing strategy to reduce loading on the ACL post-fatigue (314). The medial hamstrings, lateral hamstrings, and vastus lateralis of ACL-R individuals have also been shown to activate earlier post-fatigue compared to healthy individuals (65). This would indicate that ACL-R individuals, either consciously or unconsciously, relied on earlier muscle pre-activation to increase knee joint stability when landing in a fatigued state (65).

Conversely to these studies, two research groups showed little to no difference in ACL-R individuals landing mechanics compared to a healthy group after a fatiguing protocol (64, 162). Webster et al. (162) found that ACL-R limbs did not respond different compared to the uninvolved limb or to a healthy control, suggesting that fatigue does not influence landing

mechanics differently between these groups. Lepley et al. (64) also reported that quadriceps to hamstrings co-contraction levels were not different between ACL-R and healthy individuals post-fatigue, suggesting that ACL-R individuals are capable of using similar muscle activation levels during landing regardless of fatigue. However, both studies suggest that methodological differences may have been the primary factor influencing these results compared to other studies (64, 162).

Very few studies have observed the interaction of gender and fatigue when comparing ACL-R individuals to healthy controls. Lessi et al. (47) found that females had a greater peak knee abduction angle in the ACL-R limb post-fatigue compared to both their pre-fatigued state as well as males with an ACL-R. The authors suggested that based on the findings of a previous study, ACL-R females may be more sensitive to the effects of fatigue compared to healthy females, who have shown no significant differences in knee abduction angle during landing (41, 47). They also found that males had greater vastus lateralis muscle activation post-fatigue in the ACL-R limb compared to females (47). Another interesting finding is ACL-R females were found to have an increase in center of pressure sway speed after fatigue, indicating a decrease in postural control (46), which may predict their risk of experiencing a second ACL injury (26).

Fatigue and Neuromuscular Control

Fatigue and its relationship to neuromuscular control has been vastly studied, as muscle fatigue has been shown to create deficits in neuromuscular control (16, 34, 36). However, neuromuscular control is a modifiable factor, thus by training effectively, the decline of neuromuscular control can be slowed (16). Even though it is trainable, the loss of neuromuscular control due to fatigue cannot ever be fully avoided. As such, it is important to understand how fatigue causes these deficits in neuromuscular control and ultimately increase risk of injury.

Adverse variations in knee joint proprioception due to muscular fatigue have been reported by several studies (316-320). Skinner et al. (318) was one of the first to report that after fatigue, decreased efficiency of the muscle spindles to detect changes in muscle length, which in turn decreases the body's ability to accurately detect knee joint position. Interestingly, local fatigue and general fatigue have different mechanisms of altering knee proprioception. However, only general fatigue was shown to have a significant effect on knee proprioception (316). Miura et al. (316) saw that general fatigue decreased knee proprioception without significant deficits in peak knee extensor torque (prefatigued: 80.5 ± 11.5 %BW; general fatigue: 80.8 ± 14.4 %BW) and peak knee flexor torque (prefatigued: 46.1 ± 9.0 %BW; general fatigue: 43.0 ± 10.4 %BW), indicating that changes in the proprioception pathway does influences changes in the muscle mechanoreceptors (i.e. muscle spindles). This is further supported by Ribeiro et al. (319) who reported that changes in knee proprioception is not muscle dependent. The changes in knee proprioception independent of changes in muscle strength leads to the conclusion that proprioceptive changes are caused by central fatigue. Central fatigue may diminish motor control, thus altering the body's ability to stabilize the knee appropriately during activities such as landing and cutting, thus causing an ACL injury (316). Even though central fatigue may decrease motor control, the central nervous system does prompt the body to adjust and adapt to its new fatigued state in an effort to protect it from injury.

The central nervous system has the ability to change global inter-limb coordination following fatigue in order to maintain optimal performance (321). This can be achieved by either by reorganizing movement patterns of individual degrees of freedoms (i.e. muscles, joints), or by utilizing new movement patterns with new degrees of freedom (322-324). The changes in kinematics and kinetics are often small in magnitude between pre-fatigue and post-fatigue states.

Thus, it has been hypothesized that movement pattern reorganization may be the net sum of several small changes to many different degrees of freedom within the body (322, 323). Another interesting phenomenon that occurs after fatigue is that there is an increase in movement of different joints that are not typically involved in creating specific movements, such as increased trunk motion when the arms reach fatigue (323, 325). Cowley et al. (325) reported that an increase of inter-joint coordination is observed after fatigue, indicating that individuals adopt a new movement pattern to adapt to their newly fatigued state. These new post-fatigue movement patterns can be compared to that of movement patterns seen in individuals learning a new task (325). All these factors regarding changes in inter-joint coordination and adoption of new movement patterns could offer insight in the relationship between fatigue and ACL injuries.

One example of observing the organization of new movement patterns is through joint coordination and variability. As discussed previously, increases or decreases in variability beyond the body's "optimal variability" range will open up the individual to increased risk of injury (259-261). Few studies have described fatigue's relationship with joint coordinative variability during athletic movements like landing and cutting (326, 327). Understanding how fatigue affects joint coordinative variability gives insight to how the body reorganizes movement patterns or adopts new movement patterns to adapt to its new fatigued state. During a sidestep cutting task, Samaan et al. (326) reported lower extremity joint couplings after an isolated hamstring fatigue protocol. They found significant decreases in hip rotation/knee rotation during the initial contact and the weight acceptance phases, as well as decreases in hip adduction-abduction/knee rotation during just the weight acceptance phase (326). Decreases in the joint coordinative variability indicate that these individuals demonstrated a limited number of movement patterns they could reorganize, or a decreased ability to adapt new movement

patterns. This inability to adapt to their newly fatigue state reduced dynamic knee stability during the cutting task, thus placing them at a greater risk for musculoskeletal injury.

Interestingly, during a more generalized single-leg hopping fatigue protocol, it was reported that joint coordinative variability actually increased post-fatigue (327). Hip flexion-extension/knee flexion-extension, knee flexion-extension/ankle plantarflexion-dorsiflexion, and knee flexion-extension/ankle inversion-eversion all increased in variability during the loading phase of the single-leg hop post-fatigue compared to the pre-fatigue testing (327). During propulsion, Hip flexion-extension/knee flexion-extension and knee flexion-extension/ankle plantarflexion-dorsiflexion variability increased post-fatigue compared to pre-fatigue (327). Vertical stiffness did not change between pre and post-fatigue, indicating that the task itself remained unchanged during the testing session. This is important as it shows that the inter-joint coordination could change but not affect the overall task performance (327). The authors also speculated that the ankle could not properly adapt to the newly fatigue state, thus leading to compensatory changes at the hip and knee (327). When comparing the two studies, Mudie et al. (327) found increases in joint coordinative variability mostly in the hip and knee sagittal plane, while Samaan et al. (326) found decreases in joint coordinative variability in the hip and knee frontal and transverse planes. These differences could be task-specific, as single-leg hopping is mostly a sagittal plane movement, while sidestep cutting utilizes all three planes. They could also be attributed to the different fatigue protocols used. One used an overall general fatigue protocol, while the other used a localized fatigue protocol that only targeting the hamstrings. Therefore, future research is warranted to grasp better understanding on how fatigue affects inter-joint coordinative variability.

The human body can be considered an indeterminate system, meaning that the equations of motion (i.e. Newton's Laws of Motion) cannot be solved because there are more unknown variables (e.g. force) than there are equations of motion. Therefore, there are multiple ways that the same external movement can occur, such as knee flexion, but have an indefinite number of combinations of internal muscle forces, joint torques, etc. to cause knee flexion. Mechanical properties of muscles can be used to help solve these equations, by replacing one unknown (force) with another unknown (muscle activity). This process does not actually solve the equations of motion. However, it helps constrain the possible solutions to physiologically appropriate solutions, meaning these solutions are within the force-length and force-velocity properties of the muscles (328). As the human body can be efficient in producing new movement patterns to adapt to a fatigue state, this means that muscle activities are being reorganized to adapt to these new post-fatigue equations of motion. This could possible indicate that while no external kinematic changes are observed (i.e. decreased knee flexion angle, increased knee abduction angle, etc.) internally, muscle activities may drastically change in the muscles that directly and indirectly load the ACL, such as the quadriceps, hamstrings, gastrocnemius, soleus, and hip abductors. As such, the use of musculoskeletal modeling could open a new realm of ACL injury research and its relationship to fatigue.

Musculoskeletal Modeling

Musculoskeletal modeling provides a way to measure physiological parameters, such as muscle force, joint contact force, and ligamentous force that are difficult to measure *in vivo* (48-50) during athletic movements such as cutting and various landing tasks (51-54). With the use of musculoskeletal modeling, a more holistic understanding of these athletic movements can be achieved by observing how changes in lower extremity kinematics and kinetics are related to

changes within the neuromuscular system. Through extensive work, an open-sourced software called OpenSim was developed to allow researchers the opportunity to build computer simulated models and explore the relationship between experimentally collected data and estimated neuromuscular variables (48). Researchers can scale a musculoskeletal model of their choosing to be a participant-specific model based on specific anthropometric data. Each model contains virtual anatomical marker locations. The body segments of the participants are scaled based on the distances of the experimental markers from the motion capture system and the model virtual markers (48). Then, experimental marker coordinate and ground reaction force data can be imported and applied to the participant-specific model. An inverse kinematics solution is then found to find the joint angles and translations that best reproduce the raw marker coordinate data from the motion capture system (48). From here, researchers can either choose a number of options of simulations to run (i.e., static optimization, computed muscle control, induced acceleration, etc.) to answer their research question.

Several studies have utilized musculoskeletal modeling to determine ACL loading and contributions to variables, like anterior tibial shear force and frontal plane moments, that are known to influence ACL loading (12, 52-54, 71, 109, 329). McLean et al. (109) used a twelve degree of freedom model to create participant specific models of ten males and ten females during sidestep cutting tasks. They indirectly estimated ACL loading by using peak anterior tibial shear force as a surrogate. Monte Carlo simulations (n = 5000) were performed with the models to determine the variability of peak anterior tibial shear forces, as well as abduction and internal rotation moment. An anterior tibial shear force above a set threshold of 2000 N was used to determine the simulations that would have caused ACL injury. No simulations exceeded the 2000 N threshold, indicating no simulations for any of the models were “at risk” for an ACL

injury. However, it was shown that the abduction moment reached values that would put the ACL at risk for injury (>125 Nm). Therefore, the authors concluded that sagittal plane forces alone were not enough to injury the ACL (109).

Weinhandl et al. (54) also used musculoskeletal modeling to observe the anticipatory effects on ACL loading during sidestep cutting. They used a 21 degree of freedom model that was specifically scaled to twenty females. The authors conducted a residual reduction algorithm to calculate joint moments that would reproduce the experimentally collected sidestep cutting tasks. After the residual reduction algorithm was conducted, a computed muscle control analysis was executed to determine lower extremity muscle excitations and forces. Joint reaction forces were also calculated. Three-dimensional ACL loading was then calculated using the simulated knee joint moments, joint reaction forces, and estimated quadriceps, hamstrings, and gastrocnemius muscle forces. A previously established model were used to calculate sagittal plane (137), while frontal and transverse plane loading was based on cadaveric data and expressed as a function of the respective joint moment and knee flexion angle (54, 75, 330). They were able to observe that unanticipated sidestep cutting caused a 13% increase in overall ACL loading compared to the anticipated sidestep cutting trials. This increase was due to an increase in sagittal plane ACL loading. During the unanticipated trials, sagittal plane loading contributed 62%, frontal plane loading contributed 26%, and transverse plane loading contributed 12% to the overall ACL loading. This study confirmed others that suggested that ACL loading was multiplanar and showed that unanticipated tasks loaded the ACL more than anticipated tasks (54).

Other studies have used this same method to calculate three-dimensional planar ACL loading (51, 53, 71). However, other research groups have used variations of this method by

using point kinematics analyses to obtain the muscle line of actions from the participant specific scaled models compared to cadaveric data (52, 204). While both methods have been validated for use, the use of point kinematics to obtain the muscle line of actions may provide slightly more precise estimates of ACL loading. Since each participant will have varying heights and segment lengths, this opens the opportunity for muscle line of actions to be slightly different between all participants. Thus, depending on the research question, it may be needed to calculate participant specific muscle lines of action. While these studies have quantified ACL loading during tasks like cutting and landing, and have gone so far as quantify sagittal, frontal, and transverse plane ACL loading, it is still unclear as to what contributes to ACL loading. As discussed in a previous section, lower extremity muscles influence ACL loading, but to date no study has quantified how much individual muscles contribute to ACL loading.

Muscles directly influence joints they cross, as well as indirectly influence joints they do not cross. This phenomenon is known as dynamic coupling (11). Dynamic coupling describes how an individual muscle force acts to accelerate instantaneously not only the joint it spans, but also other joints and segments that it has no direct relationship (11, 331). This means that individual muscles also contribute to the acceleration of the body's center of mass. Because the body is multisegmented, a muscle force acting at any joint in the body also instantaneously transfers force throughout the body due to joint intersegmental forces (11, 331, 332). Therefore, a single muscle can either directly or indirectly contribute to intersegmental forces, joint accelerations, and other components like joint moments, joint power, and joint work, for all joints in the body (11, 49, 331, 332).

As such, an induced acceleration analysis (IAA) was developed to account for the dynamic coupling nature of the body during musculoskeletal modeling. In a perfectly linear

system, the summation of all the individual forces that are contributing to the total body acceleration must equal the overall total body acceleration (49). When considering the human body, the summation of the internal forces of the body (i.e. muscle forces, ligamentous forces, etc.) must equal the GRF obtained from a force plate to produce the desired body's kinematics (49). However, a major problem that researchers encounter is that a force plate cannot measure the contribution of a single muscle's force to the overall GRF, which is necessary to evaluate the intersegmental forces and accelerations induced by that specific muscle (49).

While there are various IAA methods for OpenSim available for use, one IAA method commonly used employs a multiple-point foot contact model (333, 334). This method as an advantage over other IAA methods as it is more flexible and realistic in representing the interaction between the foot and the ground (333, 334). While some methods only use one contact point between the foot and the ground, this method uses five contact points placed around the perimeter of the foot. An issue present with the methods that only use one contact point is that irregular trajectories for the muscle contributions to the GRF exist when transitioning from contralateral toe-off, ipsilateral heel-off, and ipsilateral toe-off (333, 334). Lin et al. (333) and Dorn et al. (334) method allows for much smoother muscle contribution trajectories during these transition stages, thus becoming more robust and allowing for use on all foot strike patterns, not just rearfoot strike patterned gait.

Several studies have used IAA to calculate individual muscle contributions to joint accelerations (335), acceleration of the body's center of mass (336-339), and intersegmental joint forces and moments, and GRFs (12, 204) during walking, running, and sidestep cutting. Only two studies pertain specifically to high risk ACL injury risk movements using an IAA method (333, 334). Maniar et al. (338) observed how individual lower extremity muscles contribute to

three-dimensional GRFs during unanticipated sidestep cutting. They used a 29 degree of freedom model scaled specifically to their eight male participants. An inverse kinematics algorithm was conducted to calculate lower extremity joint angles, followed by a residual reduction algorithm. Static optimization was then conducted in order to obtain the estimate muscle forces. Finally, the authors used an IAA method (333, 334) to decompose the GRFs to determine specific lower extremity muscular contribution to the GRFs (338).

They reported that during unanticipated sidestep cutting, the vasti group, gluteus maximus, soleus, and gastrocnemius were primarily responsible for contributing to the vertical GRF. These muscles acted to support bodyweight during the cutting movement by accelerating the center of mass upwards. The vasti group, along with the gluteus maximus, soleus, gastrocnemius, and hamstrings were primary contributors to the anteroposterior GRF and modulating braking and propulsion. Finally, the vasti group, gluteus maximus, and gluteus medius were the primary contributors to the mediolateral GRF, acting to accelerate the center of mass towards the sidestep cutting direction (338).

The same research group also examined how individual muscles contribute to anterior tibial shear force as well as knee abduction and rotational joint reaction moments during unanticipated sidestep cutting (12). Using a 37 degree of freedom model, eight subject specific models were computed. Inverse kinematics, inverse dynamics, and static optimization algorithms were executed to obtain joint angles, joint moments, and estimated muscle forces, respectively. An IAA method was employed to decompose the measured GRF into individual muscular contributions (333, 334). Finally, each muscle's contribution to anterior tibial shear force, as well as knee abduction and rotation moments, were calculated by applying each muscle's force and its

respective contribution to the GRF in isolation and solving for the dynamical equations of motion (12).

The authors reported that during an unanticipated sidestep cutting task, anterior tibial shear force was primarily produced by the quadriceps and the gastrocnemius. Overall, the vasti group contributed a peak 225 N of anterior tibial shear force, while the rectus femoris contributed 83 N, the lateral gastrocnemius contributed 38 N, and the medial gastrocnemius contributed 84 N, respectively. The soleus, biceps femoris long head, and medial hamstrings were the greatest contributors to posterior tibial shear force, peaking at 173 N, 111 N, and 77 N, respectively (12). These muscles actively opposed anterior tibial shear force, thus helping to unload the ACL during the sidestep cutting task. The gluteus maximus, gluteus medius, and piriformis were also reported to be the largest contributors to opposing knee abduction moment, with the gluteus medius being the overall primary contributor (12). Finally, the authors reported that a knee external rotation moment was present during the whole stance phase of the sidestep cutting task, peaking at 25 Nm. The primary contributor to the knee external rotation moment was the vasti group (~ 23 Nm), and soleus (~ 10 Nm). The gluteus maximus and gluteus medius were the largest opposers to the knee external rotation moment. However, their contributions to opposition were very small (2 Nm to 10 Nm) (12).

To date, this study is the closest any study has come to quantify how individual muscle contribute to ACL loading during athletic tasks. However, even though Maniar et al. (12) observed muscle contributions to knee kinematics and kinetics that are associated with ACL injuries (i.e. anterior tibial shear force, knee abduction moment, and knee rotation moment), they still did not actually calculate the effects individual muscles have on ACL loading. Even more so, these studies used a healthy male population. No study thus far has observed how muscles

would contribute to ACL loading in healthy females, ACL-R females, or individuals before and after a fatiguing protocol. Therefore, much more research is warranted to explore these populations.

Conclusion

Non-contact ACL injuries are extremely prevalent, costly, and often have life-long consequences following the initial injury. Young, athletic females are at the highest risk for ACL injury compared to their male counterparts. As such, every effort must continue to be made in understanding why these injuries happen and how to decrease the number that occur each year. Unfortunately, not all ACL injuries are preventable. While much a substantial amount of research exists regarding healthy females and ACL injuries, less is known about ACL-R females and their risk for sustaining a second ACL injury. One factor that could influence this risk is game fatigue. However, few studies exist that report the relationship fatigue has with lower extremity mechanics between healthy and ACL-R females. Neuromuscular control and muscle activation may be altered due to ACL-R, fatigue, or a combination of both. As it is known that lower extremity muscles influence ACL loading, it is vital to understand how individual lower extremity muscular contribution may change pre and post fatigue in healthy and ACL-R females. This information could be the key to unlocking a whole new door to ACL injury prevention and rehabilitation research and help reduce the number of ACL injuries occurring each year.

Chapter 3: Fatigue's Influence on Lower Extremity Mechanics in Healthy and ACL-Reconstructed Females: A Statistical non-Parametric Mapping Approach

Abstract

Females are 16 times greater to sustain a second ACL injury compared to their healthy female counterparts. Many of these females return to play their respective sport after an ACL-reconstruction (ACL-R). However, little is known about the influence fatigue in sport has on lower extremity mechanics of ACL-R females. The purpose of this study was to investigate the influence muscular fatigue may have on lower extremity mechanics in healthy and ACL-R females. It was hypothesized that 1) healthy control and ACL-R females would demonstrate different hip, knee, and ankle mechanics, regardless of fatigue, and 2) fatigue would influence hip, knee, and ankle mechanics, regardless of previous surgical intervention. Seven healthy and four ACL-R recreationally active females completed five anticipated box-land-and-cut trials to the right pre- and post- a fatigue protocol. Three-dimensional lower extremity kinematic and kinetic variables were measured using a motion capture system and force plate. One-dimensional statistical non-parametric mapping were used to assess changes in lower extremity mechanics between healthy control and ACL-R females over the entire stance phase. The only group × fatigue interaction found was hip flexion angle. Significant group main effects included hip flexion, abduction, and rotation angles. Significant fatigue main effects included hip flexion and knee abduction angles, as well as hip rotation moment. Hip and knee mechanics appear to be influenced by both fatigue and prior ACL surgery. However, hip mechanics seemed to be the most affected by prior ACL surgery, with fatigue being second. Therefore, future research is warranted to investigate the relationship between hip mechanics and ACL-R.

Introduction

Anterior cruciate ligament (ACL) injuries are extremely prevalent, costly, and often result in long-term consequences, such as early onset knee osteoarthritis. Approximately 200,000 ACL injuries occur every year, with 70% of these injuries considered non-contact ACL injuries (1). Epidemiologic research has shown that 100,000 to 150,000 of all ACL injuries occurring in the United States each year will undergo reconstructive surgery (13). The primary goal of conducting an ACL reconstruction is to return individuals back to an active lifestyle by regaining knee stability after the ACL injury (17). For several individuals, this means returning to sport as many ACL injuries occur in young, athletic populations. Up to 83% of ACL-reconstructed (ACL-R) athletes return to their pre-injury sport (32), however 10 to 30% of athletes who do return to sport after an ACL reconstruction will sustain a secondary ACL injury (26-28, 30). Unfortunately, females are 16 times more likely to experience a secondary ACL injury after an initial ACL reconstruction compared to their healthy female counterparts (31). As such, great effort has been placed on understanding why this high rate of ACL re-injury exists, and why ACL-R females are placed at a higher risk than healthy females.

Factors associated with re-injury of the ACL-R leg after return to sport is similar to those associated with a primary ACL injury. These factors are likely multifactorial, including altered lower extremity mechanics, such as increased hip adduction and internal rotation, decreased knee flexion, increased knee abduction, and increased ankle plantarflexion angles (61, 62, 69, 255), increased joint variability (23, 24), and altered muscle activity (19, 251, 268). Similar to a primary ACL injury, secondary ACL injuries occur most often due to non-contact mechanisms, further indicating that biomechanical and neuromuscular control is an important risk factor

(340). While it is known that biomechanical and neuromuscular control are important risk factors, one risk factor that is not well understood is muscular fatigue.

For the purposes of this study, muscular fatigue is defined as a decrease in the muscles ability to produce force after an exercise bout (303). It is hypothesized that that when an individual becomes fatigued, the fatigued musculature is not able to absorb energy as well as non-fatigued musculature (74). This in turn leads to decreases in neuromuscular control, decreased proprioception of the knee, and altered lower extremity mechanics, thus potentially overloading the ACL and causing injury (34, 35, 37, 38). Few studies have observed the effects fatigue has on healthy females during tasks such as landing and cutting (34, 35, 38, 41, 43, 44). Previous research has shown that during landing and cutting tasks, healthy females exhibit decreased initial contact hip flexion, increased initial contact internal hip rotation, internal knee rotation, knee abduction angles as well as increased peak knee abduction and internal rotation angles subsequent a fatigue protocol (34, 38, 43, 44). These mechanics reflect those commonly observed during medial knee collapse (174), a strong characteristic of high-risk non-contact ACL injury movement patterns (341). To our knowledge, only two studies exist that report the influence of fatigue on ACL-R females compared to a healthy group (46, 47). ACL-R females demonstrate decreased initial contact hip flexion angle as well as increased peak knee abduction angle (46, 47). However, due to the small amount of previous research, the mechanisms of how fatigue and ACL-reconstruction influence lower extremity mechanics in females is not well understood.

Currently, all studies that have investigated the influence of fatigue on lower extremity mechanics have limited their analyses to discrete variables, such as initial contact and peak joint angles and moments. However, by only analyzing discrete time points, it is possible that

differences in lower extremity mechanics caused by fatigue or previous surgical intervention may go undetected, thus misrepresenting the true influence fatigue and ACL-reconstruction may have on lower extremity mechanics. Therefore, using a time series-based statistical analysis, such as statistical non-parametric mapping (SnPM), allows for the entire time series of the lower extremity kinematic and kinetic data to be analyzed and provide a better understanding of how fatigue and ACL-reconstruction influences lower extremity mechanics.

Therefore, the purpose of this study was to investigate the influence muscular fatigue may have on lower extremity mechanics in healthy and ACL-R females. Because we are using non-directional statistical non-parametric mapping analyses, it was hypothesized that healthy control and ACL-R females would demonstrate different hip, knee, and ankle mechanics, regardless of fatigue. It was also hypothesized that fatigue would influence hip, knee, and ankle mechanics, regardless of previous surgical intervention.

Methods and Materials

Participants

Prior to data collection, experimental procedures received ethical approval from the university's Institutional Review Board. Eleven (seven healthy controls, four ACL-R) recreationally active females between 18 and 35 years volunteered for the study (Table 1). Inclusion criteria for both the healthy control and the ACL-R groups included being recreationally active at least 3 days per week for a minimum of 30 minutes per session, with one session being a dynamic training session, no lower extremity pain on the day, and no history of lower extremity injury within six months prior to testing. Specific inclusion criteria for the healthy control group included no history of lower back or lower extremity surgery, while specific inclusion criteria for the ACL-R group included being a minimum of one year post ACL

reconstruction, no history of multi-ligament knee surgeries, active meniscal symptoms, or bilateral knee surgery (57). There was no restriction on graft type or history of meniscal repair at the time of ACL reconstruction (26, 61, 69), and all ACL-R females were cleared to return to full sport participation by their physician. All ACL reconstructions performed on the ACL-R females were autografts. Two ACL-R females had patella tendon grafts, while the other two ACL-R females had a semitendinosus-gracilis tendon graft and a quadriceps tendon graft, respectively.

Experimental Procedures

Data collection consisted of two testing days, with a minimum of three days separation between the two testing days. On Day 1, participants provided written informed consent, as well as completed the Lower Extremity Functional Scale (LEFS) (342), the Knee injury and Osteoarthritis Outcome Score questionnaire (KOOS) (343), the International Knee Documentation Committee questionnaire (IKDC) (344), the Tampa Scale for Kinesiophobia (TSK-11) (345), a musculoskeletal health history questionnaire, and a fitness history questionnaire. Participants then completed an ankle dorsiflexion range of motion assessment, a knee joint laxity assessment, a balance assessment, and a strength assessment of the lower extremity musculature. The ankle dorsiflexion range of motion assessment was conducted using a weight-bearing lunge test as described in previous research (346, 347). Following the weight-bearing lunge test, bilateral knee joint laxity was assessed using a knee arthrometer (Prothia GNRB, Paris, FRA). Three trials of knee laxity were collected for each knee. The balance assessment consisted of a bilateral standing position with eyes open and closed, as well as a unilateral standing position with eyes open and closed on the left and right leg. Each test included three trials that lasted 20 seconds each. Finally, isokinetic strength testing at $30°\cdot s^{-1}$ on an isokinetic dynamometer (Biodex Medical Systems, System 4 Pro, NY, USA) was completed.

Three trials of isokinetic testing of the hip flexors and extensors, hip adductors and abductors, knee flexors and extensors, and ankle plantarflexors and dorsiflexors were performed on the participants' right and left leg.

On Day 2, participants returned to the laboratory to complete the biomechanical testing and fatigue protocol (Figure 1). Participants were asked to wear an athletic t-shirt, spandex shorts, and were provided with a standard laboratory shoe (Nike Pegasus, Nike Inc., Beaverton, OR, USA) to wear during testing. Height and weight were collected, and then participants completed a five-minute warm-up at a self-selected pace on a treadmill. Following the warm-up, a heart rate sensor was secured to the participant's chest (Polar T31 Heart Rate Sensor, Polar Electro Inc., Bethpage, NY, USA) and a heart rate monitor (Polar FT1 Heart Rate Monitor, Polar Electro Inc., Bethpage, NY, USA) was worn on the participant's wrist. Then, 27 anatomical, retro-reflective markers were placed on the manubrium below the sternal notch, C7, L1, and bilaterally on the right and left acromion processes, right and left iliac crests, right and left ASIS, right and left PSIS, right and left greater trochanters, medial and lateral femoral epicondyles, right and left tibial tuberosity, medial and lateral malleoli, right and left tip of the second toe, and first and fifth metatarsophalangeal joints. Clusters of four non-collinear markers on rigid thermoplastic shells were attached to the posterior trunk, posterior pelvis, and bilaterally on the lateral thighs and lateral shanks using neoprene straps to track segment movement during motion trials. Finally, clusters with four non-collinear markers on a rigid thermoplastic shell was secured directly on the posterior surface of the heel of the right and left shoes. A pre-fatigue three-second standing static calibration trial was recorded, and the 27 anatomical markers were removed.

After the anatomical markers were removed, participants were asked to complete three maximal vertical jumps to measure pre-fatigue vertical jump height. Then, participants stood on

top of a 30 cm box positioned half of the participant's body height away from the center of the force plate and were asked to jump out towards the center of the force plate and complete three anticipated landing tasks. These landing tasks included: 1) landing unilaterally on the right foot and cutting 45° to the left, 2) landing unilaterally on the left foot and cutting 45° to the right, and 3) landing bilaterally and completing a vertical jump subsequent to the initial land. While three landing tasks were performed, the box-land-and-cuts to the right were analyzed for all controls as well as ACL-R females who had a reconstruction on the right knee. Box-land-and-cuts to the left were analyzed for two ACL-R females who had a reconstruction on the left knee. The landing tasks were counterbalanced, and five successful trials of each landing task were collected prior to the start of the fatigue protocol. After the pre-fatigue data collection trials are collected, the cluster markers were removed, and participants were brought into a gym where the fatigue protocol began.

A modified fatigue protocol was used to fatigue the participants (Figure 2). Because recreationally active females participated in the current study, a modified version of an existing fatigue protocol (37) tailored to recreational individuals was created. A reactive component was added to the modified fatigue protocol as it has been shown that general fatigue protocols with a reactive component are best at creating physical overall fatigue and cognitive fatigue (298). First, participants were asked to perform a maximal vertical jump-and-reach test against a wall. Then, participants were asked to stand in the middle of four exercise stations, placed 7.5 m in front, behind, and to the left and right of the participant. Each exercise station consisted of four different body weight exercises (maximal countermovement vertical jumps, lunges, mountain climbers, and squats to parallel).

To start a round, participants stood in a standing position. They were then instructed to sprint towards the randomly assigned exercise station. If they were instructed to complete the front station, participants sprinted 7.5 m, completed the exercise, and then sprinted backwards to their starting point. If a participant was instructed to complete the back station, participants sprinted backwards 7.5 m to the station, completed the exercise, and then sprinted forward to the starting point. To reach the left or right station, participants maximally side-shuffled to the left or right station, completed the exercise, and then side-shuffled back to the starting point. Each exercise station was visited once per round. Once the participant finished the last exercise station, they sprinted to the wall to complete a maximal vertical jump-and-reach, then were asked their heart rate (HR) and rate of perceived exertion using a 6-to-20 point Borg scale, where 20 represented maximal exertion. Participants then received 60 s of rest before completing the next round. Participants completed as many rounds as possible until their maximal vertical jump-and-reach height decreased by 25% for two consecutive maximal vertical jumps.

Once maximal vertical jump-and-reach height was decreased by 25%, participants sprinted back to the laboratory, where cluster markers were placed back on the participant, and the participant completed three maximal vertical jumps to measure immediate post-fatigue maximal vertical jump. Participants were then asked to complete the round of body weight exercises they completed during the fatigue protocol (i.e. maximal countermovement vertical jumps, lunges, mountain climbers, and squats to parallel). Then, participants completed the same counterbalanced landings tasks as they did prior to completing the fatigue protocol. Between each landing task, participants were asked to complete the set of body weight exercises to ensure they remained fatigued through the post-fatigue data collection. Finally, after the last landing task was collected, one final set of three maximal vertical jumps were recorded to measure if

participants maintained a level of fatigue throughout the post-fatigue data collection. The same set of anatomical markers as described above were placed back on the participant, and finally, a post-fatigue three-second standing static trial was collected.

Data Analysis

Visual3D biomechanical software (v6.0, C-Motion, Germantown, MD, USA) was used to process and analyze three-dimensional hip, knee, and ankle joint kinematic and kinetic variables. Raw marker coordinate and ground reaction force data were filtered using a fourth-order, zero lag, Butterworth low-pass filter with a cut-off frequency of 12 Hz (36, 314, 348). Right-handed Cartesian segmental coordinate systems (x-y-z) were used for three-dimensional angular computations where x represents the medial-lateral axis, y represents the anterior-posterior axis, and z represents the longitudinal axis. Hip joint centers were determined at 25% of the distance from ipsilateral to contralateral greater trochanter markers (349). Knee joint centers were determined using the midpoint between femoral epicondyle markers (350), and ankle joint centers were determined using the midpoint between ipsilateral medial and lateral malleoli markers (351).Three-dimensional joint kinetics were calculated using standard inverse dynamics techniques and expressed as internal moments in the joint coordinate system (352). Body segment parameters were estimated from Dempster and Hanavan (353, 354). Joint moments were normalized to body mass. Stance phase was defined as the time from initial contact to toe-off which were identified using a vertical ground reaction force threshold of 10 N. Data from the right leg of the healthy controls were analyzed as all healthy controls identified as right-leg dominant while data from the ACL-reconstructed leg of the ACL-R females were analyzed. Jump height during the pre-fatigue and post-fatigue data collections in the lab were calculated

using the impulse-momentum relationship. Jump height during the fatigue protocol in the gym was calculated using a simple jump-and-reach test.

Statistical Analyses

Independent unpaired t-tests were used to calculate differences in healthy control and ACL-R descriptives as well as fatigue protocol characteristics. Differences in 3D hip, knee, and ankle joint angles and moments across the entire stance phase between healthy control and ACL-R during the two fatigue conditions were examined via one-dimensional statistical non-parametric mapping (SnPM{f}) 2 × 2 ANOVAs (group × fatigue) using Random Field Theory to correct for Type I error inflation (355, 356). MATLAB R2020a (MATLAB, MathWorks, Natick, MA, USA) was used to implement the SnPM{f} tests using the source code (http://www.spm1d.org) made available by Pataky et al. (356) Group main effects, fatigue main effects, and interactions were shown to be significant when SnPM{f} trajectory crossed the critical threshold boundary. If differences were found, the mean difference of the significant supra-threshold clusters were calculated. If a group × fatigue interaction was found, *post-hoc* SnPM *t*-tests (SnPM{t}) were conducted on each pairwise comparison separately. Significance for all tests was *a priori* set at $p < 0.05$.

Results

Participant Descriptive and Fatigue Protocol Characteristics

There were no significant differences found in age, height, mass, LEFS, IKDC, KOOS, or the TSK-11 between healthy control and ACL-R females (Table 1). There were also no significant differences found in pre-fatigue jump height, post-fatigue jump height, post-collection jump height, rounds completed, end HR, end RPE, or total time between healthy controls and ACL-R female (Table 2).

Group Differences

Hip flexion, abduction, and rotation angles were found to be significant between healthy control and ACL-R females during the anticipated cutting tasks, regardless of fatigue level (Figure 3; Table 3). Hip flexion was 15.7° degrees greater in the ACL-R group from 10 to 87% of stance phase compared to the healthy control group (p-value < 0.001). The ACL-R group also demonstrated greater hip abduction during 75 to 100% of stance phase compared to the healthy control group (mean difference: 9.3°; p-value < 0.001). Finally, the healthy control group had a mean difference of 8.7° less of hip internal rotation compared to the ACL-R group from 25 to 42% of stance phase (p-value < 0.001). There were no statistically significant group main effects found for hip moments, as well as knee or ankle angles and moments.

Fatigue Differences

Hip flexion and knee abduction angles, as well as hip rotation moment significantly differed between pre- and post-fatigue during the anticipated cutting trials, regardless of group (Figure 3 & 4; Table 4). Hip flexion decreased 3.7° from 99 to 100% of stance phase from pre-fatigue to post-fatigue (p-value < 0.001). Post-fatigue, participants experienced 0.7° more knee abduction compared to pre-fatigue from 76 to 79% of stance phase (p-value < 0.001). Finally, participants demonstrated a mean difference of 0.02 $Nm \cdot kg^{-1}$ of hip internal rotation during 53 to 70% of stance phase (p-value < 0.001). No other statistically significant group main effects were found for hip, knee, and ankle angles and moments.

Group x Fatigue Interaction

A group × fatigue interaction was identified for hip flexion, knee abduction, and ankle plantarflexion angles, as well as hip rotation moment. *Post-hoc* SnPM{t} showed that ACL-R participants had 18.7° greater hip flexion from 23 to 79% of stance phase compare to healthy

participants pre-fatigue (Healthy control pre-fatigue: 9.5° ± 7.3°; ACL-R pre-fatigue: 28.3° ± 7.7°; *p*-value = 0.009; Figure 5). Post-fatigue, hip flexion was also 15.3° greater in the ACL-R group compared to the healthy control group from 62 to 79% of stance phase (Healthy post-fatigue: 0.8° ± 3.6°; ACL-R post-fatigue: 16.1° ± 5.6°; *p*-value = 0.015; Chapter 3). Even though a significant interaction were found for knee abduction and plantarflexion angles, *post-hoc* analyses were not significant.

Discussion

The purpose of this study was to investigate the influence muscular fatigue may have on lower extremity mechanics in healthy and ACL-R females. We hypothesized that healthy control and ACL-R females would demonstrate different hip, knee, and ankle mechanics, regardless of fatigue. It was also hypothesized that fatigue would influence hip, knee, and ankle mechanics, regardless of previous surgical intervention. Finally, it was hypothesized that there would be an interaction between fatigue and previous surgical intervention.

In the present study, our first hypothesis was partially supported in that 3D hip kinematics were found to be different between the healthy control and the ACL-R females. However, there were no significant differences in knee or ankle kinematics or kinetics, as well as hip kinetics, found between the two groups. ACL-R females exhibited increased hip flexion throughout most of the stance phase (10 – 87% of stance; Table 3) compared to the healthy control group. This is similar to previous research that have studied ACL-R females completing landing and cutting tasks (46, 255). Clarke et al. (255) suggests this increased hip flexion in ACL-R females originates from deficits in trunk control. Deficits in neuromuscular control of the trunk has been associated as a predictor of knee and ACL injuries in females (357). Therefore, our results indicate that ACL-R females may be at an increased risk of ACL re-injury due to poor

control of their trunk. ACL-R females also had greater hip abduction (75 – 100% stance phase) compared to the healthy control group. Interestingly, ACL-R females exhibited 4.5° ± 0.2 of hip internal rotation, while the healthy controls exhibited approximately the same magnitude of hip external rotation (-4.2° ± 0.3) from 25 to 42% of stance phase. The combination of increased hip flexion and abduction angles as well as increased hip flexion and internal rotation angles without significant changes in knee and ankle kinematics and kinetics indicates potential compensatory mechanisms at the hip in order to maintain knee stability during a box-land-and-cut task in ACL-R females. Further investigation into trunk and hip mechanics and their relationship to ACL-reconstruction is warranted.

Our second hypothesis was also supported in that hip flexion and knee abduction angles, as well as hip rotation moment were significant between pre- and post-fatigue. However, no other hip, knee, or ankle kinematics or kinetics were found to be significant. Post-fatigue, females experienced an increase in hip flexion (99 – 100% stance phase) and knee abduction (76 – 79% stance phase) angles, as an increase in hip internal rotation moment (53 – 70% stance phase; Table 3). Even though fatigue influenced hip flexion, the significance was found during the last two percent of stance phase, indicating this finding may not be meaningful in fatigue's influence on hip flexion. Increased knee abduction angle in females post-fatigue is consistent with previous cutting research (38). Increased knee abduction angle is commonly associated with increased ACL injury risk (114, 166). However, Collins et al. (38) reported an increase in post-fatigue peak knee abduction angle, which occurred approximately between 25 – 30% of stance phase. Our results indicate that fatigue did not influence knee abduction angle until 76 – 79% of stance phase. Fatigue also did not change knee adduction moment, a known ACL injury risk mechanism (8). Therefore, fatigue may not be heavily involved in increasing ACL injury risk by

influencing prime knee mechanics. Finally, increased hip internal rotation moment was found post-fatigue compared to pre-fatigue. It is plausible that the anticipatory nature of the box-land-and-cut task caused the body's predetermined motor program to adjust muscle activation patterns and coordination during the stance phase post-fatigue (163, 310). Previous research also indicates that the body changes optimal movement strategy to perform tasks pre- and post-fatigue (312). Thus, while fatigue did not influence hip rotation angle, it can still influence hip rotation moment. However, the mean difference of hip internal rotation moment between pre- and post-fatigue was 0.02 $Nm \cdot kg^{-1}$, thus questioning the meaningfulness of this result.

Finally, an unexpected interaction was found between group and fatigue. Hip flexion, knee abduction, and ankle plantarflexion angles as well as hip rotation moment were found to have significant interactions between group and fatigue. *Post-hoc* SnPM{t} revealed that ACL-R females had 18.7° more hip flexion pre-fatigue during 23 – 79% of stance phase and had 15.3° more hip flexion post-fatigue during 62 – 79% of stance phase compared to healthy controls. As discussed previously, ACL-R females may be prone to poor neuromuscular control of the trunk, thus increasing hip flexion and potentially risk of injury. This may be indicative to clinicians and coaches that muscular strength and endurance of the hip musculature is vital in rehabilitative and injury prevention protocols for ACL-R females. Regarding the other significant interactions, further investigation conducting the *post-hoc* SnPM{t} revealed that no interaction between group and fatigue existed for knee abduction and ankle plantarflexion angles as well as hip internal rotation moment.

There are limitations to this study that must be acknowledged. First, the study contains a small sample size. An *a priori* power analysis with an *alpha* of 0.05 a *beta* of 0.80, and effect size (*f*) of 0.40 was performed based on key kinematic and kinetic variables (34, 35, 47). The

analysis indicated that a minimum of 16 participants (eight per group) were sufficient to detect any statistical differences. Due to the COVID-19 pandemic, we were not able to complete data collections that would have allowed us to meet the minimum participant number. We plan to add additional subjects to the current dataset to improve statistical power in the future.

Secondly, the fatigue protocol had to take place in a separate gym away from the testing laboratory. Consequently, participants had to run back to the laboratory after the fatigue protocol and had to stand still while the cluster markers were placed back on the participant for post-fatigue data collection. It is possible that participants received some recovery during this time. However, on average, the amount of time it took from the end of the fatigue protocol to the start of the post-fatigue data collection was approximately two minutes (Table 2). Participants were also asked to complete their fatigue protocol body weight exercises throughout the post-fatigue data collection to ensure they stayed fatigue until data collection was over. Our secondary criterion for fatigue (i.e. heart rate, RPE) also suggest that fatigue was met during the fatigue protocol.

Finally, the ACL-R females all had different surgeons that conducted their ACL-reconstruction, as well has received rehabilitation from different physical therapists. Therefore, surgical techniques and rehabilitative protocols within the ACL-R females are different, thus potentially influencing their lower extremity mechanics. ACL-R females also had a variety of graft types. While research has shown that functional outcomes of different graft types are similar after one year post-surgery (237), mechanical differences may still exist within the ACL-R group. Lastly, the small, uneven sample sizes of the healthy control and ACL-R groups may have prevented the detection of differences in some variables observed in the study, thus

increasing Type II error. Further collections of healthy control and ACL-R females are needed to decrease Type II error and to increase statistical power in the current study.

Conclusion

The present study shows that ACL-reconstruction and fatigue is influential on specific hip and knee mechanics in recreationally active females. ACL-R female displayed altered hip mechanics that may place them at a higher risk of ACL re-injury, especially after muscular fatigue has been induced, compared to healthy controls. Previous research has stated that muscle activity of the quadriceps, hamstrings, and gluteal muscles are influenced by fatigue in studies that have observed fatigues influence in ACL-R individuals (65, 314). It is important to note that these two studies grouped ACL-R males and females together in their analyses. However, understanding muscular function is influenced by fatigue in healthy and ACL-R females would give more insight into the altered hip and knee mechanics found in this study. Studying muscular function in fatigued individuals may be difficult. Therefore, future research should utilize other techniques, such as musculoskeletal modeling to better understand how fatigue influences healthy and ACL-R females.

Tables and Figures

Table 1: Mean ± SD of participant descriptive characteristics.

Variable	Total (n = 11)	Healthy (n = 7)	ACL-R (n = 4)	*p*-value
Age (yrs)	22.5 ± 2.4	23.0 ± 2.6	21.8 ± 2.1	0.205
Height (cm)	166.9 ± 5.8	165.9 ± 5.7	168.8 ± 6.3	0.238
Mass (kg)	68.5 ± 6.0	69.2 ± 6.9	67.3 ± 4.8	0.311
LEFS	79 ± 3	79 ± 2	78 ± 4	0.352
IKDC	84 ± 5	86 ± 1	81 ± 8	0.137
KOOS	97 ± 6	99 ± 2	94 ± 9	0.177
TSK-11	14 ± 3	14 ± 4	16 ± 3	0.164
Time Since Surgery (mo)	-	-	48 ± 14	-

p-value represents the comparison between Healthy and ACL-R.

Table 2: Mean ± SD of fatigue protocol characteristics.

Variable	Total (n = 11)	Healthy (n = 7)	ACL-R (n = 4)	*p*-value
Pre-Fatigue JH (m)	0.25 ± 0.04	0.24 ± 0.05	0.26 ± 0.02	0.557
Post-Fatigue JH (m)	0.22 ± 0.07	0.21 ± 0.07	0.23 ± 0.05	0.640
Post-Collection JH (m)	0.21 ± 0.06	0.21 ± 0.07	0.23 ± 0.05	0.651
Rounds Completed	7 ± 4	8 ± 5	6 ± 1	0.095
End HR (BPM)	188 ± 10	184 ± 10	195 ± 9	0.061
End RPE	19 ± 1	19 ± 2	19 ± 1	0.194
Total Time (MM:SS)	1:56 ± 0:31	2:00 ± 0:40	1:51 ± 0:03	0.352

p-value represents the comparison between Healthy and ACL-R. Total Time represents the time from the end of the fatigue protocol to the start of the post-fatigue data collections. JH represents jump height. HR represents heart rate. RPE represents rate of perceived exertion. MM:SS represents the time in minutes:seconds.

Table 3: Significant group main effects supra-threshold cluster ranges, supra-threshold cluster means ± standard deviation, and supra-threshold cluster specific p-values for the lower extremity joint kinematics.

		Range	Healthy	ACL-R	*p*-value
Joint Kinematics	Hip Flexion (°)	10 – 87%	9.5 ± 9.6	25.2 ± 10.7	< **0.001**
	Hip Abduction (°)	75 – 100%	-8.0 ± 1.3	-17.2 ± 1.5	< **0.001**
	Hip Rotation (°)	25 – 42%	-4.2 ± 0.3	4.5 ± 0.2	< **0.001**

p-value represents the cluster-specific value between Healthy and ACL-R groups. Range represents the percent of stance phase when the supra-threshold cluster was beyond the critical threshold line.

Table 4: Significant fatigue main effects supra-threshold cluster ranges, supra-threshold cluster means ± standard deviation, and supra-threshold cluster specific p-values for the lower extremity joint kinematics and kinetics.

		Range	Pre-Fatigue	Post-Fatigue	*p*-value
Joint Kinematics	Hip Flexion (°)	99 – 100%	-19.7 ± 0.3	-15.9 ± 0.4	< **0.001**
	Knee Abduction (°)	76 – 79%	-4.6 ± 0.1	-5.3 ± 0.2	< **0.001**
Joint Kinetics	Hip Rotation ($Nm \cdot kg^{-1}$)	53 – 70%	0.1 ± 0.0	0.1 ± 0.0	< **0.001**

p-value represents the cluster-specific value between the Pre-Fatigue and Post-Fatigue groups. Range represents the percent of stance phase when the supra-threshold cluster was beyond the critical threshold line.

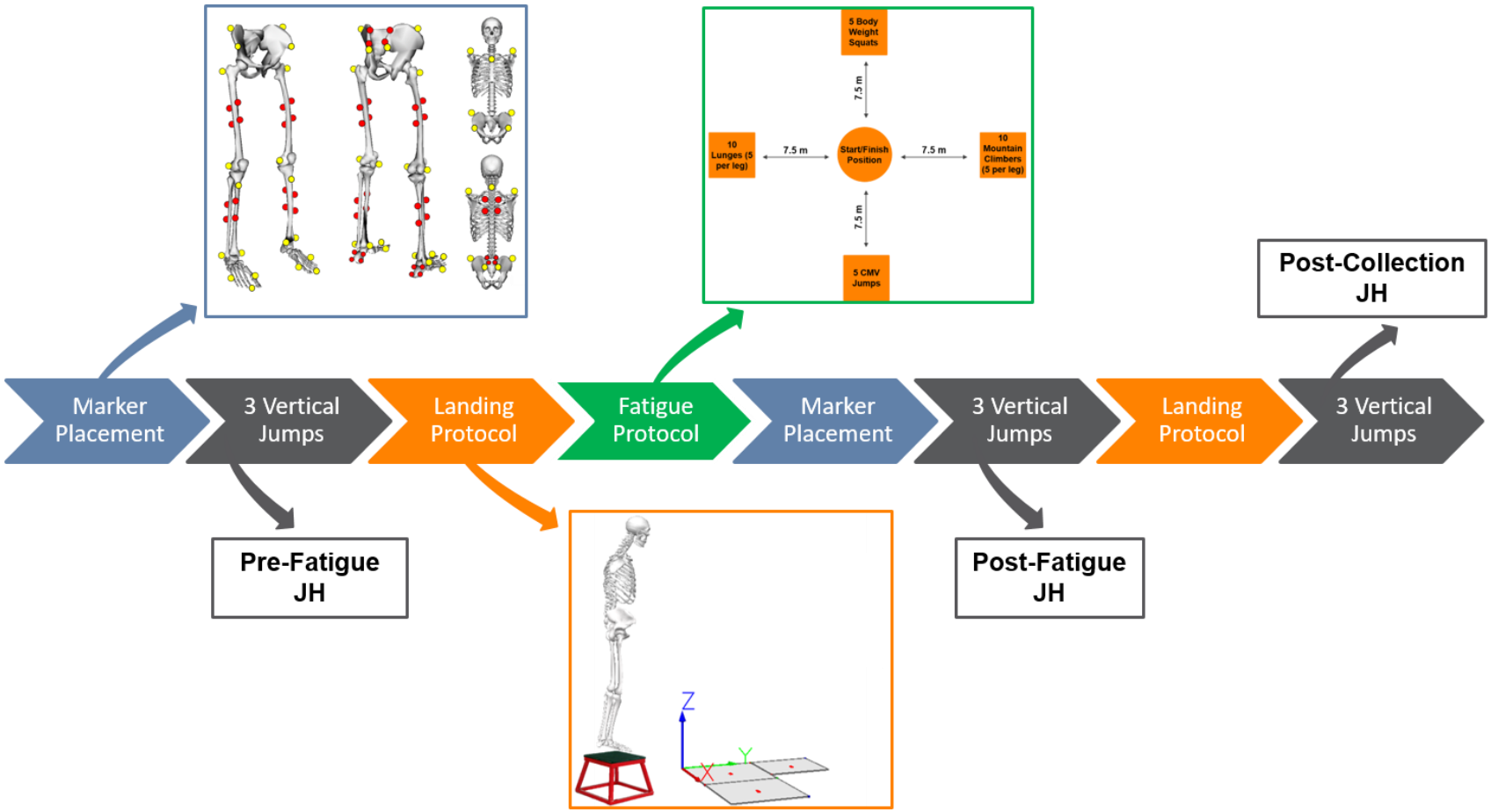

Figure 1: Visual representation of the Day 2 data collection protocol.

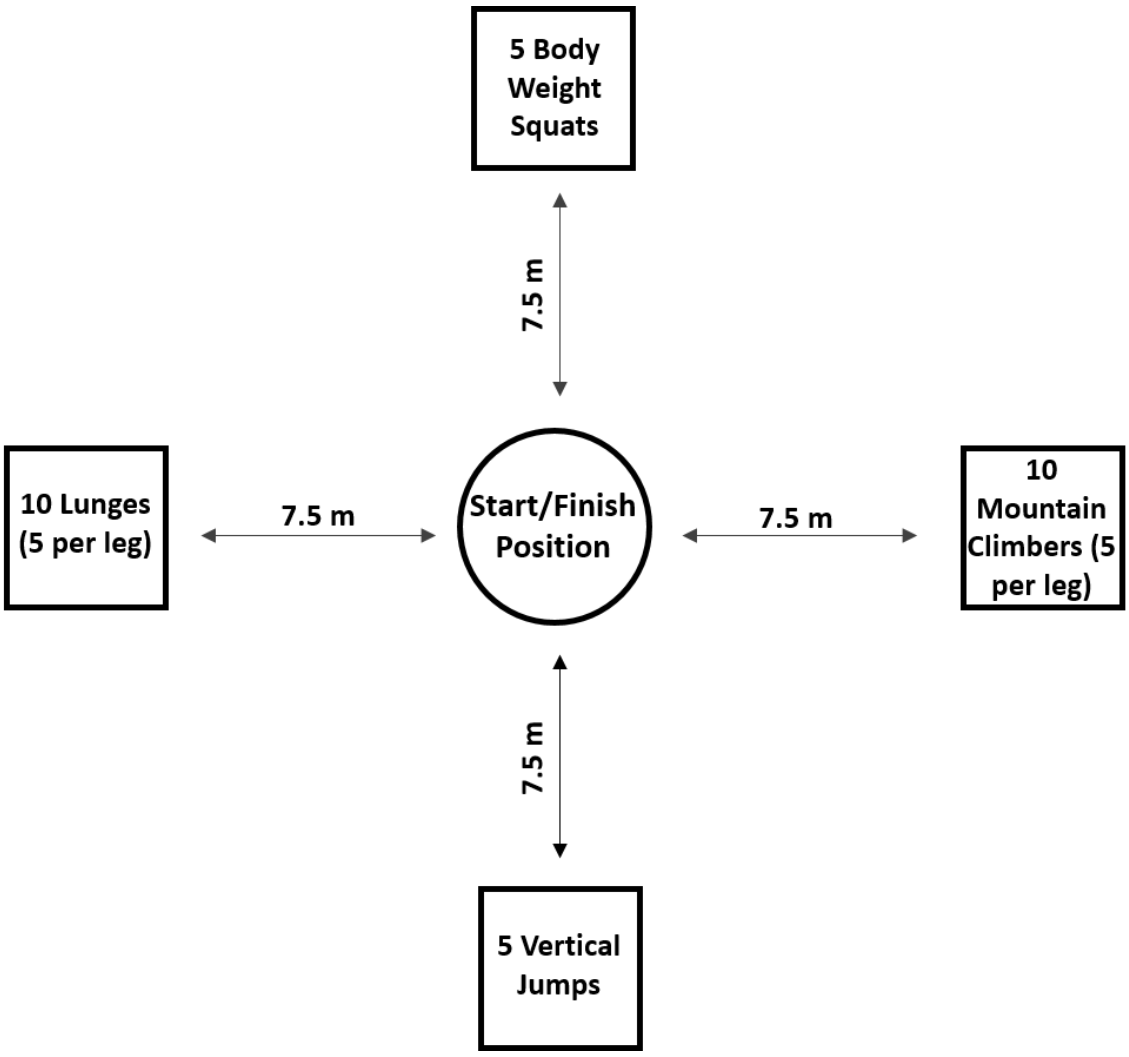

Figure 2: Visual representation of the modified fatigue protocol.

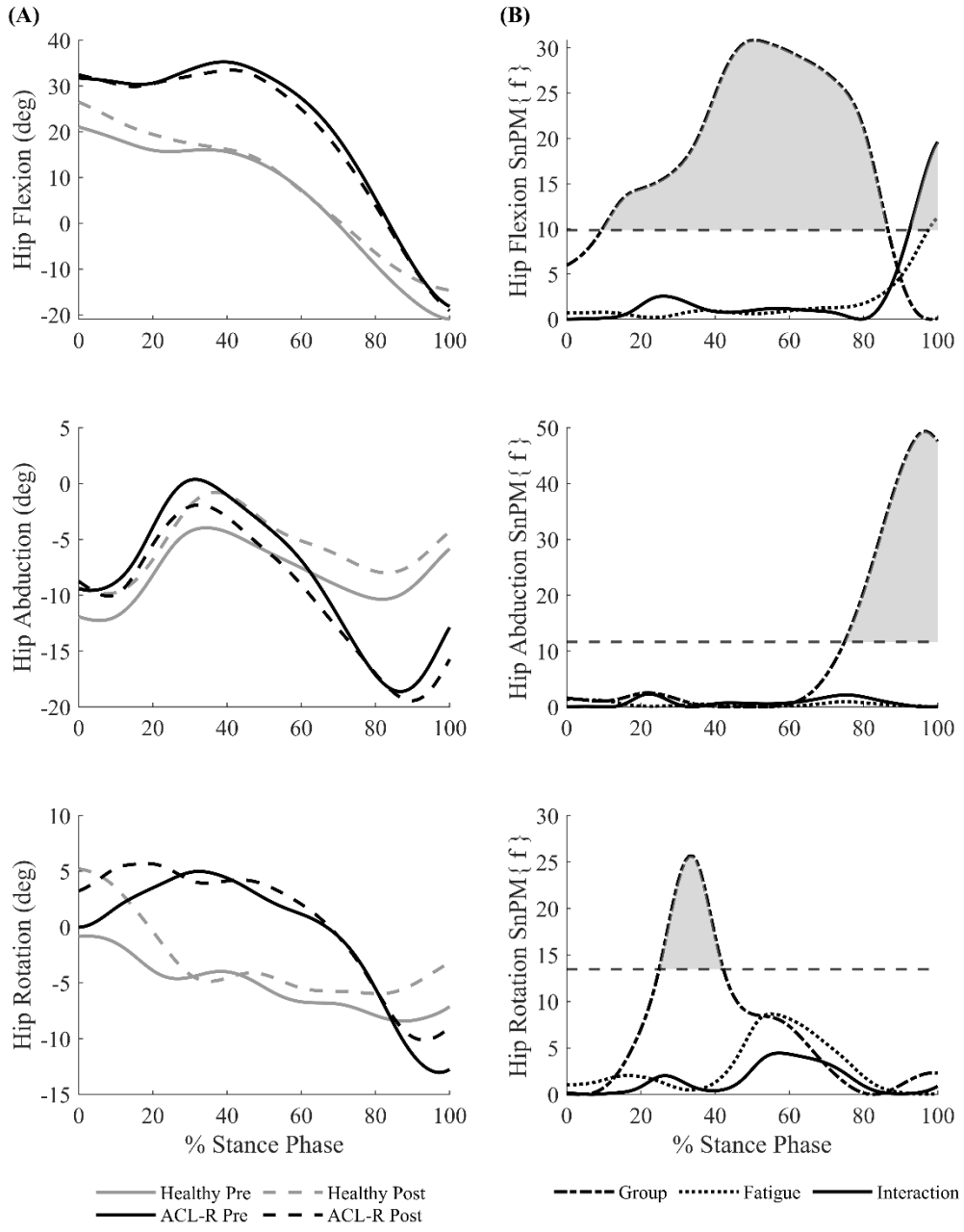

Figure 3: Mean ensemble curves for significant hip kinematic variables (A) and their respective SnPM{f} outputs (B) from 0 to 100% of stance phase. The dashed horizontal line on the SnPM{f} outputs indicates the critical threshold boundary. The grey, shaded regions indicates the significant supra-threshold clusters representing statistically significant differences.

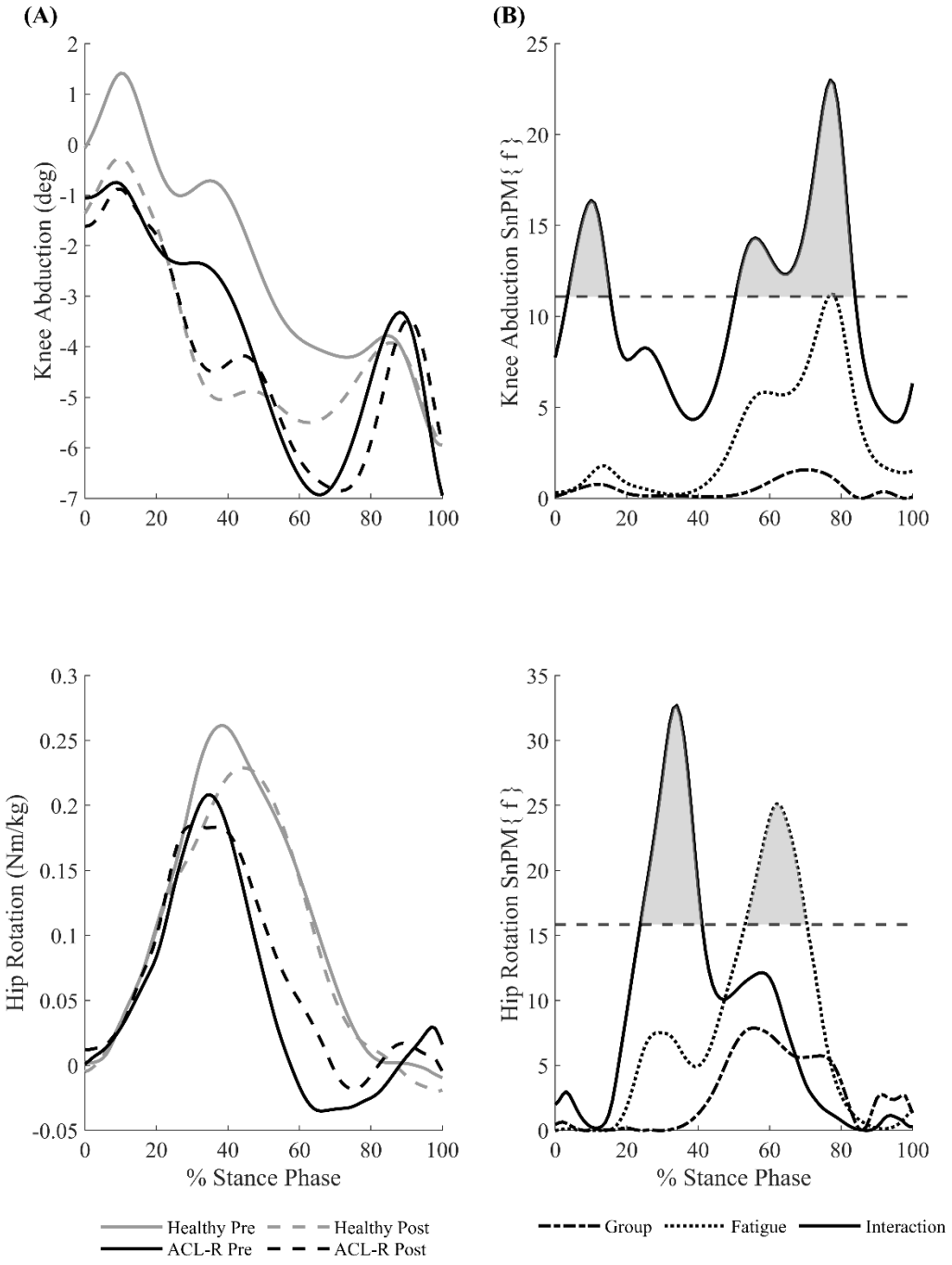

Figure 4: Mean ensemble curves for significant hip and knee kinematic and kinetic variables (A) and their respective SnPM{f} outputs (B) from 0 to 100% of stance phase. The dashed horizontal line on the SnPM{f} outputs indicates the critical threshold boundary. The grey, shaded regions indicates the significant supra-threshold clusters representing statistically significant differences.

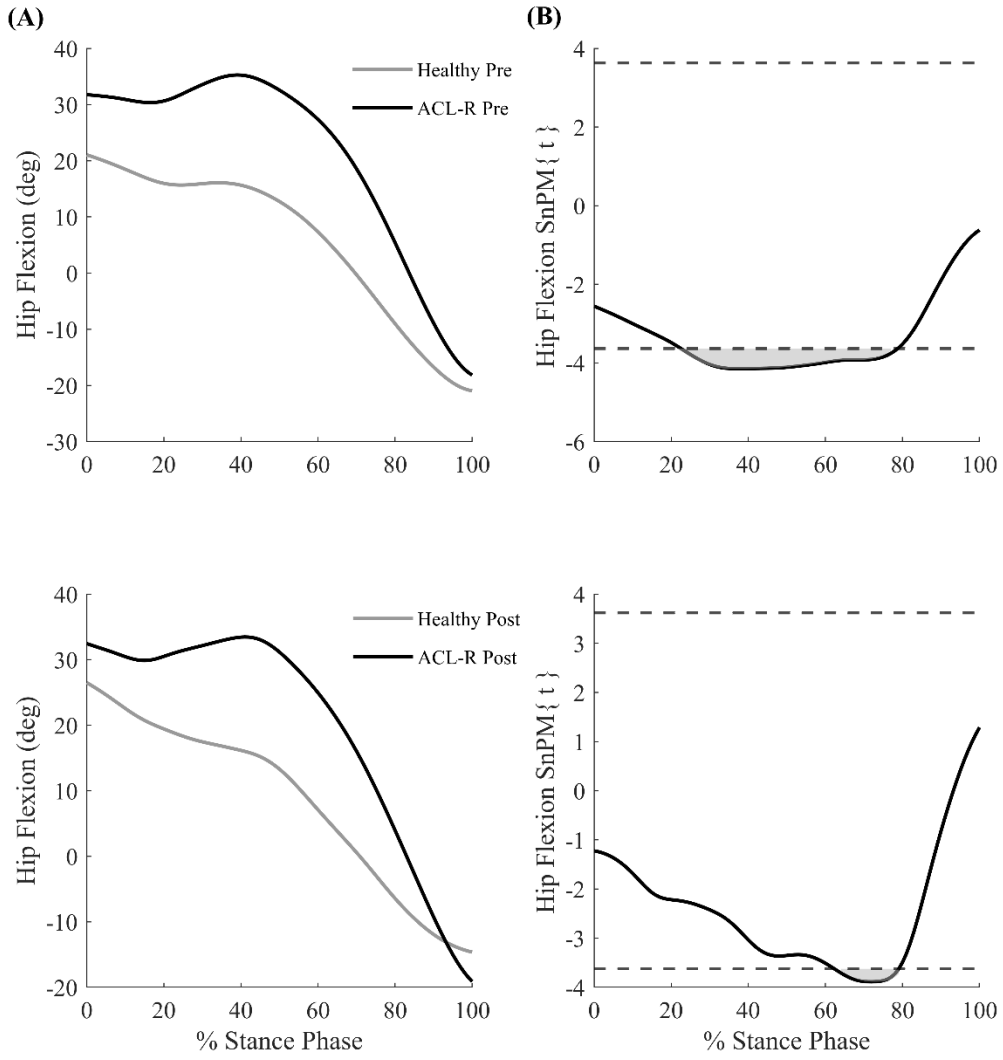

Figure 5: Mean ensemble curves for healthy and ACL-R hip flexion angles pre-fatigue and post-fatigue (A) with their respective SnPM{t} output from 0 to 100% of stance phase. The solid black line on the SnPM {t} represents the frequentist inference. The dashed horizontal lines on the SnPM{t} output indicates the critical threshold boundary. The grey, shaded region indicates the significant supra-threshold cluster representing a statistically significant difference.

Chapter 4: Fatigue's Effects on Overall ACL Loading in Healthy and ACL-Reconstructed Females

Abstract

Females are 16 times greater to sustain a second ACL injury compared to their healthy female counterparts. Many of these females return to play their respective sport after ACL-R. However, one variable hypothesized to be associated with injury that cannot be avoided is muscular fatigue. Previous studies have shown that fatigue and ACL-R can independently influence F_{ACL}. Little is known about the influence fatigue has on lower extremity mechanics of ACL-R females. However, no study thus far has observed from a musculoskeletal modeling perspective of how F_{ACL} would be influenced by fatigue concomitantly with ACL-R in recreationally active females. The purpose of this study was to investigate how F_{ACL} would be impacted before and after whole-body fatigue protocol in healthy and ACL-R females. Seven healthy and four ACL-R recreationally active males and females completed five anticipated box-land-and-cut trials to the right pre- and post- a fatigue protocol. Lower extremity kinematics and kinetics were collected with three-dimensional motion capture and force plates. A modified musculoskeletal model was scaled based on participant-specific anthropometrics, and muscle forces were obtained using static optimization. A previously established mathematical ACL loading model was used to calculate overall F_{ACL}. One-dimensional statistical non-parametric mapping were used to assess changes in F_{ACL} between healthy and ACL-R females over the entire stance phase pre- and post-fatigue. There were no significant differences in F_{ACL} due to groups, fatigue, or an interaction between the two. The lack of significance is most likely due to minimal changes in lower extremity kinematic and kinetics.

Introduction

Anterior cruciate ligament (ACL) injuries are extremely prevalent, costly, and often result in long-term consequences, such as early onset knee osteoarthritis. Approximately 200,000 ACL injuries occur every year, with 70% of these injuries considered non-contact ACL injuries (1). Epidemiologic research has shown that 100,000 to 150,000 of all ACL injuries occurring each year will undergo reconstructive surgery (13), with the primary goal of returning individuals back to an active lifestyle by regaining knee stability (17). For several individuals, this means returning to sport as many ACL injuries occur in young, athletic populations. Up to 83% of ACL-reconstructed (ACL-R) athletes return to their pre-injury sport (32), however 10 to 30% of athletes who do return to sport after an ACL reconstruction will sustain a secondary ACL injury (26-28, 30). Unfortunately, females are 16 times more likely to experience a secondary ACL injury after an initial ACL reconstruction compared to their healthy female counterparts (31). As such, great effort has been placed on understanding why this high rate of ACL re-injury exists, and why ACL-R females are placed at a higher risk than healthy females.

Re-injury of the ACL-R leg after return to sport is multifactorial, with factors including altered lower extremity mechanics (61, 62, 69, 255), increased joint variability (23, 24), and altered muscle activity (19, 251, 268). However, other lesser understood factors, such as fatigue, could play a noteworthy role in ACL-R re-injury. Few studies have observed the effects fatigue has on healthy females during tasks such as landing and cutting (34, 35, 38, 41, 43, 44). Healthy females demonstrated mechanics that reflect those commonly observed during medial knee collapse following a fatigue protocol (174), a strong characteristic of high-risk non-contact ACL injury movement patterns (341). Very few studies have observed fatigue affects in ACL-R females. However, the two studies that have compared ACL-R females to a healthy control

group pre- and post- a fatigue protocol have reported decreased initial contact hip flexion angle as well as increased peak knee abduction angle, (46, 47), both which have been associated with ACL injury.

Through the work of previous cadaveric research, it is known that lower extremity mechanics related to medial knee collapse (i.e. increased knee abduction angle, increased knee rotation, increased knee adduction moment, etc.) also increase overall ACL loading (F_{ACL}) (110). However, cadaveric research cannot describe what influences F_{ACL} in real world applications. Musculoskeletal modeling provides a way to estimate biomechanical parameters, such as ACL force, that are often difficult to measure *in vivo* during athletic movements. Several studies have utilized musculoskeletal modeling via OpenSim to determine ACL loading (52-54, 71, 109, 204, 358). Weinhandl, Earl-Boehm, Ebersole, Huddleston, Armstrong and O'Connor (53) investigated F_{ACL} during anticipated 45° cutting tasks in healthy females before and after a hamstring fatigue protocol. By acutely reducing hamstring strength by 25% using an isokinetic dynamometer, Weinhandl, Earl-Boehm, Ebersole, Huddleston, Armstrong and O'Connor (53) found that F_{ACL} loading increased by 36%, which was mostly attributed an increase in sagittal plane loading. Yet, it is currently unknown how a more whole-body fatiguing protocol that would reflect more accurately game-like fatigue would influence F_{ACL}. Conversely, Samaan, Ringleb, Bawab, Greska and Weinhandl (71) conducted a case study involving a female collegiate soccer player and investigated F_{ACL} before and after ACL-R and reported 56% higher increase in F_{ACL} in the surgical knee after ACL-R compared to before surgery. Both fatigue and ACL-R independently affected F_{ACL} in these two studies. However, no study thus far has observed from a musculoskeletal modeling perspective how F_{ACL} would be influenced by fatigue concomitantly with ACL-R in recreationally active females.

Therefore, the purpose of this study was to investigate how F_{ACL} would be impacted before and after whole-body fatigue protocol in healthy and ACL-R females. Because we are using non-directional statistical non-parametric mapping analyses, it was hypothesized that surgical intervention would influence F_{ACL}, regardless of fatigue. It was also hypothesized that fatigue would influence F_{ACL}, regardless of previous surgical intervention. Finally, it was hypothesized that there would be an interaction between fatigue and previous surgical intervention.

Methods and Materials

Participants

Prior to data collection, experimental procedures received ethical approval from the university's Institutional Review Board. Eleven (seven healthy controls, four ACL-R) recreationally active females between 18 and 35 years volunteered for the study (Chapter 3 Appendix Table 1). Inclusion criteria for both the healthy control and the ACL-R groups included being recreationally active at least 3 days per week for a minimum of 30 minutes per session, with one session being a dynamic training session, no lower extremity pain on the day, and no history of lower extremity injury within six months prior to testing. Specific inclusion criteria for the healthy control group included no history of lower back or lower extremity surgery, while specific inclusion criteria for the ACL-R group included being a minimum of one year post ACL reconstruction, no history of multi-ligament knee surgeries, active meniscal symptoms, or bilateral knee surgery (57). There was no restriction on graft type or history of meniscal repair at the time of ACL reconstruction (26, 61, 69), and all ACL-R females were cleared to return to full sport participation by their physician. All ACL reconstructions performed on the ACL-R females were autografts. Two ACL-R females had patella tendon grafts, while the

other two ACL-R females had a semitendinosus-gracilis tendon graft and a quadriceps tendon graft, respectively.

Data collection consisted of two testing days, with a minimum of three days' separation between the two testing days. A full description of the Day 1 and Day 2 testing sessions can be found in Chapter 3. Briefly, Day 1 consisted of participants providing written informed consent, as well as complete a variety of health history questionnaires. Participants then completed an ankle dorsiflexion range of motion assessment, a knee joint laxity assessment, a balance assessment, and a strength assessment of the lower extremity musculature.

On Day 2, participants were asked to wear an athletic t-shirt, spandex shorts, and provided a standard laboratory shoe (Nike Pegasus, Nike Inc., Beaverton, OR, USA) to wear during testing. Participant height and weight were collected, and then participants completed a five-minute warm-up at a self-selected pace on a treadmill. Following the warm-up, a heart rate sensor was secured to the participant's chest (Polar T31 Heart Rate Sensor, Polar Electro Inc., Bethpage, NY, USA) and a heart rate monitor (Polar FT1 Heart Rate Monitor, Polar Electro Inc., Bethpage, NY, USA) was worn on the participant's wrist. Then 27 anatomical, retro-reflective markers were placed on specific anatomical landmarks of the neck, trunk, pelvis, and bilaterally on the legs and feet (Figure 1). Clusters of four non-collinear markers on rigid thermoplastic shells were attached to the trunk, pelvis, and bilaterally on the thighs, shanks, and heels. A pre-fatigue three-second standing static calibration trail was recorded, and then the anatomical markers were removed.

After the anatomical markers were removed, participants were asked to complete three maximal vertical jumps to measure pre-fatigue vertical jump height. Then, participants stood on top of a 30 cm box positioned half of the participant's body height away from the center of the

force plate and were asked to jump out towards the center of the force plate and complete three anticipated landing tasks. These landing tasks included: 1) landing unilaterally on the right foot and cutting 45° to the left, 2) landing unilaterally on the left foot and cutting 45° cut to the right, and 3) landing bilaterally and completing a vertical jump subsequent to the initial land. While three landing tasks were performed, the box-land-and-cuts to the right were analyzed for all controls as well as ACL-R females who had a reconstruction on the right knee. Box-land-and-cuts to the left were analyzed for two ACL-R females who had a reconstruction on the left knee. The landing tasks were counterbalanced, and five successful trials of each landing task were collected prior to the start of the fatigue protocol. After the pre-fatigue data collection trials are collected, the cluster markers were removed, and participants were brought into a gym where the fatigue protocol began.

Experimental Procedures

A complete description of the modified fatigue protocol can be found in Chapter 3 (Figure 2). In short, a maximal vertical jump-and-reach test against a wall was performed. Then, participants stood in the middle of four exercise stations, placed 7.5 m in front, behind, and to the left and right of the participant. Each exercise station consisted of four different body weight exercises. To start a round, participants were instructed to sprint towards a randomly assigned exercise station. The participant would sprint, backpedal, or side-shuffle to the respective exercise station, complete the exercise, and then return back to their starting positon. Once all four stations were completed, participants sprinted back to the wall to complete a maximal vertical jump-and reach, then were asked their heart rate and rate of perceived exertion. Participants received 60 s of rest before completing the next round. Participants completed as many rounds as possible until their

maximal vertical jump-and reach height decreased by 25% for two consecutive maximal vertical jumps.

Once maximal vertical jump-and-reach height was decreased by 25%, participants sprinted back to the laboratory, where cluster markers were placed back on the participant, and the participant completed three maximal vertical jumps to measure immediate post-fatigue maximal vertical jump. Participants were then asked to complete the round of body weight exercises they completed during the fatigue protocol. Then, participants completed the same counterbalanced landings tasks as they did prior to completing the fatigue protocol. Between each landing task, participants were asked to complete the set of body weight exercises to ensure they remained fatigued through the post-fatigue data collection. Finally, after the last landing task was collected, one final set of three maximal vertical jumps were recorded to measure if participants maintained a level of fatigue throughout the post-fatigue data collection. The same set of anatomical markers as described above were placed back on the participant, and finally, a post-fatigue three-second standing static trial was collected.

Data Analysis

For all trials, raw marker coordinate data were collected at 200 Hz with a 12-camera motion capture system (Vicon, Centennial, CO, USA) while GRF data were collected synchronously at 2000 Hz (AMTI, Inc., Watertown, MA). Raw marker coordinate and ground reaction force data were filtered using a fourth-order, zero lag, Butterworth low-pass filter with cut-off frequency of 12 Hz (36, 314, 348). Visual3D biomechanical software (C-Motion, Germantown, MD, USA) was used to create a kinematic model made of eight skeletal segments (trunk, pelvis, bilateral thighs, shanks, and feet) from the standing calibration trial. Segment coordinate systems were determined using a joint coordinate system approach (350). Hip joint

centers were determined at 25% of the distance from ipsilateral to contralateral greater trochanter markers (349). Knee joint centers were determined using the midpoint between femoral epicondyle markers (350), and ankle joint centers were determined using the midpoint between ipsilateral medial and lateral malleoli markers (351). Stance phase was defined as the time from initial contact to toe-off, both of which were identified using a vertical ground reaction force threshold of 10 N. Data from the right leg of the healthy controls were analyzed as all healthy controls identified as right-leg dominant while data from the ACL-reconstructed leg of the ACL-R females were analyzed. Jump height during the pre-fatigue and post-fatigue data collections in the lab were calculated using the impulse-momentum relationship. Jump height during the fatigue protocol in the gym was calculated using a simple jump-and-reach test.

Musculoskeletal Modeling

OpenSim (v3.2, http://simtk.org) was used to simulate the pre- and post-fatigue box-land-and-cut trials (48). A generic musculoskeletal model consisting of 14 segments and 23 degrees of freedom (*dof)* (359) was scaled to match each participant's anthropometry based on experimentally measured anatomical landmarks. Each hip was modeled as a 3-*dof* ball-and-socket joint. Each knee was modeled as a 1-*dof* hinge joint with abduction-adduction and internal-external rotations as well as anteroposterior and superior-inferior translations constrained to change as a function of knee flexion angle (360). The ankles were modeled as a 1-*dof* pin joint. Once the scaled model was obtained, an inverse kinematics algorithm was used to calculate joint angles by using the sum of weighted squared errors to minimize the error between the experimental data and the model (361). Inverse dynamics was used to obtain lower extremity joint moments, which were then decomposed into individual muscle forces via a static optimization algorithm. This was accomplished by minimizing the sum of muscle activations

squared (362). Anteroposterior knee joint reaction forces using the muscle forces obtained from static optimization were computed using the JointReaction Analysis in OpenSim (363). Finally, anteroposterior knee joint reaction force was used to estimate ACL loading (F_{ACL}) relative to the tibial coordinate system (54, 137, 358). ACL loading was based on cadaveric knee measurements and expressed as an exponential function of knee flexion angle (75, 330). Therefore, using the equation below, F_{ACL} was calculated as:

$$F_{ACL} = \frac{F_{100N}(\theta_{knee}) - F_{0N}(\theta_{knee})}{100N} \cdot F_{AP} + F_{0N}(\theta_{knee})$$

Where F_{ACL} was the overall ACL loading, F_{100N} is the ACL loading when 100 Newtons of anterior tibial force was applied respective to the knee flexion angle (θ_{knee}), F_{AP} was the anteroposterior knee joint reaction force, and F_{0N} is the ACL loading when there was no applied anterior tibial force respective to the θ_{knee}.

Statistical Analysis

Independent unpaired t-tests were used to calculate differences in healthy control and ACL-R descriptives as well as fatigue protocol characteristics. Differences in F_{ACL} across the entire stance phase between healthy control and ACL-R during the two fatigue conditions was examined via one-dimensional statistical non-parametric mapping (SnPM{f}) 2 × 2 ANOVAs (group × fatigue) using Random Field Theory to correct for Type I error inflation (355, 356). MATLAB R2020a (MATLAB, MathWorks, Natick, MA, USA) was used to implement the SnPM{f} tests using the source code (http://www.spm1d.org) made available by Pataky, Robinson and Vanrenterghem (356). Group main effect, fatigue main effect, and group × fatigue interaction were shown to be significant when SnPM{f}rajectory crossed the critical threshold boundary. If differences were found, the mean difference of the significant supra-threshold clusters were calculated. If a group × fatigue interaction was found, a *post-hoc* SnPM *t*-test

(SnPM{t}) was conducted on each pairwise comparison separately. Significance for all tests was *a priori* set at $p < 0.05$.

Results

Musculoskeletal Modeling Validation

Magnitudes of the reserve moments used by the model were below 5% of the maximum net joint moments, as recommended by Hicks, Uchida, Seth, Rajagopal and Delp (364). Qualitative analysis of our predicted activations during the pre-fatigue box-land-and-cuts for the seven healthy females were in agreement with previously collected experimental EMG activations during 45° run-and-cut in healthy females for the following muscles: gluteus maximus, gluteus medius, rectus femoris, vastus medialis, vastus lateralis, biceps femoris, medial hamstrings, lateral gastrocnemius, and medial gastrocnemius (Figure 6). For most muscles, the predicted activations followed the same patterns and fell within the standard deviation of the respective experimental activations. Differences between predictive and experimental activations in muscles such as the biceps femoris, medial hamstrings, and gluteus medius are most likely due to the differences in the tasks (box-land-and-cut versus a typical 45° cut off the right foot to the left). Qualitative analysis of the F_{ACL} curves (Figure 7) were in good agreement with previous studies that have used the same F_{ACL} mathematical model used in the current study (53, 54, 71, 358).

Participant Descriptive and Fatigue Protocol Characteristics

There were no significant differences found in age, height, mass, LEFS, IKDC, KOOS, or the TSK-11 between healthy control and ACL-R females (Table 1). There were also no significant differences found in pre-fatigue jump height, post-fatigue jump height, post-collection jump

height, rounds completed, end HR, end RPE, or total time between healthy controls and ACL-R female (Table 2).

F_{ACL} Differences

There was no statistically significant group main effect, fatigue main effect, or group × fatigue interaction found for F_{ACL} between healthy controls and ACL-R females pre- and post- a fatigue protocol (Figure 8).

Discussion

The purpose of this study was to investigate how F_{ACL} would be impacted before and after whole-body fatigue protocol in healthy and ACL-R females. We hypothesized that 1) surgical intervention would influence F_{ACL}, regardless of fatigue, 2) that fatigue would influence F_{ACL}, regardless of previous surgical intervention, and 3) that there would be an interaction between fatigue and previous surgical intervention. None of our hypotheses were supported as there were no statistically significant group main effects, fatigue main effects, or group × fatigue interactions found.

There was no difference in F_{ACL} between healthy and ACL-R females, despite prior work suggesting that ACL-R could significantly influence F_{ACL} (71). Samaan, Ringleb, Bawab, Greska and Weinhandl (71) reported in a case study that a collegiate female soccer player experienced a 56% increase in F_{ACL} during unanticipated cutting following an ACL-R compared to before surgical intervention. They found that most of this increase in F_{ACL} could be mostly attributed to an increase in frontal plane ACL loading, followed by transverse plane loading. The collegiate female soccer player in their study demonstrated an increase in knee adduction moment following ACL-R. The frontal plane ACL loading calculations used in that study requires knee adduction moment as an input. Therefore, the increased knee adduction moment seen after ACL-

R may increase frontal plane ACL loading, which lead to an overall increase in F_{ACL} (71). There was no change in knee adduction moment in either the healthy or ACL-R females. The only kinematic or kinetic changes observed between the two groups were at the hip (Table 3). It appears that the combination of increased hip flexion and abduction angles as well as increased hip flexion and internal rotation angles without significant changes in knee and ankle kinematics and kinetics indicates potential compensatory mechanisms at the hip in order to maintain knee stability during the box-land-and-cut task in ACL-R females. These compensatory changes at the hip in the ACL-R females could potentially keep F_{ACL} from being significantly different between the two groups.

Previous work has shown that isolated fatigue of the hamstrings increases F_{ACL} by 36% in healthy females (53). Weinhandl, Earl-Boehm, Ebersole, Huddleston, Armstrong and O'Connor (53) reported that after the hamstring fatigue protocol, females cut with decreased knee flexion angle compared to before the hamstring fatigue protocol. Decreases in knee flexion angle caused the hamstring line of action to become more axial with the tibia. This, coupled with the hamstrings reduced ability to provide a posteriorly directed shear force to counter the quadriceps anteriorly directed shear force, lead to the net increase in F_{ACL}. There were no differences in knee flexion angle pre- and post-fatigue in the healthy or ACL-R females in the current study (Chapter 3 Results). In fact, the only lower extremity mechanics that were influenced by fatigue were hip flexion and knee abduction angle, as well as hip rotation moment (Chapter 3). As discussed in Chapter 3, the meaningfulness of these changes in joint kinematics and their impact on ACL injury should be questioned. It is important to note that Weinhandl, Earl-Boehm, Ebersole, Huddleston, Armstrong and O'Connor (53) isolated the hamstrings and targeted them specifically to fatigue. During the current study, participants completed a general fatigue protocol that would

target whole-body fatigue. During repetitive tasks, such as what was utilized in the current study, individuals may compensate for muscle fatigue by reorganizing movement patterns of individual *dof* (322) to coordinate joint motions in a way to maintain performance when fatigued (365). Since many *dofs* were being utilized by the participants in this study, it is plausible that movement reorganization was a summation of very small changes at each *dof* (323), which would result in little to no change of overall lower extremity kinematics or kinetics. If whole-body fatigue does not result in large changes in lower extremity kinematics or kinetics, it is unlikely that it would have a major impact on overall F_{ACL}.

A number of limitations exist within the current study that must be acknowledged. First, the study contains a small sample size. An *a priori* power analysis with an *alpha* of 0.05 a *beta* of 0.80, and effect size (*f*) of 0.40 was performed based on key kinematic and kinetic variables (34, 35, 47). The analysis indicated that a minimum of 16 participants (eight per group) were sufficient to detect any statistical differences. The small, uneven sample sizes of the healthy control and ACL-R groups may have prevented the detection of differences in some variables observed in the study, thus increasing Type II error. Due to the COVID-19 pandemic, we were not able to complete data collections that would have allowed us to meet the minimum participant number. We plan to add additional subjects to the current dataset to improve statistical power in the future.

Second, static optimization was used to estimate muscle forces, and limitations with using static optimization should be considered, such as the inadequacy of its ability to predict co-contractions of the muscles. However, our predicted muscle activations adequately agree with previously collected anticipated running and cutting experimental electromyography data (Figure 6). While there may be slight differences in our predicted muscle activations compared to the

experimental electromyography data due to task differences, we are confident our simulations for this study are sufficient.

Finally, the ACL-R females all had different surgeons that conducted their ACL-reconstruction, as well has received rehabilitation from different physical therapists. Therefore, surgical techniques and rehabilitative protocols within the ACL-R females are different, thus potentially influencing their lower extremity mechanics, which would in turn influence their F_{ACL}. ACL-R females also had a variety of graft types. Research has shown that functional outcomes of different graft types are similar after one year post-surgery (237). However, it is currently unknown how different graft types may influence F_{ACL}.

Conclusion

The present study suggests that fatigue, ACL-R, or a combination of both may not be enough to influence F_{ACL}. Other studies suggest that fatigue and ACL-R independently can influence F_{ACL}. Differences in methodology and fatigue protocols, as well as small sample size most likely lead to the lack of significant differences in the current study. However, given the limitations to the study, future research should focus on increasing the sample size and improving data collection techniques to grasp a better understanding of how F_{ACL} is influenced by fatigue and prior ACL surgical intervention.

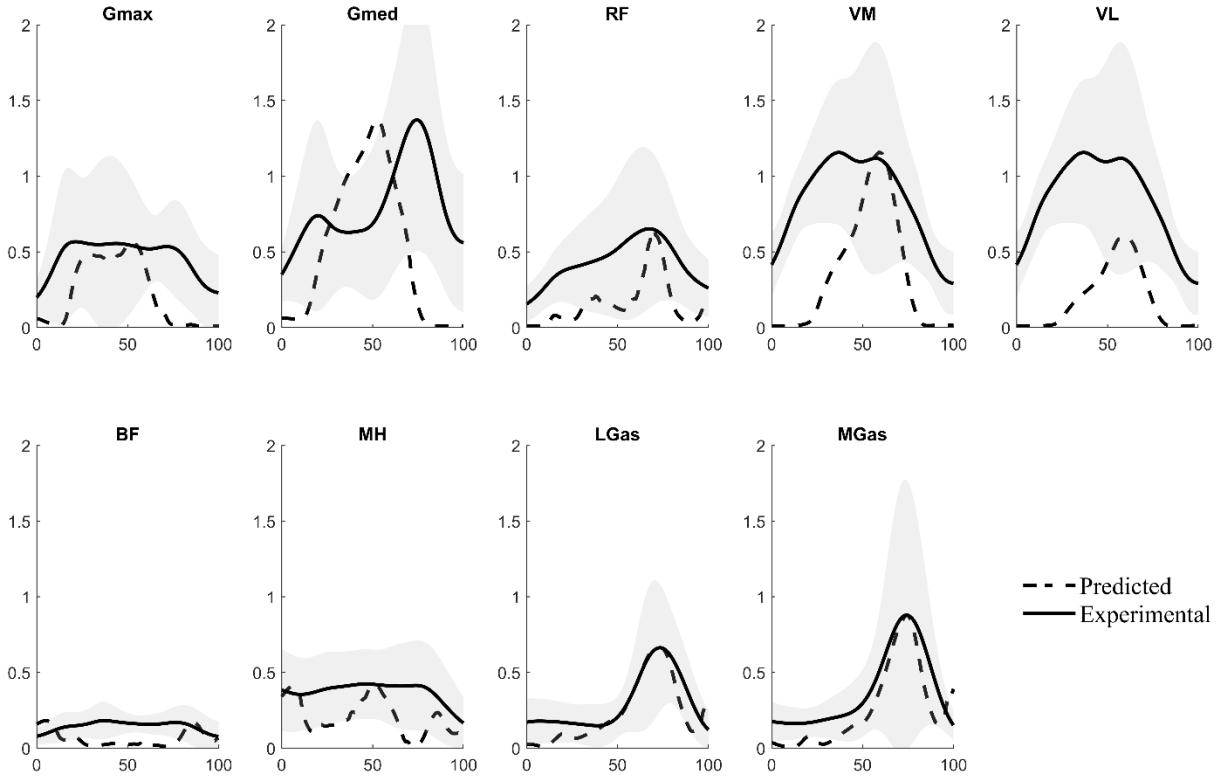

Figure 6: Comparison of previously collected experimental activations (solid black line) from a standard 45° cut and predicted (dashed black line) activations from the current study. Gray shaded region represents the standard deviation of the experimental activation. Gmax, gluteus maximus; Gmed, gluteus medius; RF, rectus femoris; VM, vastus medialis; VL, vastus lateralis; BF, biceps femoris; MH, medial hamstrings; LGas, lateral gastrocnemius; MGas, medial gastrocnemius.

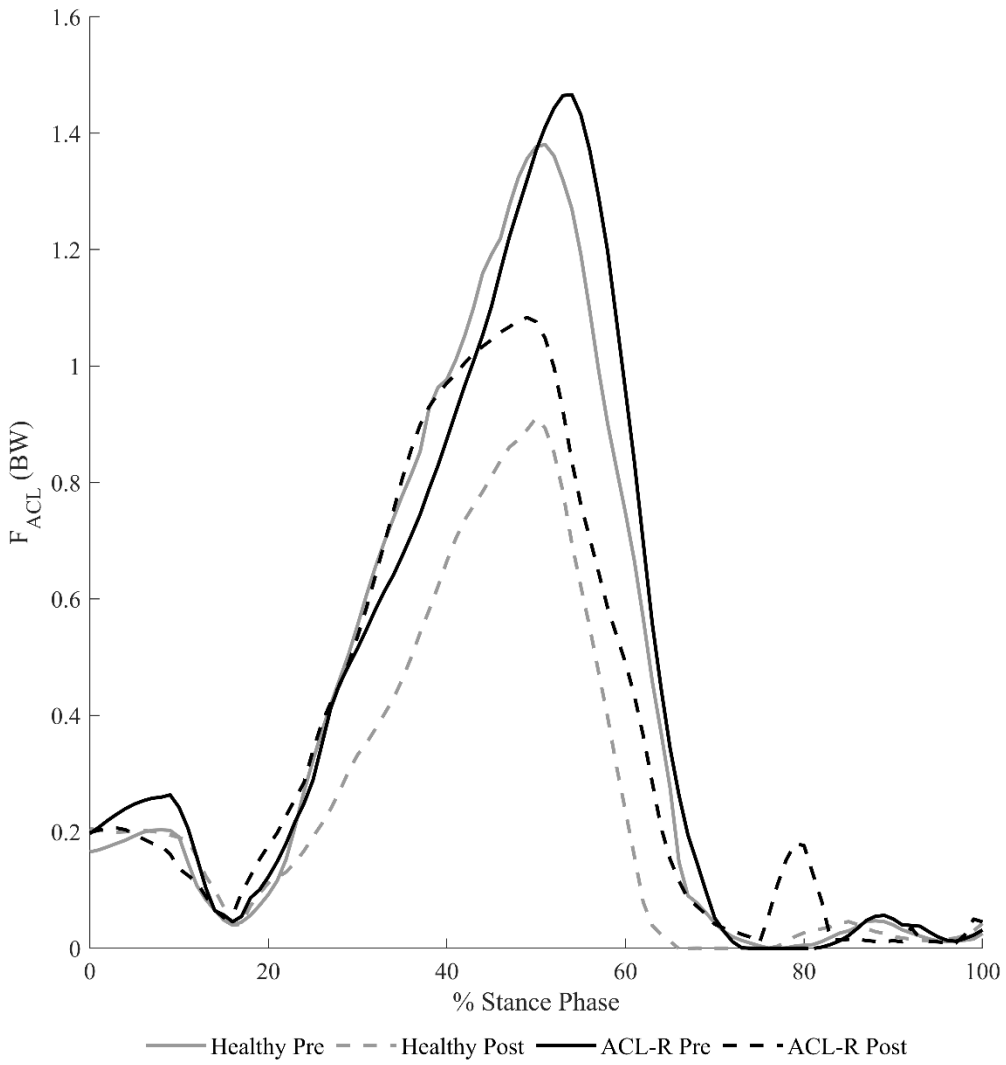

Figure 7: Mean ensemble curves for F_{ACL} from 0 to 100% of stance phase during the anticipated box-land-and-cuts pre- and post-fatigue.

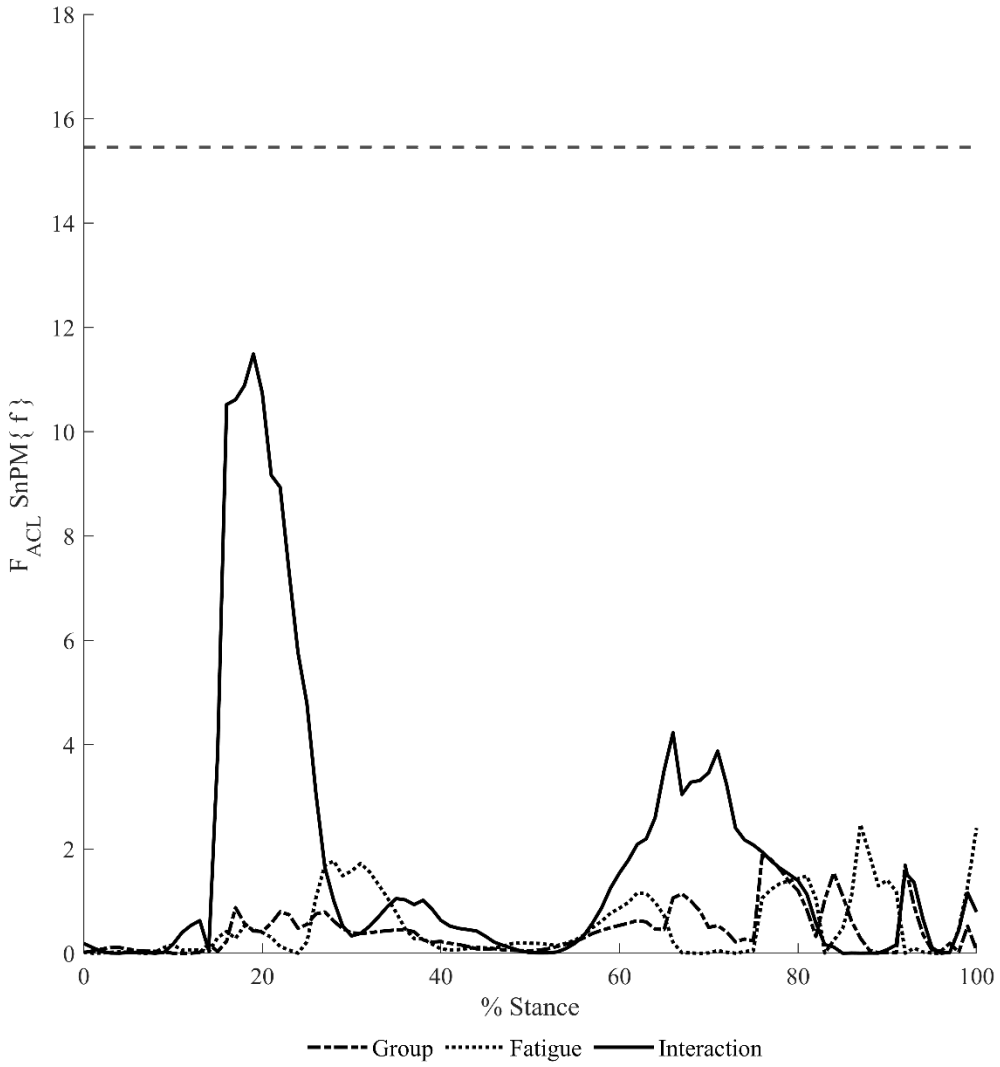

Figure 8: SnPM{f} output from 0 to 100% of stance phase during the anticipated box-land-and-cuts pre- and post-fatigue. The dashed horizontal line on the SPM{f} output indicates the critical threshold boundary.

Chapter 5: Fatigue's Effects on Individual Lower Extremity Muscle Contribution to ACL Loading in Healthy and ACL-Reconstructed Females

Abstract

Females are 16 times greater to sustain a second ACL injury compared to their healthy female counterparts. Many of these females return to play their respective sport after ACL-R. However, one variable hypothesized to be associated with injury that cannot be avoided is muscular fatigue. Previous studies have shown that fatigue and ACL-R can independently influence F_{ACL}. Little is known about the influence fatigue has on lower extremity mechanics of ACL-R females. However, no study thus far has observed from a musculoskeletal modeling perspective of how muscle contribution to F_{ACL} would be influenced by fatigue concomitantly with ACL-R in recreationally active females. The purpose of this study was to investigate how lower extremity muscle contribution to F_{ACL} would be impacted pre- and post- a fatigue protocol in healthy and ACL-R females. Seven healthy and four ACL-R recreationally active females completed five anticipated box-land-and-cutting trials pre- and post- a fatigue protocol. Lower extremity kinematics and kinetics were collected with three-dimensional motion capture and force plates. A modified musculoskeletal model was scaled based on participant-specific anthropometrics, and muscle forces were obtained using static optimization. A previously established mathematical ACL loading model was used to calculate as well as lower extremity muscle contribution to F_{ACL}. The semimembranosus, soleus, vastus lateralis, and tensor fasciae latae were found to be the largest contributors to F_{ACL}. Future ACL injury prevention and rehabilitation protocols may want to target these muscles specifically in efforts to reduce injury risk in healthy and ACL-R females.

Introduction

Approximately 100,000 and 150,000 of all anterior cruciate ligament (ACL) injuries will undergo reconstructive surgery to help individuals, such as athletes regain knee stability and return to their respective sport (13). While ACL-reconstruction (ACL-R) returns most athletes back to play, kinematic and kinetic changes to the reconstructed knee still exist compared to the contralateral knee or control knees. These include changes in knee joint kinematics and kinetics, decreased muscular strength, altered quadriceps and hamstring muscular activity, loss of proprioception, and changes in coordinative variability of the knee joint (18-25, 58). These altered mechanics are responsible for why up to 30% of these athletes will sustain a second ACL injury within 24 months of the original ACL injury (26). Unfortunately, females are 16 times more likely to experience a second ACL injury after the initial ACL-R compared to their healthy female counterparts. As such, great effort has been placed on decreasing this high re-injury rate.

Because up to 83% of ACL-R athletes return to their pre-injury sport (32), coaches and clinicians strive to implement rehabilitative programs that will put the athlete in the best position to avoid a secondary ACL injury. However, regardless if an athlete is healthy or ACL-R, muscular fatigue is one factor that cannot be avoided. Few studies exist that report the influence of fatigue on ACL-R females compared to a healthy control group (46, 47). These studies suggest that altered neuromuscular control potentially exists in ACL-R females after a fatigue protocol (46, 47). Therefore, it is plausible that lower extremity muscles may exhibit altered ACL loading patterns in a fatigued state for these two populations. Understanding specifically which muscles are most influential on ACL loading in healthy and ACL-R females may help clinicians, trainers, and coaches in preparing better ACL prevention and rehabilitation protocols

for their athletes, as well gain insight to how muscle contribution may change after ACL reconstruction.

It has been theorized that co-activation of the hamstrings and quadriceps help protect the ACL from injury during dynamic movements. Recruitment of the hamstrings help reduce ACL loading via counteracting excessive quadriceps force (9, 10). However, it is reasonable to assume that additional muscles beyond the quadriceps and hamstrings influence ACL loading. While muscles that cross the knee joint do, to various degrees, play a role in ACL loading, muscles that do not span the knee joint cannot be overlooked. It is known through dynamic coupling that an individual muscle can act to accelerate not only the joint it spans, but also other joints it has no direct relationship with (11, 331), which in turn would influence contributions to the ground reaction forces (GRF), joint reaction forces (JRF), and ultimately ACL loading. However, it is impossible to account for individual muscle contribution to ACL loading using traditional biomechanical data collection techniques.

Musculoskeletal modeling provides a way to estimate biomechanical parameters, such as individual muscle forces, joint contact forces, and ligamentous forces, such as ACL force, that are difficult to measure *in vivo* during athletic movements (48-50). Lower extremity muscle contributions to GRF have been investigated during walking (336, 337, 366-369), running (335, 339), and most recently unanticipated sidestep cutting (338). Previous work have also examined how individual muscles contribute to GRF, tibiofemoral contact forces, tibiofemoral shear force, and frontal and transverse knee moments in healthy individuals (12, 55, 56). All of these studies used an induced acceleration analysis approaches, which was developed to account for the dynamic coupling nature of the body and allow for computations of accelerations induced by individual muscles in the musculoskeletal model. Yet, no study thus far has described how

individual muscles contribute to overall ACL loading, and how those muscle contributions to ACL loading may be impacted by ACL-R or fatigue.

Therefore, the purpose of this study was to investigate how individual lower extremity muscles contribute to ACL loading in a pre-fatigued versus post-fatigue state in healthy and ACL-R females. Specifically, we used an induced acceleration approach in combination with previously established ACL load model to examine lower extremity muscle contributions to overall ACL loading and to identify which muscles have the greatest capacity to load the ACL. This in turn would help classify which lower extremity muscles could be then targeted in future ACL injury prevention protocols.

Methods and Materials

Participants

Prior to data collection, experimental procedures received ethical approval from the university's Institutional Review Board. Eleven (seven healthy controls, four ACL-R) recreationally active females between 18 and 35 years volunteered for the study (Table 1). Inclusion criteria for both the healthy control and the ACL-R groups included being recreationally active at least 3 days per week for a minimum of 30 minutes per session, with one session being a dynamic training session, no lower extremity pain on the day, and no history of lower extremity injury within six months prior to testing. Specific inclusion criteria for the healthy control group included no history of lower back or lower extremity surgery, while specific inclusion criteria for the ACL-R group included being a minimum of one year post ACL reconstruction, no history of multi-ligament knee surgeries, active meniscal symptoms, or bilateral knee surgery (57). There was no restriction on graft type or history of meniscal repair at the time of ACL reconstruction (26, 61, 69), and all ACL-R females were cleared to return to full

sport participation by their physician. All ACL reconstructions performed on the ACL-R females were autografts. Two ACL-R females had patella tendon grafts, while the other two ACL-R females had a semitendinosus-gracilis tendon graft and a quadriceps tendon graft, respectively.

Data collection consisted of two testing days, with a minimum of three days' separation between the two testing days. A full description of the Day 1 and Day 2 testing sessions can be found in Chapter 3. Briefly, Day 1 consisted of participants providing written informed consent, as well as complete a variety of health history questionnaires. Participants then completed an ankle dorsiflexion range of motion assessment, a knee joint laxity assessment, a balance assessment, and a strength assessment of the lower extremity musculature.

On Day 2, participants were asked to wear an athletic t-shirt, spandex shorts, and provided a standard laboratory shoe (Nike Pegasus, Nike Inc., Beaverton, OR, USA) to wear during testing. Participant height and weight were collected, and then participants completed a five-minute warm-up at a self-selected pace on a treadmill. Following the warm-up, a heart rate sensor was secured to the participant's chest (Polar T31 Heart Rate Sensor, Polar Electro Inc., Bethpage, NY, USA) and a heart rate monitor (Polar FT1 Heart Rate Monitor, Polar Electro Inc., Bethpage, NY, USA) was worn on the participant's wrist. Then 27 anatomical, retro-reflective markers were placed on specific anatomical landmarks of the neck, trunk, pelvis, and bilaterally on the legs and feet (Figure 1). Clusters of four non-collinear markers on rigid thermoplastic shells were attached to the trunk, pelvis, and bilaterally on the thighs, shanks, and heels. A pre-fatigue three-second standing static calibration trail was recorded, and then the anatomical markers were removed.

After the anatomical markers were removed, participants were asked to complete three maximal vertical jumps to measure pre-fatigue vertical jump height. Then, participants stood on

top of a 30 cm box positioned half of the participant's body height away from the center of the force plate and were asked to jump out towards the center of the force plate and complete three anticipated landing tasks. These landing tasks included: 1) landing unilaterally on the right foot and cutting to the left, 2) landing unilaterally on the left foot and completing a cut to the right, and 3) landing bilaterally and completing a vertical jump subsequent to the initial land. While three landing tasks were performed, the box-land-and-cuts to the right were analyzed for all healthy controls as well as ACL-R females who had a reconstruction on the right knee. Box-land-and-and-cuts to the left were analyzed for two ACL-R females who had a reconstruction on the left knee. The landing tasks were counterbalanced, and five successful trials of each landing task were collected prior to the start of the fatigue protocol. After the pre-fatigue data collection trials are collected, the cluster markers were removed, and participants were brought into a gym where the fatigue protocol began.

Experimental Protocol

A complete description of the modified fatigue protocol can be found in Chapter 3 (Figure 2). In short, a maximal vertical jump-and-reach test against a wall was performed. Then, participants stood in the middle of four exercise stations, placed 7.5 m in front, behind, and to the left and right of the participant. Each exercise station consisted of four different body weight exercises. To start a round, participants were instructed to sprint towards a randomly assigned exercise station. The participant would sprint, backpedal, or side-shuffle to the respective exercise station, complete the exercise, and then return back to their starting positon. Once all four stations were completed, participants sprinted back to the wall to complete a maximal vertical jump-and reach, then were asked their heart rate and rate of perceived exertion. Participants received 60 s of rest before completing the next round. Participants completed as many rounds as possible until their

maximal vertical jump-and reach height decreased by 25% for two consecutive maximal vertical jumps.

Once maximal vertical jump-and-reach height was decreased by 25%, participants sprinted back to the laboratory, where cluster markers were placed back on the participant, and the participant completed three maximal vertical jumps to measure immediate post-fatigue maximal vertical jump. Participants were then asked to complete the round of body weight exercises they completed during the fatigue protocol. Then, participants completed the same counterbalanced landings tasks as they did prior to completing the fatigue protocol. Between each landing task, participants were asked to complete the set of body weight exercises to ensure they remained fatigued through the post-fatigue data collection. Finally, after the last landing task was collected, one final set of three maximal vertical jumps were recorded to measure if participants maintained a level of fatigue throughout the post-fatigue data collection. The same set of anatomical markers as described above were placed back on the participant, a post-fatigue three-second standing static trial was collected, and then Day 2 data collection was ceased.

Data Analysis

For all trials, raw marker coordinate data were collected at 200 Hz with a 12-camera motion capture system (Vicon, Centennial, CO, USA) while GRF data were collected synchronously at 2000 Hz (AMTI, Inc., Watertown, MA). Raw marker coordinate and GRF data were filtered using a fourth-order, zero lag, Butterworth low-pass filter with cut-off frequency of 12 Hz (36, 314, 348). Visual3D biomechanical software (C-Motion, Germantown, MD, USA) was used to create a kinematic model made of eight skeletal segments (trunk, pelvis, bilateral thighs, shanks, and feet) from the standing calibration trial. Segment coordinate systems were determined using a joint coordinate system approach (350). Hip joint centers were determined at

25% of the distance from ipsilateral to contralateral greater trochanter markers (349, 370). Knee joint centers were determined using the midpoint between femoral epicondyle markers (350), and ankle joint centers were determined using the midpoint between ipsilateral medial and lateral malleoli markers (351). Stance phase was defined as the time from initial contact to toe-off, both of which were identified using a vertical ground reaction force threshold of 10 N. Participants involved limb were chosen for further analysis. The involved limb for the healthy females was their dominant leg (i.e. right leg for all healthy participants), and the involved limb for the ACL-R females was their ACL-R leg. Jump height during the pre-fatigue and post-fatigue data collections in the lab were calculated using the impulse-momentum relationship. Jump height during the fatigue protocol in the gym was calculated using a simple jump-and-reach test.

Musculoskeletal Modeling

OpenSim (v3.2, http://simtk.org) was used to simulate the pre- and post-fatigue box-land-and-cut trials (48). A generic musculoskeletal model consisting of 14 segments, 23 degrees of freedom (*dof*), and 80 musculotendon actuators (40 right leg, 40 left leg) (359) was scaled to match each participant's anthropometry based on experimentally measured anatomical landmarks. Each hip was modeled as a 3-*dof* ball-and-socket joint. Each knee was modeled as a 1-*dof* hinge joint with abduction-adduction and internal-external rotations as well as anteroposterior and superior-inferior translations constrained to change as a function of knee flexion angle (360). The ankles were modeled as a 1-*dof* pin joint. Once the scaled model was obtained, an inverse kinematics algorithm was used to calculate joint angles by using the sum of weighted squared errors to minimize the error between the experimental data and the model (Figure 9) (361). Inverse dynamics was used to obtain lower extremity joint moments, which were then decomposed into individual muscle forces via a static optimization algorithm. This

was accomplished by minimizing the sum of muscle activations squared (362). Anteroposterior knee JRF using the muscle forces obtained from static optimization were computed using the JointReaction Analysis in OpenSim. Anteroposterior knee JRF was used to estimate overall ACL loading (F_{ACL}) relative to the tibial coordinate system (54, 137, 358). ACL loading was based on cadaveric knee measurements and expressed as exponential functions of knee flexion angle (75, 330). Therefore, using the equation below, F_{ACL} was calculated as:

$$F_{ACL} = \frac{F_{100N}(\theta_{knee}) - F_{0N}(\theta_{knee})}{100N} \cdot F_{AP} + F_{0N}(\theta_{knee})$$

Where F_{ACL} was the overall ACL loading, F_{100N} is the ACL loading when 100 Newtons of anterior tibial force was applied respective to the knee flexion angle (θ_{knee}), F_{AP} was the anteroposterior knee JRF, and F_{0N} is the ACL loading when there was no applied anterior tibial force respective to the θ_{knee}.

The potential of all 80 musculotendon actuators to accelerate the center of mass were calculated using a previously established induced acceleration analysis (Appendix T) which included a rolling constraint foot-ground contact model (339, 371). Then, individual muscle contributions to three-dimensional GRFs were calculated by 1) calculating the potentials via the dot product of the subject-specific model mass and the induced acceleration analysis results, and 2) taking the dot product of the potentials and the individual muscle forces obtained from static optimization. Normalized root mean square error (nRMSE) and coefficients of correlation (R^2) were calculated to compare the superposition errors between the three-dimensional experimental GRFs and the summed muscle contributions to the GRFs pre- and post-fatigue.

To calculate individual muscle contribution to the $F_{ACL,}$ each muscle's contribution to the anteroposterior JRF were computed by applying each muscle's contribution to the GRF in isolation and solving the dynamical equations of motion (Figure 9). Then, each muscle's

contribution to the anteroposterior JRF (Appendix U) in isolation was used in the aforementioned equation to solve for that muscle's specific contribution to the F_{ACL}. Reported anteroposterior JRF as well as F_{ACL} were normalized to body weight.

Variables of Interest

Variables of interest were individual muscle contributions to anteroposterior JRF and peak F_{ACL} between the healthy and ACL-R females pre- and post-fatigue.

Results

Musculoskeletal Modeling Validation

Magnitudes of the reserve moments used by the model were below the 5% of the maximal of the net joint moments, as recommended by Hicks, Uchida, Seth, Rajagopal and Delp (364). Good agreement existed between the superposition errors of the pre-fatigue anteroposterior (nRMSE: 6.8% ± 3.1%; R^2: 1.0 ± 0.0), vertical (nRMSE: 2.9% ± 1.3%; R^2: 1.0 ± 0.0), and mediolateral (nRMSE: 3.4% ± 1.6%; R^2: 1.0 ± 0.0) experimental and summed muscle contribution GRFs as well as the post-fatigue anteroposterior (nRMSE: 8.1% ± 8.3%; R^2: 1.0 ± 0.0), vertical (nRMSE: 2.8% ± 1.4%; R^2: 1.0 ± 0.0), mediolateral (nRMSE: 4.2% ± 5.0%; R^2: 1.0 ± 0.0) experimental and summed muscle contribution GRFs (Figure 10) (12). Qualitative analysis of our predicted activations during the pre-fatigue box-land-and-cuts for the seven healthy females were in agreement with previously collected experimental EMG activations during 45° run-and-cut in healthy females for the following muscles: gluteus maximus, gluteus medius, rectus femoris, vastus medialis, vastus lateralis, biceps femoris, medial hamstrings, lateral gastrocnemius, and medial gastrocnemius (Figure 6). For most muscles, the predicted activations followed the same patterns and fell within the standard deviation of the respective experimental activations. Differences between predictive and experimental activations in

muscles such as the gluteus medius are most likely due to the differences in the tasks (box-land-and-cut versus a typical 45° cut off the right foot to the left). Qualitative analysis of the F_{ACL} curves (Figure 7) were in good agreement with previous studies that have used the same F_{ACL} mathematical model used in the current study (53, 54, 71, 358).

Individual Muscle Contribution to Anteroposterior JRF

Overall anteroposterior JRF in healthy females peaked at 1.71 BW approximately 51% of stance phase pre-fatigue (Figure 11). The semimembranosus was the largest contributor to anteroposterior JRF in healthy females, peaking at 0.66 BW at 55% of stance phase pre-fatigue. The soleus (0.60 BW), vastus lateralis (0.59 BW), and tensor fasciae latae (0.14 BW) were also substantial contributors to pre-fatigue anteroposterior JRF, peaking at 50%, 49%, and 42% of stance phase, respectively. The medial gastrocnemius (-1.05 BW; 73% stance phase) and lateral gastrocnemius (-0.36 BW; 72% stance phase) were the largest contributors to counteracting the anteroposterior JRF. Post-fatigue, overall anteroposterior JRF decreased, and peaked at 0.89 BW at 47% of stance phase. The soleus became the largest contributor, peaking at 0.61 BW at 46% of stance phase in healthy females. The semimembranosus (0.56 BW), vastus lateralis (0.23 BW) and the tensor fasciae latae (0.17 BW), also contributed to the post-fatigue anteroposterior JRF, peaking at 53%, 47%, and 47%, respectively. Again, the medial gastrocnemius (-1.22 BW; 66% stance phase) and lateral gastrocnemius (-0.37 BW; 67% stance phase), were the biggest contributors to opposing post-fatigue anteroposterior JRF in healthy females. All other contributions from the remaining musculotendon actuators in the model were negligible.

Overall pre-fatigue anteroposterior JRF in ACL-R females followed a similar pattern as the healthy females, peaking at 1.41 BW approximately 53% of stance phase (Figure 11). The semimembranosus was the largest contributor, peaking at 0.66 BW at 56% of stance phase. The

vastus lateralis (0.49) and the soleus (0.43 BW) were the second largest contributors, peaking at 52% and 56%, respectively. The tensor fasciae latae (0.06 BW; 34% stance phase) was small in its contributions to pre-fatigue anteroposterior JRF. The medial gastrocnemius (-0.98 BW; 77% stance phase) and lateral gastrocnemius (-0.29 BW; 78% stance phase), were the biggest contributors to opposing post-fatigue anteroposterior JRF in ACL-R females. Post-fatigue, overall anteroposterior JRF deceased, and peaked at 1.19 BW at 49% of stance phase. The soleus became the largest contributor, peaking at 0.47 BW at 51% of stance phase in ACL-R females. The vastus lateralis (0.44 BW) and the semimembranosus (0.35 BW) also contributed to the post-fatigue anteroposterior JRF, peaking at 46% and 48% of stance phase, respectively. The contributions from the tensor fasciae latae were small (0.05 BW; 30% stance phase). Again, the medial gastrocnemius (-0.93 BW; 76% stance phase) and lateral gastrocnemius (-0.32 BW; 78% stance phase), were the biggest contributors to opposing post-fatigue anteroposterior JRF in ACL-R females. All other contributions from the remaining musculotendon actuators in the model were negligible.

Individual Muscle Contribution to F_{ACL}

Overall pre-fatigue F_{ACL} in healthy females peaked at 1.38 BW approximately 51% of stance phase (Figure 12). The semimembranosus was the largest contributor, peaking at 0.55 BW at 50% of stance phase. The soleus and the vastus lateralis both peaked at 0.48 BW at 50% of stance, while the tensor fasciae latae (0.11 BW) peaked at 42% stance. F_{ACL} decreased post-fatigue and peaked at 0.91 BW at 50% of stance phase. The soleus became the largest contributor, peaking at 0.55 BW at 38% of stance phase. The semimembranosus (0.51 BW), vastus lateralis (0.23 BW) and the tensor fasciae latae (0.15 BW), also contributed to the post-

fatigue F_{ACL}, peaking at 53%, 49%, and 47%, respectively. All other contributions from the remaining musculotendon actuators in the model were negligible.

Overall pre-fatigue F_{ACL} in ACL-R females peaked at 1.47 BW approximately 55% of stance phase (Figure 12). The semimembranosus was the largest contributor, peaking at 0.57 BW at 56% of stance phase. The vastus lateralis (0.41 BW) and the soleus (0.38 BW) were the second largest contributors, peaking at 52% and 57%, respectively. The tensor fasciae latae (0.05 BW) contributed little to F_{ACL}. F_{ACL} decreased post-fatigue and peaked at 1.08 BW at 48% of stance phase. The soleus became the largest contributor, peaking at 0.47 BW at 62% of stance phase. The vastus lateralis (0.39 BW), semimembranosus (0.32 BW) also contributed to the post-fatigue F_{ACL}, peaking at 45%, 48%, respectively. Again, the tensor fasciae latae (0.04 BW), contributions to F_{ACL} were small. All other contributions from the remaining musculotendon actuators in the model were negligible.

Discussion

The purpose of this study was to investigate lower extremely muscle contribution to F_{ACL} during the stance phase of an anticipated box-land-and-cut between healthy and ACL-R females pre- and post- a fatigue protocol. We observed that pre-fatigue, the semimembranosus was the largest contributor to F_{ACL} in both healthy and ACL-R females, while the soleus was the largest contributor to F_{ACL} in both healthy and ACL-R females post-fatigue. The vastus lateralis and the tensor fasciae latae were shown to be important secondary contributors to F_{ACL} pre- and post-fatigue in healthy females, while only the vastus lateralis was an important contributor to F_{ACL} pre- and post-fatigue in ACL-R females. These same muscles were also shown to be vital in anteroposterior JRF contributions, while the medial and lateral gastrocnemius acted to counteract the anteroposterior JRF.

Overall F_{ACL} appeared to be more impacted by fatigue than by group. Weinhandl, Earl-Boehm, Ebersole, Huddleston, Armstrong and O'Connor (53) found a 36% increase in ACL loading after an isolated hamstring fatigue protocol, which would conflict with the results of the current study. However, as discussed in Chapter 4, differences between the findings of Weinhandl, Earl-Boehm, Ebersole, Huddleston, Armstrong and O'Connor (53) and our findings most likely lie in methodological differences. It is also important to note that while differences in F_{ACL} magnitude between pre- and post-fatigue for both groups are present, they were not statistically significant (Figure 8).

Several studies have established that the quadriceps (i.e. vastus lateralis, vastus intermedius, vastus medialis) are primary ACL loaders (116, 117, 124, 125, 127). The vastus lateralis was determined to be an important contributor in F_{ACL} pre- and post-fatigue in both healthy and ACL-R females. In fact, it was the only quadriceps muscle to meaningfully contribute to F_{ACL}. Zebis, Andersen, Bencke, Kjaer and Aagaard (372) prospectively investigated risk factors associated with ACL injury in athletic females. Females that sustained an ACL injury during the study period were found to have had significantly higher preactivation of vastus lateralis activity prior to injury during cutting tasks compared to females who did not sustain an ACL injury. These results in combination with ours could indicate that instead of considering the quadriceps group as primary ACL loaders, special emphasis should be placed on the specifically the vastus lateralis's role in ACL loading. In the current study, vastus lateralis contributions to ACL loading changed between groups (i.e. healthy vs ACL-R) and conditions (i.e. pre-fatigue vs post-fatigue), with the biggest difference occurring between healthy females pre-fatigue (0.48 BW) and post-fatigue (0.23 BW). While differences exist in vastus lateralis contribution magnitude, future work is needed to determine the meaningfulness of these changes.

Two hip muscles, the semimembranosus and the tensor fasciae latae were found to contribute meaningfully to F_{ACL}. Previous work described the hamstrings (i.e. biceps femoris, semitendinosus, and semimembranosus) as important ACL unloaders (10, 128). However, our data suggests that the semimembranosus is a large contributor to F_{ACL}. This is most likely due to the role the semimembranosus plays in contributing to tibiofemoral compressive JRF. The semimembranosus has been shown to be the largest hamstring contributor to tibiofemoral compressive JRF (373). During the stance phase of the box-land-and-cut, the tibia is drawn upwards into the femur. The tibial also has a posteriorly sloped tibia plateau. Thus, as the semimembranosus is a primary contributor to the compressive JRF, it may be possible that joint geometry in combination with the box-land-and-cut task lead the semimembranosus to being a contributor to F_{ACL} instead of being an ACL unloader.

The tensor fasciae latae was a surprising F_{ACL} contributor, but more interestingly it was only a meaningful contributor in healthy individuals, and was negligible in ACL-R individuals. The tensor fasciae latae connects to the iliotibial band, which runs laterally down the thigh and attaches to the anterolateral aspect of the tibia. While it is considered a dynamic knee stabilizer, the iliotibial band can also influence hip movement, specifically hip external rotation. Healthy females were observed completing the box-land-and-cutting tasks with their hips externally rotation, while the ACL-R females completed these tasks with hip internal rotation (Table 3). Therefore, it is plausible that the hip mechanics utilized by the healthy group would cause the tensor fasciae latae to be a contributor to F_{ACL} compared to the ACL-R group. There were no fatigue main effects found with hip rotation (Chapter 3), which would explain as to why tensor fasciae latae contribution is primarily affected by group and not fatigue.

Recently, speculation has arose regarding the soleus's role in F_{ACL} (130) (52). When the foot is planted, the soleus acts to resist anterior tibial translation about the ankle (130). Thus, it has been hypothesized that it could have these same resisting effects about the knee. However, it is important to note that Elias, Faust, Chu, Chao and Cosgarea (130) used cadavers to determine the role that the soleus has at the ankle and at the knee. During the current study, the participants stood on a 30 cm box one-half the distance of their body height away from the force plates. As soon as they made initial contact, they were asked to complete a 45° cut away from their planted foot. Therefore, it could be hypothesized that soleus function during such a task would be influenced by change of directions in the center of mass. Thus, the soleus could act to resist anterior tibial translation about the ankle while the foot is planted, yet may not have the same resisting effects about the knee during this specific task. We chose to use an induced acceleration analysis which included a rolling constraint foot-ground contact model (339, 371). While this is a well-established foot-ground contact model, soleus contributions to vertical and anteroposterior center of mass accelerations have been shown to differ between various foot-ground contact models (334, 371). Therefore, the magnitude of our soleus contributions to F_{ACL} may be impacted by rolling constraint foot-ground contact model.

A number of limitations exist within the current study that must be acknowledged. First, the study contains a small sample size. An *a priori* power analysis with an *alpha* of 0.05 a *beta* of 0.80, and effect size (*f*) of 0.40 was performed based on key kinematic and kinetic variables (34, 35, 47). The analysis indicated that a minimum of 16 participants (eight per group) were sufficient to detect any statistical differences. The small, uneven sample sizes of the healthy control and ACL-R groups may have prevented the detection of differences in some variables observed in the study, thus increasing Type II error. Due to the COVID-19 pandemic, we were

not able to complete data collections that would have allowed us to meet the minimum participant number. We plan to add additional subjects to the current dataset to improve statistical power in the future.

Second, static optimization was used to estimate muscle forces, and limitations with using static optimization should be considered, such as the inadequacy of its ability to predict co-contractions of the muscles. However, our predicted muscle activations adequately agree with previously collected anticipated running and cutting experimental electromyography data (Chapter 4 Appendix: Figure 5). While there may be slight differences in our predicted muscle activations compared to the experimental electromyography data due to task differences, we are confident our simulations for this study are sufficient.

Finally, the ACL-R females all had different surgeons that conducted their ACL-reconstruction, as well has received rehabilitation from different physical therapists. Therefore, surgical techniques and rehabilitative protocols within the ACL-R females are different, thus potentially influencing their lower extremity mechanics, which would in turn influence their F_{ACL}. ACL-R females also had a variety of graft types. Research has shown that functional outcomes of different graft types are similar after one year post-surgery (237). However, it is currently unknown how different graft types may influence F_{ACL}.

Conclusion

This study is the first to describe the lower extremity muscle contribution to the anteroposterior JRF and F_{ACL} during the stance phase of an anticipated box-land-and-cut between healthy and ACL-R females pre- and post- a fatigue protocol. These data could suggest muscle groups to target in improving athletic performance as well as injury prevention and rehabilitation protocols for not only healthy female athletes, but to ACL-R females returning back to sport.

However, due to conflicting results with previous studies, further work is needed to determine how muscles such as the semimembranosus and the soleus contribute to F_{ACL}.

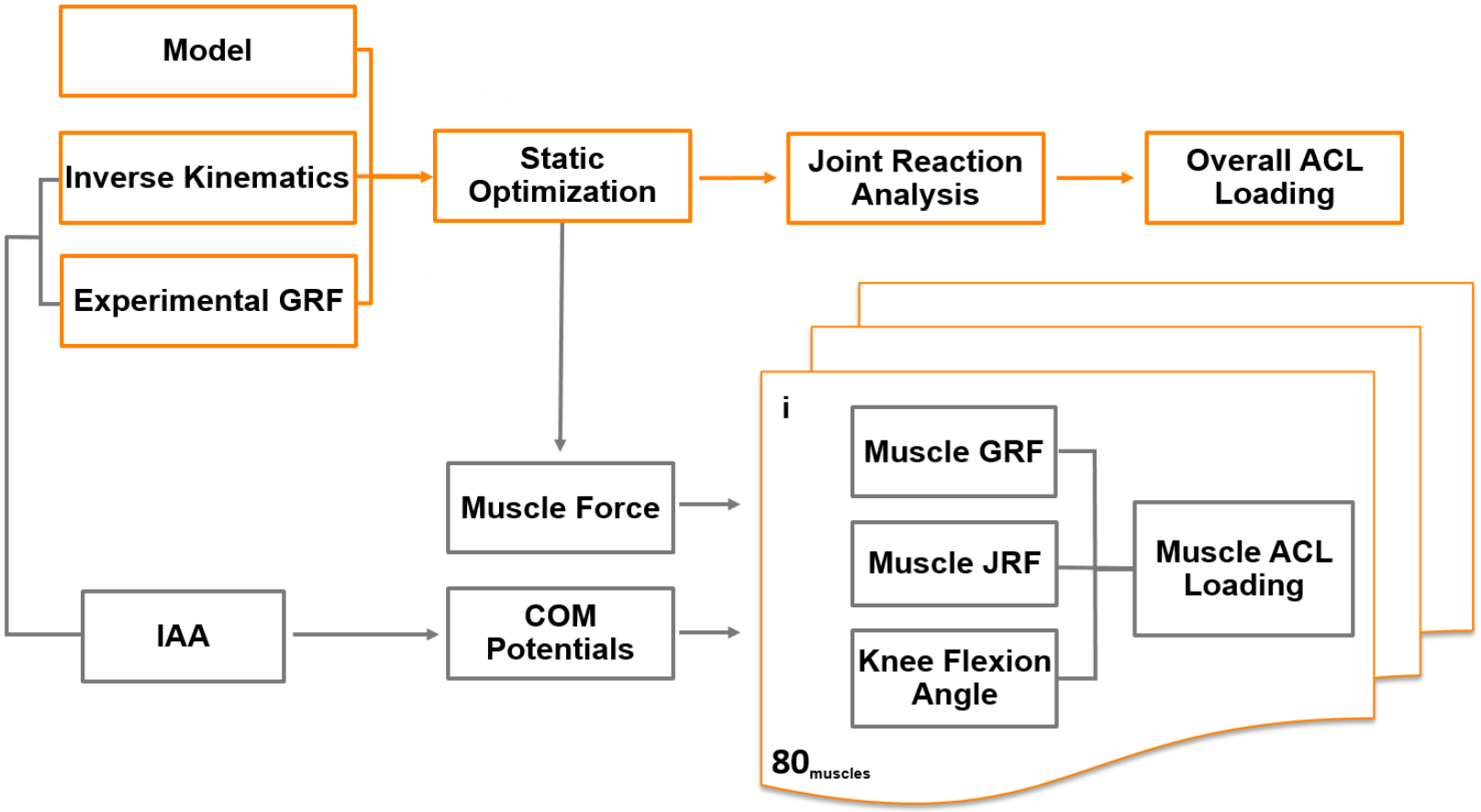

Figure 9: Visual representation of the musculoskeletal modeling workflow for calculating overall F_{ACL} and individual muscle contribution to F_{ACL}.

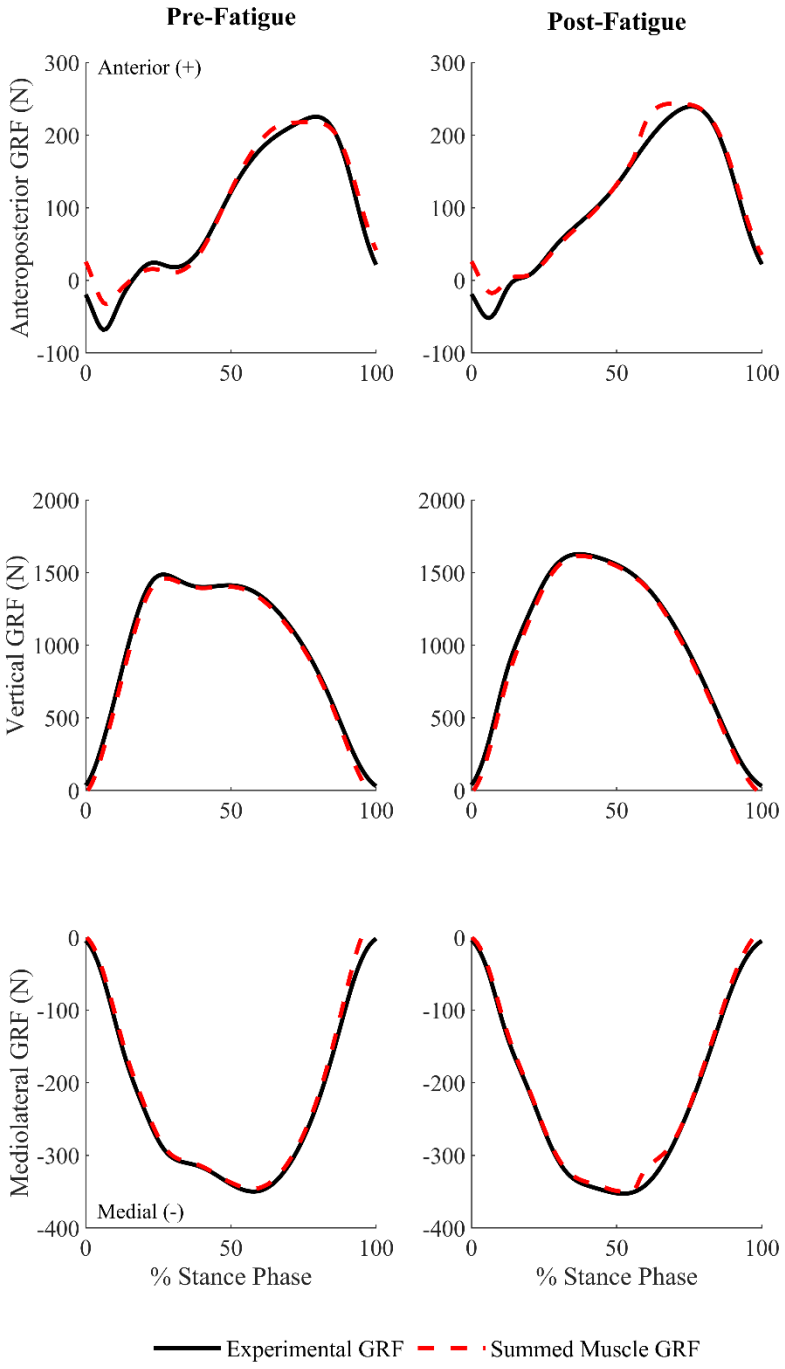

Figure 10: Muscle contributions to the anteroposterior GRF, mediolateral GRF, and the vertical GRF during stance phase (i.e. initial contact to toe-off) pre- and post-fatigue. Anterior GRF is indicated as positive and medial GRF is indicated as negative. The black solid line represents the experimental GRF while the red dashed line represents the sum of all 80 musculotendon actuators contributions to each GRF, respectively.

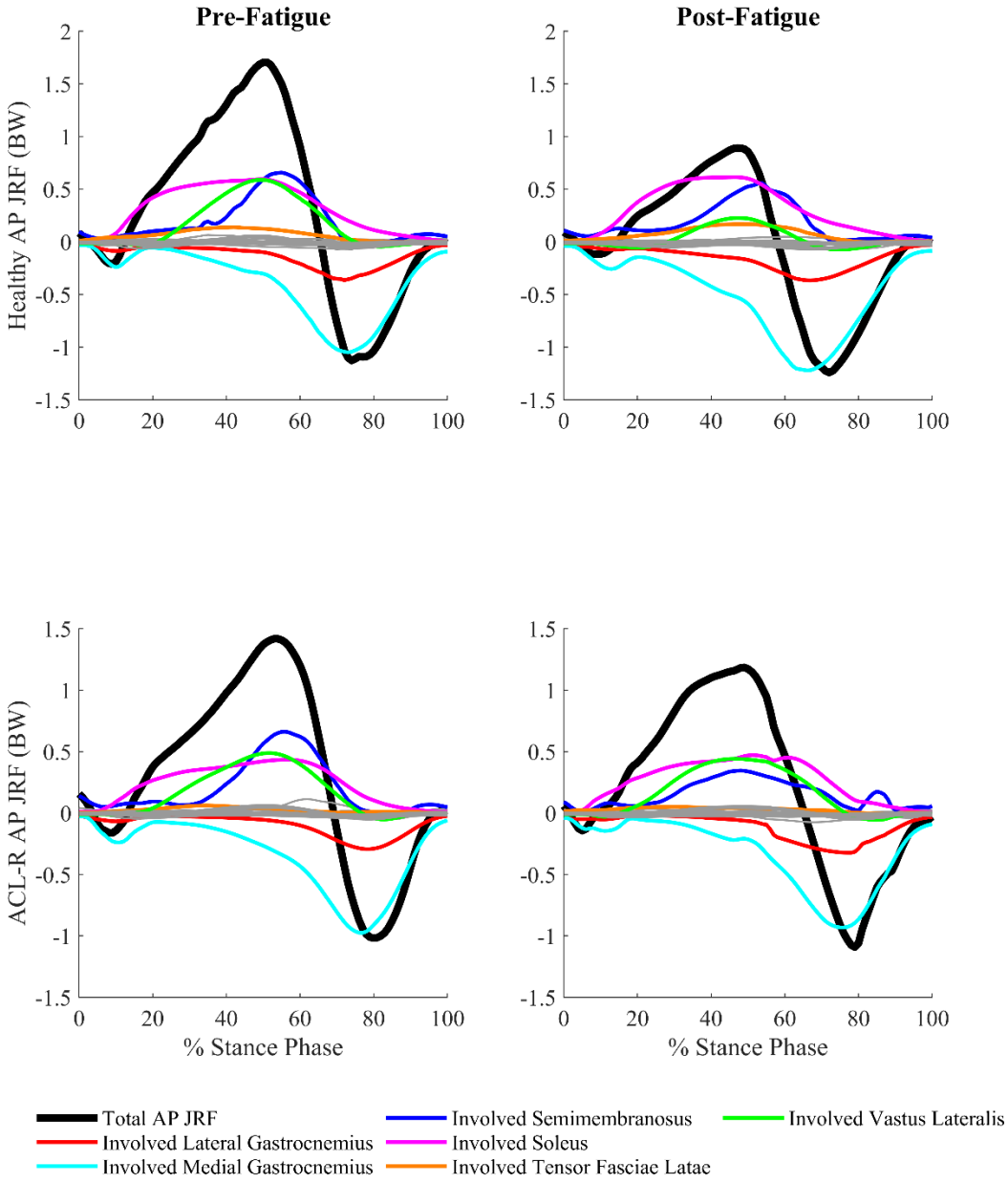

Figure 11: Muscle contributions to the anteroposterior JRF during stance phase (i.e. initial contact to toe-off) pre- and post-fatigue in healthy and ACL-R females. The colored muscles represent the involved leg (i.e. the right leg for healthy females, ACL-R leg for ACL-R females).

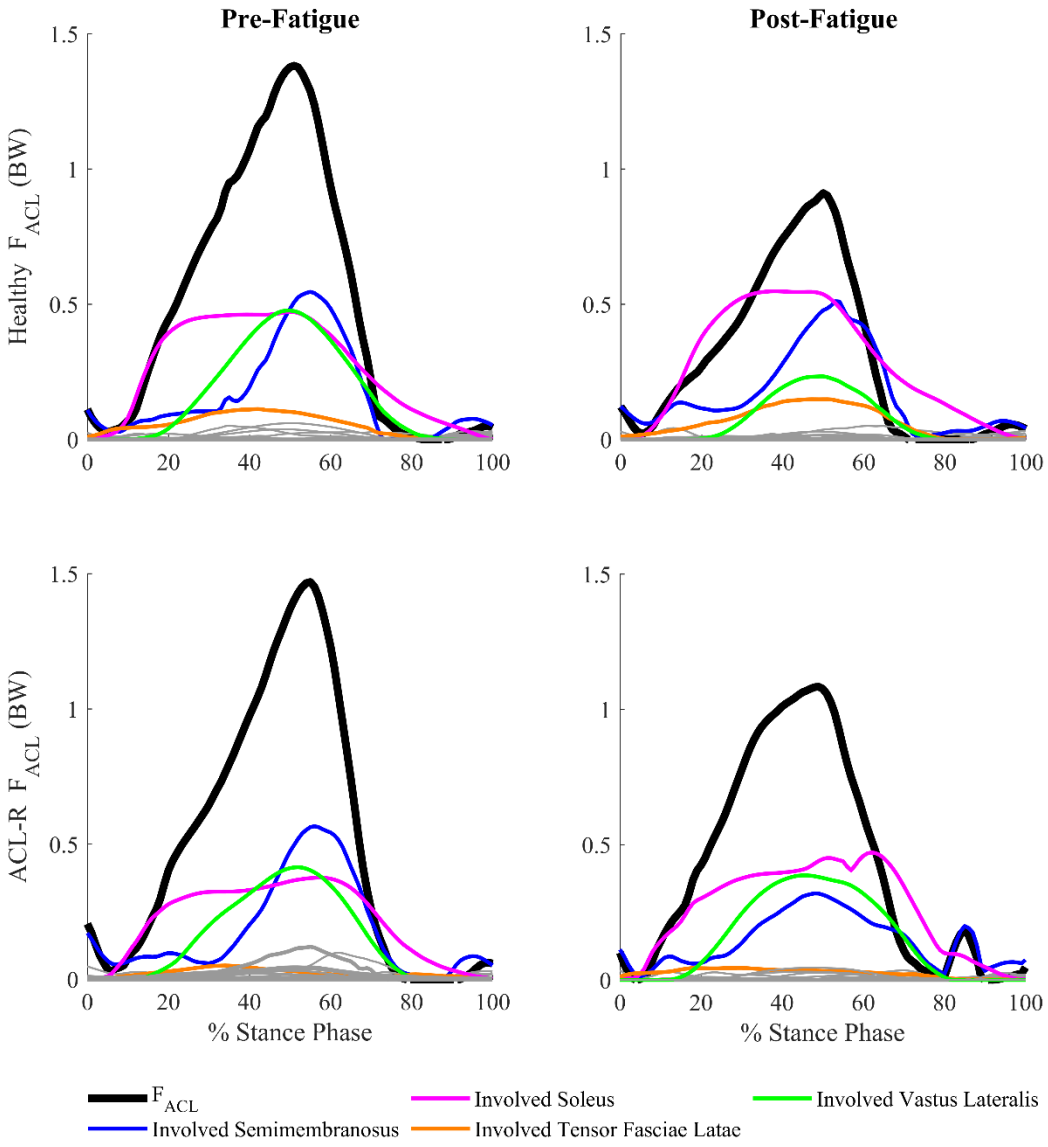

Figure 12: Muscle contributions to the F_{ACL} during stance phase (i.e. initial contact to toe-off) pre- and post-fatigue in healthy and ACL-R females. The colored muscles represent the involved leg (i.e. the right leg for healthy females, ACL-R leg for ACL-R females).

Chapter 6: Conclusion

The purpose of this dissertation was to determine how fatigue and surgical intervention of the ACL influenced lower extremity mechanics as well as how is to determine how individual lower extremity muscles contributed to ACL healthy and ACL-R females. Chapter 3 showed that ACL-reconstruction and fatigue is influential on specific hip and knee mechanics in recreationally active females. ACL-R females displayed altered hip mechanics that may place them at a higher risk of ACL re-injury, especially after muscular fatigue has been induced, compared to healthy females. Chapter 4 found that neither fatigue nor surgical intervention influenced F_{ACL}. Finally, Chapter 5 showed that fatigue and surgical intervention also did not influence individual muscle contributions to F_{ACL}. Future research should focus on the effects fatigue did have on hip mechanics in ACL-R females as a way to improve injury prevention as well as rehabilitation protocols. Future research should also focus on improving the limitations of this dissertation.

REFERENCES

1. Prodromos CC, Han Y, Rogowski J, Joyce B, Shi K. A meta-analysis of the incidence of anterior cruciate ligament tears as a function of gender, sport, and a knee injury-reduction regimen. *Arthroscopy*. 2007;23(12):1320-5.e6.

2. Paterno MV, Rauh MJ, Schmitt LC, Ford KR, Hewett TE. Incidence of Second ACL Injuries 2 Years After Primary ACL Reconstruction and Return to Sport. *Am J Sports Med*. 2014;42(7):1567-73.

3. Walden M, Hagglund M, Werner J, Ekstrand J. The epidemiology of anterior cruciate ligament injury in football (soccer): a review of the literature from a gender-related perspective. *Knee Surg Sports Traumatol Arthrosc*. 2011;19(1):3-10.

4. Agel J, Arendt EA, Bershadsky B. Anterior cruciate ligament injury in national collegiate athletic association basketball and soccer: a 13-year review. *Am J Sports Med*. 2005;33(4):524-30.

5. Sigward SM, Cesar GM, Havens KL. Predictors of Frontal Plane Knee Moments During Side-Step Cutting to 45 and 110 Degrees in Men and Women: Implications for Anterior Cruciate Ligament Injury. *Clin J Sport Med*. 2015;25(6):529-34.

6. Arendt E, Dick R. Knee injury patterns among men and women in collegiate basketball and soccer. NCAA data and review of literature. *Am J Sports Med*. 1995;23(6):694-701.

7. Norwood LA, Cross MJ. Anterior cruciate ligament: functional anatomy of its bundles in rotatory instabilities. *Am J Sports Med*. 1979;7(1):23-6.

8. Hewett TE, Myer GD, Ford KR et al. Biomechanical measures of neuromuscular control and valgus loading of the knee predict anterior cruciate ligament injury risk in female athletes: a prospective study. *Am J Sports Med*. 2005;33(4):492-501.

9. Beynnon BD, Fleming BC. Anterior cruciate ligament strain in-vivo: a review of previous work. *J Biomech*. 1998;31(6):519-25.

10. Li G, Rudy TW, Sakane M, Kanamori A, Ma CB, Woo SL. The importance of quadriceps and hamstring muscle loading on knee kinematics and in-situ forces in the ACL. *J Biomech*. 1999;32(4):395-400.

11. Zajac FE, Gordon ME. Determining muscle's force and action in multi-articular movement. *Exerc Sport Sci Rev*. 1989;17:187-230.

12. Maniar N, Schache AG, Sritharan P, Opar DA. Non-knee-spanning muscles contribute to tibiofemoral shear as well as valgus and rotational joint reaction moments during unanticipated sidestep cutting. *Sci Rep*. 2018;8(1):2501.

13. Spindler KP, Wright RW. Clinical practice. Anterior cruciate ligament tear. *N Engl J Med*. 2008;359(20):2135-42.

14. Bates NA, McPherson AL, Rao MB, Myer GD, Hewett TE. Characteristics of inpatient anterior cruciate ligament reconstructions and concomitant injuries. *Knee Surg Sports Traumatol Arthrosc*. 2016;24(9):2778-86.

15. Freedman KB, Glasgow MT, Glasgow SG, Bernstein J. Anterior cruciate ligament injury and reconstruction among university students. *Clin Orthop Relat Res*. 1998;(356):208-12.

16. Hewett TE, Ford KR, Myer GD. Anterior cruciate ligament injuries in female athletes: Part 2, a meta-analysis of neuromuscular interventions aimed at injury prevention. *Am J Sports Med*. 2006;34(3):490-8.

17. Segawa H, Omori G, Koga Y. Long-term results of non-operative treatment of anterior cruciate ligament injury. *Knee*. 2001;8(1):5-11.

18. Holsgaard-Larsen A, Jensen C, Mortensen NH, Aagaard P. Concurrent assessments of lower limb loading patterns, mechanical muscle strength and functional performance in ACL-patients--a cross-sectional study. *Knee*. 2014;21(1):66-73.

19. Konrath JM, Vertullo CJ, Kennedy BA, Bush HS, Barrett RS, Lloyd DG. Morphologic Characteristics and Strength of the Hamstring Muscles Remain Altered at 2 Years After Use of a Hamstring Tendon Graft in Anterior Cruciate Ligament Reconstruction. *Am J Sports Med*. 2016;44(10):2589-98.

20. Setuain I, Izquierdo M, Idoate F et al. Differential Effects of 2 Rehabilitation Programs Following Anterior Cruciate Ligament Reconstruction. *J Sport Rehabil*. 2017;26(6):544-55.

21. Zhou MW, Gu L, Chen YP et al. Factors affecting proprioceptive recovery after anterior cruciate ligament reconstruction. *Chin Med J (Engl)*. 2008;121(22):2224-8.

22. Laboute E, Verhaeghe E, Ucay O, Minden A. Evaluation kinaesthetic proprioceptive deficit after knee anterior cruciate ligament (ACL) reconstruction in athletes. *J Exp Orthop*. 2019;6(1):6.

23. Pollard CD, Stearns KM, Hayes AT, Heiderscheit BC. Altered lower extremity movement variability in female soccer players during side-step cutting after anterior cruciate ligament reconstruction. *Am J Sports Med*. 2015;43(2):460-5.

24. Kurz MJ, Stergiou N, Buzzi UH, Georgoulis AD. The effect of anterior cruciate ligament reconstruction on lower extremity relative phase dynamics during walking and running. *Knee Surg Sports Traumatol Arthrosc*. 2005;13(2):107-15.

25. Srinivasan D, Tengman E, Hager CK. Increased movement variability in one-leg hops about 20years after treatment of anterior cruciate ligament injury. *Clin Biomech (Bristol, Avon)*. 2018;53:37-45.

26. Paterno MV, Schmitt LC, Ford KR et al. Biomechanical measures during landing and postural stability predict second anterior cruciate ligament injury after anterior cruciate ligament reconstruction and return to sport. *Am J Sports Med*. 2010;38(10):1968-78.

27. Salmon L, Russell V, Musgrove T, Pinczewski L, Refshauge K. Incidence and risk factors for graft rupture and contralateral rupture after anterior cruciate ligament reconstruction. *Arthroscopy*. 2005;21(8):948-57.

28. Shelbourne KD, Gray T, Haro M. Incidence of subsequent injury to either knee within 5 years after anterior cruciate ligament reconstruction with patellar tendon autograft. *Am J Sports Med*. 2009;37(2):246-51.

29. Schilaty ND, Nagelli C, Bates NA et al. Incidence of Second Anterior Cruciate Ligament Tears and Identification of Associated Risk Factors From 2001 to 2010 Using a Geographic Database. *Orthop J Sports Med*. 2017;5(8):2325967117724196.

30. Hui C, Salmon LJ, Kok A, Maeno S, Linklater J, Pinczewski LA. Fifteen-year outcome of endoscopic anterior cruciate ligament reconstruction with patellar tendon autograft for "isolated" anterior cruciate ligament tear. *Am J Sports Med*. 2011;39(1):89-98.

31. Paterno MV, Rauh MJ, Schmitt LC, Ford KR, Hewett TE. Incidence of contralateral and ipsilateral anterior cruciate ligament (ACL) injury after primary ACL reconstruction and return to sport. *Clin J Sport Med*. 2012;22(2):116-21.

32. Lai CCH, Ardern CL, Feller JA, Webster KE. Eighty-three per cent of elite athletes return to preinjury sport after anterior cruciate ligament reconstruction: a systematic review with meta-analysis of return to sport rates, graft rupture rates and performance outcomes. *Br J Sports Med*. 2018;52(2):128-38.

33. Mair SD, Seaber AV, Glisson RR, Garrett WE, Jr. The role of fatigue in susceptibility to acute muscle strain injury. *Am. J. Sports Med.* 1996;24(2):137-43.

34. Borotikar BS, Newcomer R, Koppes R, McLean SG. Combined effects of fatigue and decision making on female lower limb landing postures: central and peripheral contributions to ACL injury risk. *Clin Biomech (Bristol, Avon)*. 2008;23(1):81-92.

35. McLean SG, Fellin RE, Suedekum N, Calabrese G, Passerallo A, Joy S. Impact of fatigue on gender-based high-risk landing strategies. *Med Sci Sports Exerc*. 2007;39(3):502-14.

36. McLean SG, Samorezov JE. Fatigue-induced ACL injury risk stems from a degradation in central control. *Med Sci Sports Exerc*. 2009;41(8):1661-72.

37. Chappell JD, Herman DC, Knight BS, Kirkendall DT, Garrett WE, Yu B. Effect of fatigue on knee kinetics and kinematics in stop-jump tasks. *Am J Sports Med*. 2005;33(7):1022-9.

38. Collins JD, Almonroeder TG, Ebersole KT, O'Connor KM. The effects of fatigue and anticipation on the mechanics of the knee during cutting in female athletes. *Clin Biomech (Bristol, Avon)*. 2016;35:62-7.

39. Moreau NG, Li L, Geaghan JP, Damiano DL. Fatigue resistance during a voluntary performance task is associated with lower levels of mobility in cerebral palsy. *Arch Phys Med Rehabil*. 2008;89(10):2011-6.

40. Iguchi J, Tateuchi H, Taniguchi M, Ichihashi N. The effect of sex and fatigue on lower limb kinematics, kinetics, and muscle activity during unanticipated side-step cutting. *Knee Surg Sports Traumatol Arthrosc*. 2014;22(1):41-8.

41. Lessi GC, Dos Santos AF, Batista LF, de Oliveira GC, Serrao FV. Effects of fatigue on lower limb, pelvis and trunk kinematics and muscle activation: Gender differences. *J Electromyogr Kinesiol*. 2017;32:9-14.

42. Patrek MF, Kernozek TW, Willson JD, Wright GA, Doberstein ST. Hip-abductor fatigue and single-leg landing mechanics in women athletes. *J Athl Train*. 2011;46(1):31-42.

43. Cortes N, Greska E, Ambegaonkar JP, Kollock RO, Caswell SV, Onate JA. Knee kinematics is altered post-fatigue while performing a crossover task. *Knee Surg Sports Traumatol Arthrosc*. 2014;22(9):2202-8.

44. Sanna G, O'Connor KM. Fatigue-related changes in stance leg mechanics during sidestep cutting maneuvers. *Clin Biomech (Bristol, Avon)*. 2008;23(7):946-54.

45. Mejane J, Faubert J, Romeas T, Labbe DR. The combined impact of a perceptual-cognitive task and neuromuscular fatigue on knee biomechanics during landing. *Knee*. 2019;26(1):52-60.

46. Frank BS, Gilsdorf CM, Goerger BM, Prentice WE, Padua DA. Neuromuscular fatigue alters postural control and sagittal plane hip biomechanics in active females with anterior cruciate ligament reconstruction. *Sports Health*. 2014;6(4):301-8.

47. Lessi GC, Silva RS, Serrao FV. Comparison of the effects of fatigue on kinematics and muscle activation between men and women after anterior cruciate ligament reconstruction. *Phys Ther Sport*. 2018;31:29-34.

48. Delp SL, Anderson FC, Arnold AS et al. OpenSim: open-source software to create and analyze dynamic simulations of movement. *IEEE Trans Biomed Eng*. 2007;54(11):1940-50.

49. Seth A, Sherman M, Reinbolt JA, Delp SL. OpenSim: a musculoskeletal modeling and simulation framework for in silico investigations and exchange. *Procedia IUTAM*. 2011;2:212-32.

50. Thelen DG, Anderson FC. Using computed muscle control to generate forward dynamic simulations of human walking from experimental data. *J Biomech*. 2006;39(6):1107-15.

51. Laughlin WA, Weinhandl JT, Kernozek TW, Cobb SC, Keenan KG, O'Connor KM. The effects of single-leg landing technique on ACL loading. *J Biomech*. 2011;44(10):1845-51.

52. Mokhtarzadeh H, Yeow CH, Hong Goh JC, Oetomo D, Malekipour F, Lee PV. Contributions of the soleus and gastrocnemius muscles to the anterior cruciate ligament loading during single-leg landing. *J Biomech*. 2013;46(11):1913-20.

53. Weinhandl JT, Earl-Boehm JE, Ebersole KT, Huddleston WE, Armstrong BS, O'Connor KM. Reduced hamstring strength increases anterior cruciate ligament loading during anticipated sidestep cutting. *Clin Biomech (Bristol, Avon)*. 2014;29(7):752-9.

54. Weinhandl JT, Earl-Boehm JE, Ebersole KT, Huddleston WE, Armstrong BS, O'Connor KM. Anticipatory effects on anterior cruciate ligament loading during sidestep cutting. *Clin Biomech (Bristol, Avon)*. 2013;28(6):655-63.

55. Saxby DJ, Modenese L, Bryant AL et al. Tibiofemoral contact forces during walking, running and sidestepping. *Gait Posture*. 2016;49:78-85.

56. Killen BA, Saxby DJ, Fortin K et al. Individual muscle contributions to tibiofemoral compressive articular loading during walking, running and sidestepping. *J Biomech*. 2018;80:23-31.

57. Goetschius J, Hertel J, Saliba SA, Brockmeier SF, Hart JM. Gait Biomechanics in Anterior Cruciate Ligament-reconstructed Knees at Different Time Frames Postsurgery. *Med Sci Sports Exerc*. 2018;50(11):2209-16.

58. Bryant AL, Kelly J, Hohmann E. Neuromuscular adaptations and correlates of knee functionality following ACL reconstruction. *J Orthop Res*. 2008;26(1):126-35.

59. Meyer CAG, Gette P, Mouton C, Seil R, Theisen D. Side-to-side asymmetries in landing mechanics from a drop vertical jump test are not related to asymmetries in knee joint laxity following anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc*. 2018;26(2):381-90.

60. Decker MJ, Torry MR, Noonan TJ, Riviere A, Sterett WI. Landing adaptations after ACL reconstruction. *Med Sci Sports Exerc*. 2002;34(9):1408-13.

61. Delahunt E, Sweeney L, Chawke M et al. Lower limb kinematic alterations during drop vertical jumps in female athletes who have undergone anterior cruciate ligament reconstruction. *J Orthop Res*. 2012;30(1):72-8.

62. Gokeler A, Hof AL, Arnold MP, Dijkstra PU, Postema K, Otten E. Abnormal landing strategies after ACL reconstruction. *Scand J Med Sci Sports*. 2010;20(1):e12-9.

63. Xergia SA, Pappas E, Zampeli F, Georgiou S, Georgoulis AD. Asymmetries in functional hop tests, lower extremity kinematics, and isokinetic strength persist 6 to 9 months

following anterior cruciate ligament reconstruction. *J Orthop Sports Phys Ther*. 2013;43(3):154-62.

64. Lepley LK, Thomas AC, McLean SG, Palmieri-Smith RM. Fatigue's lack of effect on thigh-muscle activity in anterior cruciate ligament-reconstructed patients during a dynamic-landing task. *J Sport Rehabil*. 2013;22(2):83-92.

65. Rostami KD, Alizadeh MH, Minoonejad H, Yazdi H, Thomas A. Effect of Fatigue on Electromyographic Activity Patterns of the Knee Joint Muscles in Anterior Cruciate Ligament Reconstructed and Deficient Patients during Landing Task. *J Funct Morphol Kinesiol*. 2018;3(2):22.

66. Thomas AC, Lepley LK, Wojtys EM, McLean SG, Palmieri-Smith RM. Effects of Neuromuscular Fatigue on Quadriceps Strength and Activation and Knee Biomechanics in Individuals Post-Anterior Cruciate Ligament Reconstruction and Healthy Adults. *J Orthop Sports Phys Ther*. 2015;45(12):1042-50.

67. Matsumoto H, Suda Y, Otani T, Niki Y, Seedhom BB, Fujikawa K. Roles of the anterior cruciate ligament and the medial collateral ligament in preventing valgus instability. *J Orthop Sci*. 2001;6(1):28-32.

68. Sakane M, Fox RJ, Woo SL, Livesay GA, Li G, Fu FH. In situ forces in the anterior cruciate ligament and its bundles in response to anterior tibial loads. *J Orthop Res*. 1997;15(2):285-93.

69. Stearns KM, Pollard CD. Abnormal frontal plane knee mechanics during sidestep cutting in female soccer athletes after anterior cruciate ligament reconstruction and return to sport. *Am J Sports Med*. 2013;41(4):918-23.

70. Lee SP, Chow JW, Tillman MD. Persons with reconstructed ACL exhibit altered knee mechanics during high-speed maneuvers. *Int J Sports Med*. 2014;35(6):528-33.

71. Samaan MA, Ringleb SI, Bawab SY, Greska EK, Weinhandl JT. Anterior cruciate ligament (ACL) loading in a collegiate athlete during sidestep cutting after ACL reconstruction: A case study. *Knee*. 2016;23(4):744-52.

72. Okoroha KR, Marfo K, Meta F et al. Amount of Minutes Played Does Not Contribute to Anterior Cruciate Ligament Injury in National Basketball Association Athletes. *Orthopedics*. 2017;40(4):e658-e62.

73. Harris JD, Erickson BJ, Bach BR, Jr. et al. Return-to-Sport and Performance After Anterior Cruciate Ligament Reconstruction in National Basketball Association Players. *Sports Health*. 2013;5(6):562-8.

74. Mair SD, Seaber AV, Glisson RR, Garrett WE, Jr. The role of fatigue in susceptibility to acute muscle strain injury. *Am J Sports Med*. 1996;24(2):137-43.

75. Markolf KL, Burchfield DM, Shapiro MM, Shepard MF, Finerman GA, Slauterbeck JL. Combined knee loading states that generate high anterior cruciate ligament forces. *J Orthop Res*. 1995;13(6):930-5.

76. Ng AW, Lee RK, Ho EP, Law BK, Griffith JF. Anterior cruciate ligament bundle measurement by MRI. *Skeletal Radiol*. 2013;42(11):1549-54.

77. Ellison AE, Berg EE. Embryology, anatomy, and function of the anterior cruciate ligament. *Orthop Clin North Am*. 1985;16(1):3-14.

78. Markatos K, Kaseta MK, Lallos SN, Korres DS, Efstathopoulos N. The anatomy of the ACL and its importance in ACL reconstruction. *Eur J Orthop Surg Traumatol*. 2013;23(7):747-52.

79. Arliani GG, Astur DC, Moraes ER et al. Three dimensional anatomy of the anterior cruciate ligament: a new approach in anatomical orthopedic studies and a literature review. *Open Access J Sports Med*. 2012;3:183-8.

80. Baek GH, Carlin GJ, Vogrin TM, Woo SL, Harner CD. Quantitative analysis of collagen fibrils of human cruciate and meniscofemoral ligaments. *Clin Orthop Relat Res*. 1998;(357):205-11.

81. Giron F, Cuomo P, Aglietti P, Bull AM, Amis AA. Femoral attachment of the anterior cruciate ligament. *Knee Surg Sports Traumatol Arthrosc*. 2006;14(3):250-6.

82. Furman W, Marshall JL, Girgis FG. The anterior cruciate ligament. A functional analysis based on postmortem studies. *J Bone Joint Surg Am*. 1976;58(2):179-85.

83. Girgis FG, Marshall JL, Monajem A. The cruciate ligaments of the knee joint. Anatomical, functional and experimental analysis. *Clin Orthop Relat Res*. 1975;(106):216-31.

84. Hole RL, Lintner DM, Kamaric E, Moseley JB. Increased tibial translation after partial sectioning of the anterior cruciate ligament. The posterolateral bundle. *Am J Sports Med*. 1996;24(4):556-60.

85. Arnoczky SP. Anatomy of the anterior cruciate ligament. *Clin Orthop Relat Res*. 1983;(172):19-25.

86. Cohen SB, VanBeek C, Starman JS, Armfield D, Irrgang JJ, Fu FH. MRI measurement of the 2 bundles of the normal anterior cruciate ligament. *Orthopedics*. 2009;32(9).

87. Amis AA, Dawkins GP. Functional anatomy of the anterior cruciate ligament. Fibre bundle actions related to ligament replacements and injuries. *J Bone Joint Surg Br*. 1991;73(2):260-7.

88. Duthon VB, Barea C, Abrassart S, Fasel JH, Fritschy D, Menetrey J. Anatomy of the anterior cruciate ligament. *Knee Surg Sports Traumatol Arthrosc*. 2006;14(3):204-13.

89. Harner CD, Baek GH, Vogrin TM, Carlin GJ, Kashiwaguchi S, Woo SL. Quantitative analysis of human cruciate ligament insertions. *Arthroscopy*. 1999;15(7):741-9.

90. Petersen W, Zantop T. Anatomy of the anterior cruciate ligament with regard to its two bundles. *Clin Orthop Relat Res*. 2007;454:35-47.

91. Odensten M, Gillquist J. Functional anatomy of the anterior cruciate ligament and a rationale for reconstruction. *J Bone Joint Surg Am*. 1985;67(2):257-62.

92. Hollis JM, Takai S, Adams DJ, Horibe S, Woo SL. The effects of knee motion and external loading on the length of the anterior cruciate ligament (ACL): a kinematic study. *J Biomech Eng*. 1991;113(2):208-14.

93. Colombet P, Robinson J, Christel P et al. Morphology of anterior cruciate ligament attachments for anatomic reconstruction: a cadaveric dissection and radiographic study. *Arthroscopy*. 2006;22(9):984-92.

94. Butler DL, Noyes FR, Grood ES. Ligamentous restraints to anterior-posterior drawer in the human knee. A biomechanical study. *J Bone Joint Surg Am*. 1980;62(2):259-70.

95. Li G, DeFrate LE, Sun H, Gill TJ. In vivo elongation of the anterior cruciate ligament and posterior cruciate ligament during knee flexion. *Am J Sports Med*. 2004;32(6):1415-20.

96. Kawaguchi Y, Kondo E, Takeda R, Akita K, Yasuda K, Amis AA. The role of fibers in the femoral attachment of the anterior cruciate ligament in resisting tibial displacement. *Arthroscopy*. 2015;31(3):435-44.

97. Müller W. *The knee: form, function, and ligament reconstruction.* New York: Springer-Verlag Berlin Heidelberg; 1983, 314 p.

98. Kennedy JC, Alexander IJ, Hayes KC. Nerve supply of the human knee and its functional importance. *Am J Sports Med*. 1982;10(6):329-35.

99. Kennedy JC, Weinberg HW, Wilson AS. The anatomy and function of the anterior cruciate ligament. As determined by clinical and morphological studies. *J Bone Joint Surg Am*. 1974;56(2):223-35.

100. Schutte MJ, Dabezies EJ, Zimny ML, Happel LT. Neural anatomy of the human anterior cruciate ligament. *J Bone Joint Surg Am*. 1987;69(2):243-7.

101. Johansson H, Sjolander P, Sojka P. A sensory role for the cruciate ligaments. *Clin Orthop Relat Res*. 1991;(268):161-78.

102. Tsuda E, Okamura Y, Otsuka H, Komatsu T, Tokuya S. Direct evidence of the anterior cruciate ligament-hamstring reflex arc in humans. *Am J Sports Med*. 2001;29(1):83-7.

103. Johansson H, Sjolander P, Sojka P. Activity in receptor afferents from the anterior cruciate ligament evokes reflex effects on fusimotor neurones. *Neurosci Res*. 1990;8(1):54-9.

104. Solomonow M, Baratta R, Zhou BH et al. The synergistic action of the anterior cruciate ligament and thigh muscles in maintaining joint stability. *Am J Sports Med*. 1987;15(3):207-13.

105. Smith HC, Vacek P, Johnson RJ et al. Risk factors for anterior cruciate ligament injury: a review of the literature - part 1: neuromuscular and anatomic risk. *Sports Health*. 2012;4(1):69-78.

106. Noyes FR, Grood ES. The strength of the anterior cruciate ligament in humans and Rhesus monkeys. *J Bone Joint Surg Am*. 1976;58(8):1074-82.

107. Woo SL, Hollis JM, Adams DJ, Lyon RM, Takai S. Tensile properties of the human femur-anterior cruciate ligament-tibia complex. The effects of specimen age and orientation. *Am J Sports Med*. 1991;19(3):217-25.

108. Chandrashekar N, Mansouri H, Slauterbeck J, Hashemi J. Sex-based differences in the tensile properties of the human anterior cruciate ligament. *J Biomech*. 2006;39(16):2943-50.

109. McLean SG, Huang X, Su A, Van Den Bogert AJ. Sagittal plane biomechanics cannot injure the ACL during sidestep cutting. *Clin Biomech (Bristol, Avon)*. 2004;19(8):828-38.

110. Kiapour AM, Demetropoulos CK, Kiapour A et al. Strain Response of the Anterior Cruciate Ligament to Uniplanar and Multiplanar Loads During Simulated Landings: Implications for Injury Mechanism. *Am J Sports Med*. 2016;44(8):2087-96.

111. Shin CS, Chaudhari AM, Andriacchi TP. Valgus plus internal rotation moments increase anterior cruciate ligament strain more than either alone. *Med Sci Sports Exerc*. 2011;43(8):1484-91.

112. Oh YK, Lipps DB, Ashton-Miller JA, Wojtys EM. What strains the anterior cruciate ligament during a pivot landing? *Am J Sports Med*. 2012;40(3):574-83.

113. Quatman CE, Kiapour AM, Demetropoulos CK et al. Preferential loading of the ACL compared with the MCL during landing: a novel in sim approach yields the multiplanar mechanism of dynamic valgus during ACL injuries. *Am J Sports Med*. 2014;42(1):177-86.

114. Olsen OE, Myklebust G, Engebretsen L, Bahr R. Injury mechanisms for anterior cruciate ligament injuries in team handball: a systematic video analysis. *Am J Sports Med*. 2004;32(4):1002-12.

115. Baratta R, Solomonow M, Zhou BH, Letson D, Chuinard R, D'Ambrosia R. Muscular coactivation. The role of the antagonist musculature in maintaining knee stability. *Am J Sports Med*. 1988;16(2):113-22.

116. Draganich LF, Vahey JW. An in vitro study of anterior cruciate ligament strain induced by quadriceps and hamstrings forces. *J Orthop Res*. 1990;8(1):57-63.

117. Durselen L, Claes L, Kiefer H. The influence of muscle forces and external loads on cruciate ligament strain. *Am J Sports Med*. 1995;23(1):129-36.

118. Markolf KL, O'Neill G, Jackson SR, McAllister DR. Effects of applied quadriceps and hamstrings muscle loads on forces in the anterior and posterior cruciate ligaments. *Am J Sports Med*. 2004;32(5):1144-9.

119. Adouni M, Shirazi-Adl A, Marouane H. Role of gastrocnemius activation in knee joint biomechanics: gastrocnemius acts as an ACL antagonist. *Comput Methods Biomech Biomed Engin*. 2016;19(4):376-85.

120. Waligora AC, Johanson NA, Hirsch BE. Clinical anatomy of the quadriceps femoris and extensor apparatus of the knee. *Clin Orthop Relat Res*. 2009;467(12):3297-306.

121. Brownstein B, Lamb RE, Mangine RE. Quadriceps torque and integrated electromyography*. *J Orthop Sports Phys Ther*. 1985;6(6):309-14.

122. Warren LF, Marshall JL. The supporting structures and layers on the medial side of the knee: an anatomical analysis. *J Bone Joint Surg Am*. 1979;61(1):56-62.

123. Woodley SJ, Mercer SR. Hamstring muscles: architecture and innervation. *Cells Tissues Organs*. 2005;179(3):125-41.

124. Arms SW, Pope MH, Johnson RJ, Fischer RA, Arvidsson I, Eriksson E. The biomechanics of anterior cruciate ligament rehabilitation and reconstruction. *Am J Sports Med*. 1984;12(1):8-18.

125. Beynnon BD, Fleming BC, Johnson RJ, Nichols CE, Renstrom PA, Pope MH. Anterior cruciate ligament strain behavior during rehabilitation exercises in vivo. *Am J Sports Med*. 1995;23(1):24-34.

126. More RC, Karras BT, Neiman R, Fritschy D, Woo SL, Daniel DM. Hamstrings--an anterior cruciate ligament protagonist. An in vitro study. *Am J Sports Med*. 1993;21(2):231-7.

127. Yasuda K, Sasaki T. Exercise after anterior cruciate ligament reconstruction. The force exerted on the tibia by the separate isometric contractions of the quadriceps or the hamstrings. *Clin Orthop Relat Res*. 1987;(220):275-83.

128. Renstrom P, Arms SW, Stanwyck TS, Johnson RJ, Pope MH. Strain within the anterior cruciate ligament during hamstring and quadriceps activity. *Am J Sports Med*. 1986;14(1):83-7.

129. Pandy MG, Shelburne KB. Dependence of cruciate-ligament loading on muscle forces and external load. *J Biomech*. 1997;30(10):1015-24.

130. Elias JJ, Faust AF, Chu YH, Chao EY, Cosgarea AJ. The soleus muscle acts as an agonist for the anterior cruciate ligament. An in vitro experimental study. *Am J Sports Med*. 2003;31(2):241-6.

131. Fleming BC, Renstrom PA, Ohlen G et al. The gastrocnemius muscle is an antagonist of the anterior cruciate ligament. *J Orthop Res*. 2001;19(6):1178-84.

132. Imwalle LE, Myer GD, Ford KR, Hewett TE. Relationship between hip and knee kinematics in athletic women during cutting maneuvers: a possible link to noncontact anterior cruciate ligament injury and prevention. *J Strength Cond Res*. 2009;23(8):2223-30.

133. Lass P, Kaalund S, leFevre S, Arendt-Nielsen L, Sinkjaer T, Simonsen O. Muscle coordination following rupture of the anterior cruciate ligament. Electromyographic studies of 14 patients. *Acta Orthop Scand*. 1991;62(1):9-14.

134. O'Connor JJ. Can muscle co-contraction protect knee ligaments after injury or repair? *J Bone Joint Surg Br*. 1993;75(1):41-8.

135. Geiser CF, O'Connor KM, Earl JE. Effects of isolated hip abductor fatigue on frontal plane knee mechanics. *Med Sci Sports Exerc*. 2010;42(3):535-45.

136. Khayambashi K, Ghoddosi N, Straub RK, Powers CM. Hip Muscle Strength Predicts Noncontact Anterior Cruciate Ligament Injury in Male and Female Athletes: A Prospective Study. *Am J Sports Med*. 2016;44(2):355-61.

137. Kernozek TW, Ragan RJ. Estimation of anterior cruciate ligament tension from inverse dynamics data and electromyography in females during drop landing. *Clin Biomech (Bristol, Avon)*. 2008;23(10):1279-86.

138. Flaxman TE, Alkjaer T, Smale KB, Simonsen EB, Krogsgaard MR, Benoit DL. Differences in EMG-moment relationships between ACL-injured and uninjured adults during a weight-bearing multidirectional force control task. *J Orthop Res*. 2019;37(1):113-23.

139. Majewski M, Susanne H, Klaus S. Epidemiology of athletic knee injuries: A 10-year study. *Knee*. 2006;13(3):184-8.

140. Griffin LY, Albohm MJ, Arendt EA et al. Understanding and preventing noncontact anterior cruciate ligament injuries: a review of the Hunt Valley II meeting, January 2005. *Am J Sports Med*. 2006;34(9):1512-32.

141. Gornitzky AL, Lott A, Yellin JL, Fabricant PD, Lawrence JT, Ganley TJ. Sport-Specific Yearly Risk and Incidence of Anterior Cruciate Ligament Tears in High School Athletes: A Systematic Review and Meta-analysis. *Am J Sports Med*. 2016;44(10):2716-23.

142. Mall NA, Chalmers PN, Moric M et al. Incidence and trends of anterior cruciate ligament reconstruction in the United States. *Am J Sports Med*. 2014;42(10):2363-70.

143. Herzog MM, Marshall SW, Lund JL, Pate V, Mack CD, Spang JT. Trends in Incidence of ACL Reconstruction and Concomitant Procedures Among Commercially Insured Individuals in the United States, 2002-2014. *Sports Health*. 2018;10(6):523-31.

144. Parkkari J, Pasanen K, Mattila VM, Kannus P, Rimpela A. The risk for a cruciate ligament injury of the knee in adolescents and young adults: a population-based cohort study of 46 500 people with a 9 year follow-up. *Br J Sports Med*. 2008;42(6):422-6.

145. Nordenvall R, Bahmanyar S, Adami J, Stenros C, Wredmark T, Fellander-Tsai L. A population-based nationwide study of cruciate ligament injury in Sweden, 2001-2009: incidence, treatment, and sex differences. *Am J Sports Med*. 2012;40(8):1808-13.

146. Gianotti SM, Marshall SW, Hume PA, Bunt L. Incidence of anterior cruciate ligament injury and other knee ligament injuries: a national population-based study. *J Sci Med Sport*. 2009;12(6):622-7.

147. Zbrojkiewicz D, Vertullo C, Grayson JE. Increasing rates of anterior cruciate ligament reconstruction in young Australians, 2000-2015. *Med J Aust*. 2018;208(8):354-8.

148. Beck NA, Lawrence JTR, Nordin JD, DeFor TA, Tompkins M. ACL Tears in School-Aged Children and Adolescents Over 20 Years. *Pediatrics*. 2017;139(3).

149. Werner BC, Yang S, Looney AM, Gwathmey FW, Jr. Trends in Pediatric and Adolescent Anterior Cruciate Ligament Injury and Reconstruction. *J Pediatr Orthop*. 2016;36(5):447-52.

150. Hewett TE, Di Stasi SL, Myer GD. Current concepts for injury prevention in athletes after anterior cruciate ligament reconstruction. *Am J Sports Med*. 2013;41(1):216-24.

151. Sanders TL, Maradit Kremers H, Bryan AJ et al. Incidence of Anterior Cruciate Ligament Tears and Reconstruction: A 21-Year Population-Based Study. *Am J Sports Med*. 2016;44(6):1502-7.

152. Mountcastle SB, Posner M, Kragh JF, Jr., Taylor DC. Gender differences in anterior cruciate ligament injury vary with activity: epidemiology of anterior cruciate ligament injuries in a young, athletic population. *Am J Sports Med*. 2007;35(10):1635-42.

153. Stanley LE, Kerr ZY, Dompier TP, Padua DA. Sex Differences in the Incidence of Anterior Cruciate Ligament, Medial Collateral Ligament, and Meniscal Injuries in Collegiate and High School Sports: 2009-2010 Through 2013-2014. *Am J Sports Med*. 2016;44(6):1565-72.

154. Gans I, Retzky JS, Jones LC, Tanaka MJ. Epidemiology of Recurrent Anterior Cruciate Ligament Injuries in National Collegiate Athletic Association Sports: The Injury Surveillance Program, 2004-2014. *Orthop J Sports Med*. 2018;6(6):2325967118777823.

155. McLean SG, Myers PT, Neal RJ, Walters MR. A quantitative analysis of knee joint kinematics during the sidestep cutting maneuver. Implications for non-contact anterior cruciate ligament injury. *Bull Hosp Jt Dis*. 1998;57(1):30-8.

156. Noyes FR, Mooar PA, Matthews DS, Butler DL. The symptomatic anterior cruciate-deficient knee. Part I: the long-term functional disability in athletically active individuals. *J Bone Joint Surg Am*. 1983;65(2):154-62.

157. Boden BP, Dean GS, Feagin JA, Jr., Garrett WE, Jr. Mechanisms of anterior cruciate ligament injury. *Orthopedics*. 2000;23(6):573-8.

158. Renstrom P, Ljungqvist A, Arendt E et al. Non-contact ACL injuries in female athletes: an International Olympic Committee current concepts statement. *Br J Sports Med*. 2008;42(6):394-412.

159. Wojtys EM, Huston LJ, Lindenfeld TN, Hewett TE, Greenfield ML. Association between the menstrual cycle and anterior cruciate ligament injuries in female athletes. *Am J Sports Med*. 1998;26(5):614-9.

160. Mack CD, Hershman EB, Anderson RB et al. Higher Rates of Lower Extremity Injury on Synthetic Turf Compared With Natural Turf Among National Football League Athletes: Epidemiologic Confirmation of a Biomechanical Hypothesis. *Am J Sports Med*. 2019;47(1):189-96.

161. Olsen OE, Myklebust G, Engebretsen L, Holme I, Bahr R. Relationship between floor type and risk of ACL injury in team handball. *Scand J Med Sci Sports*. 2003;13(5):299-304.

162. Webster KE, Santamaria LJ, McClelland JA, Feller JA. Effect of fatigue on landing biomechanics after anterior cruciate ligament reconstruction surgery. *Med Sci Sports Exerc*. 2012;44(5):910-6.

163. Kernozek TW, Torry MR, Iwasaki M. Gender differences in lower extremity landing mechanics caused by neuromuscular fatigue. *Am J Sports Med*. 2008;36(3):554-65.

164. Shin CS, Chaudhari AM, Andriacchi TP. The influence of deceleration forces on ACL strain during single-leg landing: a simulation study. *J Biomech*. 2007;40(5):1145-52.

165. Koga H, Nakamae A, Shima Y et al. Mechanisms for noncontact anterior cruciate ligament injuries: knee joint kinematics in 10 injury situations from female team handball and basketball. *Am J Sports Med*. 2010;38(11):2218-25.

166. Krosshaug T, Nakamae A, Boden BP et al. Mechanisms of anterior cruciate ligament injury in basketball: video analysis of 39 cases. *Am J Sports Med*. 2007;35(3):359-67.

167. Kristianslund E, Faul O, Bahr R, Myklebust G, Krosshaug T. Sidestep cutting technique and knee abduction loading: implications for ACL prevention exercises. *Br J Sports Med*. 2014;48(9):779-83.

168. Pollard CD, Sigward SM, Powers CM. Gender differences in hip joint kinematics and kinetics during side-step cutting maneuver. *Clin J Sport Med*. 2007;17(1):38-42.

169. Sell TC, Ferris CM, Abt JP et al. The effect of direction and reaction on the neuromuscular and biomechanical characteristics of the knee during tasks that simulate the noncontact anterior cruciate ligament injury mechanism. *Am J Sports Med*. 2006;34(1):43-54.

170. Ford KR, Myer GD, Toms HE, Hewett TE. Gender differences in the kinematics of unanticipated cutting in young athletes. *Med Sci Sports Exerc*. 2005;37(1):124-9.

171. Landry SC, McKean KA, Hubley-Kozey CL, Stanish WD, Deluzio KJ. Neuromuscular and lower limb biomechanical differences exist between male and female elite adolescent soccer players during an unanticipated run and crosscut maneuver. *Am J Sports Med*. 2007;35(11):1901-11.

172. Hanson AM, Padua DA, Troy Blackburn J, Prentice WE, Hirth CJ. Muscle activation during side-step cutting maneuvers in male and female soccer athletes. *J Athl Train*. 2008;43(2):133-43.

173. Weinhandl JT, Joshi M, O'Connor KM. Gender comparisons between unilateral and bilateral landings. *J Appl Biomech*. 2010;26(4):444-53.

174. Taylor JB, Ford KR, Nguyen AD, Shultz SJ. Biomechanical comparison of single- and double-leg jump landings in the sagittal and frontal plane. *Orthop J Sports Med*. 2016;4(6).

175. Chappell JD, Creighton RA, Giuliani C, Yu B, Garrett WE. Kinematics and electromyography of landing preparation in vertical stop-jump: risks for noncontact anterior cruciate ligament injury. *Am J Sports Med*. 2007;35(2):235-41.

176. Bates NA, Ford KR, Myer GD, Hewett TE. Kinetic and kinematic differences between first and second landings of a drop vertical jump task: implications for injury risk assessments. *Clin Biomech*. 2013;28(4):459-66.

177. Tran AA, Gatewood C, Harris AH, Thompson JA, Dragoo JL. The effect of foot landing position on biomechanical risk factors associated with anterior cruciate ligament injury. *J Exp Orthop*. 2016;3(1):13.

178. Myers CA, Torry MR, Peterson DS et al. Measurements of tibiofemoral kinematics during soft and stiff drop landings using biplane fluoroscopy. *Am J Sports Med*. 2011;39(8):1714-22.

179. Cortes N, Onate J, Abrantes J, Gagen L, Dowling E, Van Lunen B. Effects of gender and foot-landing techniques on lower extremity kinematics during drop-jump landings. *J Appl Biomech*. 2007;23(4):289-99.

180. Pappas E, Hagins M, Sheikhzadeh A, Nordin M, Rose D. Biomechanical differences between unilateral and bilateral landings from a jump: gender differences. *Clin J Sport Med*. 2007;17(4):263-8.

181. Ireland ML. Anterior cruciate ligament injury in female athletes: epidemiology. *J Athl Train*. 1999;34(2):150-4.

182. Kernozek TW, Torry MR, H VANH, Cowley H, Tanner S. Gender differences in frontal and sagittal plane biomechanics during drop landings. *Med Sci Sports Exerc*. 2005;37(6):1003-12; discussion 13.

183. Decker MJ, Torry MR, Wyland DJ, Sterett WI, Steadman JR. Gender differences in lower extremity kinematics, kinetics and energy absorption during landing. *Clin Biomech*. 2003;18(7):662-9.

184. Nagano Y, Ida H, Akai M, Fukubayashi T. Gender differences in knee kinematics and muscle activity during single limb drop landing. *Knee*. 2007;14(3):218-23.

185. Russell KA, Palmieri RM, Zinder SM, Ingersoll CD. Sex differences in valgus knee angle during a single-leg drop jump. *J Athl Train*. 2006;41(2):166-71.

186. Hughes G, Watkins J. Lower limb coordination and stiffness during landing from volleyball block jumps. *Res Sports Med*. 2008;16(2):138-54.

187. Huston LJ, Vibert B, Ashton-Miller JA, Wojtys EM. Gender differences in knee angle when landing from a drop-jump. *Am J Knee Surg*. 2001;14(4):215-20.

188. Ford KR, Myer GD, Hewett TE. Longitudinal effects of maturation on lower extremity joint stiffness in adolescent athletes. *Am J Sports Med*. 2010;38(9):1829-37.

189. Weinhandl JT, Irmischer BS, Sievert ZA. Sex differences in unilateral landing mechanics from absolute and relative heights. *Knee*. 2015;22(4):298-303.

190. Hewett TE, Myer GD, Ford KR. Decrease in neuromuscular control about the knee with maturation in female athletes. *J Bone Joint Surg Am*. 2004;86(8):1601-8.

191. Yu B, Lin CF, Garrett WE. Lower extremity biomechanics during the landing of a stop-jump task. *Clin Biomech (Bristol, Avon)*. 2006;21(3):297-305.

192. Pollard CD, Sigward SM, Powers CM. Limited hip and knee flexion during landing is associated with increased frontal plane knee motion and moments. *Clin Biomech (Bristol, Avon)*. 2010;25(2):142-6.

193. Podraza JT, White SC. Effect of knee flexion angle on ground reaction forces, knee moments and muscle co-contraction during an impact-like deceleration landing: implications for the non-contact mechanism of ACL injury. *Knee*. 2010;17(4):291-5.

194. Devita P, Skelly WA. Effect of landing stiffness on joint kinetics and energetics in the lower extremity. *Med Sci Sports Exerc*. 1992;24(1):108-15.

195. Padua DA, Marshall SW, Boling MC, Thigpen CA, Garrett WE, Jr., Beutler AI. The Landing Error Scoring System (LESS) Is a valid and reliable clinical assessment tool of jump-landing biomechanics: The JUMP-ACL study. *Am J Sports Med*. 2009;37(10):1996-2002.

196. Ishida T, Yamanaka M, Takeda N et al. The effect of changing toe direction on knee kinematics during drop vertical jump: a possible risk factor for anterior cruciate ligament injury. *Knee Surg Sports Traumatol Arthrosc*. 2015;23(4):1004-9.

197. Lloyd DG, Buchanan TS, Besier TF. Neuromuscular biomechanical modeling to understand knee ligament loading. *Med Sci Sports Exerc*. 2005;37(11):1939-47.

198. Shimokochi Y, Shultz SJ. Mechanisms of noncontact anterior cruciate ligament injury. *J Athl Train*. 2008;43(4):396-408.

199. Myer GD, Ford KR, Hewett TE. The effects of gender on quadriceps muscle activation strategies during a maneuver that mimics a high ACL injury risk position. *J Electromyogr Kinesiol*. 2005;15(2):181-9.

200. Palmieri-Smith RM, Wojtys EM, Ashton-Miller JA. Association between preparatory muscle activation and peak valgus knee angle. *J Electromyogr Kinesiol*. 2008;18(6):973-9.

201. Palmieri-Smith RM, McLean SG, Ashton-Miller JA, Wojtys EM. Association of quadriceps and hamstrings cocontraction patterns with knee joint loading. *J Athl Train*. 2009;44(3):256-63.

202. Brown TN, McLean SG, Palmieri-Smith RM. Associations between lower limb muscle activation strategies and resultant multi-planar knee kinetics during single leg landings. *J Sci Med Sport*. 2014;17(4):408-13.

203. Sell TC, Ferris CM, Abt JP et al. Predictors of proximal tibia anterior shear force during a vertical stop-jump. *J Orthop Res*. 2007;25(12):1589-97.

204. Mokhtarzadeh H, Ewing K, Janssen I, Yeow CH, Brown N, Lee PVS. The effect of leg dominance and landing height on ACL loading among female athletes. *J Biomech*. 2017;60:181-7.

205. Nadler SF, Malanga GA, DePrince M, Stitik TP, Feinberg JH. The relationship between lower extremity injury, low back pain, and hip muscle strength in male and female collegiate athletes. *Clin J Sport Med*. 2000;10(2):89-97.

206. Beard DJ, Kyberd PJ, Fergusson CM, Dodd CA. Proprioception after rupture of the anterior cruciate ligament. An objective indication of the need for surgery? *J Bone Joint Surg Br*. 1993;75(2):311-5.

207. Chinnasee C, Weir G, Sasimontonkul S, Alderson J, Donnelly C. A Biomechanical Comparison of Single-Leg Landing and Unplanned Sidestepping. *Int J Sports Med*. 2018;39(8):636-45.

208. Dai B, Garrett WE, Gross MT, Padua DA, Queen RM, Yu B. The effect of performance demands on lower extremity biomechanics during landing and cutting tasks. *J Sport Health Sci*. 2019;8(3):228-34.

209. Kristianslund E, Krosshaug T. Comparison of drop jumps and sport-specific sidestep cutting: implications for anterior cruciate ligament injury risk screening. *Am J Sports Med*. 2013;41(3):684-8.

210. Bencke J, Naesborg H, Simonsen EB, Klausen K. Motor pattern of the knee joint muscles during side-step cutting in European team handball. Influence on muscular co-ordination after an intervention study. *Scand J Med Sci Sports*. 2000;10(2):68-77.

211. Xie D, Urabe Y, Ochiai J, Kobayashi E, Maeda N. Sidestep cutting maneuvers in female basketball players: stop phase poses greater risk for anterior cruciate ligament injury. *Knee*. 2013;20(2):85-9.

212. Peel SA, Schroeder LE, Sievert ZA, Weinhandl JT. Comparing Anterior Cruciate Ligament Injury Risk Variables Between Unanticipated Cutting and Decelerating Tasks. *J Appl Biomech*. 2019;35(2):101-6.

213. McLean SG, Huang X, van den Bogert AJ. Association between lower extremity posture at contact and peak knee valgus moment during sidestepping: implications for ACL injury. *Clin Biomech (Bristol, Avon)*. 2005;20(8):863-70.

214. Sigward SM, Powers CM. The influence of gender on knee kinematics, kinetics and muscle activation patterns during side-step cutting. *Clin Biomech (Bristol, Avon)*. 2006;21(1):41-8.

215. Sigward SM, Powers CM. Loading characteristics of females exhibiting excessive valgus moments during cutting. *Clin Biomech (Bristol, Avon)*. 2007;22(7):827-33.

216. McLean SG, Neal RJ, Myers PT, Walters MR. Knee joint kinematics during the sidestep cutting maneuver: potential for injury in women. *Med Sci Sports Exerc*. 1999;31(7):959-68.

217. Malinzak RA, Colby SM, Kirkendall DT, Yu B, Garrett WE. A comparison of knee joint motion patterns between men and women in selected athletic tasks. *Clin Biomech (Bristol, Avon)*. 2001;16(5):438-45.

218. Pollard CD, Davis IM, Hamill J. Influence of gender on hip and knee mechanics during a randomly cued cutting maneuver. *Clin Biomech (Bristol, Avon)*. 2004;19(10):1022-31.

219. Ireland ML. The female ACL: why is it more prone to injury? *Orthop Clin North Am*. 2002;33(4):637-51.

220. Christensen JC, Goldfine LR, Barker T, Collingridge DS. What can the first 2 months tell us about outcomes after anterior cruciate ligament reconstruction? *J Athl Train*. 2015;50(5):508-15.

221. Lohmander LS, Englund PM, Dahl LL, Roos EM. The long-term consequence of anterior cruciate ligament and meniscus injuries: osteoarthritis. *Am J Sports Med*. 2007;35(10):1756-69.

222. Ichiba A, Kishimoto I. Effects of articular cartilage and meniscus injuries at the time of surgery on osteoarthritic changes after anterior cruciate ligament reconstruction in patients under 40 years old. *Arch Orthop Trauma Surg*. 2009;129(3):409-15.

223. Yagi M, Wong EK, Kanamori A, Debski RE, Fu FH, Woo SL. Biomechanical analysis of an anatomic anterior cruciate ligament reconstruction. *Am J Sports Med*. 2002;30(5):660-6.

224. Woo SL, Kanamori A, Zeminski J, Yagi M, Papageorgiou C, Fu FH. The effectiveness of reconstruction of the anterior cruciate ligament with hamstrings and patellar tendon . A cadaveric study comparing anterior tibial and rotational loads. *J Bone Joint Surg Am*. 2002;84(6):907-14.

225. Mascarenhas R, Cvetanovich GL, Sayegh ET et al. Does Double-Bundle Anterior Cruciate Ligament Reconstruction Improve Postoperative Knee Stability Compared With Single-Bundle Techniques? A Systematic Review of Overlapping Meta-analyses. *Arthroscopy*. 2015;31(6):1185-96.

226. Li YL, Ning GZ, Wu Q et al. Single-bundle or double-bundle for anterior cruciate ligament reconstruction: a meta-analysis. *Knee*. 2014;21(1):28-37.

227. Hoshino Y, Fu FH, Irrgang JJ, Tashman S. Can joint contact dynamics be restored by anterior cruciate ligament reconstruction? *Clin Orthop Relat Res*. 2013;471(9):2924-31.

228. Gifstad T, Foss OA, Engebretsen L et al. Lower risk of revision with patellar tendon autografts compared with hamstring autografts: a registry study based on 45,998 primary ACL reconstructions in Scandinavia. *Am J Sports Med*. 2014;42(10):2319-28.

229. Tibor L, Chan PH, Funahashi TT, Wyatt R, Maletis GB, Inacio MC. Surgical Technique Trends in Primary ACL Reconstruction from 2007 to 2014. *J Bone Joint Surg Am*. 2016;98(13):1079-89.

230. Abdalla RJ, Monteiro DA, Dias L, Correia DM, Cohen M, Forgas A. Comparison Between The Results Achieved In Anterior Cruciate Ligament Reconstruction With Two

Kinds Of Autologous Grafts: Patellar Tendon Versus Semitendinous And Gracilis. *Rev Bras Ortop*. 2009;44(3):204-7.

231. Eriksson K, Anderberg P, Hamberg P et al. A comparison of quadruple semitendinosus and patellar tendon grafts in reconstruction of the anterior cruciate ligament. *J Bone Joint Surg Br*. 2001;83(3):348-54.

232. Mohtadi N, Chan D, Barber R, Oddone Paolucci E. A Randomized Clinical Trial Comparing Patellar Tendon, Hamstring Tendon, and Double-Bundle ACL Reconstructions: Patient-Reported and Clinical Outcomes at a Minimal 2-Year Follow-up. *Clin J Sport Med*. 2015;25(4):321-31.

233. Webster KE, Feller JA, Hartnett N, Leigh WB, Richmond AK. Comparison of Patellar Tendon and Hamstring Tendon Anterior Cruciate Ligament Reconstruction: A 15-Year Follow-up of a Randomized Controlled Trial. *Am J Sports Med*. 2016;44(1):83-90.

234. Zoran Z, Ivan V, Egon B, Dubravka B, Vjekoslav W, Vjekoslav K. Knee stability after arthroscopic anterior cruciate ligament reconstruction using the middle third of the patellar ligament and quadrupled hamstring tendons grafts - A two-year follow-up. *Injury*. 2015;46 Suppl 6:S91-5.

235. Xie X, Liu X, Chen Z, Yu Y, Peng S, Li Q. A meta-analysis of bone-patellar tendon-bone autograft versus four-strand hamstring tendon autograft for anterior cruciate ligament reconstruction. *Knee*. 2015;22(2):100-10.

236. Feller JA, Webster KE. A randomized comparison of patellar tendon and hamstring tendon anterior cruciate ligament reconstruction. *Am J Sports Med*. 2003;31(4):564-73.

237. Stanczak K, Zielinska M, Synder M, Domzalski M, Polguj M, Sibinski M. Comparison of hamstring and patellar tendon grafts in anterior cruciate ligament reconstruction: A prospective randomized study. *J Int Med Res*. 2018;46(2):785-91.

238. Steiner ME, Hecker AT, Brown CH, Jr., Hayes WC. Anterior cruciate ligament graft fixation. Comparison of hamstring and patellar tendon grafts. *Am J Sports Med*. 1994;22(2):240-6; discussion 6-7.

239. Laboute E, James-Belin E, Puig PL, Trouve P, Verhaeghe E. Graft failure is more frequent after hamstring than patellar tendon autograft. *Knee Surg Sports Traumatol Arthrosc*. 2018;26(12):3537-46.

240. Pinczewski LA, Lyman J, Salmon LJ, Russell VJ, Roe J, Linklater J. A 10-year comparison of anterior cruciate ligament reconstructions with hamstring tendon and patellar tendon autograft: a controlled, prospective trial. *Am J Sports Med*. 2007;35(4):564-74.

241. Goldblatt JP, Fitzsimmons SE, Balk E, Richmond JC. Reconstruction of the anterior cruciate ligament: meta-analysis of patellar tendon versus hamstring tendon autograft. *Arthroscopy*. 2005;21(7):791-803.

242. Yunes M, Richmond JC, Engels EA, Pinczewski LA. Patellar versus hamstring tendons in anterior cruciate ligament reconstruction: A meta-analysis. *Arthroscopy*. 2001;17(3):248-57.

243. Samuelsen BT, Webster KE, Johnson NR, Hewett TE, Krych AJ. Hamstring Autograft versus Patellar Tendon Autograft for ACL Reconstruction: Is There a Difference in Graft Failure Rate? A Meta-analysis of 47,613 Patients. *Clin Orthop Relat Res*. 2017;475(10):2459-68.

244. Baverel L, Demey G, Odri GA, Leroy P, Saffarini M, Dejour D. Do outcomes of outpatient ACL reconstruction vary with graft type? *Orthop Traumatol Surg Res*. 2015;101(7):803-6.

245. Kohn D, Sander-Beuermann A. Donor-site morbidity after harvest of a bone-tendon-bone patellar tendon autograft. *Knee Surg Sports Traumatol Arthrosc*. 1994;2(4):219-23.

246. Miller MD, Nichols T, Butler CA. Patella fracture and proximal patellar tendon rupture following arthroscopic anterior cruciate ligament reconstruction. *Arthroscopy*. 1999;15(6):640-3.

247. Sachs RA, Daniel DM, Stone ML, Garfein RF. Patellofemoral problems after anterior cruciate ligament reconstruction. *Am J Sports Med*. 1989;17(6):760-5.

248. Wright RW, Dunn WR, Amendola A et al. Risk of tearing the intact anterior cruciate ligament in the contralateral knee and rupturing the anterior cruciate ligament graft during the first 2 years after anterior cruciate ligament reconstruction: a prospective MOON cohort study. *Am J Sports Med*. 2007;35(7):1131-4.

249. Wiggins AJ, Grandhi RK, Schneider DK, Stanfield D, Webster KE, Myer GD. Risk of Secondary Injury in Younger Athletes After Anterior Cruciate Ligament Reconstruction: A Systematic Review and Meta-analysis. *Am J Sports Med*. 2016;44(7):1861-76.

250. Messer DJ, Shield AJ, Williams MD, Timmins RG, Bourne MN. Hamstring muscle activation and morphology are significantly altered 1-6 years after anterior cruciate ligament reconstruction with semitendinosus graft. *Knee Surg Sports Traumatol Arthrosc*. 2019.

251. Ward SH, Blackburn JT, Padua DA et al. Quadriceps Neuromuscular Function and Jump-Landing Sagittal-Plane Knee Biomechanics After Anterior Cruciate Ligament Reconstruction. *J Athl Train*. 2018;53(2):135-43.

252. Vairo GL, Myers JB, Sell TC, Fu FH, Harner CD, Lephart SM. Neuromuscular and biomechanical landing performance subsequent to ipsilateral semitendinosus and gracilis autograft anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc*. 2008;16(1):2-14.

253. Deneweth JM, Bey MJ, McLean SG, Lock TR, Kolowich PA, Tashman S. Tibiofemoral joint kinematics of the anterior cruciate ligament-reconstructed knee during a single-legged hop landing. *Am J Sports Med*. 2010;38(9):1820-8.

254. Orishimo KF, Kremenic IJ, Mullaney MJ, McHugh MP, Nicholas SJ. Adaptations in single-leg hop biomechanics following anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc*. 2010;18(11):1587-93.

255. Clarke SB, Kenny IC, Harrison AJ. Dynamic knee joint mechanics after anterior cruciate ligament reconstruction. *Med Sci Sports Exerc*. 2015;47(1):120-7.

256. Ortiz A, Olson S, Libby CL et al. Landing mechanics between noninjured women and women with anterior cruciate ligament reconstruction during 2 jump tasks. *Am J Sports Med*. 2008;36(1):149-57.

257. Hadders-Algra M. Variation and variability: key words in human motor development. *Phys Ther*. 2010;90(12):1823-37.

258. Davis K, Williams JL, Sanford BA, Zucker-Levin A. Assessing lower extremity coordination and coordination variability in individuals with anterior cruciate ligament reconstruction during walking. *Gait Posture*. 2019;67:154-9.

259. Hamill J, Palmer C, Van Emmerik RE. Coordinative variability and overuse injury. *Sports Med Arthrosc Rehabil Ther Technol*. 2012;4(1):45.

260. Bartlett R, Wheat J, Robins M. Is movement variability important for sports biomechanists? *Sports Biomech*. 2007;6(2):224-43.

261. Preatoni E, Hamill J, Harrison AJ et al. Movement variability and skills monitoring in sports. *Sports Biomech*. 2013;12(2):69-92.

262. Moraiti CO, Stergiou N, Ristanis S et al. The effect of anterior cruciate ligament reconstruction on stride-to-stride variability. *Arthroscopy*. 2009;25(7):742-9.

263. Moraiti CO, Stergiou N, Vasiliadis HS, Motsis E, Georgoulis A. Anterior cruciate ligament reconstruction results in alterations in gait variability. *Gait Posture*. 2010;32(2):169-75.

264. Armitano CN, Morrison S, Russell DM. Coordination stability between the legs is reduced after anterior cruciate ligament reconstruction. *Clin Biomech (Bristol, Avon)*. 2018;58:28-33.

265. Blache Y, Pairot de Fontenay B, Argaud S, Monteil K. Asymmetry of Inter-joint Coordination during Single Leg Jump after Anterior Cruciate Ligament Reconstruction. *Int J Sports Med*. 2017;38(2):159-67.

266. Pandy MG, Zajac FE. Optimal muscular coordination strategies for jumping. *J Biomech*. 1991;24(1):1-10.

267. Di Stasi S, Myer GD, Hewett TE. Neuromuscular training to target deficits associated with second anterior cruciate ligament injury. *J Orthop Sports Phys Ther*. 2013;43(11):777-92, a1-11.

268. Bourne MN, Bruder AM, Mentiplay BF, Carey DL, Patterson BE, Crossley KM. Eccentric knee flexor weakness in elite female footballers 1-10 years following anterior cruciate ligament reconstruction. *Phys Ther Sport*. 2019;37:144-9.

269. Kuenze CM, Hertel J, Weltman A, Diduch D, Saliba SA, Hart JM. Persistent neuromuscular and corticomotor quadriceps asymmetry after anterior cruciate ligament reconstruction. *J Athl Train*. 2015;50(3):303-12.

270. Lepley LK. Deficits in Quadriceps Strength and Patient-Oriented Outcomes at Return to Activity After ACL Reconstruction: A Review of the Current Literature. *Sports Health*. 2015;7(3):231-8.

271. Palmieri-Smith RM, Lepley LK. Quadriceps Strength Asymmetry After Anterior Cruciate Ligament Reconstruction Alters Knee Joint Biomechanics and Functional Performance at Time of Return to Activity. *Am J Sports Med*. 2015;43(7):1662-9.

272. Ithurburn MP, Paterno MV, Ford KR, Hewett TE, Schmitt LC. Young Athletes With Quadriceps Femoris Strength Asymmetry at Return to Sport After Anterior Cruciate Ligament Reconstruction Demonstrate Asymmetric Single-Leg Drop-Landing Mechanics. *Am J Sports Med*. 2015;43(11):2727-37.

273. Thomas AC, Villwock M, Wojtys EM, Palmieri-Smith RM. Lower extremity muscle strength after anterior cruciate ligament injury and reconstruction. *J Athl Train*. 2013;48(5):610-20.

274. Yasuda K, Ohkoshi Y, Tanabe Y, Kaneda K. Muscle weakness after anterior cruciate ligament reconstruction using patellar and quadriceps tendons. *Bull Hosp Jt Dis Orthop Inst*. 1991;51(2):175-85.

275. Drechsler WI, Cramp MC, Scott OM. Changes in muscle strength and EMG median frequency after anterior cruciate ligament reconstruction. *Eur J Appl Physiol*. 2006;98(6):613-23.

276. Konishi Y, Ikeda K, Nishino A, Sunaga M, Aihara Y, Fukubayashi T. Relationship between quadriceps femoris muscle volume and muscle torque after anterior cruciate ligament repair. *Scand J Med Sci Sports*. 2007;17(6):656-61.

277. Karanikas K, Arampatzis A, Bruggemann GP. Motor task and muscle strength followed different adaptation patterns after anterior cruciate ligament reconstruction. *Eur J Phys Rehabil Med*. 2009;45(1):37-45.

278. Konishi Y, Fukubayashi T. Relationship between muscle volume and muscle torque of the hamstrings after anterior cruciate ligament reconstruction. *J Sci Med Sport*. 2010;13(1):101-5.

279. Hart JM, Pietrosimone B, Hertel J, Ingersoll CD. Quadriceps activation following knee injuries: a systematic review. *J Athl Train*. 2010;45(1):87-97.

280. Snyder-Mackler L, Delitto A, Bailey SL, Stralka SW. Strength of the quadriceps femoris muscle and functional recovery after reconstruction of the anterior cruciate ligament. A prospective, randomized clinical trial of electrical stimulation. *J Bone Joint Surg Am*. 1995;77(8):1166-73.

281. Pietrosimone BG, Lepley AS, Ericksen HM, Gribble PA, Levine J. Quadriceps strength and corticospinal excitability as predictors of disability after anterior cruciate ligament reconstruction. *J Sport Rehabil*. 2013;22(1):1-6.

282. Bodkin SG, Norte GE, Hart JM. Corticospinal excitability can discriminate quadriceps strength indicative of knee function after ACL-reconstruction. *Scand J Med Sci Sports*. 2019;29(5):716-24.

283. Konishi Y, Fukubayashi T, Takeshita D. Mechanism of quadriceps femoris muscle weakness in patients with anterior cruciate ligament reconstruction. *Scand J Med Sci Sports*. 2002;12(6):371-5.

284. Kouzaki M, Shinohara M, Fukunaga T. Decrease in maximal voluntary contraction by tonic vibration applied to a single synergist muscle in humans. *J Appl Physiol (1985)*. 2000;89(4):1420-4.

285. Cross MJ, Roger G, Kujawa P, Anderson IF. Regeneration of the semitendinosus and gracilis tendons following their transection for repair of the anterior cruciate ligament. *Am J Sports Med*. 1992;20(2):221-3.

286. Papandrea P, Vulpiani MC, Ferretti A, Conteduca F. Regeneration of the semitendinosus tendon harvested for anterior cruciate ligament reconstruction. Evaluation using ultrasonography. *Am J Sports Med*. 2000;28(4):556-61.

287. Rispoli DM, Sanders TG, Miller MD, Morrison WB. Magnetic resonance imaging at different time periods following hamstring harvest for anterior cruciate ligament reconstruction. *Arthroscopy*. 2001;17(1):2-8.

288. Burks RT, Crim J, Fink BP, Boylan DN, Greis PE. The effects of semitendinosus and gracilis harvest in anterior cruciate ligament reconstruction. *Arthroscopy*. 2005;21(10):1177-85.

289. Nomura Y, Kuramochi R, Fukubayashi T. Evaluation of hamstring muscle strength and morphology after anterior cruciate ligament reconstruction. *Scand J Med Sci Sports*. 2015;25(3):301-7.

290. Snow BJ, Wilcox JJ, Burks RT, Greis PE. Evaluation of muscle size and fatty infiltration with MRI nine to eleven years following hamstring harvest for ACL reconstruction. *J Bone Joint Surg Am*. 2012;94(14):1274-82.

291. Lloyd DG, Buchanan TS. Strategies of muscular support of varus and valgus isometric loads at the human knee. *J Biomech*. 2001;34(10):1257-67.

292. Ageberg E, Roos HP, Silbernagel KG, Thomee R, Roos EM. Knee extension and flexion muscle power after anterior cruciate ligament reconstruction with patellar tendon graft or hamstring tendons graft: a cross-sectional comparison 3 years post surgery. *Knee Surg Sports Traumatol Arthrosc*. 2009;17(2):162-9.

293. Nakamura N, Horibe S, Sasaki S et al. Evaluation of active knee flexion and hamstring strength after anterior cruciate ligament reconstruction using hamstring tendons. *Arthroscopy*. 2002;18(6):598-602.

294. Viola RW, Sterett WI, Newfield D, Steadman JR, Torry MR. Internal and external tibial rotation strength after anterior cruciate ligament reconstruction using ipsilateral semitendinosus and gracilis tendon autografts. *Am J Sports Med*. 2000;28(4):552-5.

295. Armour T, Forwell L, Litchfield R, Kirkley A, Amendola N, Fowler PJ. Isokinetic evaluation of internal/external tibial rotation strength after the use of hamstring tendons for anterior cruciate ligament reconstruction. *Am J Sports Med*. 2004;32(7):1639-43.

296. Timmins RG, Bourne MN, Shield AJ, Williams MD, Lorenzen C, Opar DA. Short biceps femoris fascicles and eccentric knee flexor weakness increase the risk of hamstring injury in elite football (soccer): a prospective cohort study. *Br J Sports Med*. 2016;50(24):1524-35.

297. Hawkins RD, Hulse MA, Wilkinson C, Hodson A, Gibson M. The association football medical research programme: an audit of injuries in professional football. *Br J Sports Med*. 2001;35(1):43-7.

298. Barber-Westin SD, Noyes FR. Effect of Fatigue Protocols on Lower Limb Neuromuscular Function and Implications for Anterior Cruciate Ligament Injury Prevention Training: A Systematic Review. *Am J Sports Med*. 2017;45(14):3388-96.

299. Hawkins RD, Fuller CW. A prospective epidemiological study of injuries in four English professional football clubs. *Br J Sports Med*. 1999;33(3):196-203.

300. Williams JM, Andersen MB. Psychosocial influences on central and peripheral vision and reaction time during demanding tasks. *Behav Med*. 1997;22(4):160-7.

301. Andersen MB, Williams JM. Athletic injury, psychosocial factors and perceptual changes during stress. *J Sports Sci*. 1999;17(9):735-41.

302. Swanik CB. Brains and Sprains: The Brain's Role in Noncontact Anterior Cruciate Ligament Injuries. *J Athl Train*. 2015;50(10):1100-2.

303. Barry BK, Enoka RM. The neurobiology of muscle fatigue: 15 years later. *Integr Comp Biol*. 2007;47(4):465-73.

304. Gandevia SC. Some central and peripheral factors affecting human motoneuronal output in neuromuscular fatigue. *Sports Med*. 1992;13(2):93-8.

305. Gandevia SC. Spinal and supraspinal factors in human muscle fatigue. *Physiol Rev*. 2001;81(4):1725-89.

306. Gandevia SC, Allen GM, Butler JE, Taylor JL. Supraspinal factors in human muscle fatigue: evidence for suboptimal output from the motor cortex. *J Physiol*. 1996;490 (Pt 2):529-36.

307. Walker S, Peltonen J, Ahtiainen JP, Avela J, Hakkinen K. Neuromuscular fatigue induced by an isotonic heavy-resistance loading protocol in knee extensors. *J Sports Sci*. 2009;27(12):1271-9.

308. Cortes N, Greska E, Kollock R, Ambegaonkar J, Onate JA. Changes in lower extremity biomechanics due to a short-term fatigue protocol. *J Athl Train*. 2013;48(3):306-13.

309. Lucci S, Cortes N, Van Lunen B, Ringleb S, Onate J. Knee and hip sagittal and transverse plane changes after two fatigue protocols. *J Sci Med Sport*. 2011;14(5):453-9.

310. Xia R, Zhang X, Wang X, Sun X, Fu W. Effects of Two Fatigue Protocols on Impact Forces and Lower Extremity Kinematics during Drop Landings: Implications for Noncontact Anterior Cruciate Ligament Injury. *J Healthc Eng*. 2017;2017:5690519.

311. Gleeson NP, Reilly T, Mercer TH, Rakowski S, Rees D. Influence of acute endurance activity on leg neuromuscular and musculoskeletal performance. *Med Sci Sports Exerc*. 1998;30(4):596-608.

312. Monjo F, Terrier R, Forestier N. Muscle fatigue as an investigative tool in motor control: A review with new insights on internal models and posture-movement coordination. *Hum Mov Sci*. 2015;44:225-33.

313. van Melick N, van Rijn L, Nijhuis-van der Sanden MWG, Hoogeboom TJ, van Cingel REH. Fatigue affects quality of movement more in ACL-reconstructed soccer players than in healthy soccer players. *Knee Surg Sports Traumatol Arthrosc*. 2019;27(2):549-55.

314. Lessi GC, Serrao FV. Effects of fatigue on lower limb, pelvis and trunk kinematics and lower limb muscle activity during single-leg landing after anterior cruciate ligament reconstruction. *Knee Surg Sports Traumatol Arthrosc*. 2017;25(8):2550-8.

315. Gokeler A, Eppinga P, Dijkstra PU et al. Effect of fatigue on landing performance assessed with the landing error scoring system (less) in patients after ACL reconstruction. A pilot study. *Int J Sports Phys Ther*. 2014;9(3):302-11.

316. Miura K, Ishibashi Y, Tsuda E, Okamura Y, Otsuka H, Toh S. The effect of local and general fatigue on knee proprioception. *Arthroscopy*. 2004;20(4):414-8.

317. Hiemstra LA, Lo IK, Fowler PJ. Effect of fatigue on knee proprioception: implications for dynamic stabilization. *J Orthop Sports Phys Ther*. 2001;31(10):598-605.

318. Skinner HB, Wyatt MP, Hodgdon JA, Conard DW, Barrack RL. Effect of fatigue on joint position sense of the knee. *J Orthop Res*. 1986;4(1):112-8.

319. Ribeiro F, Venancio J, Quintas P, Oliveira J. The effect of fatigue on knee position sense is not dependent upon the muscle group fatigued. *Muscle Nerve*. 2011;44(2):217-20.

320. Ribeiro F, Santos F, Gonçalves P, Oliveira J. Effects of volleyball match-induced fatigue on knee joint position sense. *Eur J Sport Sci*. 2008;8(6):397-402.

321. Forestier N, Nougier V. The effects of muscular fatigue on the coordination of a multijoint movement in human. *Neurosci Lett*. 1998;252(3):187-90.

322. McDonald AC, Tse CT, Keir PJ. Adaptations to isolated shoulder fatigue during simulated repetitive work. Part II: Recovery. *J Electromyogr Kinesiol*. 2016;29:42-9.

323. Cote JN, Mathieu PA, Levin MF, Feldman AG. Movement reorganization to compensate for fatigue during sawing. *Exp Brain Res*. 2002;146(3):394-8.

324. Cote JN, Raymond D, Mathieu PA, Feldman AG, Levin MF. Differences in multi-joint kinematic patterns of repetitive hammering in healthy, fatigued and shoulder-injured individuals. *Clin Biomech (Bristol, Avon)*. 2005;20(6):581-90.

325. Cowley JC, Gates DH. Inter-joint coordination changes during and after muscle fatigue. *Hum Mov Sci*. 2017;56(Pt B):109-18.

326. Samaan MA, Hoch MC, Ringleb SI, Bawab S, Weinhandl JT. Isolated hamstrings fatigue alters hip and knee joint coordination during a cutting maneuver. *J Appl Biomech*. 2015;31(2):102-10.

327. Mudie KL, Gupta A, Green S, Clothier PJ. Adaptation of lower limb movement patterns when maintaining performance in the presence of muscle fatigue. *Hum Mov Sci*. 2016;48:28-36.

328. van den Bogert AJ. Analysis and simulation of mechanical loads on the human musculoskeletal system: a methodological overview. *Exerc Sport Sci Rev*. 1994;22:23-51.

329. McLean SG, Huang X, van den Bogert AJ. Investigating isolated neuromuscular control contributions to non-contact anterior cruciate ligament injury risk via computer simulation methods. *Clin Biomech (Bristol, Avon)*. 2008;23(7):926-36.

330. Markolf KL, Gorek JF, Kabo JM, Shapiro MS. Direct measurement of resultant forces in the anterior cruciate ligament. An in vitro study performed with a new experimental technique. *J Bone Joint Surg Am*. 1990;72(4):557-67.

331. Zajac FE. Muscle coordination of movement: a perspective. *J Biomech*. 1993;26 Suppl 1:109-24.

332. Zajac FE, Neptune RR, Kautz SA. Biomechanics and muscle coordination of human walking. Part I: introduction to concepts, power transfer, dynamics and simulations. *Gait Posture*. 2002;16(3):215-32.

333. Lin YC, Kim, H.J., Pandy, M.G. A computationally efficient method for assessing muscle function during human locomotion. *Int J Numer Meth Biomed Eng*. 2011;27(3):436-49.

334. Dorn TW, Lin YC, Pandy MG. Estimates of muscle function in human gait depend on how foot-ground contact is modelled. *Comput Methods Biomech Biomed Engin*. 2012;15(6):657-68.

335. Dorn TW, Schache AG, Pandy MG. Muscular strategy shift in human running: dependence of running speed on hip and ankle muscle performance. *J Exp Biol*. 2012;215(Pt 11):1944-56.

336. Anderson FC, Pandy MG. Individual muscle contributions to support in normal walking. *Gait Posture*. 2003;17(2):159-69.

337. Lim YP, Lin YC, Pandy MG. Muscle function during gait is invariant to age when walking speed is controlled. *Gait Posture*. 2013;38(2):253-9.

338. Maniar N, Schache AG, Cole MH, Opar DA. Lower-limb muscle function during sidestep cutting. *J Biomech*. 2019;82:186-92.

339. Hamner SR, Seth A, Delp SL. Muscle contributions to propulsion and support during running. *J Biomech*. 2010;43(14):2709-16.

340. Wright RW, Huston LJ, Spindler KP et al. Descriptive epidemiology of the Multicenter ACL Revision Study (MARS) cohort. *Am J Sports Med*. 2010;38(10):1979-86.

341. Kim JH, Lee KK, Kong SJ, An KO, Jeong JH, Lee YS. Effect of Anticipation on Lower Extremity Biomechanics During Side- and Cross-Cutting Maneuvers in Young Soccer Players. *Am J Sports Med*. 2014;42(8):1985-92.

342. Binkley JM, Stratford PW, Lott SA, Riddle DL. The Lower Extremity Functional Scale (LEFS): scale development, measurement properties, and clinical application. North American Orthopaedic Rehabilitation Research Network. *Phys Ther*. 1999;79(4):371-83.

343. Roos EM, Roos HP, Lohmander LS, Ekdahl C, Beynnon BD. Knee Injury and Osteoarthritis Outcome Score (KOOS)--development of a self-administered outcome measure. *J Orthop Sports Phys Ther*. 1998;28(2):88-96.

344. Higgins LD, Taylor MK, Park D et al. Reliability and validity of the International Knee Documentation Committee (IKDC) Subjective Knee Form. *Joint Bone Spine*. 2007;74(6):594-9.

345. Woby SR, Roach NK, Urmston M, Watson PJ. Psychometric properties of the TSK-11: a shortened version of the Tampa Scale for Kinesiophobia. *Pain*. 2005;117(1-2):137-44.

346. Bennell KL, Talbot RC, Wajswelner H, Techovanich W, Kelly DH, Hall AJ. Intra-rater and inter-rater reliability of a weight-bearing lunge measure of ankle dorsiflexion. *Aust J Physiother*. 1998;44(3):175-80.

347. Hoch MC, McKeon PO. Joint mobilization improves spatiotemporal postural control and range of motion in those with chronic ankle instability. *J Orthop Res*. 2011;29(3):326-32.

348. Kristianslund E, Krosshaug T, van den Bogert AJ. Effect of low pass filtering on joint moments from inverse dynamics: implications for injury prevention. *J Biomech*. 2012;45(4):666-71.

349. Weinhandl JT, O'Connor KM. Assessment of a greater trochanter-based method of locating the hip joint center. *J Biomech*. 2010;43(13):2633-6.

350. Grood ES, Suntay WJ. A joint coordinate system for the clinical description of three-dimensional motions: application to the knee. *J Biomech Eng*. 1983;105(2):136-44.

351. Wu G, Siegler S, Allard P et al. ISB recommendation on definitions of joint coordinate system of various joints for the reporting of human joint motion--part I: ankle, hip, and spine. International Society of Biomechanics. *J Biomech*. 2002;35(4):543-8.

352. Kristianslund E, Krosshaug T, Mok KM, McLean S, van den Bogert AJ. Expressing the joint moments of drop jumps and sidestep cutting in different reference frames--does it matter? *J Biomech*. 2014;47(1):193-9.

353. Dempster WT, Gabel WC, Felts WJ. The anthropometry of the manual work space for the seated subject. *Am J Phys Anthropol*. 1959;17:289-317.

354. Hanavan EP. A Mathematical Model of the Human Body. AMRL-TR-64-102. *AMRL TR*. 1964:1-149.

355. Pataky TC, Robinson MA, Vanrenterghem J. Vector field statistical analysis of kinematic and force trajectories. *J Biomech*. 2013;46(14):2394-401.

356. Pataky TC, Robinson MA, Vanrenterghem J. Region-of-interest analyses of one-dimensional biomechanical trajectories: bridging 0D and 1D theory, augmenting statistical power. *PeerJ*. 2016;4:e2652.

357. Zazulak BT, Hewett TE, Reeves NP, Goldberg B, Cholewicki J. Deficits in neuromuscular control of the trunk predict knee injury risk: a prospective biomechanical-epidemiologic study. *Am J Sports Med*. 2007;35(7):1123-30.

358. Weinhandl JT, Hoch MC, Bawab SY, Ringleb SI. Comparison of ACL strain estimated via a data-driven model with in vitro measurements. *Comput Methods Biomech Biomed Engin*. 2016;19(14):1550-6.

359. Lai AKM, Arnold AS, Wakeling JM. Why are Antagonist Muscles Co-activated in My Simulation? A Musculoskeletal Model for Analysing Human Locomotor Tasks. *Ann Biomed Eng*. 2017;45(12):2762-74.

360. Walker PS, Rovick JS, Robertson DD. The effects of knee brace hinge design and placement on joint mechanics. *J Biomech*. 1988;21(11):965-74.

361. Lu TW, O'Connor JJ. Bone position estimation from skin marker co-ordinates using global optimisation with joint constraints. *J Biomech*. 1999;32(2):129-34.

362. Crowninshield RD, Brand RA. A physiologically based criterion of muscle force prediction in locomotion. *J Biomech*. 1981;14(11):793-801.

363. Steele KM, Demers MS, Schwartz MH, Delp SL. Compressive tibiofemoral force during crouch gait. *Gait Posture*. 2012;35(4):556-60.

364. Hicks JL, Uchida TK, Seth A, Rajagopal A, Delp SL. Is my model good enough? Best practices for verification and validation of musculoskeletal models and simulations of movement. *J Biomech Eng*. 2015;137(2):020905.

365. Cowley JC, Dingwell JB, Gates DH. Effects of local and widespread muscle fatigue on movement timing. *Exp Brain Res*. 2014;232(12):3939-48.

366. Liu MQ, Anderson FC, Pandy MG, Delp SL. Muscles that support the body also modulate forward progression during walking. *J Biomech*. 2006;39(14):2623-30.

367. Liu MQ, Anderson FC, Schwartz MH, Delp SL. Muscle contributions to support and progression over a range of walking speeds. *J Biomech*. 2008;41(15):3243-52.

368. Neptune RR, Kautz SA, Zajac FE. Contributions of the individual ankle plantar flexors to support, forward progression and swing initiation during walking. *J Biomech*. 2001;34(11):1387-98.

369. Pandy MG, Lin YC, Kim HJ. Muscle coordination of mediolateral balance in normal walking. *J Biomech*. 2010;43(11):2055-64.

370. Bennett HJ, Shen G, Weinhandl JT, Zhang S. Validation of the greater trochanter method with radiographic measurements of frontal plane hip joint centers and knee mechanical axis angles and two other hip joint center methods. *J Biomech*. 2016;49(13):3047-51.

371. Hamner SR, Seth A, Steele KM, Delp SL. A rolling constraint reproduces ground reaction forces and moments in dynamic simulations of walking, running, and crouch gait. *J Biomech*. 2013;46(10):1772-6.

372. Zebis MK, Andersen LL, Bencke J, Kjaer M, Aagaard P. Identification of athletes at future risk of anterior cruciate ligament ruptures by neuromuscular screening. *Am J Sports Med*. 2009;37(10):1967-73.

373. Biscarini A, Botti FM, Pettorossi VE. Selective contribution of each hamstring muscle to anterior cruciate ligament protection and tibiofemoral joint stability in leg-extension exercise: a simulation study. *Eur J Appl Physiol*. 2013;113(9):2263-73.

374. Millard M, Uchida T, Seth A, Delp SL. Flexing computational muscle: modeling and simulation of musculotendon dynamics. *J Biomech Eng*. 2013;135(2):021005.

375. Tijs C, van Dieën JH, Baan GC, Maas H. Three-dimensional ankle moments and nonlinear summation of rat triceps surae muscles. *PloS one*. 2014;9(10):e111595.

Appendices

Appendix A. IRB Approval Letter

THE UNIVERSITY OF TENNESSEE KNOXVILLE

August 30, 2019

Joshua Weinhandl,
UTK - Coll of Education, Hlth, & Human - Kinesiology Recreation & Sport Studies

Re: UTK IRB-19-05383-XP
Study Title: Lower Extremity Muscle Contributions to ACL Loading in Healthy and ACL-Reconstructed Females

Dear Joshua Weinhandl:

The UTK Institutional Review Board (IRB) reviewed your application for the above referenced project. It determined that your application is eligible for expedited review under 45 CFR 46.110(b)(1), Category 4: Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing
Category 6: Collection of data from voice, video, digital, or image recordings made for research purposes
Category 7: Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. The IRB has reviewed these materials and determined that they do comply with proper consideration for the rights and welfare of human subjects and the regulatory requirements for the protection of human subjects. Therefore, this letter constitutes full approval by the IRB of your application (version 1.0).

Approval Information:

- Categories 4, 6, and 7
- 80 participants
- Written informed consent

Approved Documents:

Institutional Review Board | Office of Research & Engagement
1534 White Avenue Knoxville, TN 37996-1529
865-974-7697 865-974-7400 fax irb.utk.edu

- UTK Knoxville Main Campus IRB Application – Version 1.0
- Lower Extremity Muscle Contributions to ACL Loading in Healthy and ACL-Reconstructed Males and Females - Version 1.0
- Recruitment Flyer Dis 2019 - Version 1.0
- Twitter announcement - Version 1.0
- Screening Questions-Dis 2019 - Version 1.0
- Recruitment Email-Dis 2019 - Version 1.0
- TSK-11 - Version 1.0
- KOOS - Version 1.0
- IKDC - Version 1.0
- Musculoskeletal Questionnaire-Dis 2019 - Version 1.0
- LEFS - Version 1.0
- Fitness Activity Questionnaire - Version 1.0

The above documents have been dated and stamped IRB approved. Approval of this study will be valid from August 30, 2019 to 08/29/2020.

In the event that subjects are to be recruited using solicitation materials, such as brochures, posters, web-based advertisements, etc., these materials must receive prior approval of the IRB. Any revisions in the approved application must also be submitted to and approved by the IRB prior to implementation. In addition, you are responsible for reporting any unanticipated serious adverse events or other problems involving risks to subjects or others in the manner required by the local IRB policy.

Finally, re-approval of your project is required by the IRB in accord with the conditions specified above. You may not continue the research study beyond the time or other limits specified unless you obtain prior written approval of the IRB.

Sincerely,

Colleen P. Gilrane

Colleen P. Gilrane, Ph.D.
Chair

Institutional Review Board | Office of Research & Engagement
1534 White Avenue Knoxville, TN 37996-1529
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Appendix B. Informed Consent

Consent for Research Participation

Research Study Title: Lower Extremity Muscle Contributions to ACL Loading in Healthy and ACL-Reconstructed Males and Females

Researcher(s): Joshua T. Weinhandl, PhD, University of Tennessee, Knoxville
Shelby A. Peel, MS, University of Tennessee, Knoxville
Jake A. Melaro, MS, University of Tennessee, Knoxville
Lauren E. Schroeder, MS, University of Tennessee, Knoxville

Why am I being asked to be in this research study?

We are asking you to be in this research study because you are between the ages of 18 to 35 years old and are recreationally active. We are also asking you to be in this research study because you are either healthy or have experienced an ACL-reconstruction. We define being recreationally active as being physically active at least 3 times per week for a minimum of 30 minutes each session, with one of these sessions including dynamic movements, such as jumping and cutting. Individuals who are not between the ages of 18 to 35, not recreationally active 3 times a week, or have sustained a lower back or leg injury within the past 6 months will not be asked to be in this research study.

How long will I be in the research study?

If you agree to be in the study, your participation will involve 2 study visits, each lasting approximately 2.5 hours long.

What will happen if I say "Yes, I want to be in this research study"?

If you agree to be in this study, we will ask you to come to the Biomechanics Lab for two testing session.

On Day 1, you will come to the Biomechanics Lab. You will fill out the informed consent, as well as complete the Lower Extremity Functional Scale (LEFS), Knee Injury and Osteoarthritis Outcome form (KOOS), the International Knee Documentation Committee Subjective Knee form (IKDC), the Tampa Scale for Kinesiophobia form (TSK-11), a musculoskeletal health history form, and a fitness activity questionnaire. After these forms are completed, you will change into compression shorts and a generic t-shirt, which will be provided if you do not have them. After you change, you will be asked to complete a weight-bearing ankle joint range of motion assessment, a knee joint laxity assessment, a single-leg balance assessment, and finally a muscle strength assessment of your hip, knee, and ankle muscles.

On Day 2, you will come to the Biomechanics Lab. You will change into compression shorts and a generic t-shirt, which will be provided if you do not have them. You will also be fitted with a heart rate monitor to wear during your data collection. Your height and weight will be collected. You will then complete a 5-minute warm-up jog at a self-selected pace. After the warm-up, motion capture data collection will start. Reflective markers will be placed on your right leg and pelvis, which will be used to track your movement for each trial. You will perform three maximal vertical jumps, and then begin the landing protocol. For the landing protocol, you will complete three different tasks. For tasks one and two, you will stand on a 30-cm tall box that will be
placed ½ the distance of your height (in cm) away from the force plate. For the first task, you will jump with both legs onto the force plate, and then perform a maximum vertical jump immediately after landing. For the second task, you will land with your right leg on the force plate, then cut to the left at a 45-degree angle. The path that you will need to run will be marked with duct tape on the ground. For the third task, you will land with your left leg on the force plate, then cut to the right at a 45-degree angle. Five trials will be completed for each task. After the landing protocol is complete, you will then complete

a fatigue protocol. The fatigue protocol consists of you running to four different exercise stations. There will be an exercise station in front of you, one to your left, one to your right, and one directly behind you, placed 7.5-m from your starting position. You will be directed to run to a randomly selected exercise station, and complete five repetitions of the given exercise at that station, and then run back to your starting position where you then then receive instruction to run to a different exercise station. You will visit each station once in a round. After the completion of a round, you will complete 3 maximal vertical jumps, and then have 60 seconds of rest before the start of the next round. You will complete as many rounds as possible until your vertical jump height decreases by 25% of your pre-fatigue height. After the completion of the fatigue protocol, you will complete 3 maximal vertical jumps and complete the same landing protocol as described previously. After the completion of the second landing protocol, you will then complete a final round of 3 maximal vertical jumps. Day 2 session will then be completed.

What happens if I say "No, I do not want to be in this research study"?

Being in this study is up to you. You can say no now or leave the study later. Either way, your decision won't affect your grades, your relationship with your instructors, or standing with the University of Tennessee, Knoxville. Additionally, your decision won't affect your relationship with the University of Tennessee, Knoxville.

What happens if I say "Yes" but change my mind later?

Even if you decide to be in the study now, you can change your mind and stop at any time. If you decide to stop before the study is completed, you can tell the PI and/or co-PI that you want to withdraw from the study at any time. If you decide to withdraw from the study, your information will be kept de-identified and kept in a locked drawer in the Biomechanics lab. Only study personnel will have access to any forms and data that have already been collected.

Are there any possible risks to me?

It is possible that someone could find out you were in this study or see your study information, but we believe this risk is small because of the procedures we use to protect your information. These procedures are described later in this form.

Possible risks include lower extremity injury during the landings of the study movements and possible soreness from the leg assessments. These risks will be minimized. The movements that are included are movements you should be familiar with, due to you being recreationally active. You are also required to warm up before data collection, so your muscles are ready to move.

Are there any benefits to being in this research study?

We do not expect you to benefit from being in this study. Your participation may help us to learn more about the relationship between fatigue and its relationship to traumatic knee injuries. We hope the knowledge gained from this study will benefit others in the future.

Who can see or use the information collected for this research study?

We will protect the confidentiality of your information by keeping all forms in a locker drawer in the Biomechanics lab, which is locked every day. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used. We will make every effort to prevent anyone who is not on the research team from knowing that you gave us information or what information came from you. Although it is unlikely, there are time when others may need to see the information we collect about you. These include people at the University of Tennessee, Knoxville who oversee research to make sure it is conducted properly.

What will happen to my information after this study is over?

We will keep your information to use for future research. Your name and other information that can directly identify you will be kept secure and stored separately from your research data collected as part of the study. We will not share your research data with other researchers.

Will I be paid for being in this research study?

You will not be paid for being in this study.

Will it cost me anything to be in this research study?

It will not cost you anything to be in this study

Who can answer my questions about this research study?

If you have questions or concerns about this study, or have experienced a research related problem or injury, contact the researchers, Dr. Joshua Weinhandl (jweinhan@utk.edu, 865-974-9556), Shelby Peel (speel@vols.utk.edu, 865-974-2091), Jake Melaro (jmelaro@vols.utk.edu, 865-974-2091) or Lauren Schroeder (lschroe1@vols.utk.edu, 865-974-2091).

For questions or concerns about your rights or to speak with someone other than the research team about the study, please contact:

Institutional Review Board
The University of Tennessee, Knoxville
1534 White Avenue
Blount Hall, Room 408
Knoxville, TN 37996-1529
Phone: 865-974-7697
Email: utkirb@utk.edu

STATEMENT OF CONSENT

I have read this form and the research study has been explained to me. I have been given the chance to ask questions and my questions have been answered. If I have more questions, I have been told who to contact. By signing this document, I am agreeing to be in this study. I will receive a copy of this document after I sign it.

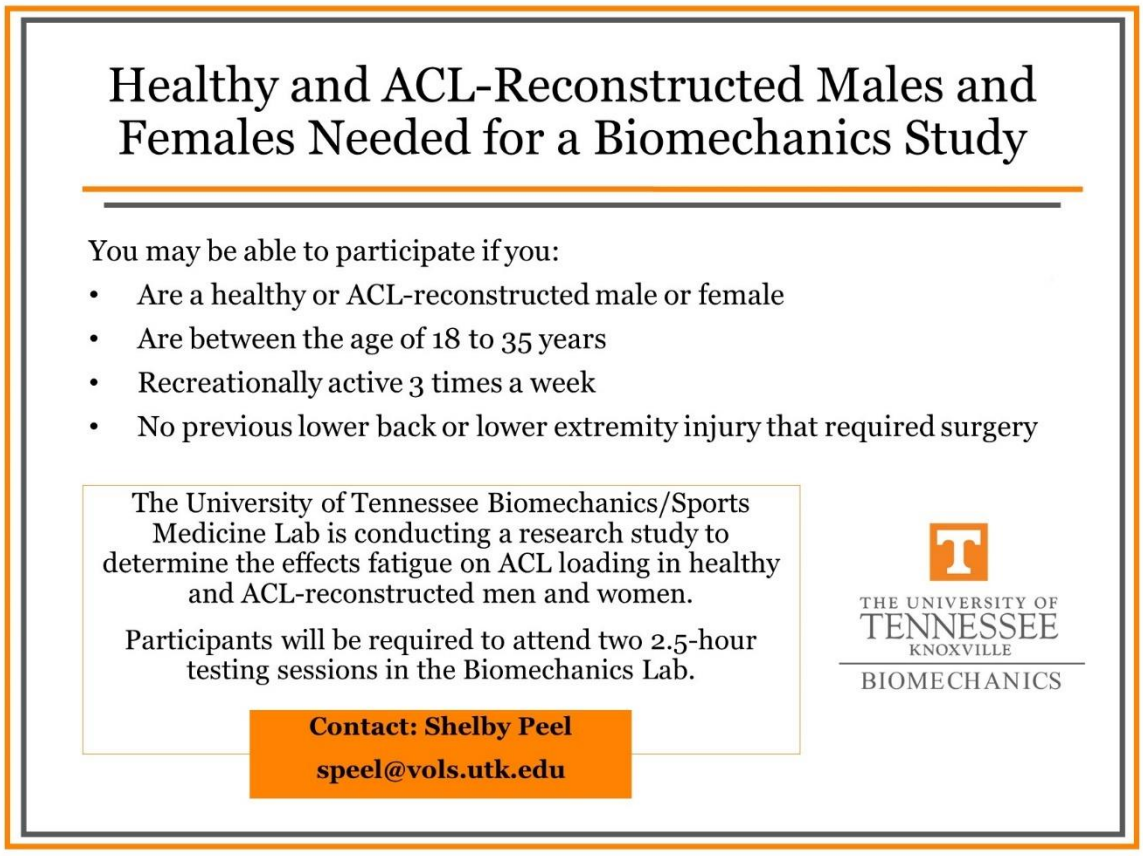
_____	_____	_____
Name of Adult Participant	Signature of Adult Participant	Date

Researcher Signature (to be completed at time of informed consent)

I have explained the study to the participant and answered all his/her questions. I believe that he/she understands the information described in this consent form and freely consents to be in the study.

_____	_____	_____
Name of Research Team Member	Signature of Research Team Member	Date

Appendix C. Recruitment Announcement



Appendix D. International Knee Documentation Committee Form

2000 IKDC SUBJECTIVE KNEE EVALUATION FORM

Your Full Name_____

Today's Date: _____/_____/_____ (Day / Month / Year) Date of Injury: _____/_____/_____ (Day / Month / Year)

SYMPTOMS*:

*Grade symptoms at the highest activity level at which you think you could function without significant symptoms, even if you are not actually performing activities at this level.

1. What is the highest level of activity that you can perform without significant knee pain?

   4❑ Very strenuous activities like jumping or pivoting as in basketball or soccer
   3❑ Strenuous activities like heavy physical work, skiing or tennis
   2❑ Moderate activities like moderate physical work, running or jogging
   1❑ Light activities like walking, housework or yard work
   0❑ Unable to perform any of the above activities due to knee pain

2. During the past 4 weeks, or since your injury, how often have you had pain?

	10	9	8	7	6	5	4	3	2	1	0	
Never	❑	❑	❑	❑	❑	❑	❑	❑	❑	❑	❑	Constant

3. If you have pain, how severe is it?

	10	9	8	7	6	5	4	3	2	1	0	
No pain	❑	❑	❑	❑	❑	❑	❑	❑	❑	❑	❑	Worst pain imaginable

4. During the past 4 weeks, or since your injury, how stiff or swollen was your knee?

   4❑ Not at all
   3❑ Mildly
   2❑ Moderately
   1❑ Very
   0❑ Extremely

5. What is the highest level of activity you can perform without significant swelling in your knee?

   4❑ Very strenuous activities like jumping or pivoting as in basketball or soccer
   3❑ Strenuous activities like heavy physical work, skiing or tennis
   2❑ Moderate activities like moderate physical work, running or jogging
   1❑ Light activities like walking, housework, or yard work
   0❑ Unable to perform any of the above activities due to knee swelling

6. During the past 4 weeks, or since your injury, did your knee lock or catch?

   0❑ Yes 1❑ No

7. What is the highest level of activity you can perform without significant giving way in your knee?
   4❑ Very strenuous activities like jumping or pivoting as in basketball or soccer
   3❑ Strenuous activities like heavy physical work, skiing or tennis
   2❑ Moderate activities like moderate physical work, running or jogging
   1❑ Light activities like walking, housework or yard work
   0❑ Unable to perform any of the above activities due to giving way of the knee

EMORY CLINIC
Physical Therapy

Page 2 – 2000 IKDC SUBJECTIVE KNEE EVALUATION FORM

SPORTS ACTIVITIES:

8. What is the highest level of activity you can participate in on a regular basis?

4❑ Very strenuous activities like jumping or pivoting as in basketball or soccer
3❑ Strenuous activities like heavy physical work, skiing or tennis
2❑ Moderate activities like moderate physical work, running or jogging
1❑ Light activities like walking, housework or yard work
0❑ Unable to perform any of the above activities due to knee

9. How does your knee affect your ability to:

		Not difficult at all	Minimally difficult	Moderately Difficult	Extremely difficult	Unable to do
a.	Go up stairs	4❑	3❑	2❑	1❑	0❑
b.	Go down stairs	4❑	3❑	2❑	1❑	0❑
c.	Kneel on the front of your knee	4❑	3❑	2❑	1❑	0❑
d.	Squat	4❑	3❑	2❑	1❑	0❑
e.	Sit with your knee bent	4❑	3❑	2❑	1❑	0❑
f.	Rise from a chair	4❑	3❑	2❑	1❑	0❑
g.	Run straight ahead	4❑	3❑	2❑	1❑	0❑
h.	Jump and land on your involved leg	4❑	3❑	2❑	1❑	0❑
i.	Stop and start quickly	4❑	3❑	2❑	1❑	0❑

FUNCTION:

10. How would you rate the function of your knee on a scale of 0 to 10 with 10 being normal, excellent function and 0 being the inability to perform any of your usual daily activities which may include sports?

FUNCTION PRIOR TO YOUR KNEE INJURY:

Couldn't perform daily activities	0 ❑	1 ❑	2 ❑	3 ❑	4 ❑	5 ❑	6 ❑	7 ❑	8 ❑	9 ❑	10 ❑	No limitation in daily activities

CURRENT FUNCTION OF YOUR KNEE:

Cannot perform daily activities	0 ❑	1 ❑	2 ❑	3 ❑	4 ❑	5 ❑	6 ❑	7 ❑	8 ❑	9 ❑	10 ❑	No limitation in daily activities

Appendix E. Knee Injury and Osteoarthritis Outcome Score Form

KOOS KNEE SURVEY

Today's date: _____/_____/_____ Date of birth: _____/_____/_____

Name: _____

INSTRUCTIONS: This survey asks for your view about your knee. This information will help us keep track of how you feel about your knee and how well you are able to perform your usual activities.
Answer every question by ticking the appropriate box, only one box for each question. If you are unsure about how to answer a question, please give the best answer you can.

Symptoms
These questions should be answered thinking of your knee symptoms during the **last week**.

S1. Do you have swelling in your knee?

Never	Rarely	Sometimes	Often	Always
☐	☐	☐	☐	☐

S2. Do you feel grinding, hear clicking or any other type of noise when your knee moves?

Never	Rarely	Sometimes	Often	Always
☐	☐	☐	☐	☐

S3. Does your knee catch or hang up when moving?

Never	Rarely	Sometimes	Often	Always
☐	☐	☐	☐	☐

S4. Can you straighten your knee fully?

Always	Often	Sometimes	Rarely	Never
☐	☐	☐	☐	☐

S5. Can you bend your knee fully?

Always	Often	Sometimes	Rarely	Never
☐	☐	☐	☐	☐

Stiffness
The following questions concern the amount of joint stiffness you have experienced during the **last week** in your knee. Stiffness is a sensation of restriction or slowness in the ease with which you move your knee joint.

S6. How severe is your knee joint stiffness after first wakening in the morning?

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

S7. How severe is your knee stiffness after sitting, lying or resting **later in the day**?

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

Pain

P1. How often do you experience knee pain?

Never	Monthly	Weekly	Daily	Always
☐	☐	☐	☐	☐

What amount of knee pain have you experienced the **last week** during the following activities?

P2. Twisting/pivoting on your knee

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P3. Straightening knee fully

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P4. Bending knee fully

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P5. Walking on flat surface

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P6. Going up or down stairs

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P7. At night while in bed

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P8. Sitting or lying

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

P9. Standing upright

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

Function, daily living

The following questions concern your physical function. By this we mean your ability to move around and to look after yourself. For each of the following activities please indicate the degree of difficulty you have experienced in the **last week** due to your knee.

A1. Descending stairs

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A2. Ascending stairs

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

For each of the following activities please indicate the degree of difficulty you have experienced in the **last week** due to your knee.

A3. Rising from sitting

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A4. Standing

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A5. Bending to floor/pick up an object

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A6. Walking on flat surface

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A7. Getting in/out of car

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A8. Going shopping

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A9. Putting on socks/stockings

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A10. Rising from bed

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A11. Taking off socks/stockings

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A12. Lying in bed (turning over, maintaining knee position)

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A13. Getting in/out of bath

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A14. Sitting

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A15. Getting on/off toilet

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

For each of the following activities please indicate the degree of difficulty you have experienced in the **last week** due to your knee.

A16. Heavy domestic duties (moving heavy boxes, scrubbing floors, etc)

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

A17. Light domestic duties (cooking, dusting, etc)

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

Function, sports and recreational activities

The following questions concern your physical function when being active on a higher level. The questions should be answered thinking of what degree of difficulty you have experienced during the **last week** due to your knee.

SP1. Squatting

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

SP2. Running

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

SP3. Jumping

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

SP4. Twisting/pivoting on your injured knee

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

SP5. Kneeling

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

Quality of Life

Q1. How often are you aware of your knee problem?

Never	Monthly	Weekly	Daily	Constantly
☐	☐	☐	☐	☐

Q2. Have you modified your life style to avoid potentially damaging activities to your knee?

Not at all	Mildly	Moderately	Severely	Totally
☐	☐	☐	☐	☐

Q3. How much are you troubled with lack of confidence in your knee?

Not at all	Mildly	Moderately	Severely	Extremely
☐	☐	☐	☐	☐

Q4. In general, how much difficulty do you have with your knee?

None	Mild	Moderate	Severe	Extreme
☐	☐	☐	☐	☐

Thank you very much for completing all the questions in this questionnaire.

Appendix F. Lower Extremity Functional Scale Form

Lower Extremity Functional Scale

We are interested in knowing whether or not you are having any difficulty at all with the activities listed below. Please provide an honest answer for each activity.

KEY
0 - Extreme difficulty or unable to perform activity
1 - Quite a bit of difficulty
2 - Moderate difficulty
3 - A little bit of difficulty
4 - No difficulty

Today, ***do you*** or ***would you*** have any difficulty at all with:	Extreme 0	Quite a bit 1	Moderate 2	Minimal 3	None 4
1. Any of your usual work, housework or school activities	☐	☐	☐	☐	☐
2. Your usual hobbies, recreational or sporting activities	☐	☐	☐	☐	☐
3. Getting into or out of the bath	☐	☐	☐	☐	☐
4. Walking between rooms	☐	☐	☐	☐	☐
5. Putting on your shoes or socks	☐	☐	☐	☐	☐
6. Squatting	☐	☐	☐	☐	☐
7. Lifting an object, like a bag of groceries from the floor	☐	☐	☐	☐	☐
8. Performing light activities around your home	☐	☐	☐	☐	☐
9. Performing heavy activities around your home	☐	☐	☐	☐	☐
10. Getting into or out of a car	☐	☐	☐	☐	☐
11. Walking 2 blocks	☐	☐	☐	☐	☐
12. Walking a mile	☐	☐	☐	☐	☐
13. Going up or down 10 stairs (about 1 flight)	☐	☐	☐	☐	☐
14. Standing for 1 hour	☐	☐	☐	☐	☐
15. Sitting for 1 hour	☐	☐	☐	☐	☐
16. Running on even ground	☐	☐	☐	☐	☐
17. Running on uneven ground	☐	☐	☐	☐	☐
18. Making sharp turns while running fast	☐	☐	☐	☐	☐
19. Hopping	☐	☐	☐	☐	☐
20. Rolling over in bed	☐	☐	☐	☐	☐

Appendix G. Tampa Scale for Kinesiophobia-11 Form

Tampa Scale-11 (TSK-11) **Name:** **Date:**

This is a list of phrases which other patients have used to express how the view their condition. Please circle the number that best describes how you feel about each statement.

	Strongly Disagree	Somewhat Disagree	Somewhat Agree	Strongly Agree
1. I'm afraid I might injure myself if I exercise.	1	2	3	4
2. If I were to try to overcome it, my pain would increase.	1	2	3	4
3. My body is telling me I have something dangerously wrong.	1	2	3	4
4. People aren't taking my medical condition serious enough.	1	2	3	4
5. My accident/problem has put my body at risk for the rest of my life.	1	2	3	4
6. Pain always means I have injured my body.	1	2	3	4
7. Simply being careful that I do not make any unnecessary movements is the safest thing I can do to prevent my pain from worsening.	1	2	3	4
8. I wouldn't have this much pain if there wasn't something potentially dangerous going on in my body.	1	2	3	4
9. Pain lets me know when to stop exercising so that I don't injure myself.	1	2	3	4
10. I can't do all the things normal people do because it's too easy for me to get injured.	1	2	3	4
11. No one should have to exercise when he/she is in pain.	1	2	3	4

Source: Woby et al. (2005), Psychometric properties of the TSK-11: A shortened version of the Tampa Scale for Kinesiophobia. Pain, 117, 137-144.

MUSCULOSKELETAL QUESTIONNAIRE

Spine / Low Back / Sacroiliac Joint:

Have You Ever Suffered An Injury To Your Spine / Low Back / Sacroiliac Joint?

☐ YES ☐ NO

- ♦ List Time Missed _____
- ♦ Please Describe _____

Were Any Diagnostic Tests Performed? (check all that apply)

☐ X-Rays ☐ MRI ☐ CT-Scan ☐ Bone Scan

Have You Ever Been Hospitalized For A Spine / Low Back / Sacroiliac Joint Injury?

☐ YES ☐ NO

- ♦ When? _____
- ♦ Please Describe _____

Have You Ever Had Surgery of Any Kind on Your Spine / Low Back / Sacroiliac Joint?

☐ YES ☐ NO

- ♦ When? _____
- ♦ Please Describe _____

Have You Ever Had Numbness/Tingling Down One (1) or Both Legs?

☐ YES ☐ NO

- ♦ Date(s)/Time Missed? _____
- ♦ Please Describe? _____

Have You Ever Been Advised Not To Participate In Athletic Activities Due To A Spine, Low Back, or SI Joint Injury?

☐ YES ☐ NO

- ♦ Please Describe _____

Hip/Groin

Have You Ever Suffered An Injury To Your Hip / Groin *(including hernias and/or sports hernias)?* ☐ YES ☐ NO

- ♦ List Time Missed _____
- ♦ Please Describe _____

Were Any Diagnostic Tests Performed? (check all that apply)

☐ X-Rays ☐ MRI ☐ CT-Scan ☐ Bone Scan

Have You Ever Had Surgery For A Hip / Groin Injury?

☐ YES ☐ NO

- ♦ When? _____
- ♦ Please Describe _____

Have You Ever Been Advised Not To Participate In Athletic Activities Due To A Hip and/or Groin Injury?

☐ YES ☐ NO

- ♦ Please Describe _____

Thigh / Hamstring / Quadriceps:

Have You Ever Suffered An Injury To Your Thigh, Hamstring, and/or Quadriceps?

☐ YES ☐ NO

- ♦ List Time Missed _____
- ♦ Please Describe _____

Were Any Diagnostic Tests Performed? (check all that apply)

☐ X-Rays ☐ MRI ☐ CT-Scan ☐ Bone Scan

Have You Ever Been Hospitalized For A Thigh, Hamstring, and/or Quadriceps Injury?

☐ YES ☐ NO

- ♦ When? _____
- ♦ Please Describe _____

Have You Ever Had Surgery For A Thigh, Hamstring, and/or Quadriceps Injury?

☐ YES ☐ NO

- ♦ When? _____

- Please Describe _____

Have You Ever Been Advised Not To Participate In Athletic Activities Due To A Thigh, Hamstring, or Quadriceps Injury?

☐ YES ☐ NO

- Please Describe _____

Knee / Patella:

Have You Ever Suffered An Injury To Your Knee and/or Patella (kneecap)?

☐ YES ☐ NO

- List Time Missed _____
- Please Describe _____
- Were Any Diagnostic Tests Performed? (check all that apply)

  ☐ X-Rays ☐ MRI ☐ CT-Scan ☐ Bone Scan

Have You Ever Been Hospitalized For A Knee and/or Patella Injury?

☐ YES ☐ NO

- When? _____
- Please Describe _____

Have You Ever Had Surgery For A Knee and/or Patella Injury?

☐ YES ☐ NO

- When? _____
- Please Describe _____

Have You Ever Been Advised Not To Participate In Athletic Activities Due To A Knee/Patella Injury?

☐ YES ☐ NO

- Please Describe _____

Have You Ever/Do You Presently Wear A Knee Brace?

☐ YES ☐ NO

- Which Knee? _____ Brand / Model of Brace? _____
- Reason for Wearing ? _____

XVI. Ankle / Lower Leg:

Have You Ever Suffered An Injury To Your Ankle / Lower Leg?

☐ YES ☐ NO

- ♦ List Time Missed _____
- ♦ Please Describe _____

Were Any Diagnostic Tests Performed? (check all that apply)

☐ X-Rays ☐ MRI ☐ CT-Scan ☐ Bone Scan

Have You Ever Been Hospitalized For An Ankle / Lower Leg Injury?

☐ YES ☐ NO

- ♦ When? _____
- ♦ Please Describe _____

Have You Ever Had Surgery For An Ankle / Lower Leg Injury?

☐ YES ☐ NO

- ♦ When? _____
- ♦ Please Describe _____

Have You Ever Been Advised Not To Participate In Athletic Activities Due To An Ankle / Lower Leg Injury?

☐ YES ☐ NO

- ♦ Please Describe _____

Do You Presently ☐ Tape Your Ankle(s) ☐ Use Ankle Brace(s) ☐ Other

- ♦ Please Describe _____

XII. Foot / Toes:

Have You Ever Suffered An Injury To Your Foot / Toe(s)?

☐ YES ☐ NO

- ♦ List Time Missed _____
- ♦ Please Describe _____

Were Any Diagnostic Tests Performed? (check all that apply)

☐ X-Rays ☐ MRI ☐ CT-Scan ☐ Bone Scan

Have You Ever Had Surgery For A Foot / Toe Injury?

☐ YES ☐ NO

- When? _____
- Please Describe _____

Have You Ever Been Advised Not To Participate In Athletic Activities Due To An Foot and/or Toe Injury?

☐ YES ☐ NO

- Please Describe _____

XIII. Anterior Cruciate Ligament:

Have You Ever Experienced An Anterior Cruciate Ligament (ACL) Injury?

☐ YES ☐ NO

- List Time Missed _____
- Please Describe _____

What Knee? (check all that apply)

☐ Left Knee ☐ Right Knee ☐ Both

Were Any Diagnostic Tests Performed? (check all that apply)

☐ X-Rays ☐ MRI ☐ CT-Scan ☐ Bone Scan

- Please Describe _____

What Activity Were You Doing At The Time Of Injury?

- Please Describe _____

Have You Ever Had An ACL Reconstruction?

☐ YES ☐ NO

- List Time Missed _____
- Please Describe _____

What Knee? (check all that apply)

☐ Left Knee ☐ Right Knee ☐ Both

What Type Of Graft Did You Receive During Your ACL Reconstruction?

☐Semitendinosus-Gracillis Graft ☐Patellar Tendon Graft ☐Donor Graft ☐Other

- Please Describe _____

Did You Participate in Any Prehabilitation (i.e. Physical Therapy) Before Surgery?

☐ YES ☐ NO

- Please Describe _____
- How Long? _____

Did You Participate in Any Rehabilitation (i.e. Physical Therapy) After Surgery?

☐ YES ☐ NO

- Please Describe _____
- How Long? _____

How Long Was It Until You Returned Back To Play (i.e. Time Between Surgery To Clearance Back To Sport)

- Please Describe _____

Have You Ever Multiple ACL Reconstructions?

☐ YES ☐ NO

- Please Describe _____

IX. Menstrual Cycle

Are You Currently On Your Menstrual Cycle?

☐ YES ☐ NO

- How Long? _____

How Long Does Your Typical Menstrual Cycle Last?

- Please Describe _____

When Was Your Last Menstrual Cycle?

- Please Describe _____
- How Long? _____

When Was Your First Menstrual Cycle?

- Please Describe _____

Have You Ever Been Pregnant?

☐ YES ☐ NO

Appendix I. Fitness Activity Questionnaire

FITNESS ACTIVITY QUESTIONNAIRE

Please describe your current participation in the following types of exercise:

1. Aerobic (aerobic classes, walking, jogging, stair climbing, hiking, cycling, etc.)
Frequency (# of days per week): _____
Duration (time spent per session): _____minutes
Intensity (difficulty level): light somewhat hard hard very hard
How long have you been participating in aerobic activity as described above?
_____Years

2. Anaerobic (weight training, sprinting, etc.)
Frequency (# of days per week): _____
Duration (time spent per session): _____minutes
Intensity (difficulty level): light somewhat hard hard very hard
How long have you been participating in anaerobic activity as described above?
_____Years

3. Organized or Recreational sports
Type of sport(s):_____
Frequency (# of days per week): _____
Duration (time spent per session): _____minutes
Intensity (difficulty level): light somewhat hard hard very hard
How long have you been participating in sports activity as described above?
_____Years

Appendix J. Individual Subject Characteristics

Table 5: Individual subject characteristics.

Subject	Age (yrs)	Height (cm)	Mass (kg)	Leg Dominance	ACL-R Leg	IKDC	KOOS	LEFS	TSK-11
S01	27	171.5	74.5	R	-	84	96	76	11
S02	24	163.0	65.5	R	L	86	99	80	12
S03	25	163.0	62.6	R	-	87	100	80	11
S05	22	166.0	61.8	R	-	87	100	78	11
S06	20	166.0	61.6	R	L	83	97	80	18
S07	21	158.0	62.2	R	-	86	100	78	13
S08	25	172.0	77.8	R	-	87	98	80	21
S09	20	160.0	70.2	R	-	87	100	80	15
S10	20	177.5	69.9	R	R	86	100	80	16
S12	21	170.5	75.0	R	-	87	100	80	13
S15	23	168.5	72.5	R	R	69	81	72	16
Mean ± SD	22.5 ± 2.4	166.9 ± 59.0	68.5 ± 6.0			84 ± 5	87 ± 6	79 ± 3	14 ± 3

Appendix K. Individual Fatigue Protocol Characteristics

Table 6: Individual fatigue protocol characteristics.

Subject	Pre-Fatigue JH (m)	Post-Fatigue JH (m)	Post-Collection JH (m)	Rounds Completed	End HR (BPM)	End RPE	Total Time (MM:SS)
S01	0.30	0.26	0.24	9	179	17	2:13
S02	0.27	0.27	0.26	5	195	18	1:49
S03	0.20	0.19	0.16	19	171	19	2:22
S05	0.28	0.24	0.24	5	177	17	1:38
S06	0.28	0.26	0.26	6	201	20	1:48
S07	0.24	0.23	0.25	6	187	20	1:39
S08	0.30	0.33	0.30	8	190	17	1:43
S09	0.23	0.12	0.12	5	186	20	1:36
S10	0.23	0.16	0.15	6	182	18	1:54
S12	0.16	0.12	0.14	6	201	20	1:27
S15	0.27	0.25	0.24	5	200	20	1:52
Mean ± SD	0.25 ± 0.04	0.22 ± 0.07	0.21 ± 0.06	7 ± 4	188 ± 10	19 ± 1	2:00 ± 0.3

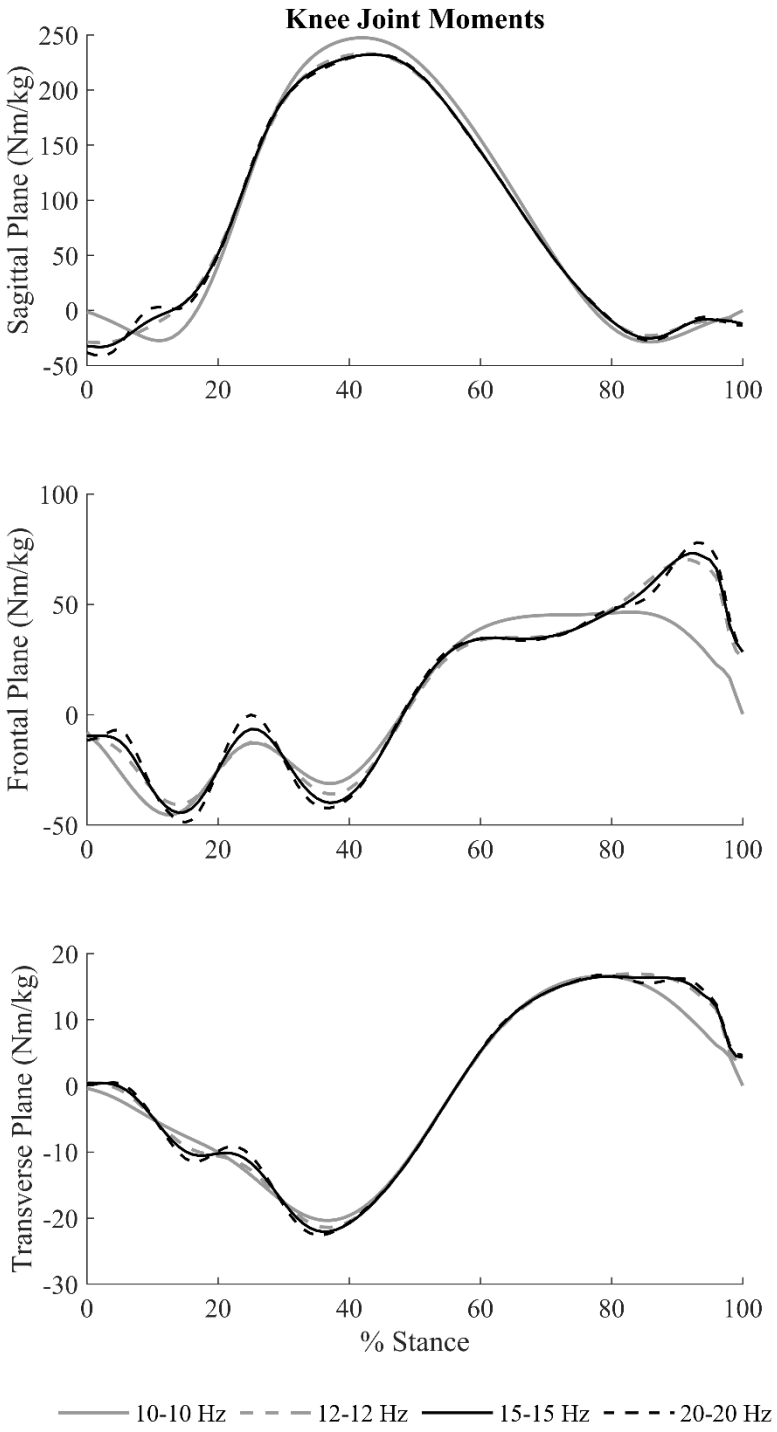


Figure 13: Various cut-off frequencies (i.e. 10-10 Hz, 12-12 Hz, 15-15 Hz, 20-20 Hz) used on three-dimensional knee joint moments to determine which cut-off frequency was most appropriate to filter the raw marker coordinate and GRF data.

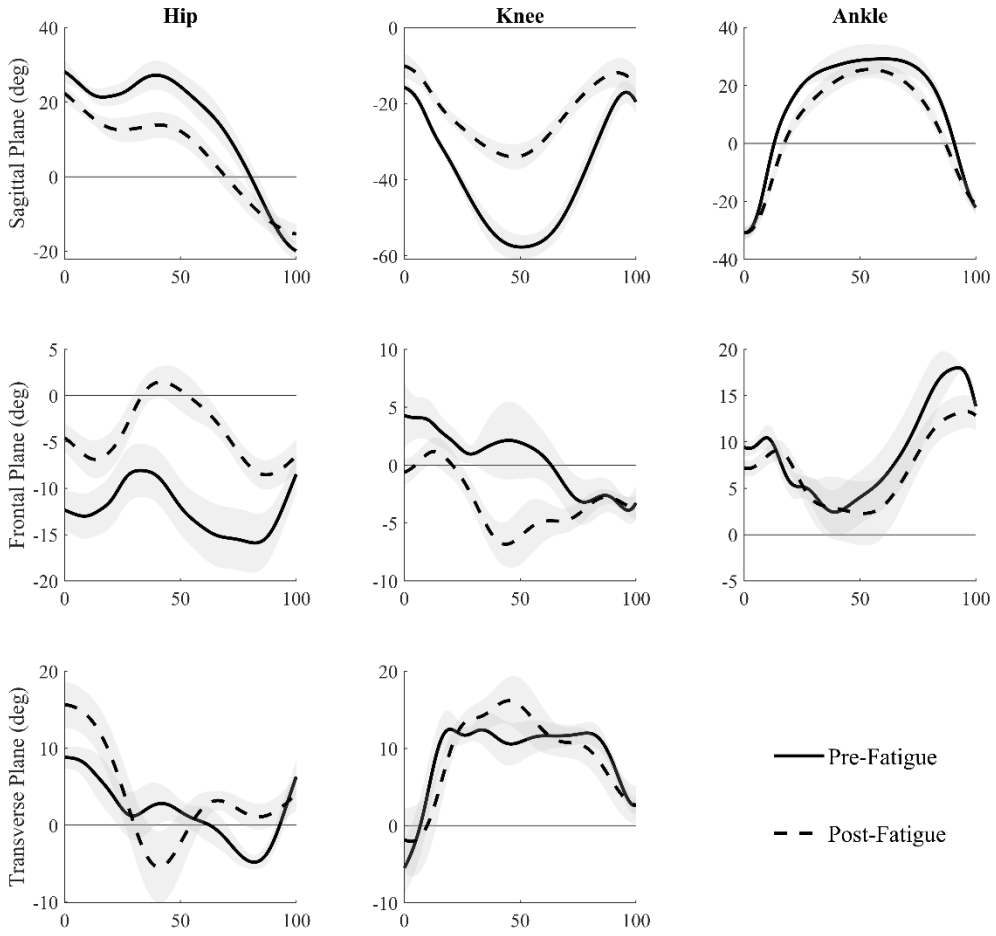


Figure 14: Subject 01 three-dimensional hip, knee, and ankle joint angles from 0 to 100% of stance phase. The shaded regions represent the standard deviation of the pre- and post-fatigue joint angles.

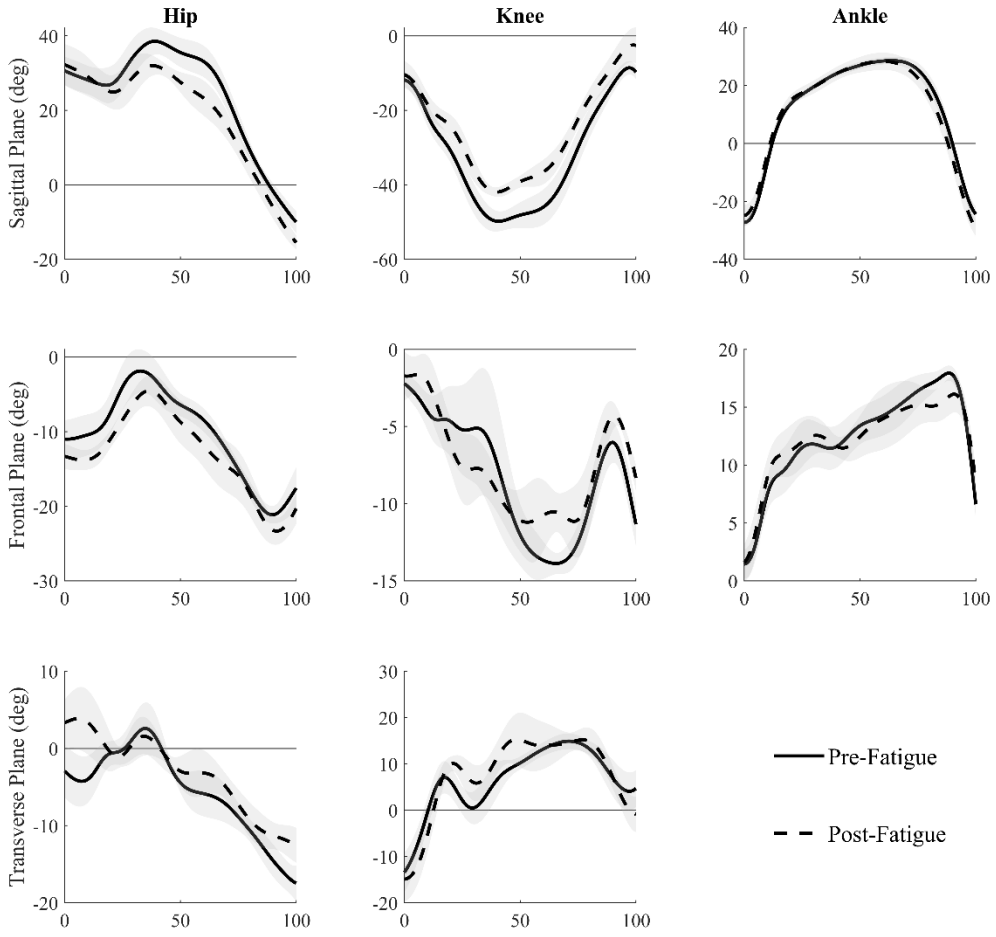


Figure 15: Subject 02 three-dimensional hip, knee, and ankle joint angles from 0 to 100% of stance phase. The shaded regions represent the standard deviation of the pre- and post-fatigue joint angles.

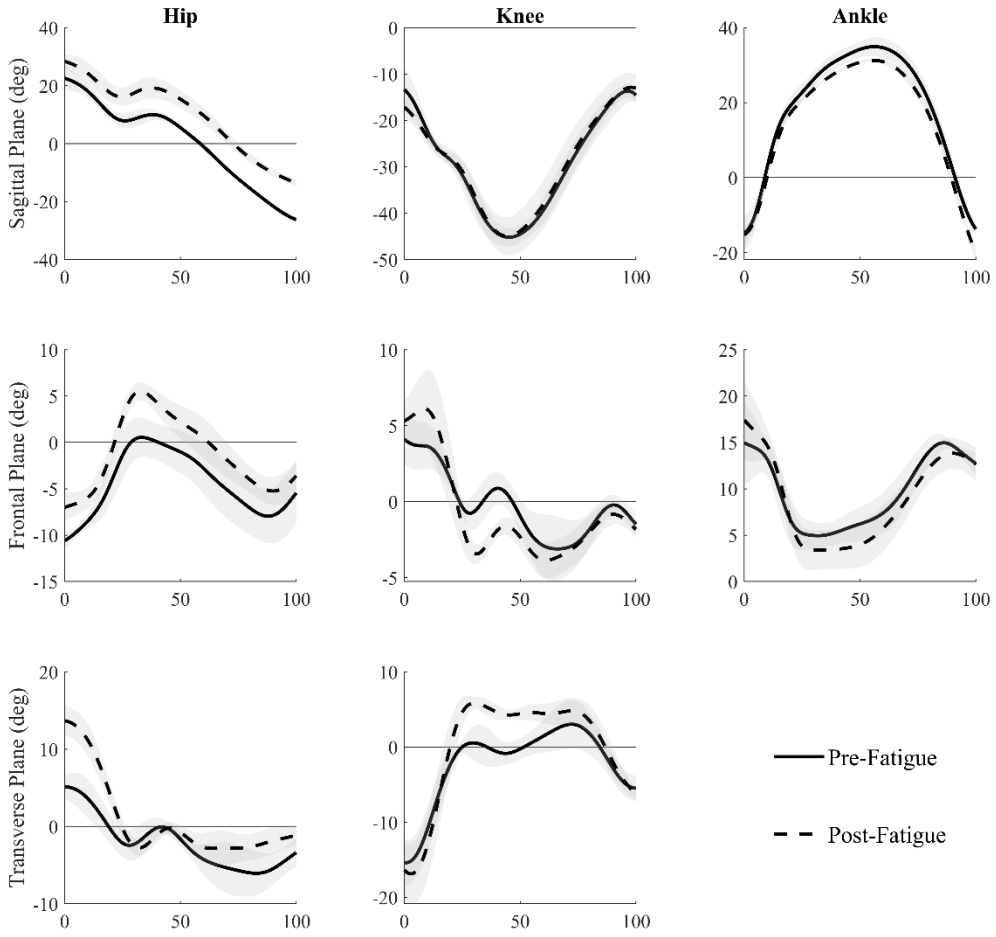


Figure 16: Subject 03 three-dimensional hip, knee, and ankle joint angles from 0 to 100% of stance phase. The shaded regions represent the standard deviation of the pre- and post-fatigue joint angles.

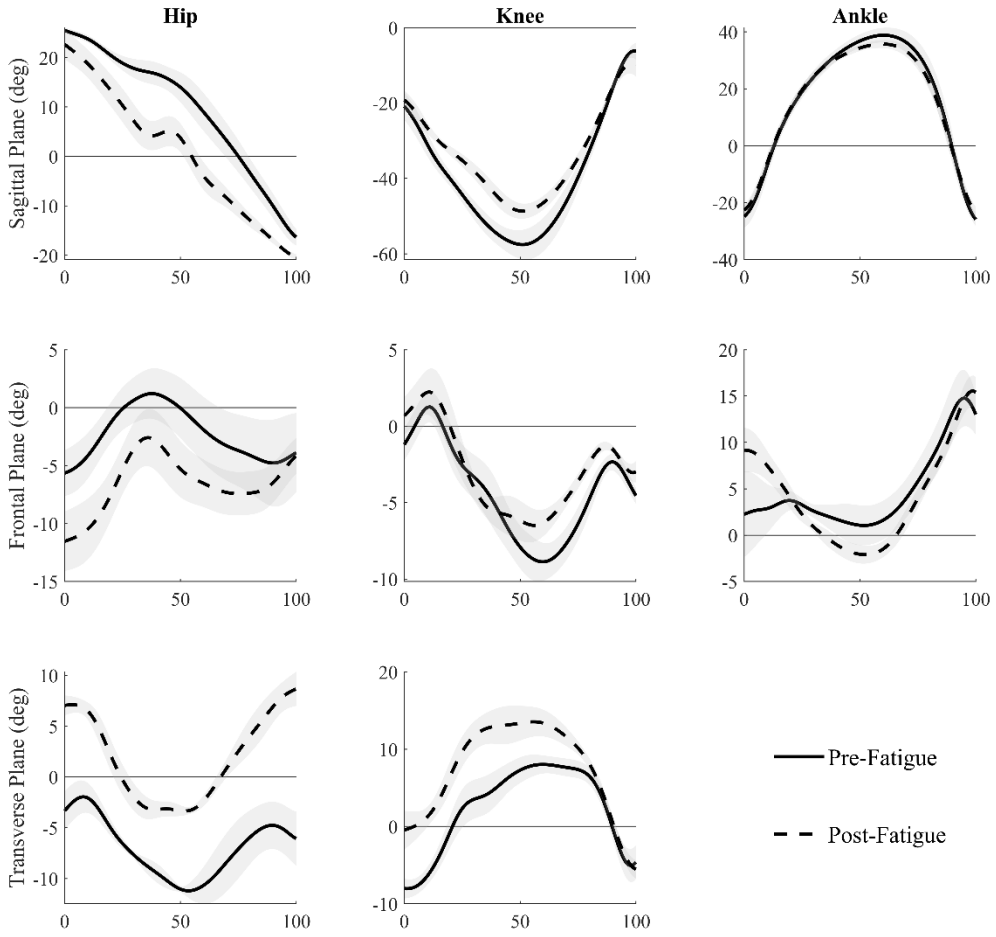


Figure 17: Subject 05 three-dimensional hip, knee, and ankle joint angles from 0 to 100% of stance phase. The shaded regions represent the standard deviation of the pre- and post-fatigue joint angles.

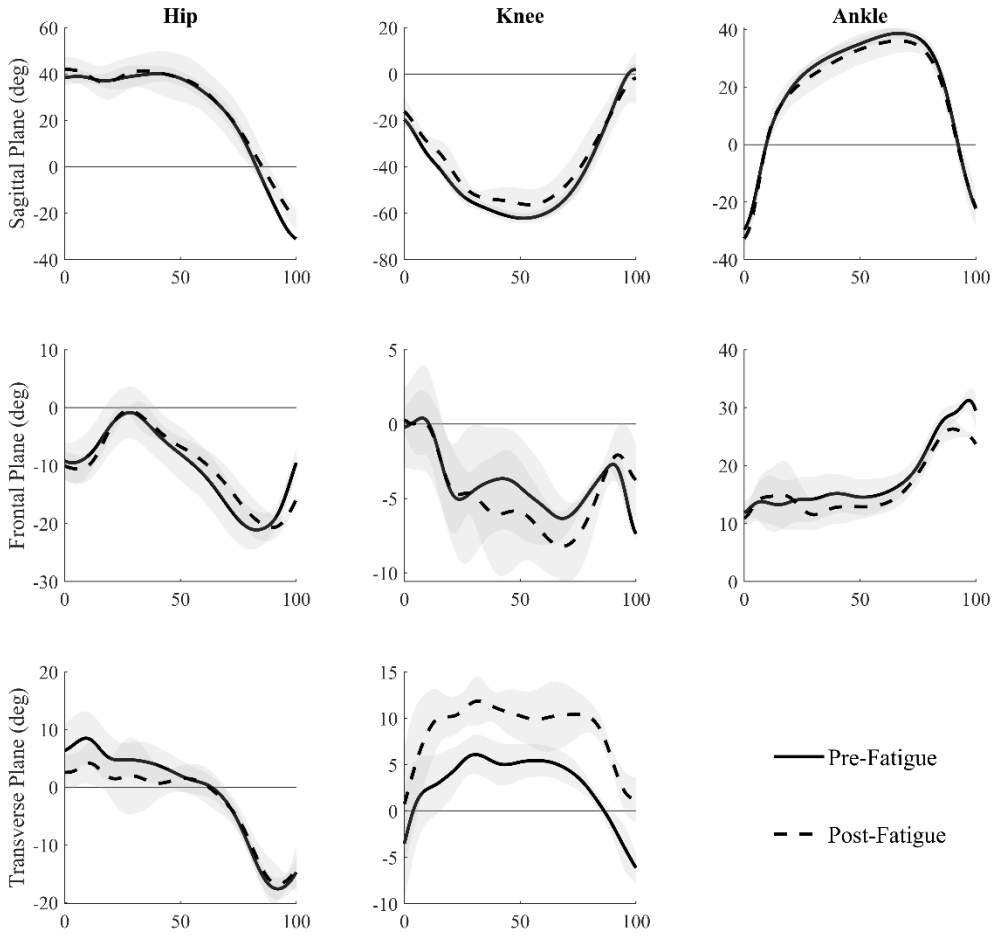


Figure 18: Subject 06 three-dimensional hip, knee, and ankle joint angles from 0 to 100% of stance phase. The shaded regions represent the standard deviation of the pre- and post-fatigue joint angles.

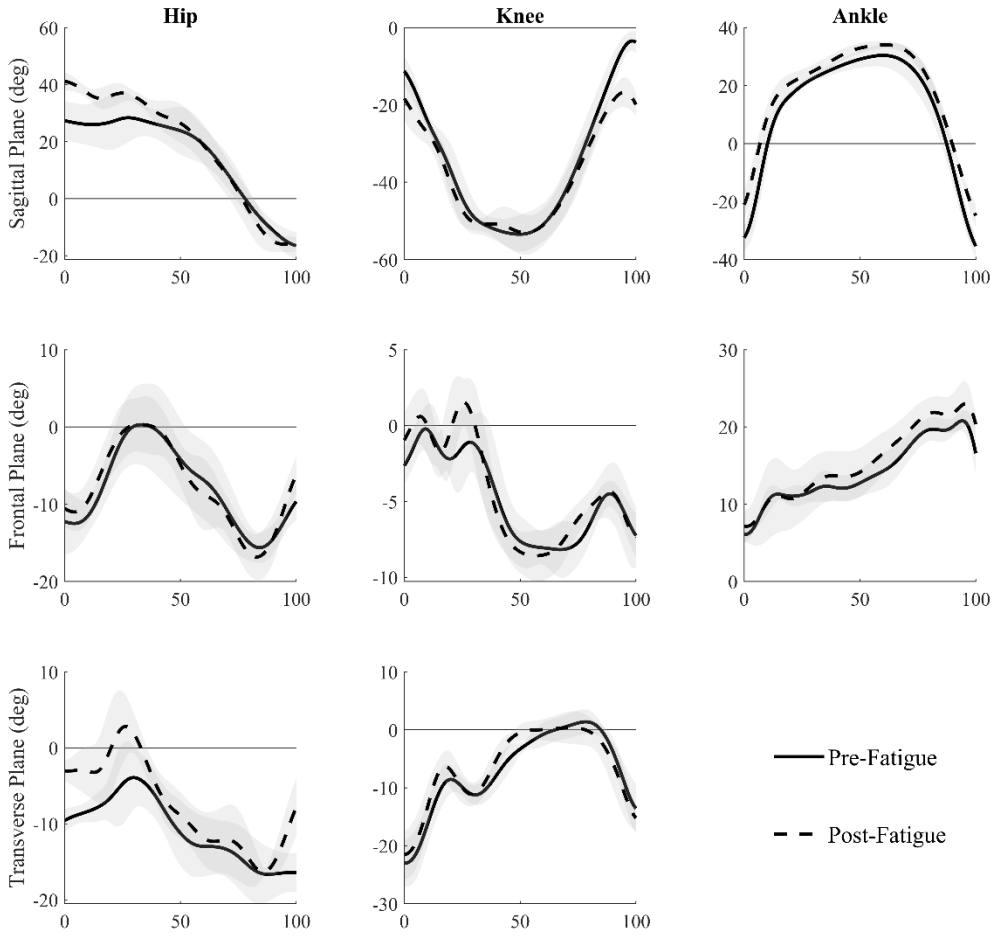


Figure 19: Subject 07 three-dimensional hip, knee, and ankle joint angles from 0 to 100% of stance phase. The shaded regions represent the standard deviation of the pre- and post-fatigue joint angles.

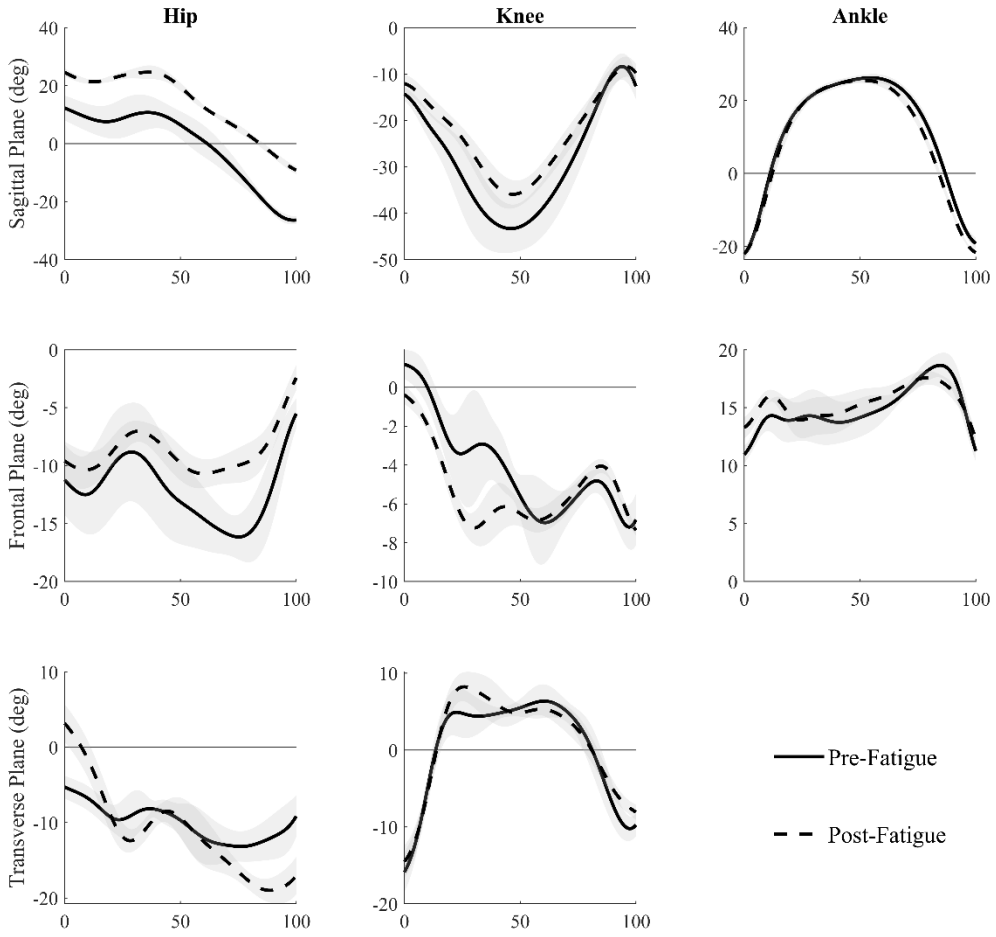


Figure 20: Subject 08 three-dimensional hip, knee, and ankle joint angles from 0 to 100% of stance phase. The shaded regions represent the standard deviation of the pre- and post-fatigue joint angles.

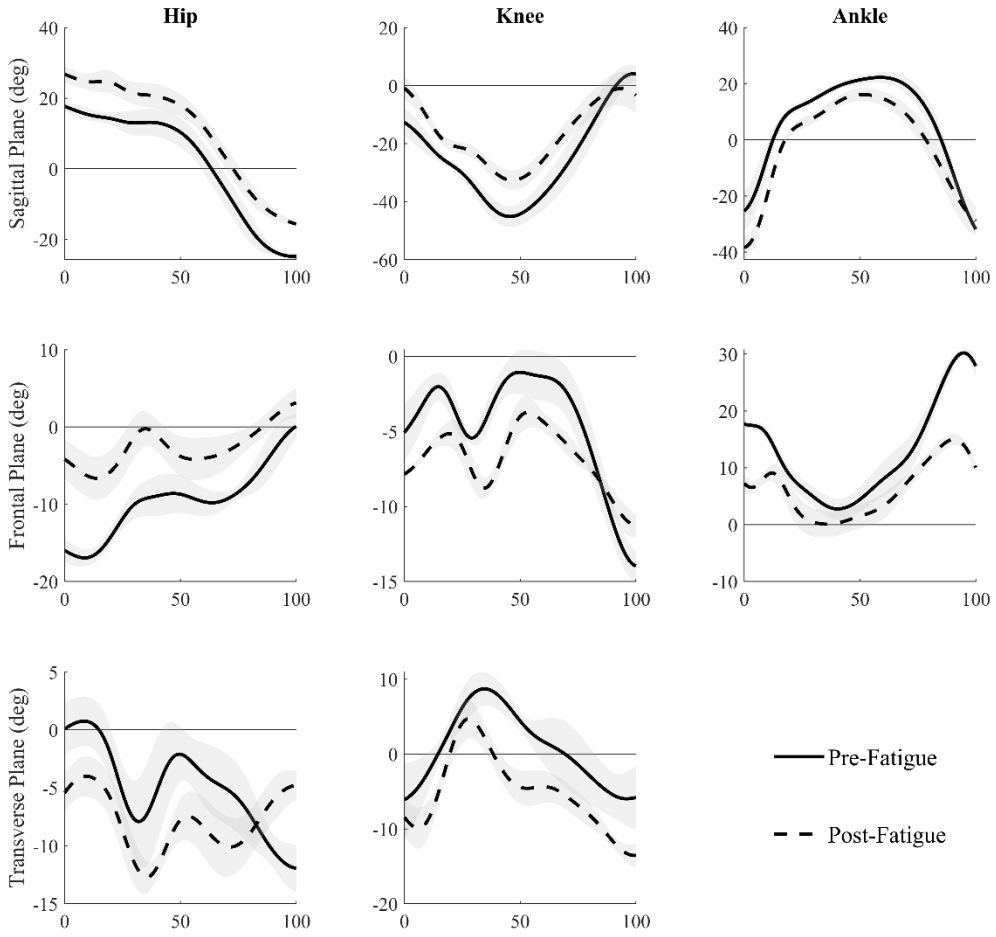


Figure 21: Subject 09 three-dimensional hip, knee, and ankle joint angles from 0 to 100% of stance phase. The shaded regions represent the standard deviation of the pre- and post-fatigue joint angles.

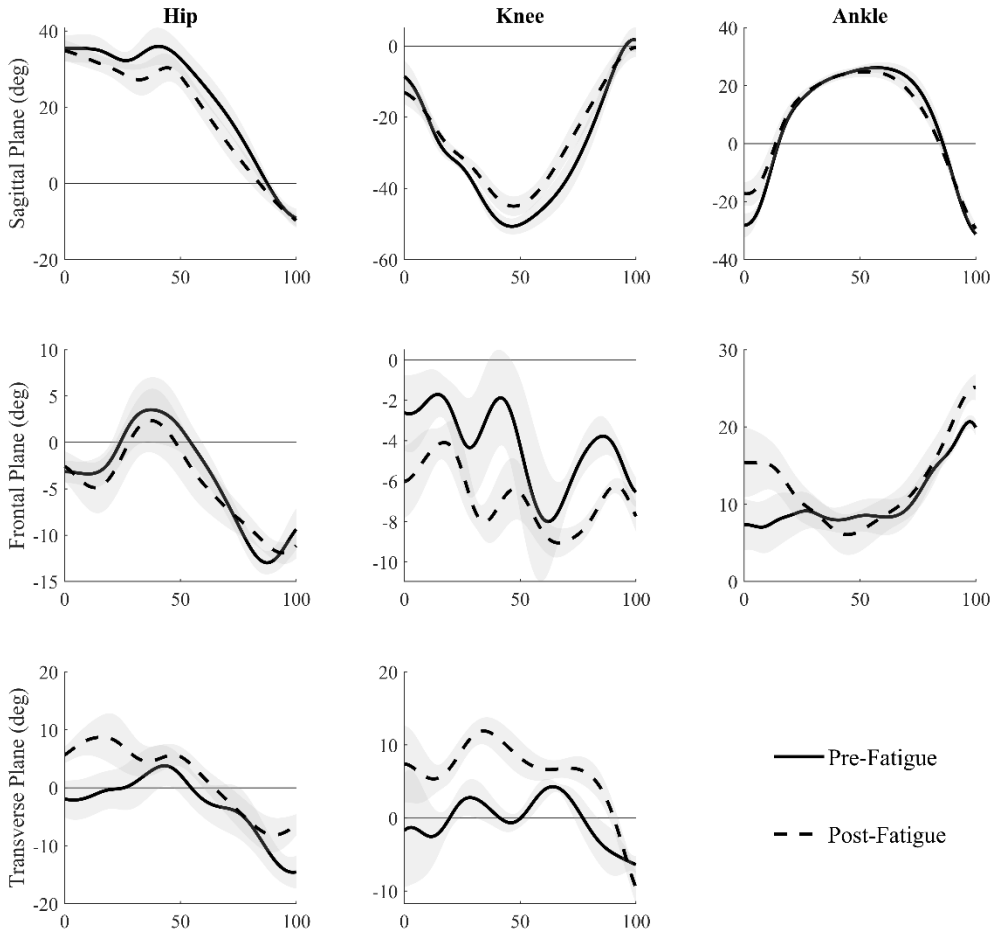


Figure 22: Subject 10 three-dimensional hip, knee, and ankle joint angles from 0 to 100% of stance phase. The shaded regions represent the standard deviation of the pre- and post-fatigue joint angles.

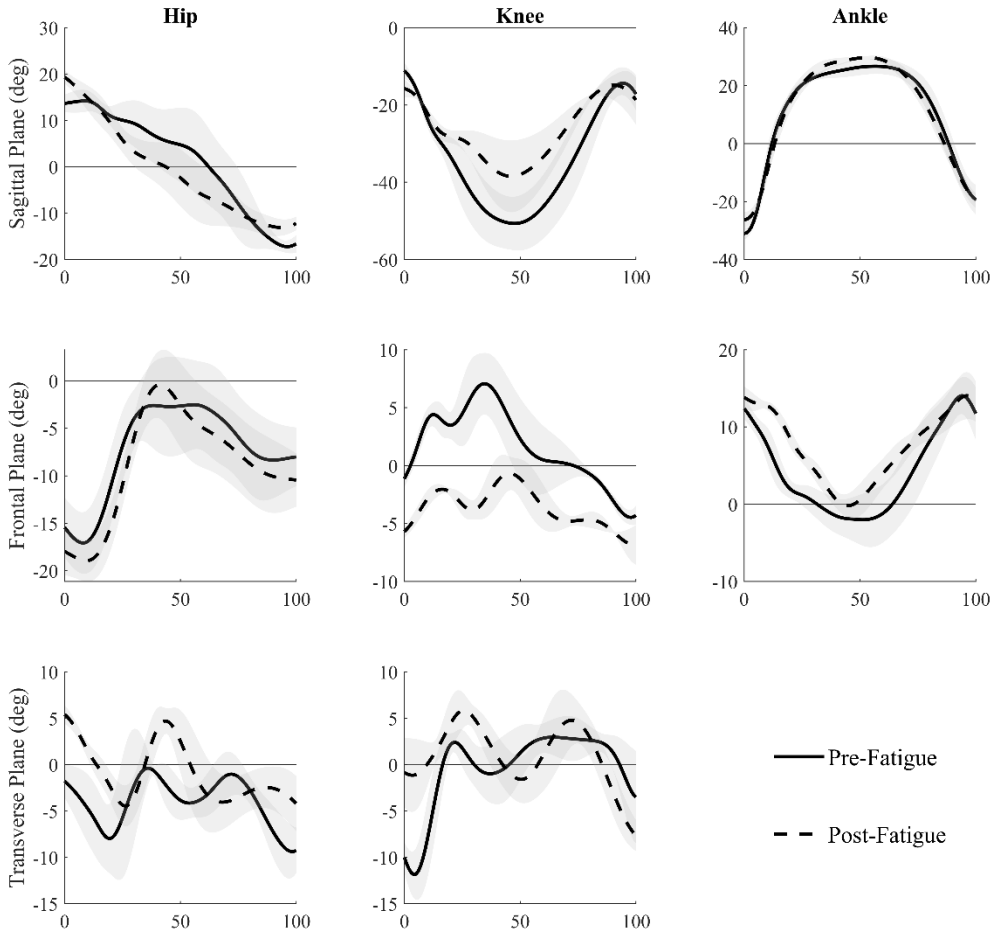


Figure 23: Subject 12 three-dimensional hip, knee, and ankle joint angles from 0 to 100% of stance phase. The shaded regions represent the standard deviation of the pre- and post-fatigue joint angles.

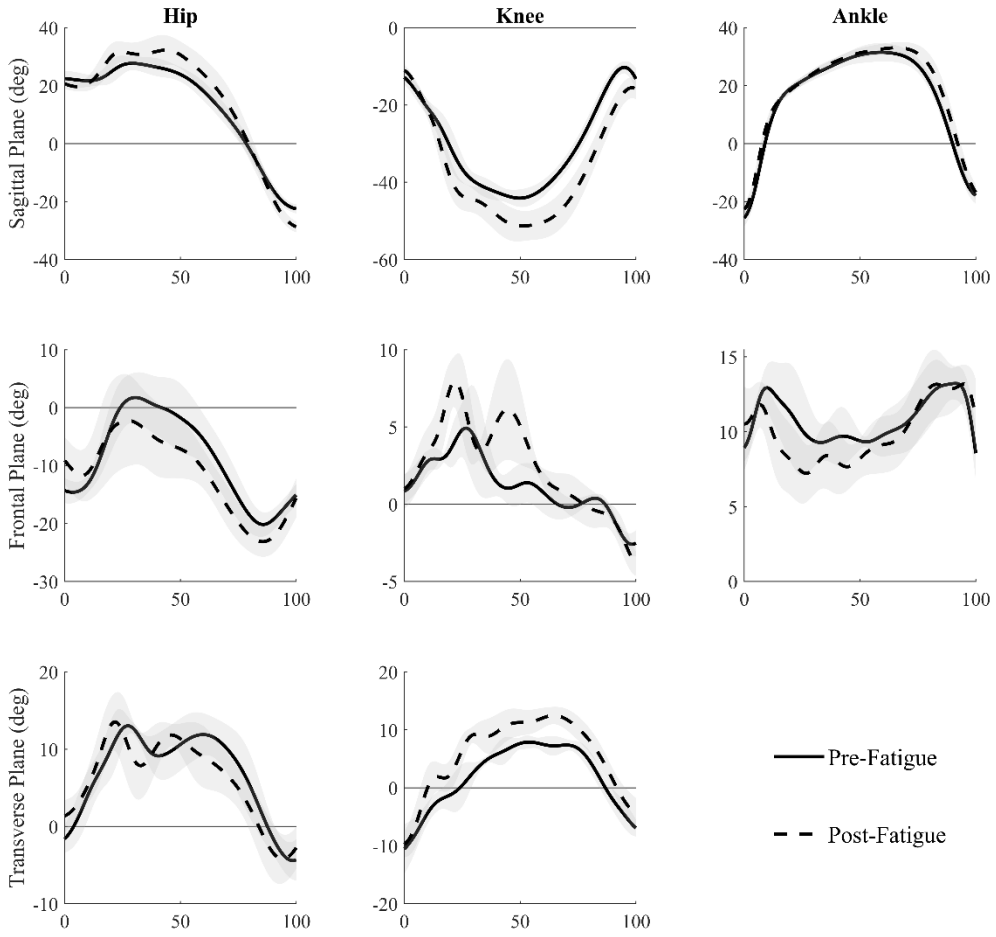


Figure 24: Subject 15 three-dimensional hip, knee, and ankle joint angles from 0 to 100% of stance phase. The shaded regions represent the standard deviation of the pre- and post-fatigue joint angles.

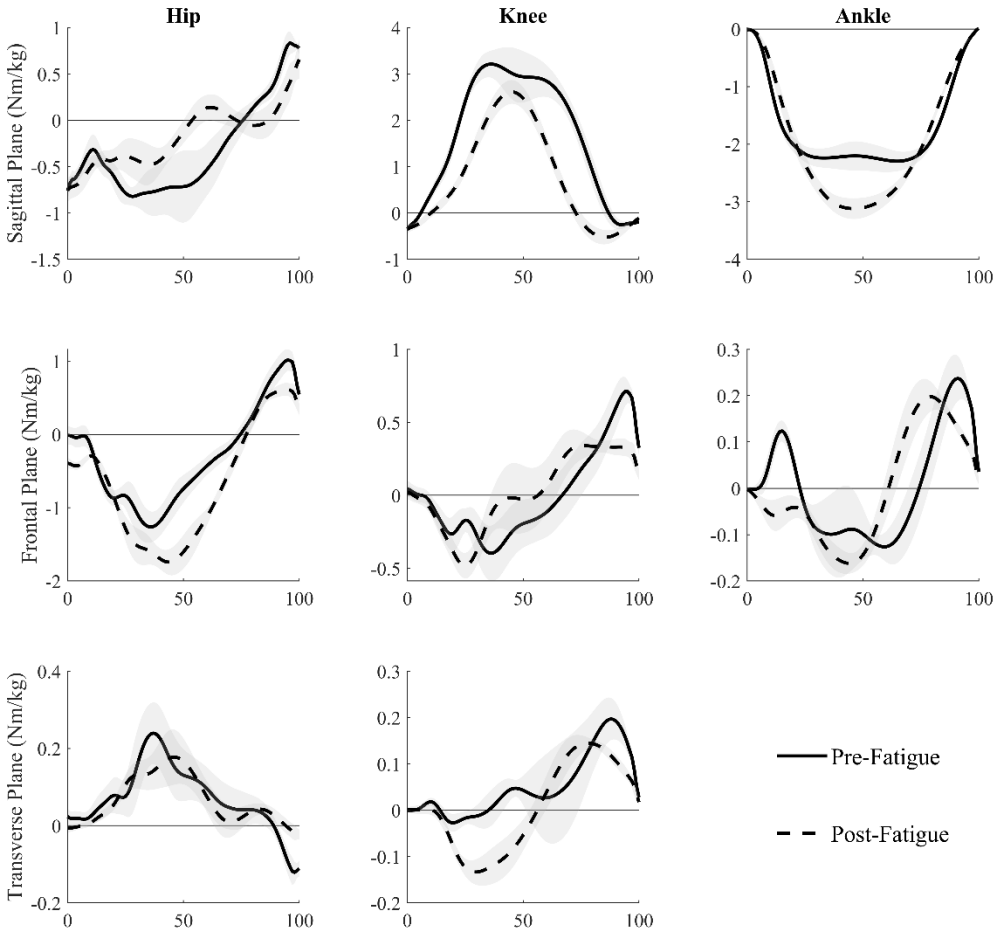


Figure 25: Subject 01 three-dimensional hip, knee, and ankle joint moments from 0 to 100% of stance phase. The shaded regions represent the standard deviation of the pre- and post-fatigue joint moments.

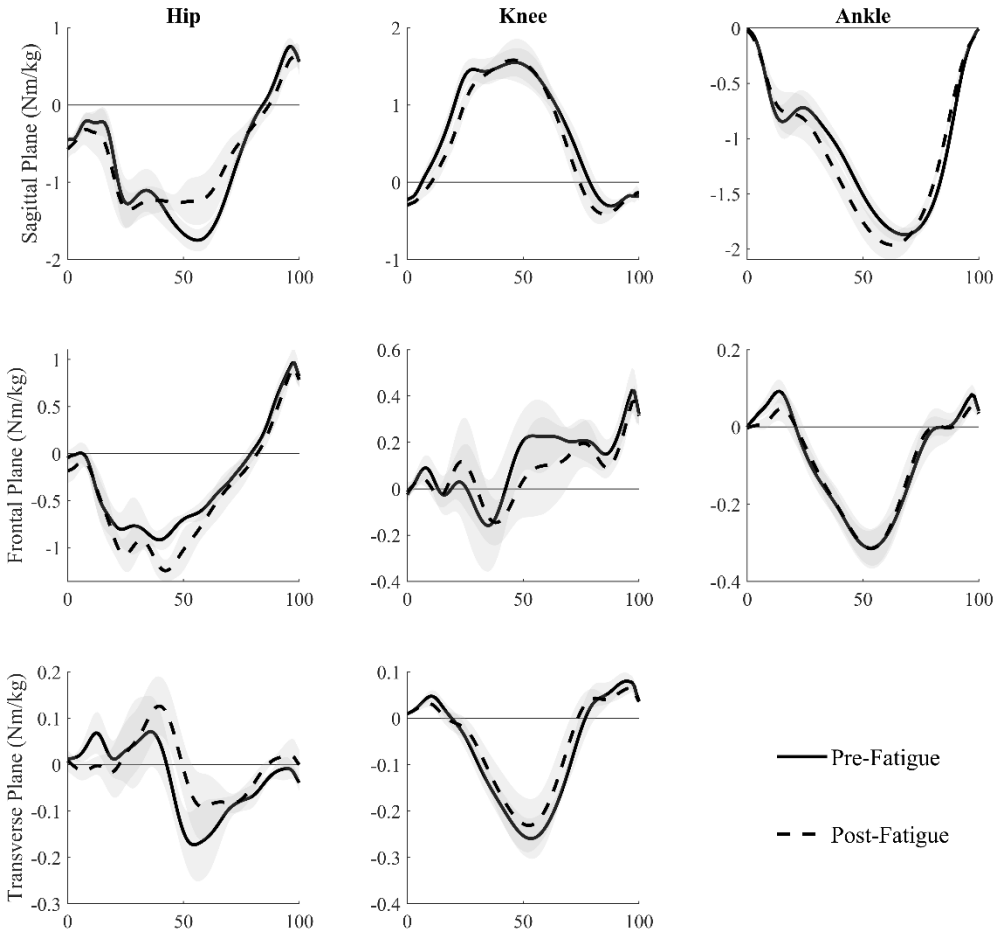


Figure 26: Subject 02 three-dimensional hip, knee, and ankle joint moments from 0 to 100% of stance phase. The shaded regions represent the standard deviation of the pre- and post-fatigue joint moments.

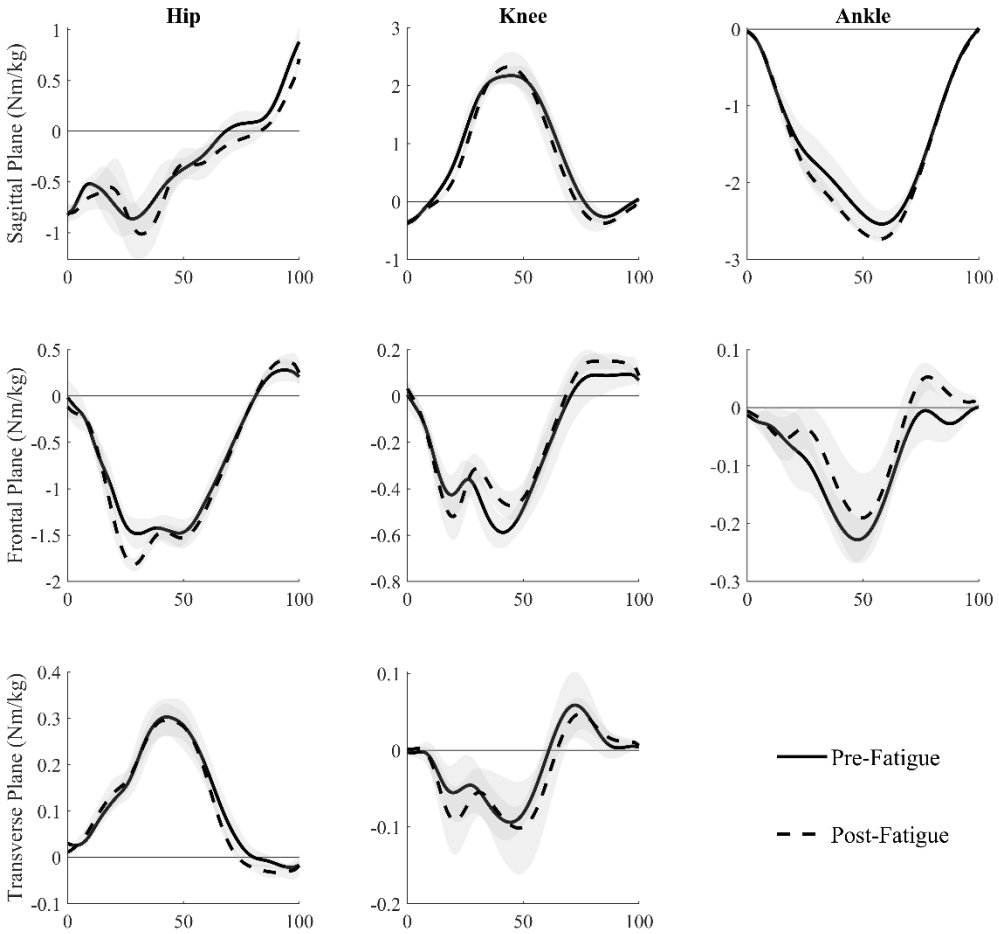


Figure 27: Subject 03 three-dimensional hip, knee, and ankle joint moments from 0 to 100% of stance phase. The shaded regions represent the standard deviation of the pre- and post-fatigue joint moments.

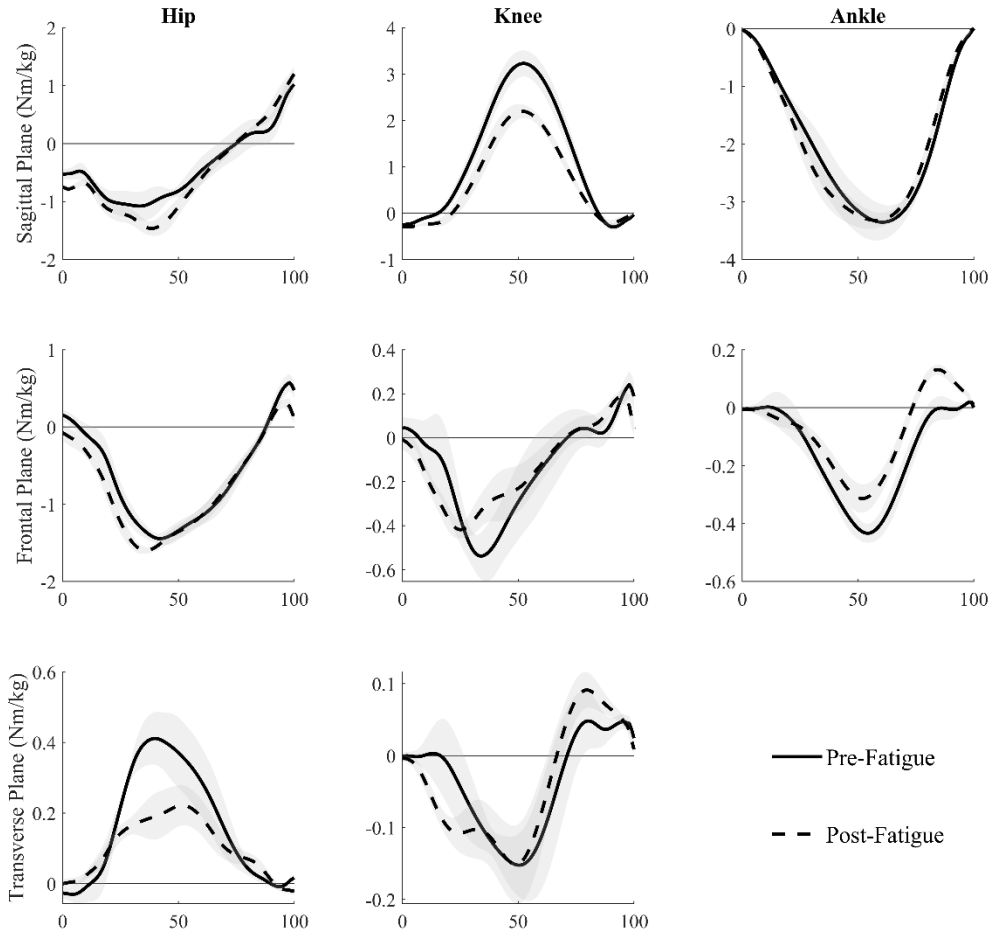


Figure 28: Subject 05 three-dimensional hip, knee, and ankle joint moments from 0 to 100% of stance phase. The shaded regions represent the standard deviation of the pre- and post-fatigue joint moments.

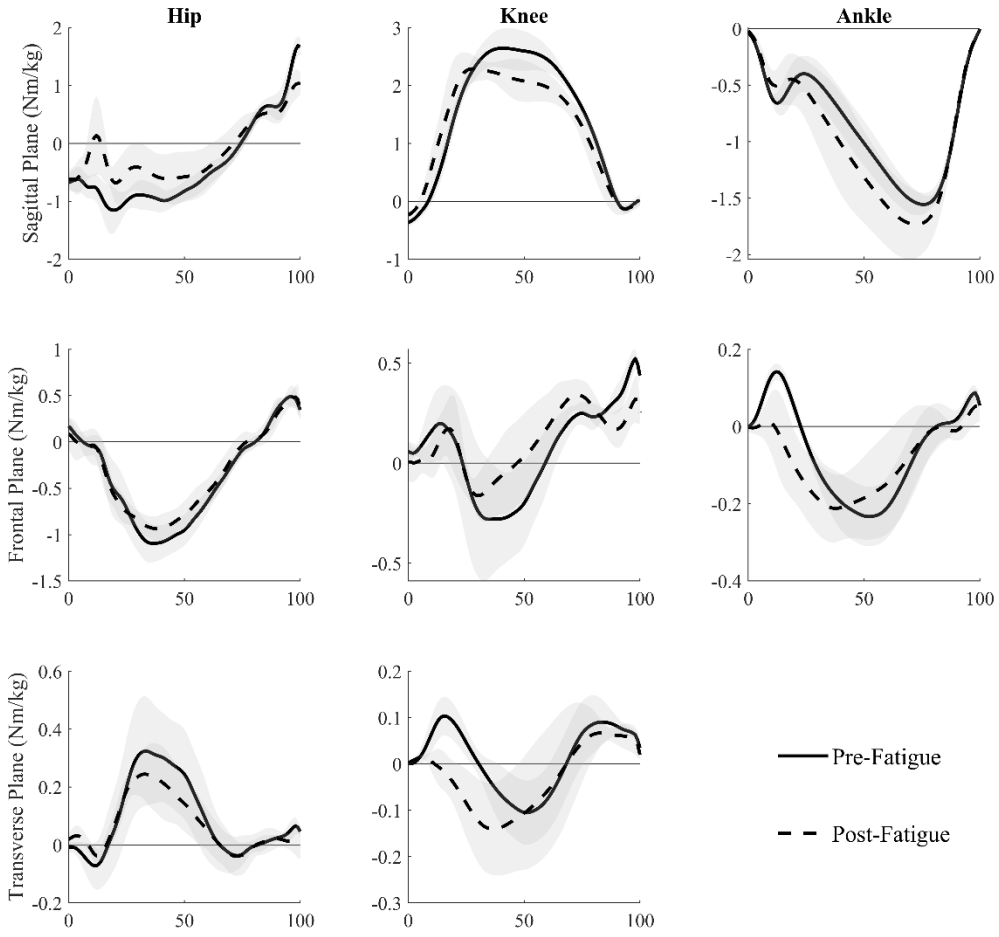


Figure 29: Subject 06 three-dimensional hip, knee, and ankle joint moments from 0 to 100% of stance phase. The shaded regions represent the standard deviation of the pre- and post-fatigue joint moments.

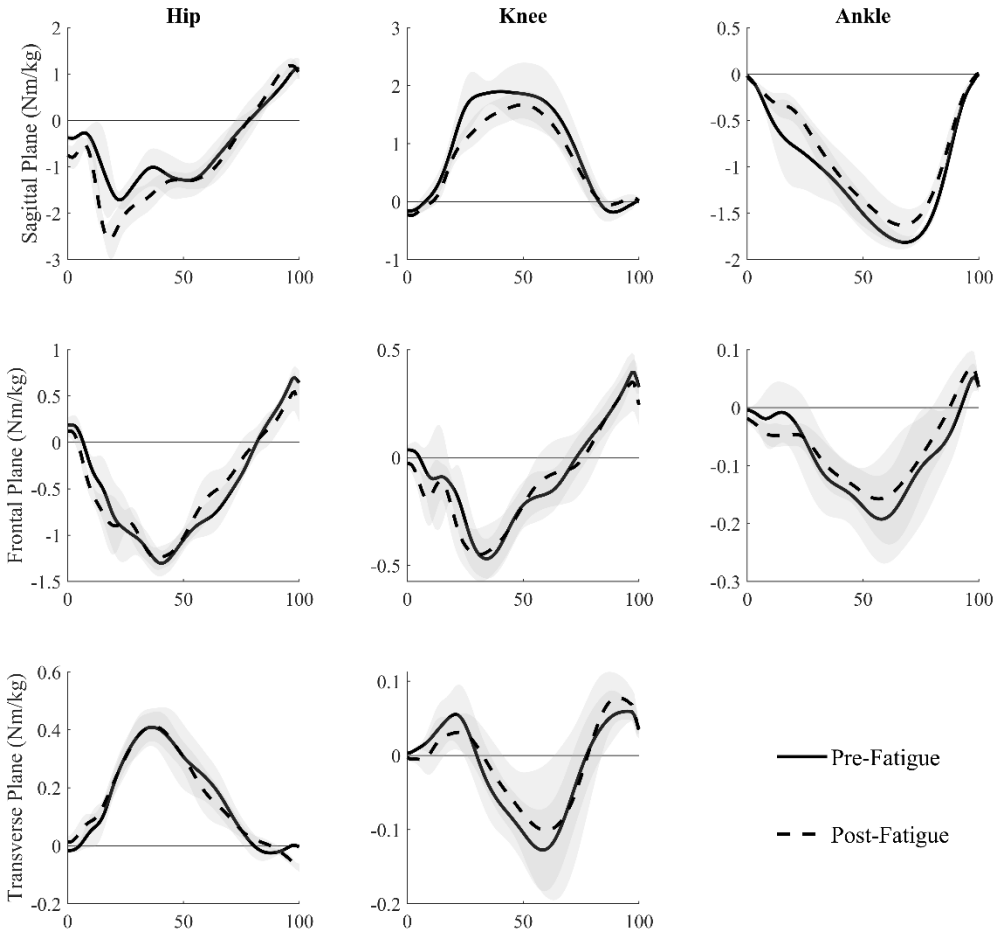


Figure 30:Subject 07 three-dimensional hip, knee, and ankle joint moments from 0 to 100% of stance phase. The shaded regions represent the standard deviation of the pre- and post-fatigue joint moments.

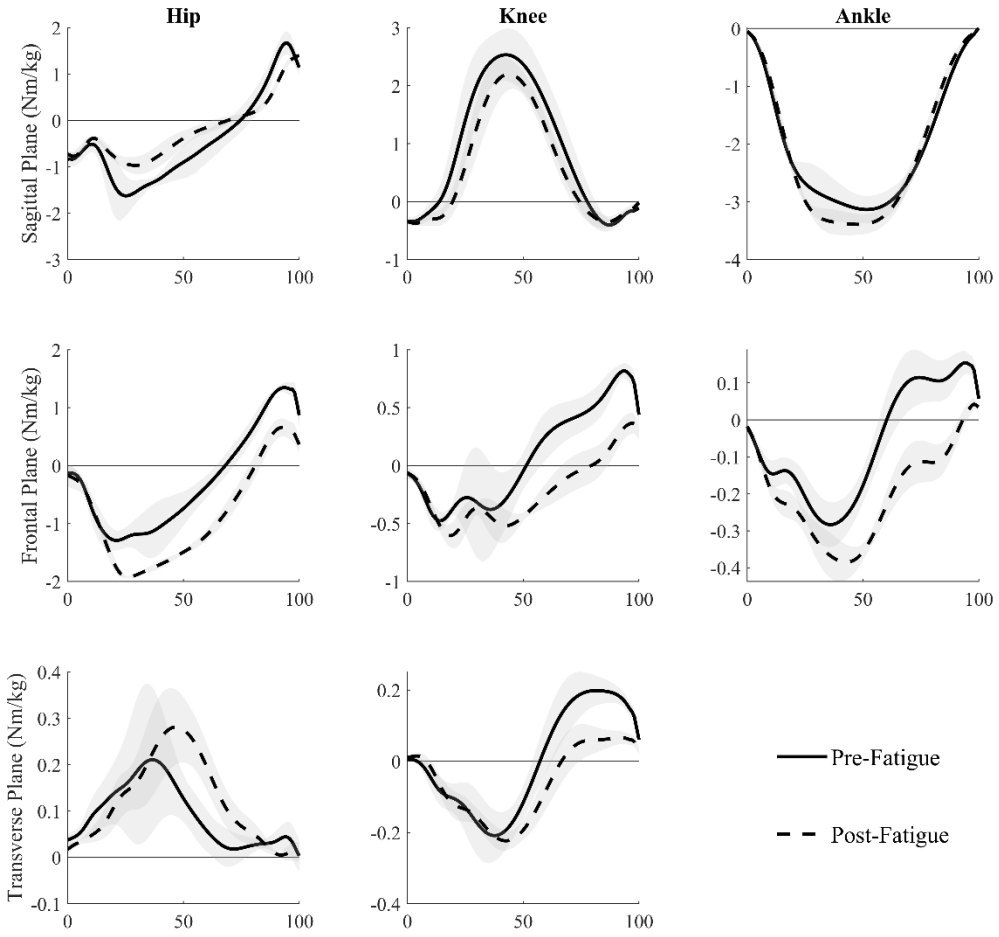


Figure 31: Subject 08 three-dimensional hip, knee, and ankle joint moments from 0 to 100% of stance phase. The shaded regions represent the standard deviation of the pre- and post-fatigue joint moments.

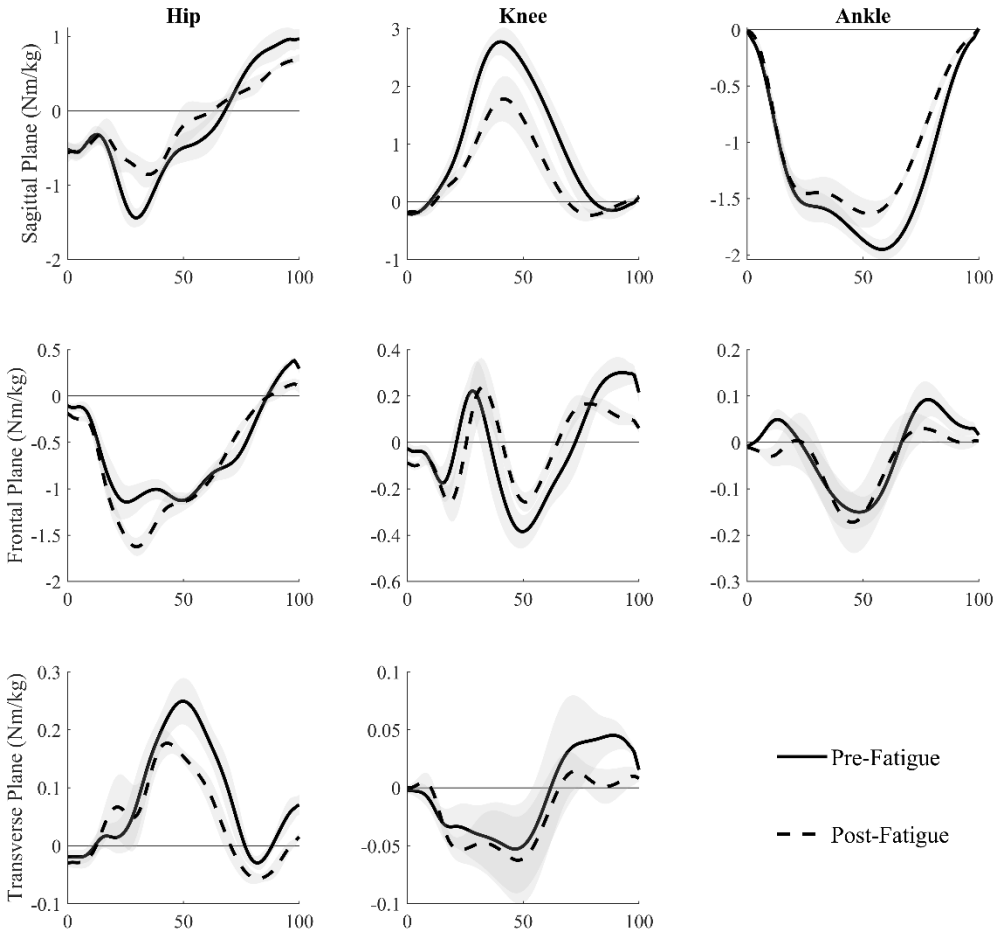


Figure 32: Subject 09 three-dimensional hip, knee, and ankle joint moments from 0 to 100% of stance phase. The shaded regions represent the standard deviation of the pre- and post-fatigue joint moments.

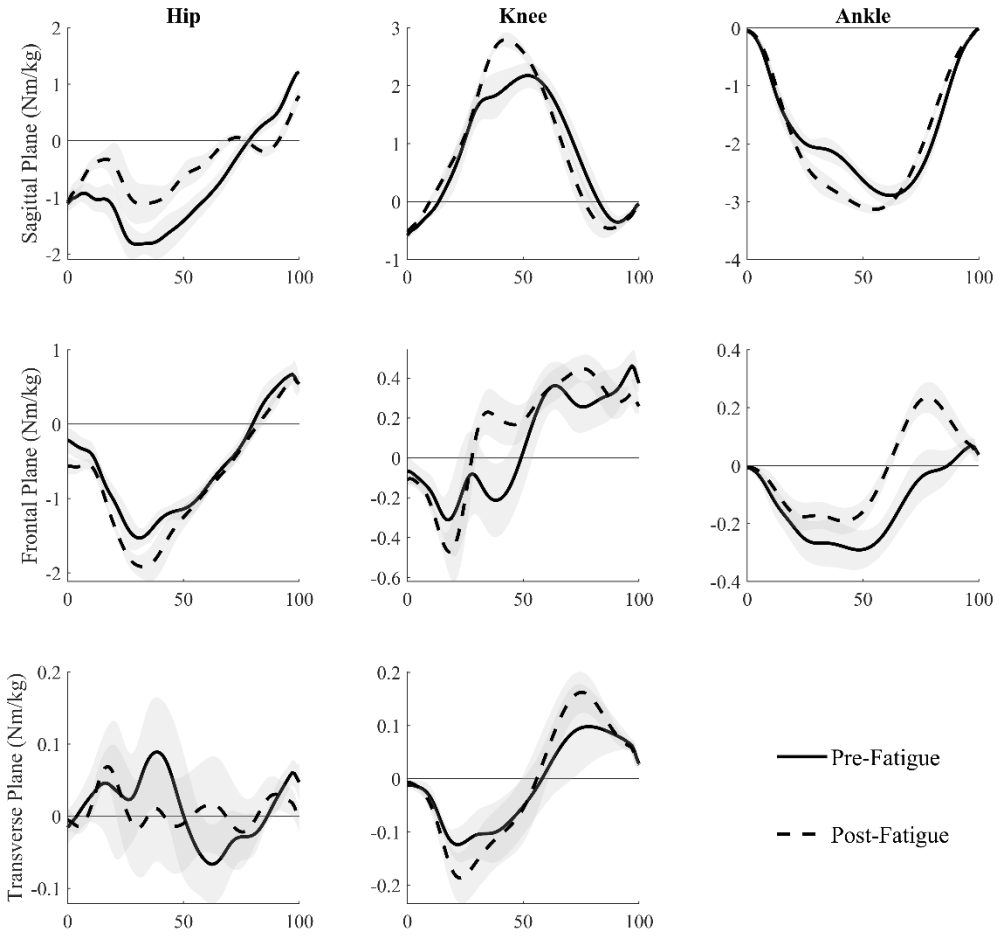


Figure 33: Subject 10 three-dimensional hip, knee, and ankle joint moments from 0 to 100% of stance phase. The shaded regions represent the standard deviation of the pre- and post-fatigue joint moments.

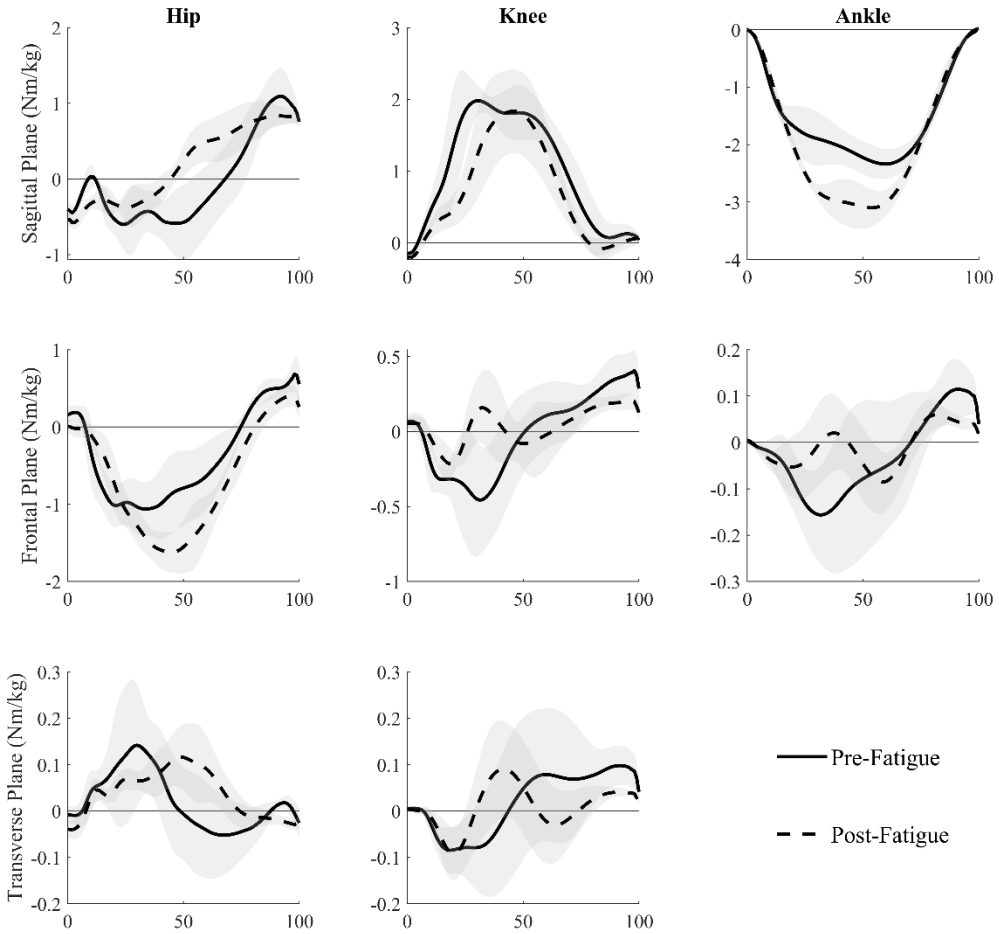


Figure 34: Subject 12 three-dimensional hip, knee, and ankle joint moments from 0 to 100% of stance phase. The shaded regions represent the standard deviation of the pre- and post-fatigue joint moments.

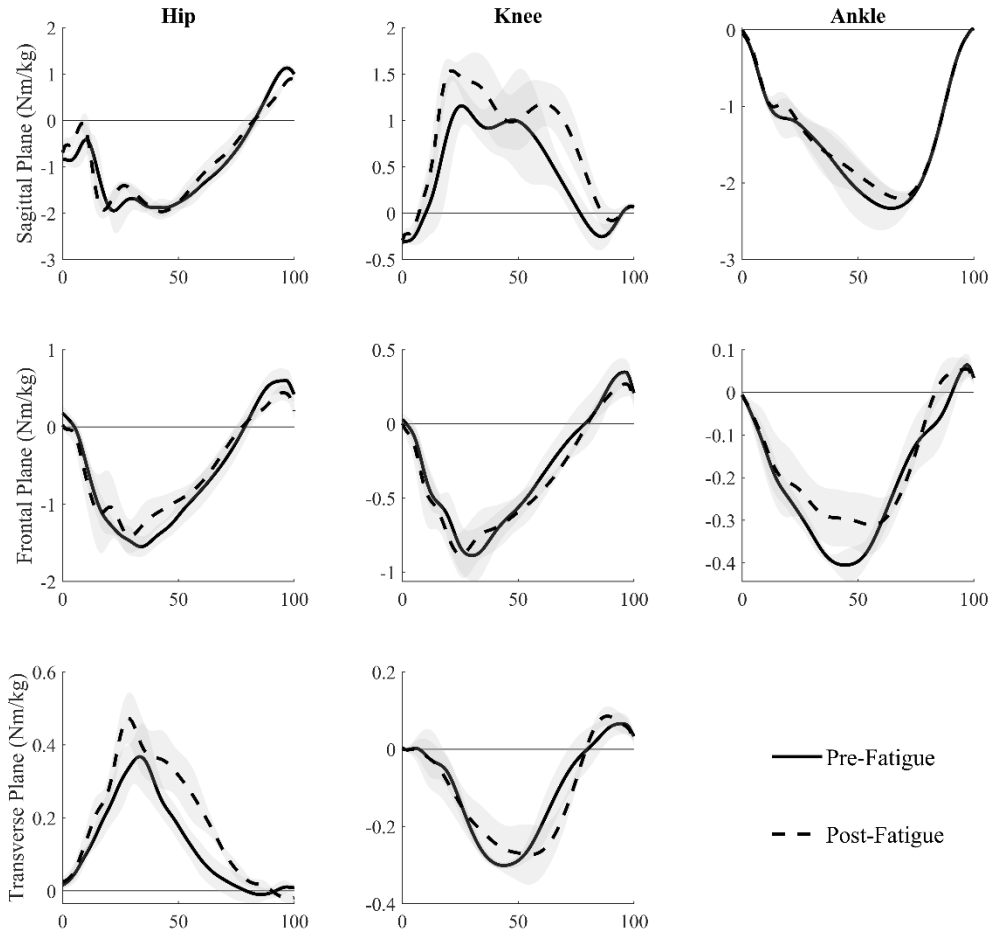


Figure 35: Subject 15 three-dimensional hip, knee, and ankle joint moments from 0 to 100% of stance phase. The shaded regions represent the standard deviation of the pre- and post-fatigue joint moments.

Appendix O. Individual Subject Hicks Recommendations for Static Optimization Reserves

Table 7: Individual subject Hicks recommendations for the maximum static optimization reserves as well as the average subject static optimization reserves for the right hip pre fatigue ACR trials.

Subject	Right Hip Flexion		Right Hip Adduction		Right Hip Rotation	
	Hicks	Average	Hicks	Average	Hicks	Average
S01	-6.97	0.00	-6.26	0.00	1.73	0.01
S02	-4.33	0.01	-1.90	-0.03	0.74	-0.08
S03	-4.54	0.00	-6.55	-0.02	1.67	0.03
S05	-4.12	-0.24	-5.87	-0.37	1.76	0.90
S06	-3.92	0.02	-1.74	-0.03	0.77	-0.04
S07	-5.06	0.00	-5.95	-0.02	1.84	0.03
S08	-8.85	0.16	-8.11	-0.07	1.66	0.23
S09	-5.56	0.01	-6.22	-0.01	1.12	0.02
S10	-7.77	0.00	-7.93	-0.01	1.39	0.00
S12	-3.77	0.00	-7.60	-0.02	1.55	0.02
S15	-8.67	0.00	-6.51	-0.01	1.91	0.02
Mean ± SD	-5.78 ± 1.94	0.00 ± 0.09	-5.88 ± 2.15	-0.05 ± 0.11	1.47 ± 0.41	0.10 ± 0.27

Table 8: Individual subject Hicks recommendations for the maximum static optimization reserves as well as the average subject static optimization reserves for the right knee and ankle pre fatigue ACR trials.

Subject	Right Knee Angle		Right Ankle Angle	
	Hicks	Average	Hicks	Average
S01	-11.89	0.00	-9.11	0.00
S02	-0.22	0.02	-0.06	0.01
S03	-6.21	0.00	-7.33	0.00
S05	-7.42	0.00	-9.44	0.00
S06	-0.21	0.02	-0.03	0.01
S07	-7.37	0.00	-5.75	0.00
S08	-10.10	0.09	-11.32	0.00
S09	-11.53	0.01	-6.25	0.00
S10	-6.80	0.00	-10.16	0.00
S12	-8.86	0.00	-7.57	0.00
S15	-7.27	0.00	-7.73	0.00
Mean ± SD	-7.08 ± 3.88	0.01 ± 0.03	-6.80 ± 3.72	0.00 ± 0.00

Table 9: Individual subject Hicks recommendations for the maximum static optimization reserves as well as the average subject static optimization reserves for the left hip pre fatigue ACR trials.

Subject	Left Hip Flexion		Left Hip Adduction		Left Hip Rotation	
	Hicks	Average	Hicks	Average	Hicks	Average
S01	1.04	0.01	-2.83	-0.01	1.04	-0.01
S02	0.71	0.00	-5.21	-0.01	0.71	0.00
S03	0.51	0.02	-1.20	-0.01	0.51	-0.01
S05	0.61	0.02	-1.40	-0.01	0.61	-0.01
S06	1.63	-0.01	-4.08	-0.01	1.63	0.01
S07	0.58	0.01	-1.62	-0.01	0.58	0.00
S08	1.31	0.02	-2.56	-0.01	1.31	0.00
S09	0.92	0.02	-2.72	-0.02	0.92	-0.01
S10	0.70	0.02	-2.21	-0.03	0.70	-0.01
S12	0.66	0.01	-1.47	-0.02	0.69	-0.04
S15	0.66	0.01	-2.29	-0.01	0.66	-0.02
Mean ± SD	0.85 ± 0.35	0.01 ± 0.01	-2.51 ± 1.22	-0.01 ± 0.01	0.85 ± 0.35	0.01 ± 0.01

Table 10: Individual subject Hicks recommendations for the maximum static optimization reserves as well as the average subject static optimization reserves for the left knee and ankle pre fatigue ACR trials.

Subject	Left Knee Angle		Left Ankle Angle	
	Hicks	Average	Hicks	Average
S01	-0.20	0.02	-0.19	0.01
S02	-3.99	0.00	-6.36	0.00
S03	-0.28	0.02	-0.06	0.01
S05	-0.53	0.01	-0.04	0.01
S06	-8.25	0.00	-5.46	0.00
S07	-0.29	0.02	-0.04	0.01
S08	-0.43	0.03	-0.15	0.02
S09	-0.85	0.02	-0.07	0.01
S10	-0.81	0.02	-0.05	0.01
S12	-0.47	0.02	-0.04	0.01
S15	-0.53	0.02	-0.16	0.01
Mean ± SD	-1.51 ± 2.48	0.02 ± 0.01	-1.15 ± 2.36	0.01 ± 0.01

Table 11: Individual subject Hicks recommendations for the maximum static optimization reserves as well as the average subject static optimization reserves for the right hip post fatigue ACR trials.

Subject	Right Hip Flexion		Right Hip Adduction		Right Hip Rotation	
	Hicks	Average	Hicks	Average	Hicks	Average
S01	-5.41	-0.01	-8.53	-0.03	1.51	0.07
S02	-4.29	0.02	-1.13	-0.03	0.56	0.00
S03	-4.43	0.00	-6.15	-0.01	1.42	0.02
S05	-4.45	-0.78	-5.34	-0.98	1.02	2.15
S06	-3.69	0.01	-2.03	-0.02	0.86	-0.03
S07	-9.25	-0.01	-4.76	-0.03	1.62	0.06
S08	-7.39	0.01	-8.80	-0.01	1.55	0.00
S09	-3.76	0.00	-6.59	-0.01	0.90	-0.01
S10	-5.92	0.00	-10.19	-0.01	1.43	0.01
S12	-5.14	0.00	-8.25	-0.03	0.85	0.02
S15	-8.27	0.00	-5.00	-0.01	1.76	0.02
Mean ± SD	-5.64 ± 1.88	-0.07 ± 0.24	-6.07 ± 2.82	-0.11 ± 0.29	1.23 ± 0.40	0.21 ± 0.64

Table 12: Individual subject Hicks recommendations for the maximum static optimization reserves as well as the average subject static optimization reserves for the right knee and ankle post fatigue ACR trials.

Subject	Right Knee Angle		Right Ankle Angle	
	Hicks	Average	Hicks	Average
S01	-8.81	0.01	-12.46	0.00
S02	-0.32	0.02	-0.05	0.01
S03	-7.17	0.00	-8.68	0.00
S05	-5.03	0.01	-10.75	0.00
S06	-0.09	0.02	-0.02	0.01
S07	-4.86	0.00	-5.21	0.00
S08	-10.00	0.01	-14.11	-0.01
S09	-7.31	0.01	-6.21	0.00
S10	-10.54	0.00	-10.55	0.00
S12	-7.71	0.01	-10.75	-0.01
S15	-7.97	0.00	-7.46	0.00
Mean ± SD	-6.35 ± 3.50	0.01 ± 0.01	-7.84 ± 4.66	0.00 ± 0.01

Table 13: Individual subject Hicks recommendations for the maximum static optimization reserves as well as the average subject static optimization reserves for the left hip post fatigue ACR trials.

Subject	Left Hip Flexion		Left Hip Adduction		Left Hip Rotation	
	Hicks	Average	Hicks	Average	Hicks	Average
S01	1.34	0.02	-2.46	-0.02	1.34	-0.03
S02	0.71	0.00	-5.97	-0.01	0.71	0.01
S03	0.54	0.02	-1.34	-0.01	0.54	-0.03
S05	0.68	0.02	-1.13	-0.01	0.68	-0.01
S06	1.50	0.00	-4.97	-0.01	1.50	0.01
S07	0.66	0.02	-1.12	-0.01	0.66	0.00
S08	1.11	0.02	-3.14	-0.03	1.11	-0.02
S09	0.49	0.01	-1.58	-0.01	0.49	-0.01
S10	0.81	0.02	-2.95	-0.03	0.81	-0.01
S12	0.65	0.01	-1.45	-0.01	0.65	-0.03
S15	0.73	0.01	-1.89	-0.01	0.73	-0.02
Mean ± SD	0.84 ± 0.33	0.01 ± 0.01	-2.55 ± 1.62	-0.01 ± 0.01	0.84 ± 0.33	-0.01 ± 0.01

Table 14: Individual subject Hicks recommendations for the maximum static optimization reserves as well as the average subject static optimization reserves for the left knee and ankle post fatigue ACR trials.

Subject	Left Knee Angle		Left Ankle Angle	
	Hicks	Average	Hicks	Average
S01	-0.41	0.01	-0.13	0.01
S02	-2.68	0.01	-5.94	0.00
S03	-0.40	0.02	-0.03	0.01
S05	-0.44	0.01	-0.03	0.01
S06	-6.99	0.00	-6.64	0.00
S07	-0.20	0.03	-0.07	0.02
S08	-0.57	0.04	-0.06	0.03
S09	-0.76	0.03	-0.08	0.01
S10	-0.74	0.01	-0.07	0.01
S12	-0.36	0.02	-0.02	0.01
S15	-0.21	0.02	0.00	0.02
Mean ± SD	-1.25 ± 2.03	0.02 ± 0.01	-1.19 ± 2.53	0.01 ± 0.01

Appendix P. Individual Subject Normalized RMSE and R^2 Values for Experimental versus Summed Muscle GRF Comparisons

Table 15: Individual subject pre-fatigue normalized root mean square error and coefficients of correlations for the anteroposterior, mediolateral, and vertical GRFs to compare the superposition errors between the experimental and summed muscle GRFs.

Subject	Anteroposterior		Mediolateral		Vertical	
	nRMSE	R^2	nRMSE	R^2	nRMSE	R^2
S01	7.8	0.96	3.3	1.0	2.8	1.00
S02	5.7	0.98	4.0	0.99	2.9	1.00
S03	7.1	0.96	0.9	1.0	2.1	1.00
S05	3.2	0.99	1.5	1.0	1.4	1.00
S06	8.2	0.95	3.5	1.0	4.2	1.00
S07	5.1	0.98	4.6	0.98	6.1	0.95
S08	12.6	0.87	6.7	0.98	3.5	1.00
S09	4.8	0.98	2.7	1.0	1.4	1.00
S10	12.2	0.87	4.3	0.99	3.0	1.00
S12	4.4	0.98	3.5	1.0	2.0	1.00
S15	4.2	0.99	2.4	1.0	2.9	0.99
Mean ± SD	6.8 ± 3.1	0.95 ± 0.04	3.4 ± 1.6	0.99 ± 0.01	2.9 ± 1.3	0.99 ± 0.01

Table 16: Individual subject post-fatigue normalized root mean square error and coefficients of correlations for the anteroposterior, mediolateral, and vertical GRFs to compare the superposition errors between the experimental and summed muscle GRFs.

Subject	Anteroposterior		Mediolateral		Vertical	
	nRMSE	R^2	nRMSE	R^2	nRMSE	R^2
S01	5.2	0.99	1.4	1.00	2.3	1.00
S02	32.4	0.86	19.0	0.90	5.1	0.97
S03	5.9	0.98	1.4	1.00	1.7	1.00
S05	3.5	0.99	2.5	1.00	2.2	1.00
S06	7.1	0.94	4.3	0.99	3.5	0.99
S07	5.5	0.97	4.4	0.99	5.6	0.98
S08	5.1	0.98	1.5	1.00	1.5	1.00
S09	5.1	0.98	2.9	1.00	1.8	1.00
S10	10.3	0.93	3.4	1.00	2.1	1.00
S12	5.2	0.98	2.0	1.00	1.7	1.00
S15	3.9	0.99	2.8	0.99	3.3	0.99
Mean ± SD	8.1 ± 8.3	0.96 ± 0.04	4.2 ± 5.0	0.99 ± 0.03	2.8 ± 1.4	0.99 ± 0.01

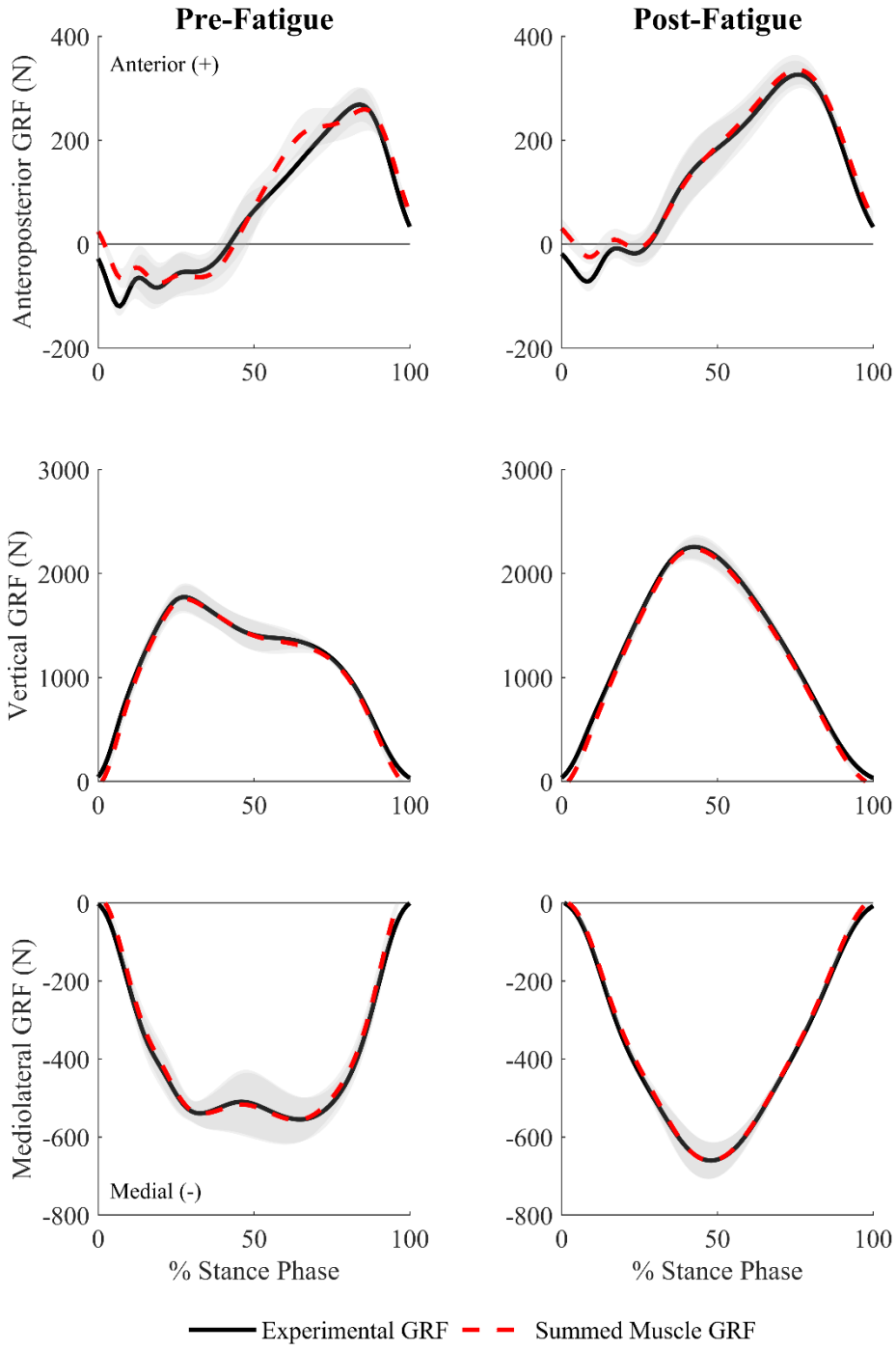


Figure 36: Subject 01 three-dimensional superimposed experimental and summed muscle GRFs from 0 to 100% of stance phase. The shaded regions represent the standard deviation of the experimental and summed muscle GRFs.

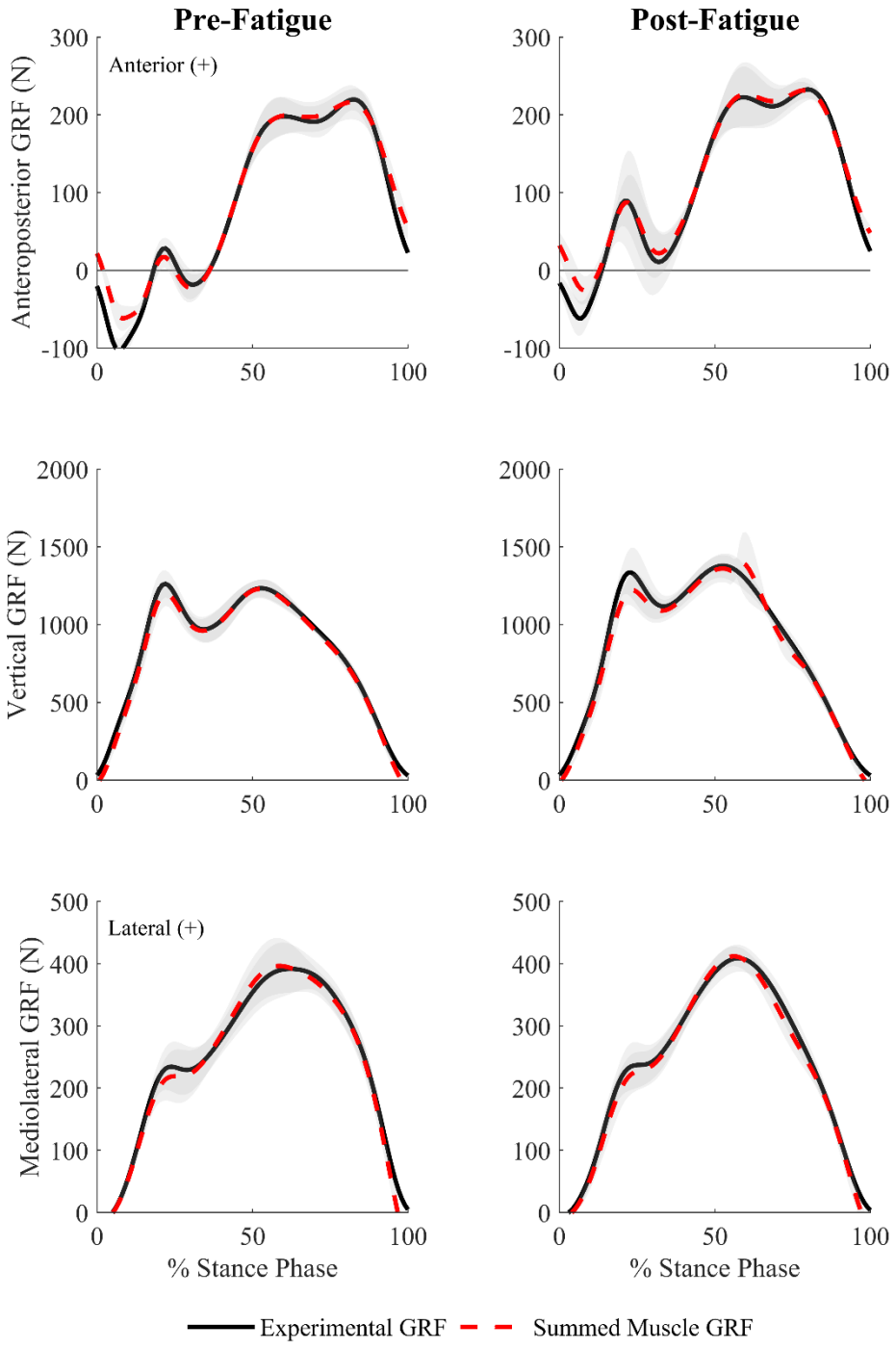


Figure 37: Subject 02 three-dimensional superimposed experimental and summed muscle GRFs from 0 to 100% of stance phase. The shaded regions represent the standard deviation of the experimental and summed muscle GRFs.

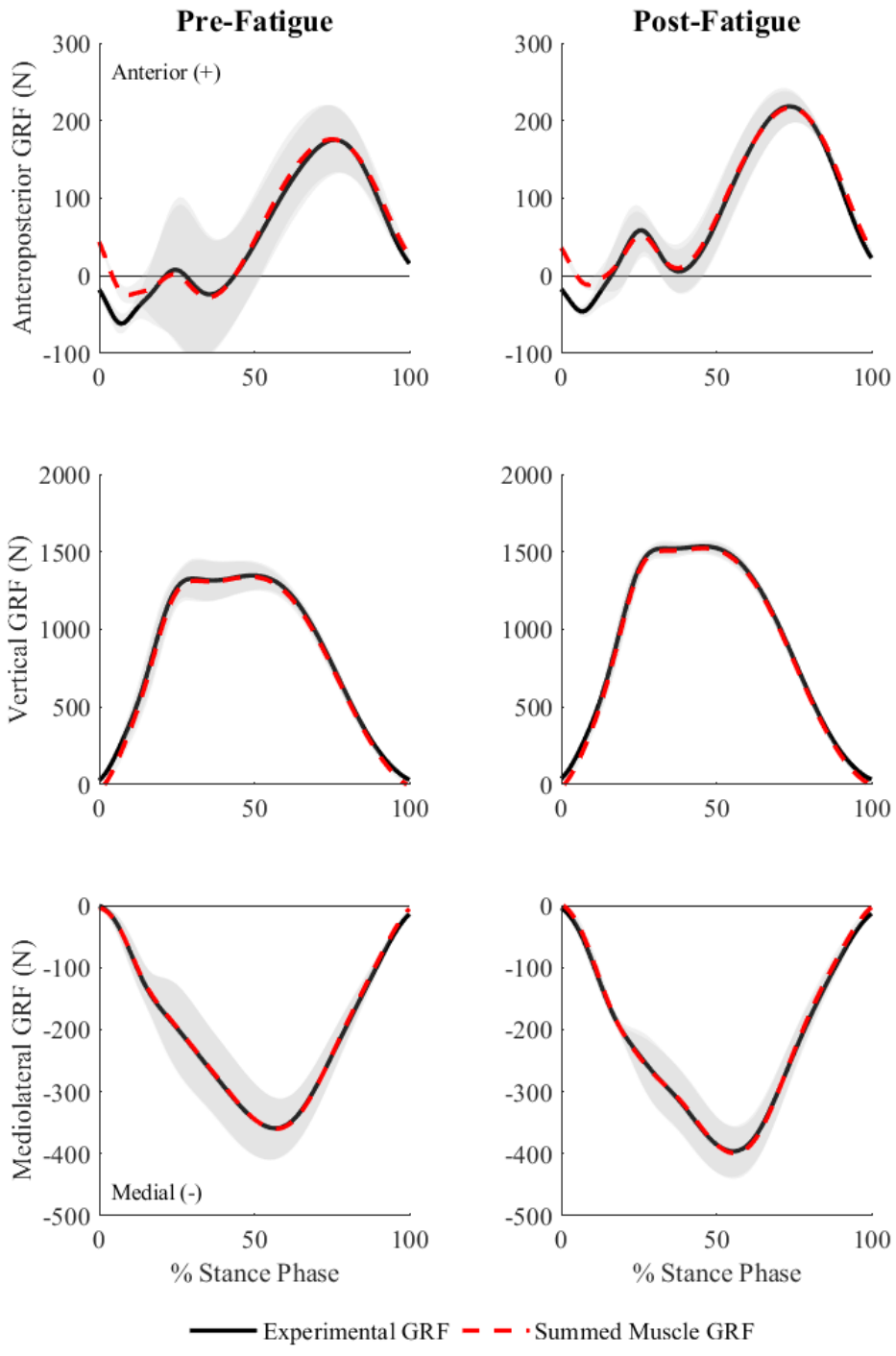


Figure 38: Subject 03 three-dimensional superimposed experimental and summed muscle GRFs from 0 to 100% of stance phase. The shaded regions represent the standard deviation of the experimental and summed muscle GRFs.

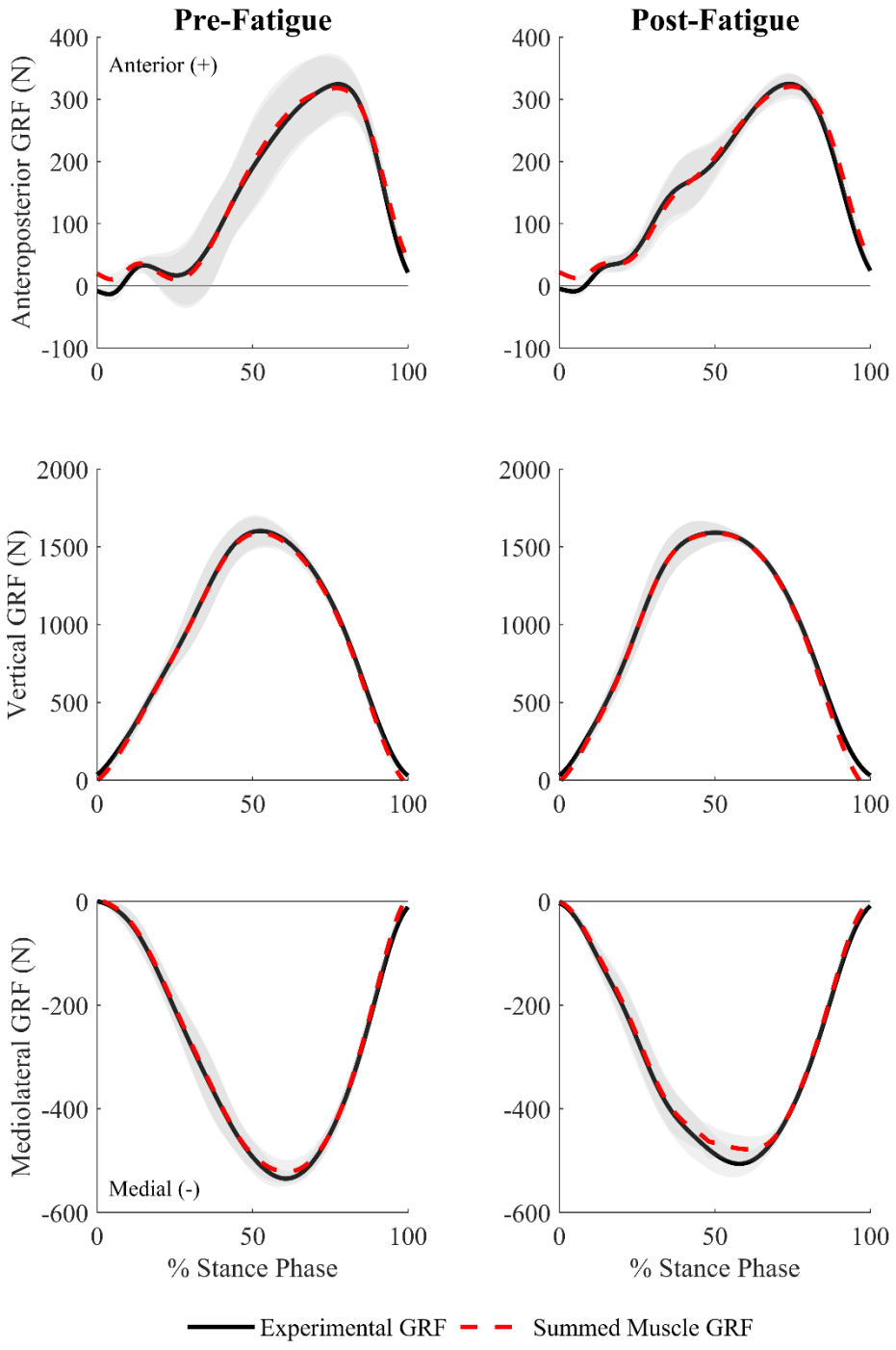


Figure 39: Subject 05 three-dimensional superimposed experimental and summed muscle GRFs from 0 to 100% of stance phase. The shaded regions represent the standard deviation of the experimental and summed muscle GRFs.

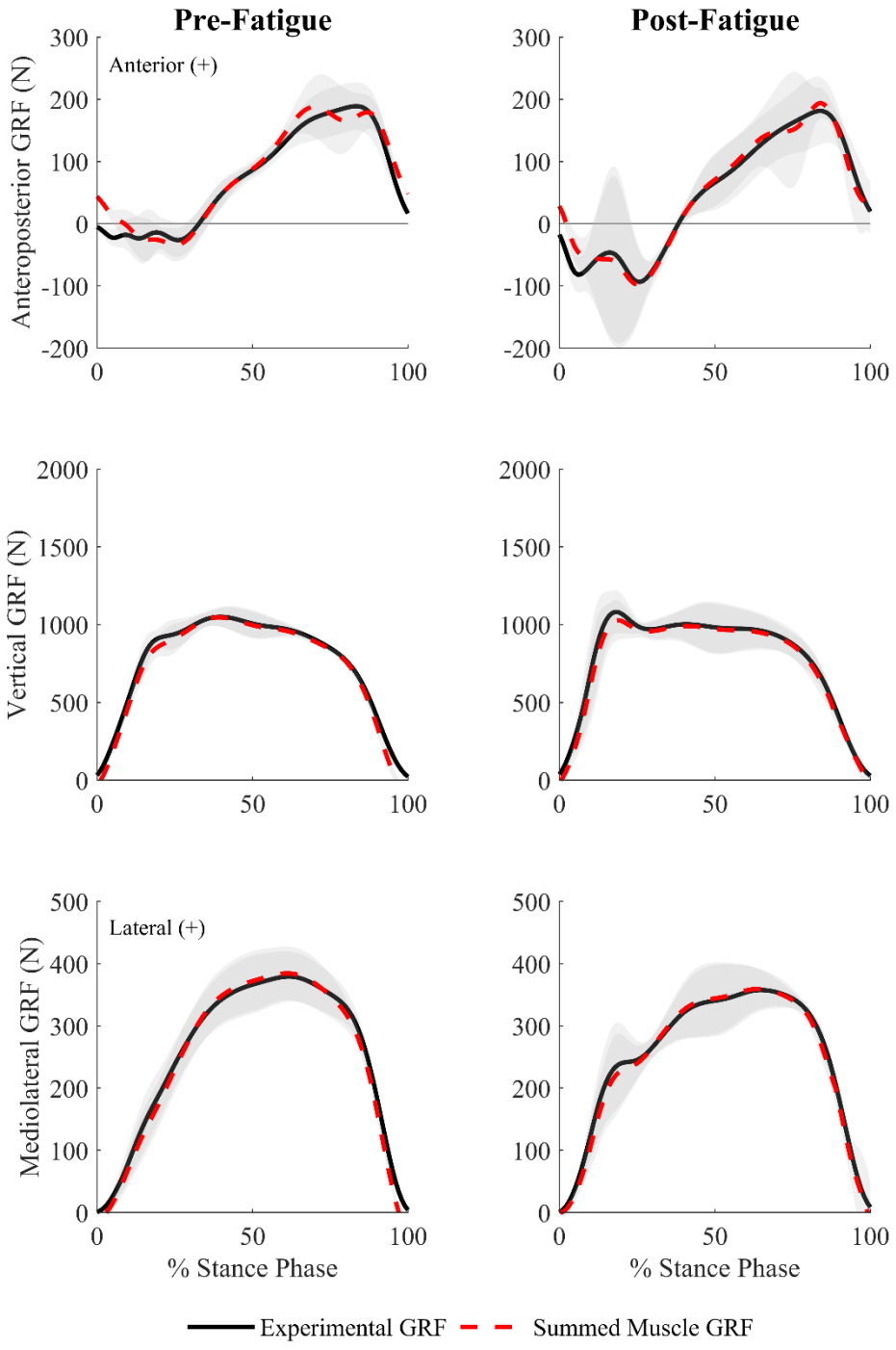


Figure 40: Subject 06 three-dimensional superimposed experimental and summed muscle GRFs from 0 to 100% of stance phase. The shaded regions represent the standard deviation of the experimental and summed muscle GRFs.

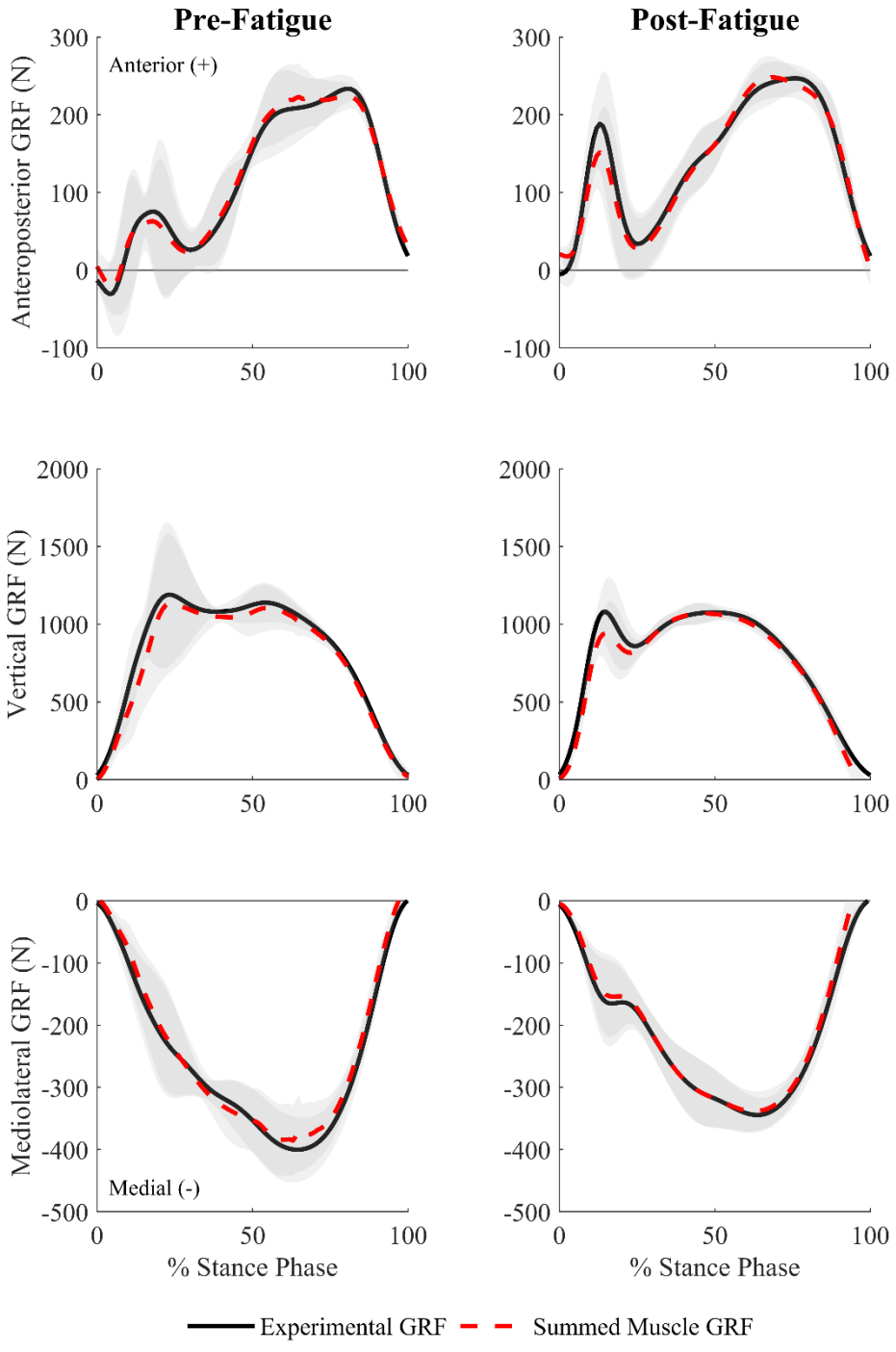


Figure 41: Subject 07 three-dimensional superimposed experimental and summed muscle GRFs from 0 to 100% of stance phase. The shaded regions represent the standard deviation of the experimental and summed muscle GRFs.

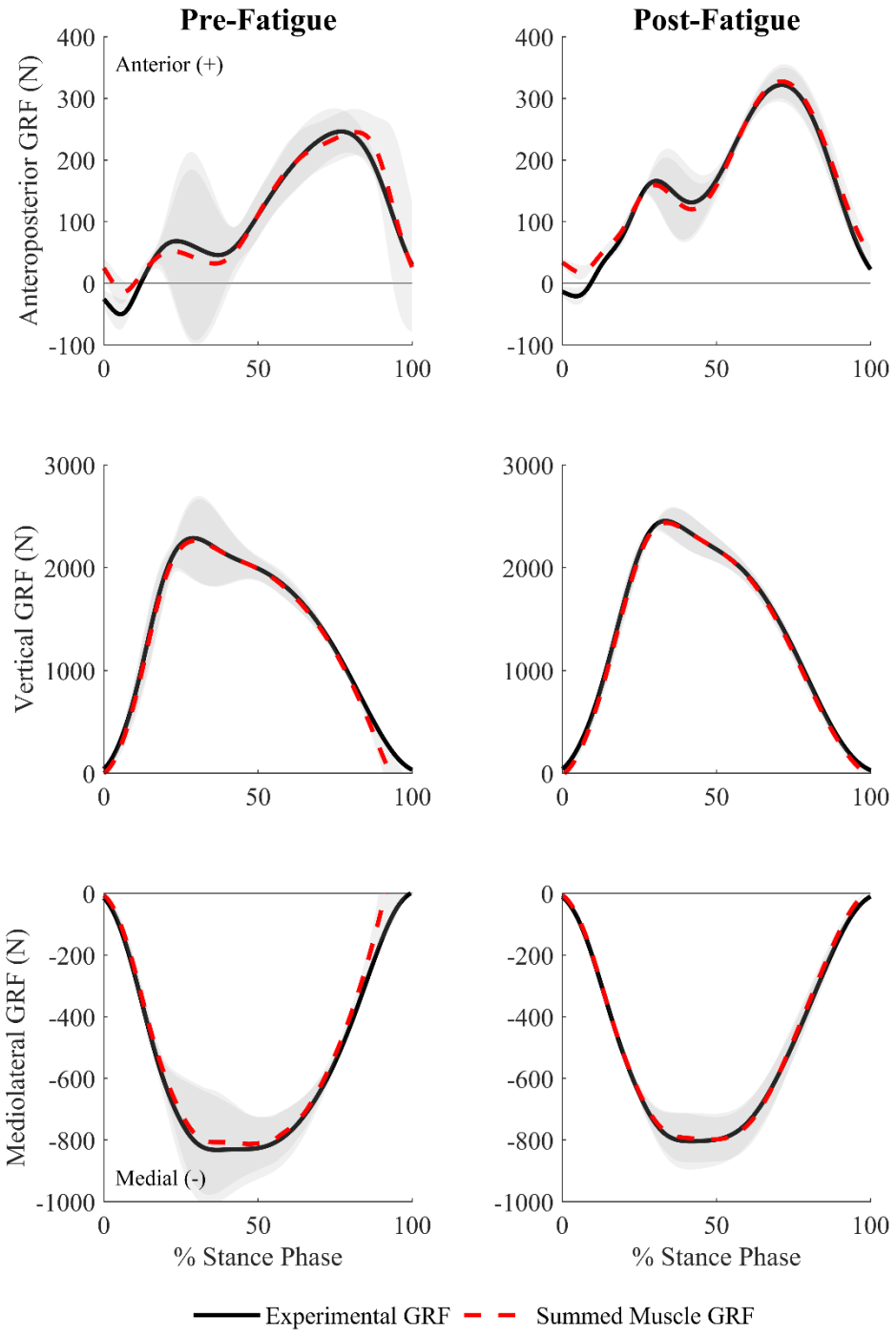


Figure 42: Subject 08 three-dimensional superimposed experimental and summed muscle GRFs from 0 to 100% of stance phase. The shaded regions represent the standard deviation of the experimental and summed muscle GRFs.

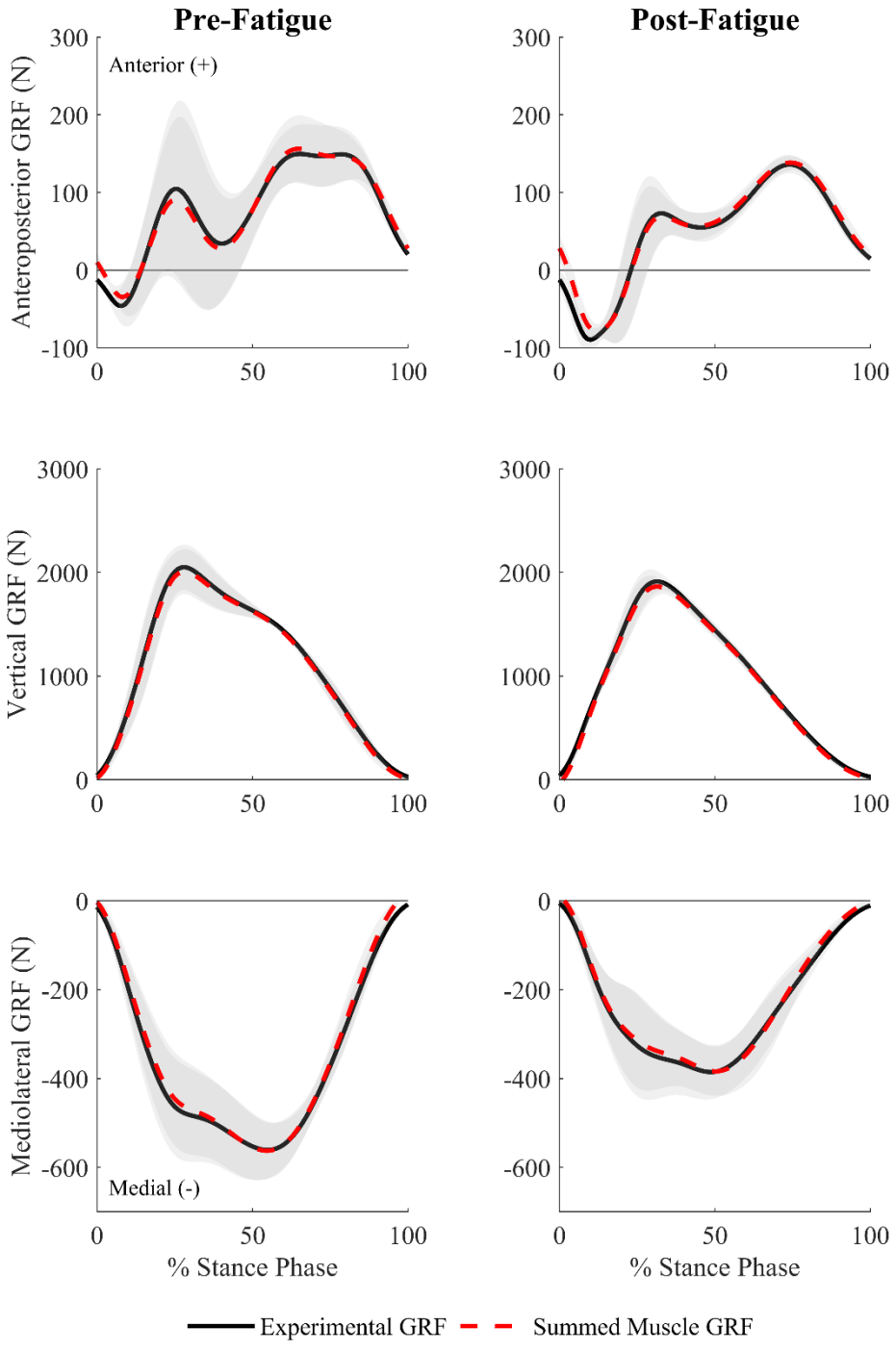


Figure 43: Subject 09 three-dimensional superimposed experimental and summed muscle GRFs from 0 to 100% of stance phase. The shaded regions represent the standard deviation of the experimental and summed muscle GRFs.

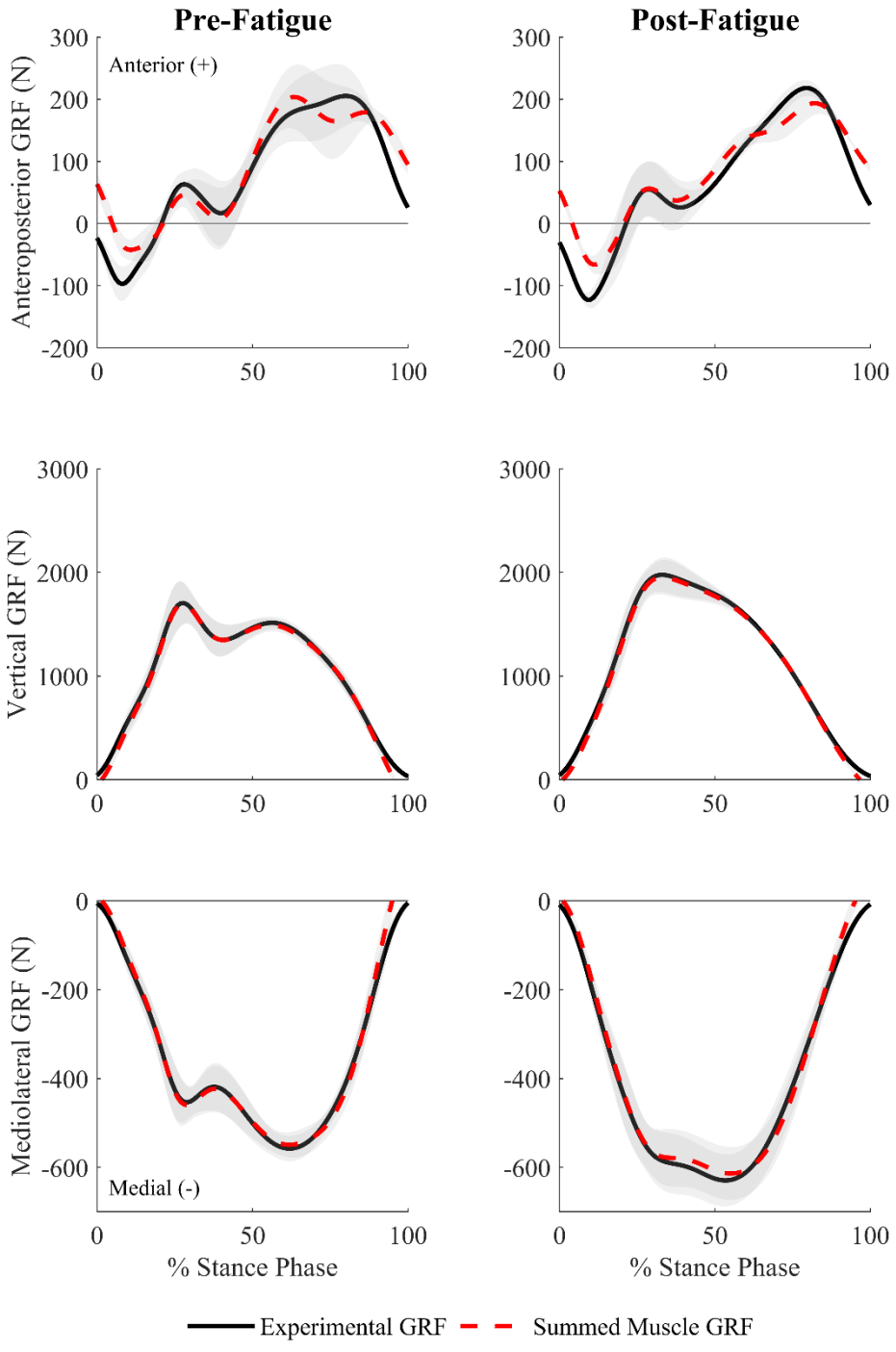


Figure 44: Subject 10 three-dimensional superimposed experimental and summed muscle GRFs from 0 to 100% of stance phase. The shaded regions represent the standard deviation of the experimental and summed muscle GRFs.

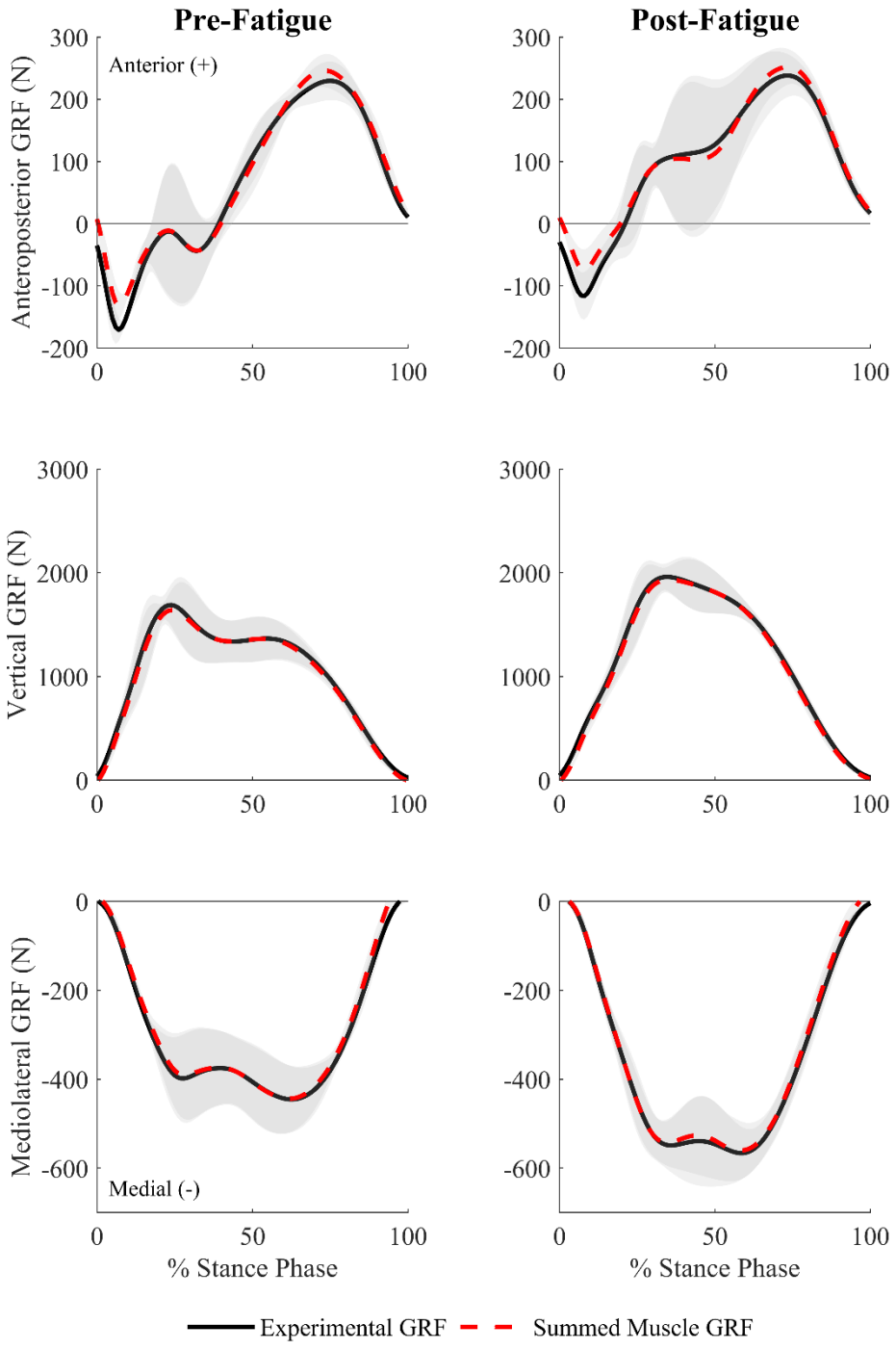


Figure 45: Subject 12 three-dimensional superimposed experimental and summed muscle GRFs from 0 to 100% of stance phase. The shaded regions represent the standard deviation of the experimental and summed muscle GRFs.

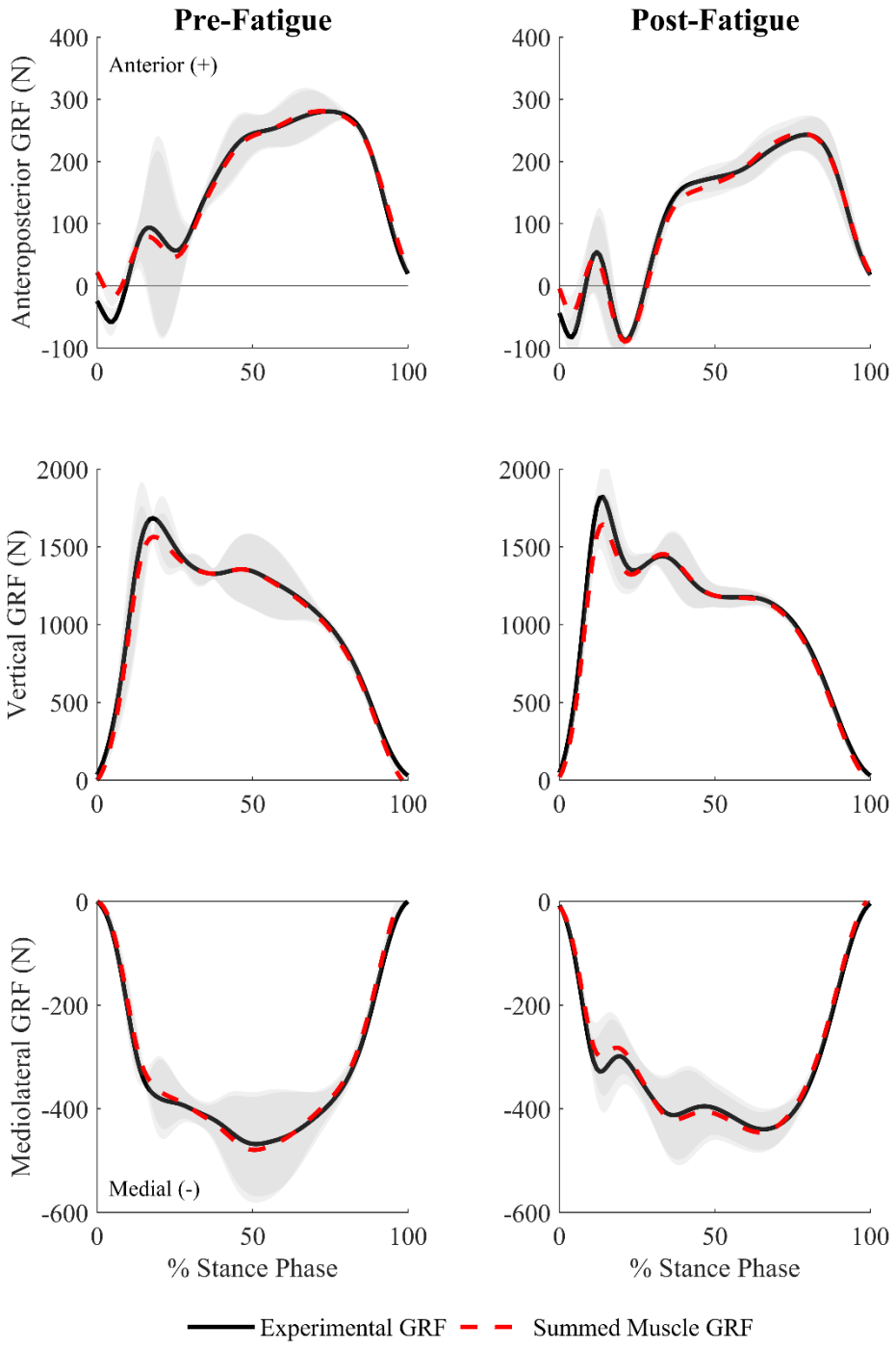


Figure 46: Subject 15 three-dimensional superimposed experimental and summed muscle GRFs from 0 to 100% of stance phase. The shaded regions represent the standard deviation of the experimental and summed muscle GRFs.

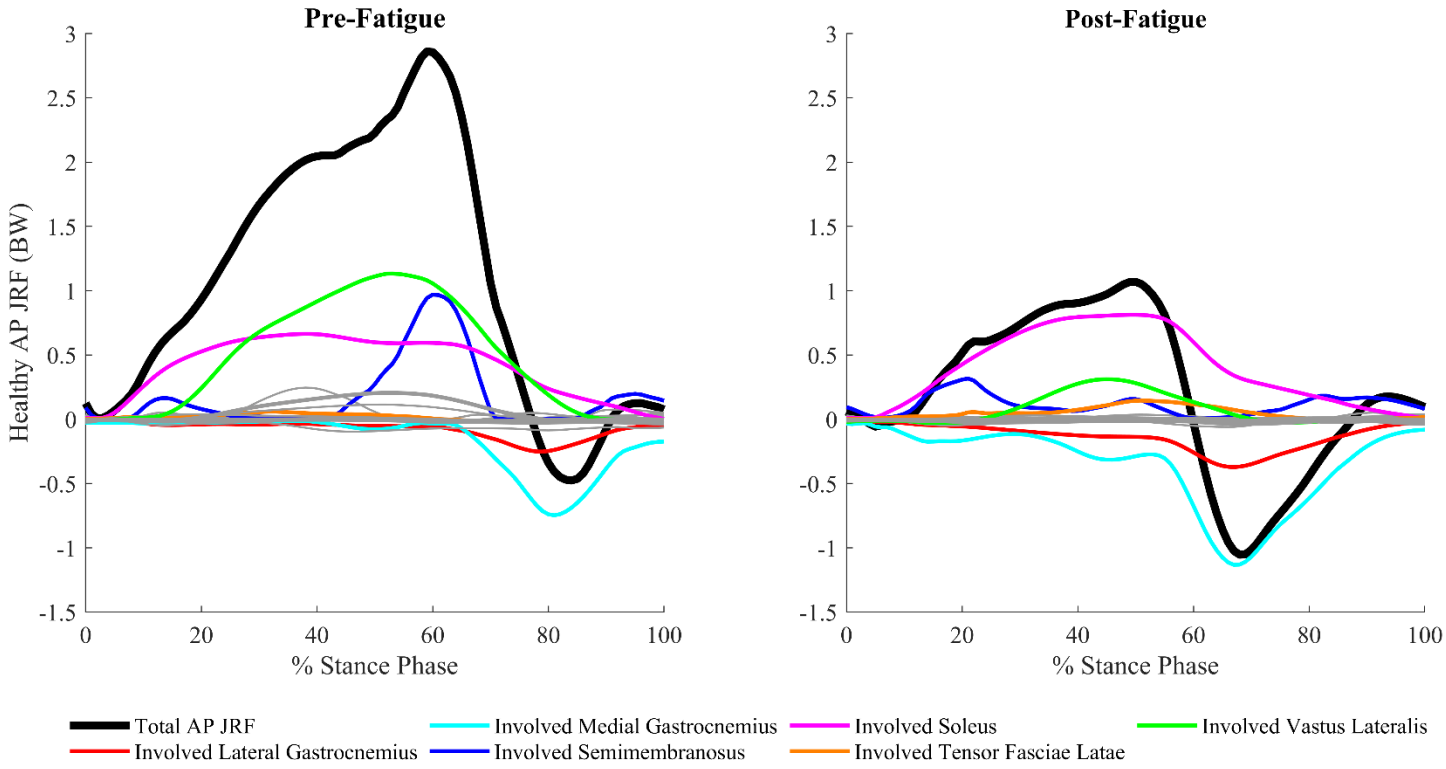


Figure 47: Subject 01 individual muscle contributions to the anteroposterior joint reaction force. Colored lines represent muscles that meaningfully contributed to the anteroposterior joint reaction force. Grey lines represent muscles that did not meaningfully contribute to the anteroposterior joint reaction force.

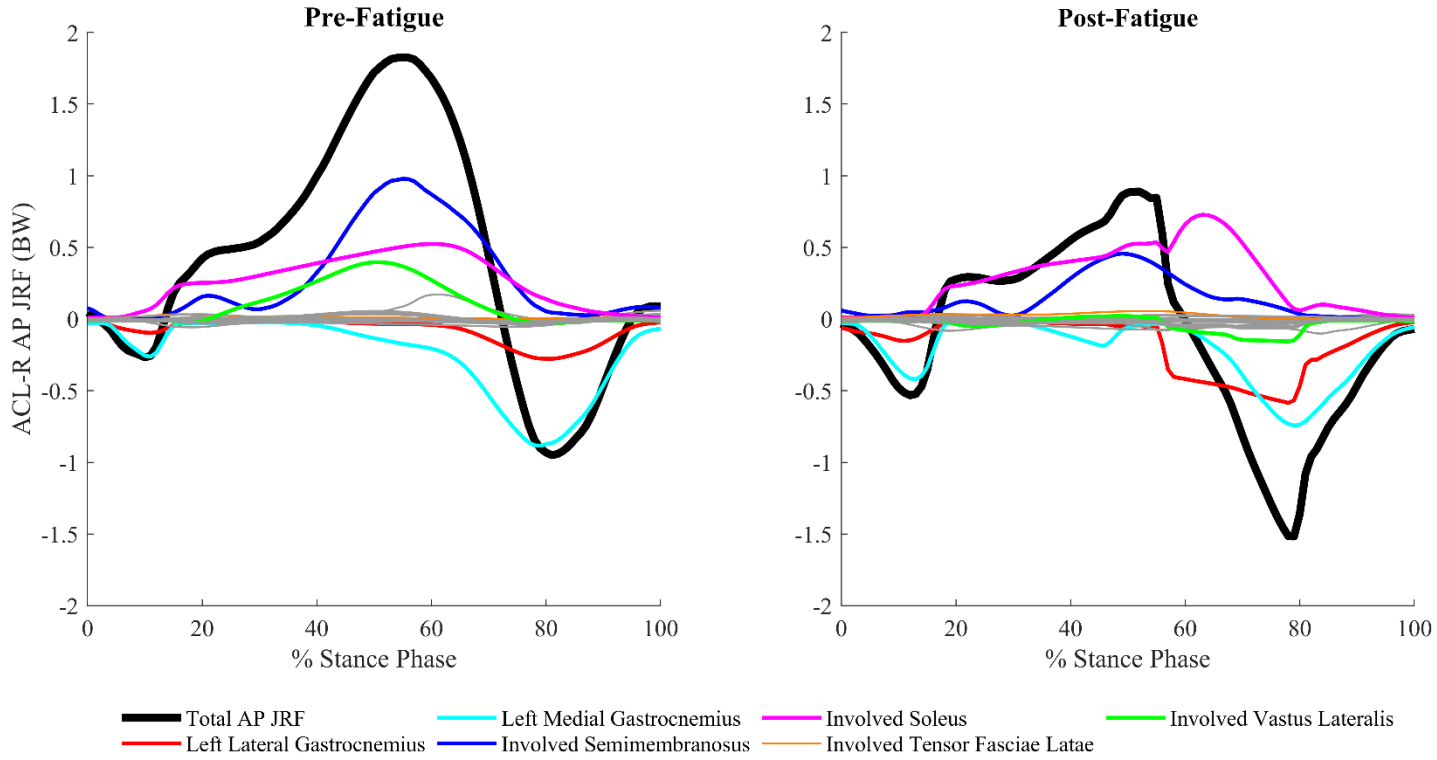


Figure 48: Subject 02 individual muscle contributions to the anteroposterior joint reaction force. Colored lines represent muscles that meaningfully contributed to the anteroposterior joint reaction force. Grey lines represent muscles that did not meaningfully contribute to the anteroposterior joint reaction force.

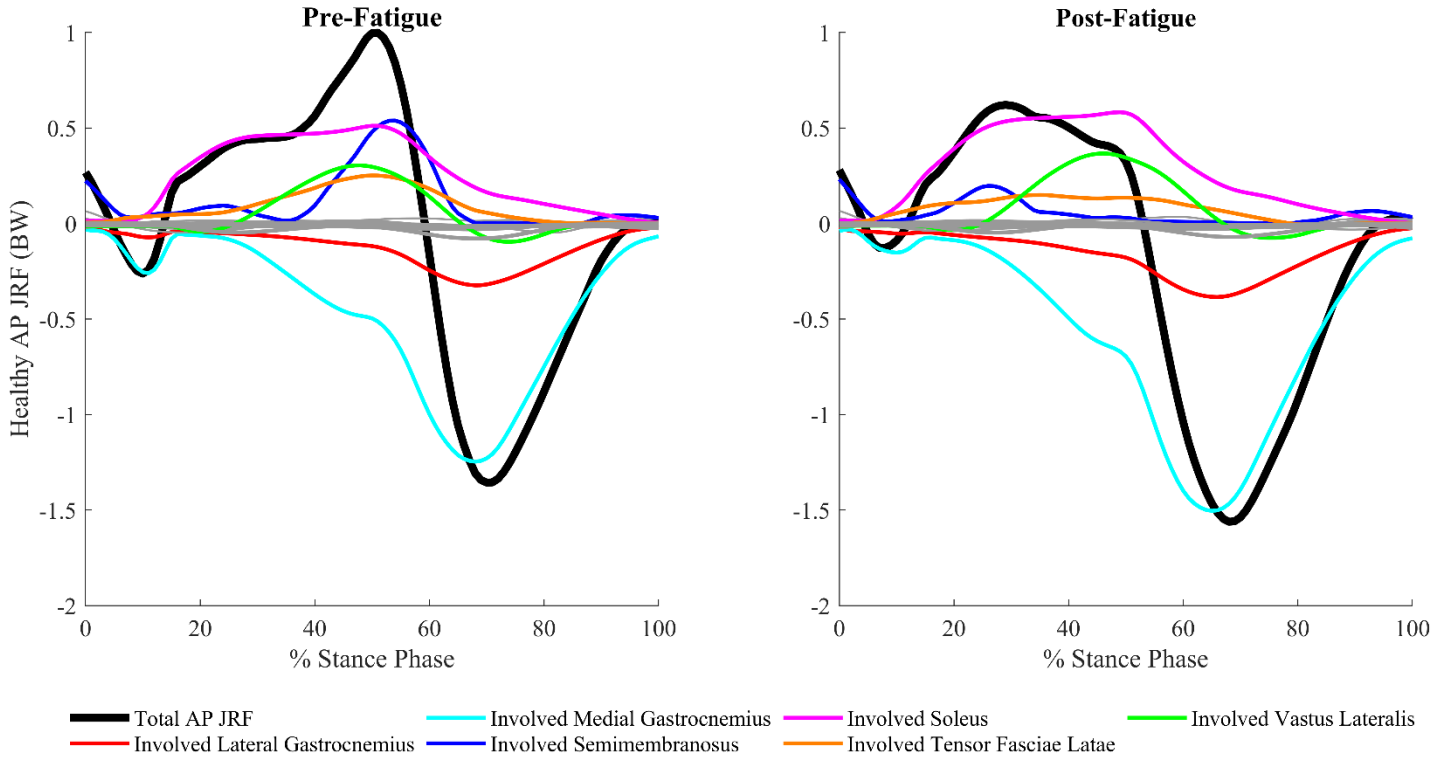


Figure 49: Subject 03 individual muscle contributions to the anteroposterior joint reaction force. Colored lines represent muscles that meaningfully contributed to the anteroposterior joint reaction force. Grey lines represent muscles that did not meaningfully contribute to the anteroposterior joint reaction force.

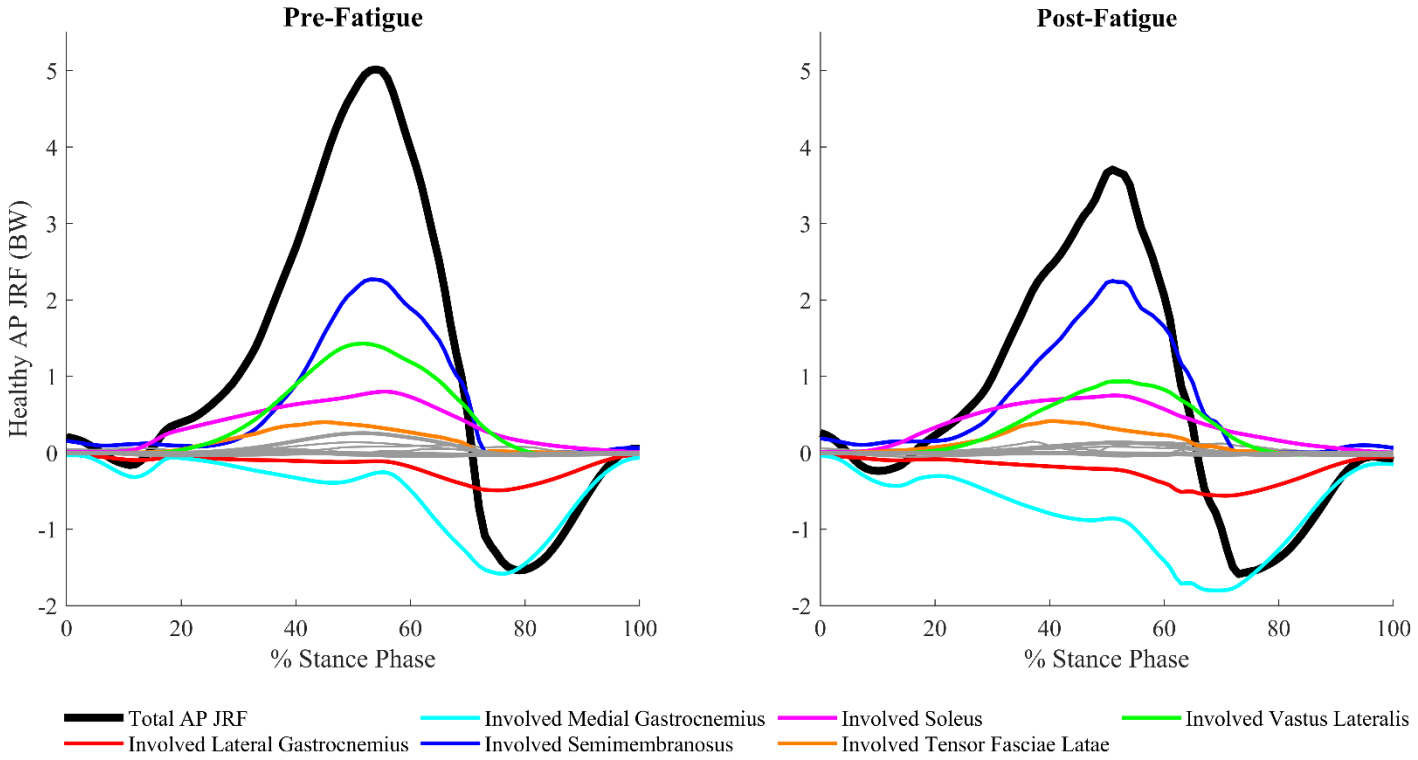


Figure 50: Subject 05 individual muscle contributions to the anteroposterior joint reaction force. Colored lines represent muscles that meaningfully contributed to the anteroposterior joint reaction force. Grey lines represent muscles that did not meaningfully contribute to the anteroposterior joint reaction force.

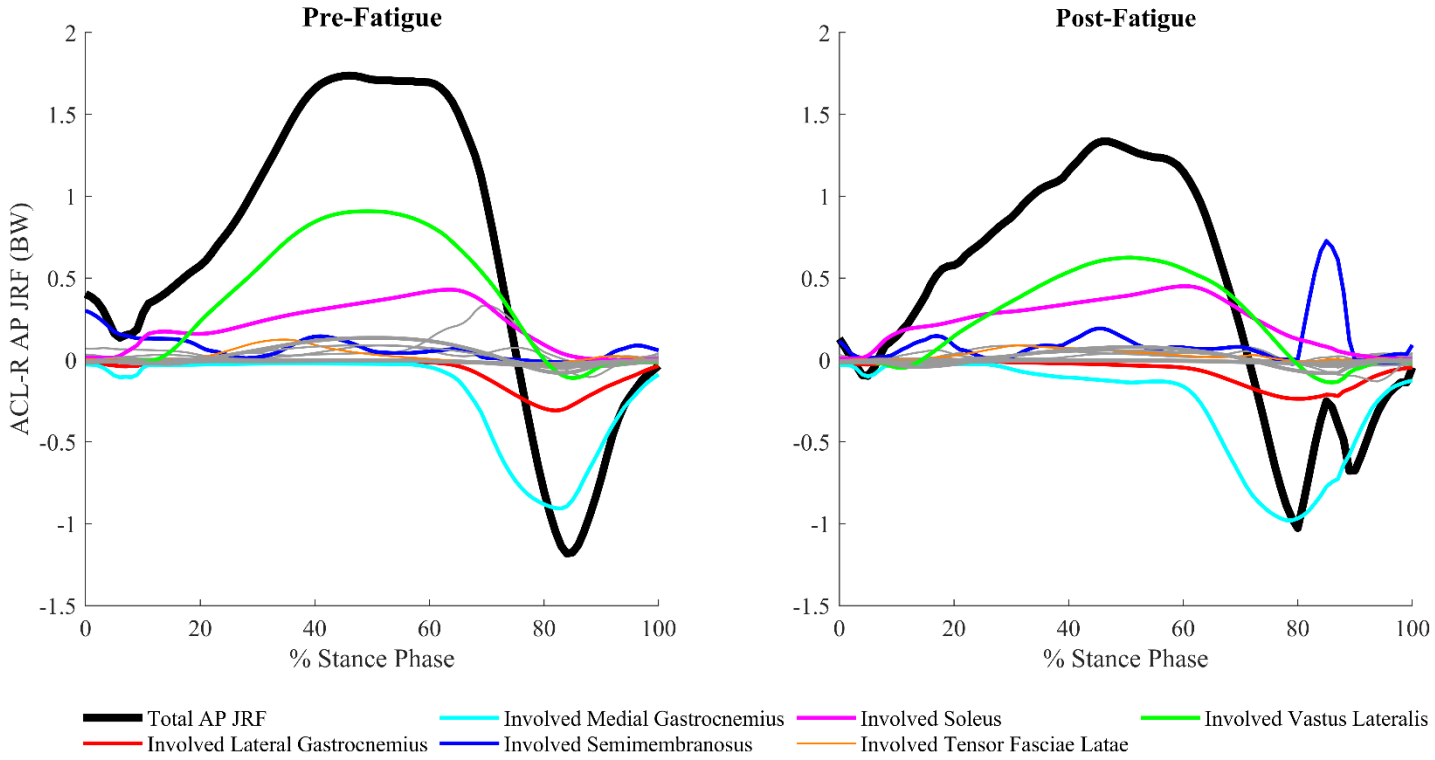


Figure 51: Subject 06 individual muscle contributions to the anteroposterior joint reaction force. Colored lines represent muscles that meaningfully contributed to the anteroposterior joint reaction force. Grey lines represent muscles that did not meaningfully contribute to the anteroposterior joint reaction force.

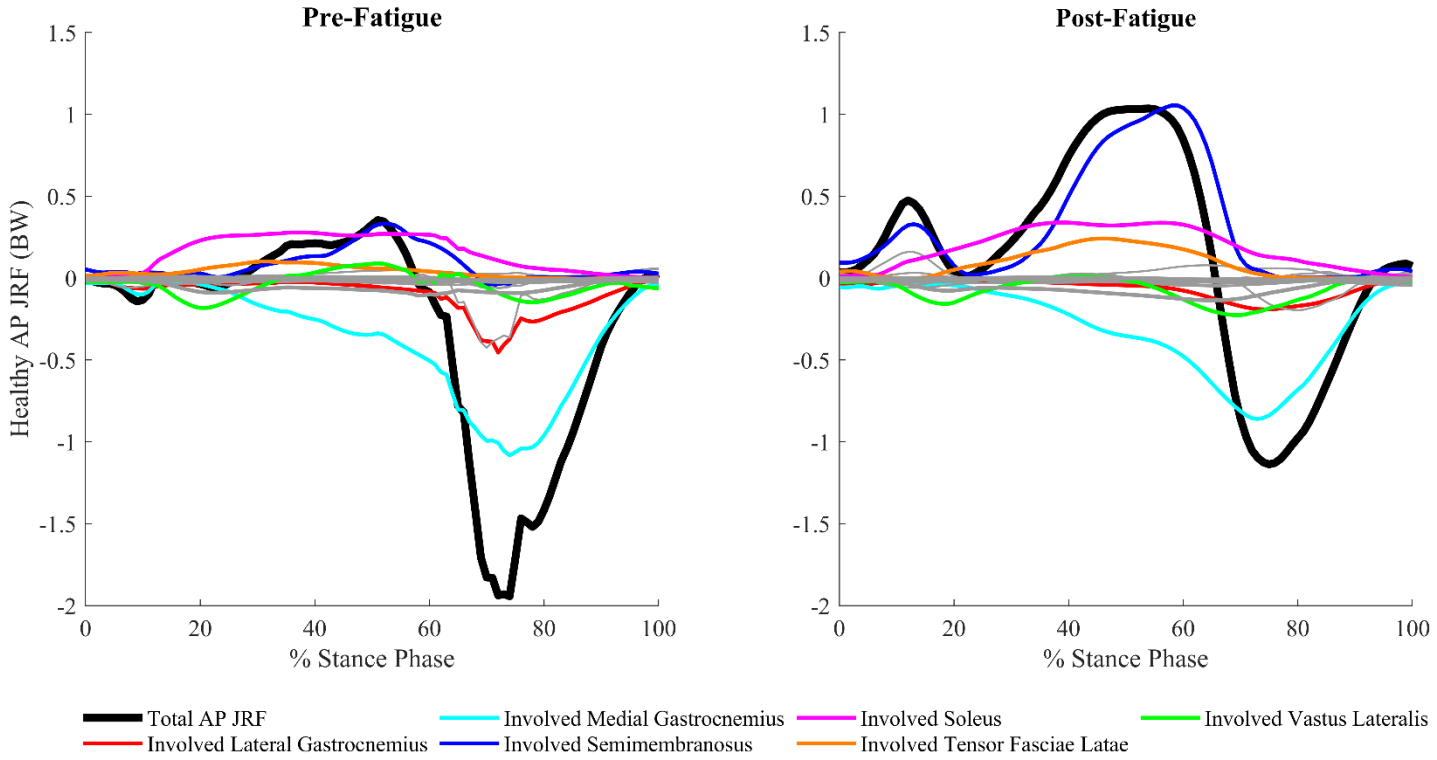


Figure 52: Subject 07 individual muscle contributions to the anteroposterior joint reaction force. Colored lines represent muscles that meaningfully contributed to the anteroposterior joint reaction force. Grey lines represent muscles that did not meaningfully contribute to the anteroposterior joint reaction force.

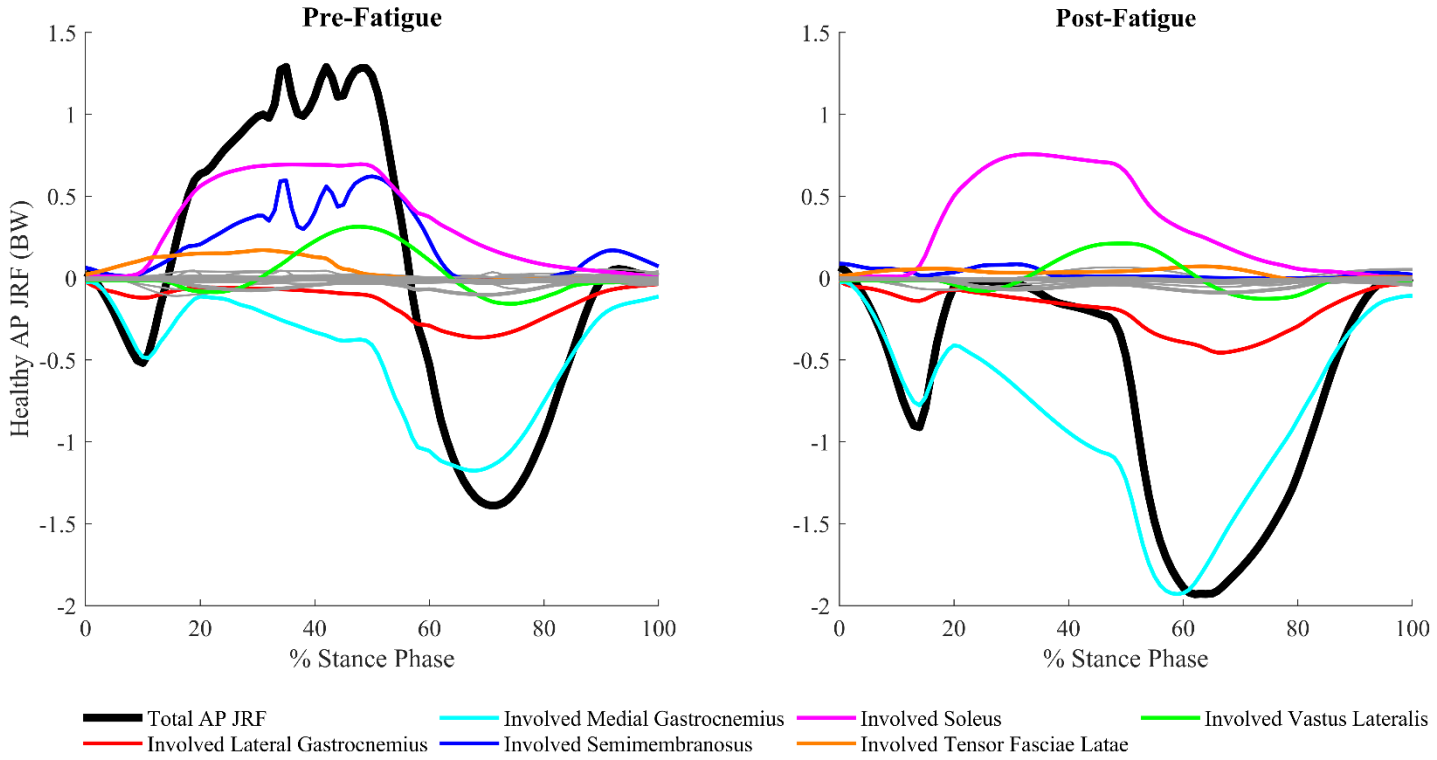


Figure 53: Subject 08 individual muscle contributions to the anteroposterior joint reaction force. Colored lines represent muscles that meaningfully contributed to the anteroposterior joint reaction force. Grey lines represent muscles that did not meaningfully contribute to the anteroposterior joint reaction force.

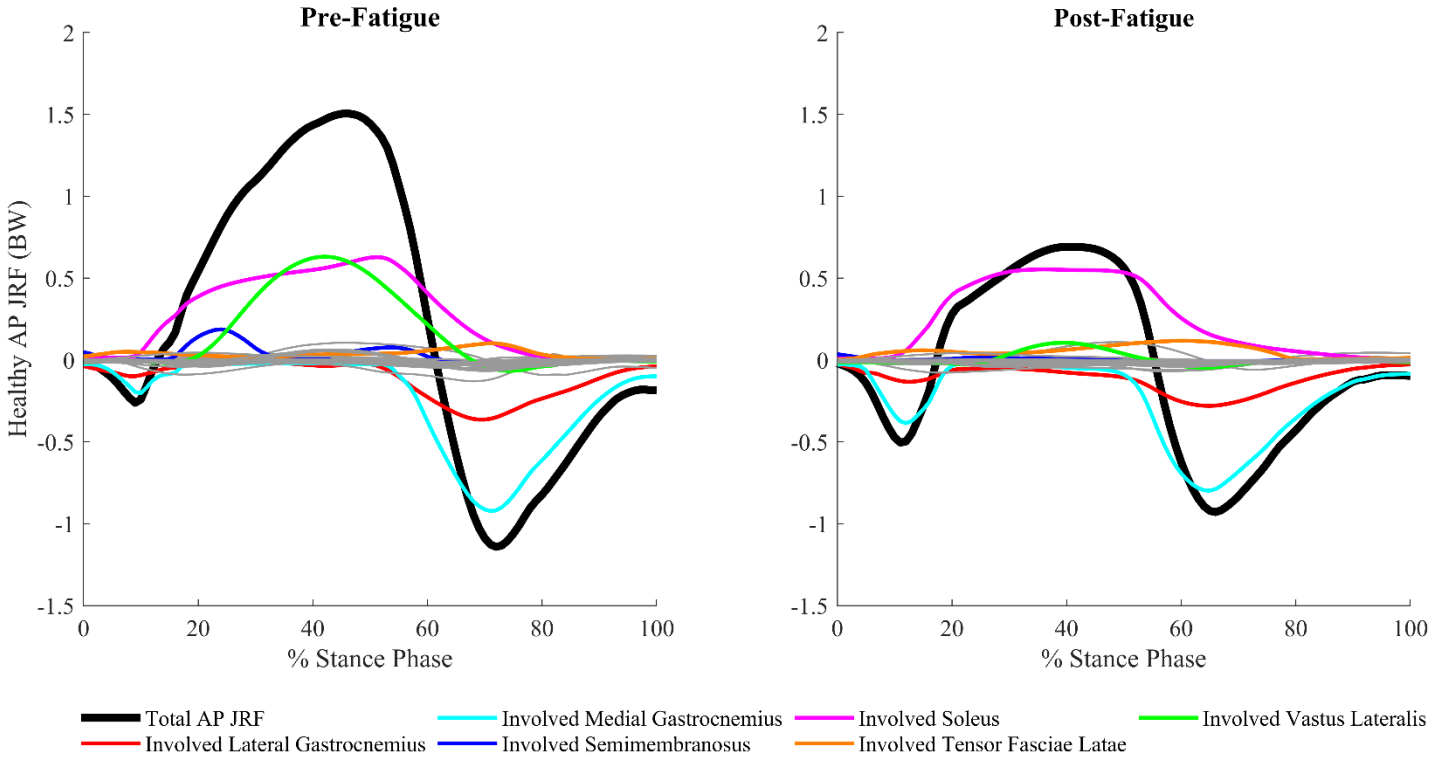


Figure 54: Subject 09 individual muscle contributions to the anteroposterior joint reaction force. Colored lines represent muscles that meaningfully contributed to the anteroposterior joint reaction force. Grey lines represent muscles that did not meaningfully contribute to the anteroposterior joint reaction force.

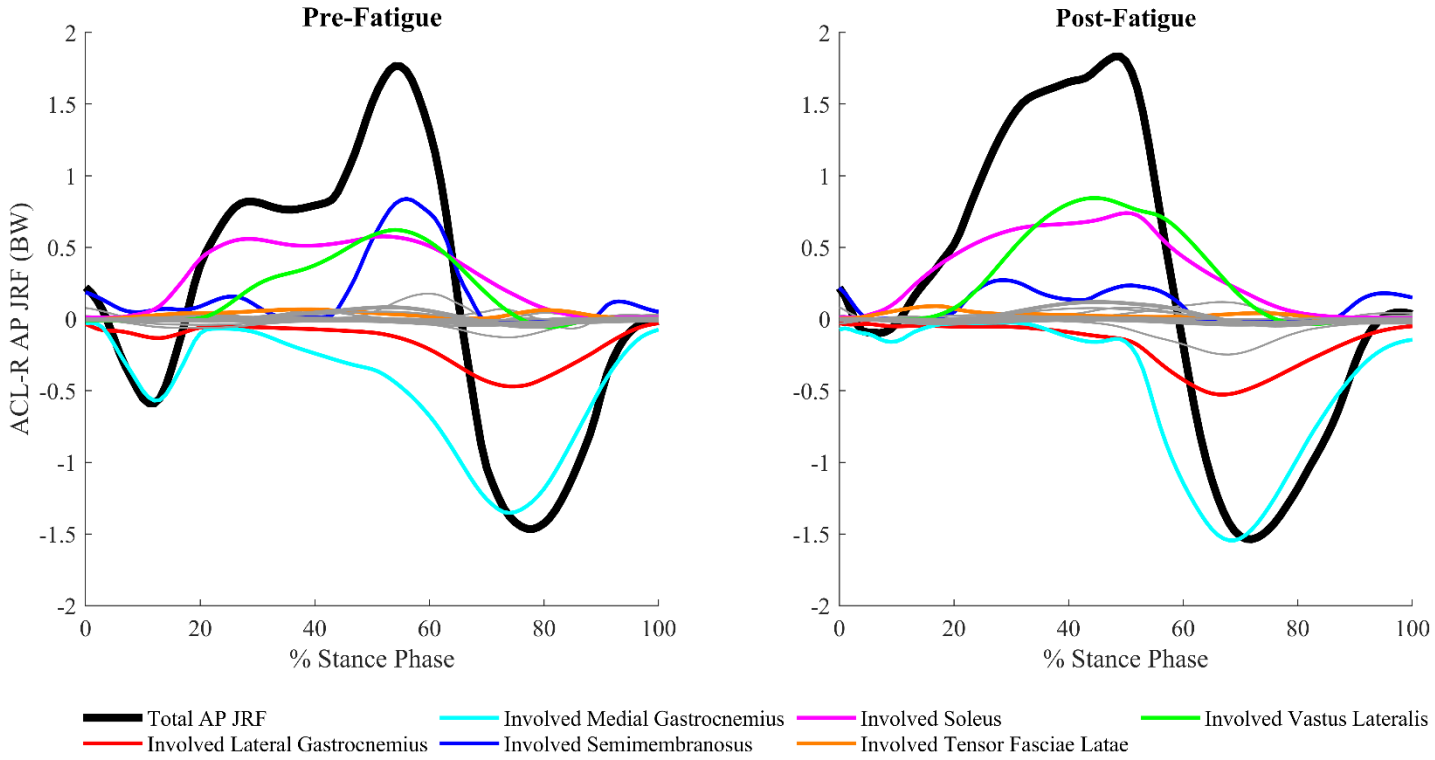


Figure 55: Subject 10 individual muscle contributions to the anteroposterior joint reaction force. Colored lines represent muscles that meaningfully contributed to the anteroposterior joint reaction force. Grey lines represent muscles that did not meaningfully contribute to the anteroposterior joint reaction force.

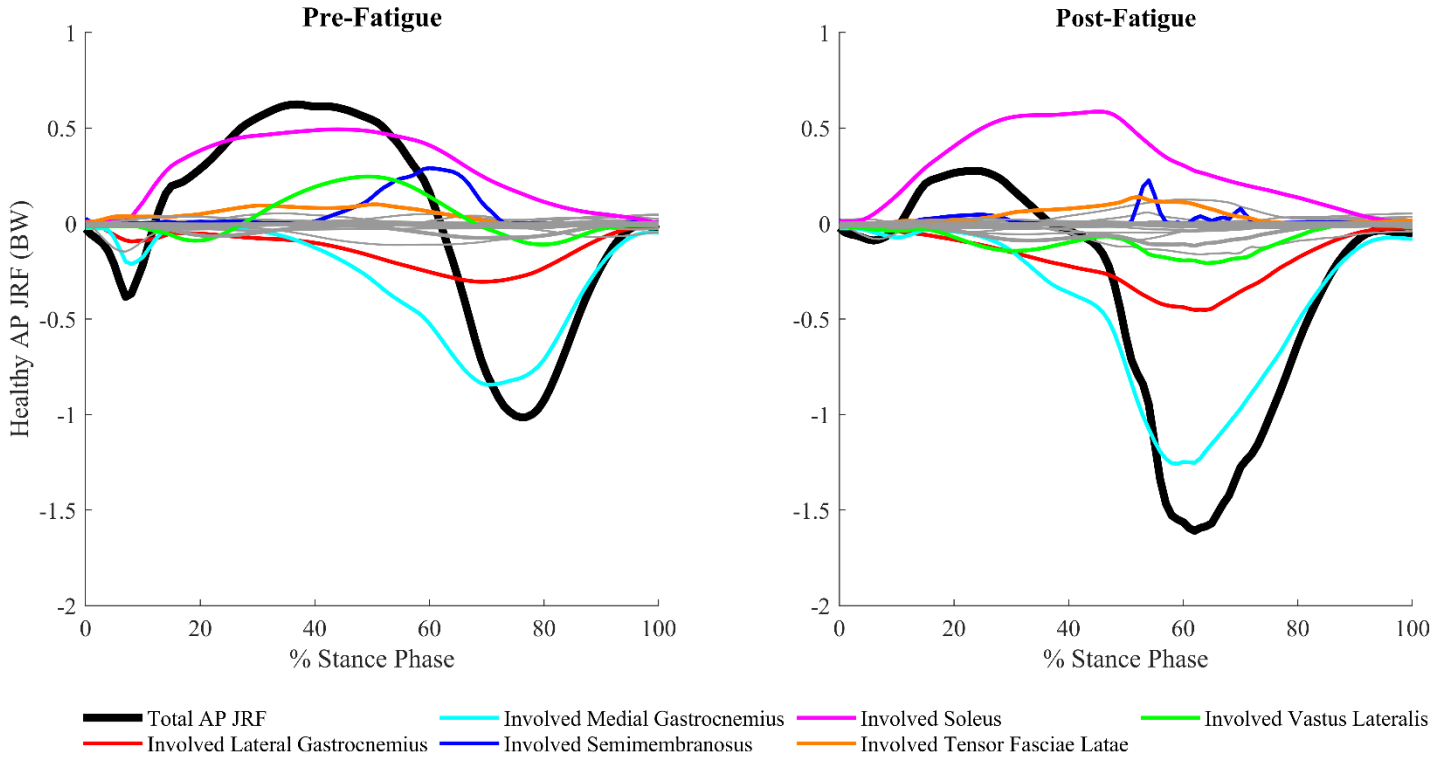


Figure 56: Subject 12 individual muscle contributions to the anteroposterior joint reaction force. Colored lines represent muscles that meaningfully contributed to the anteroposterior joint reaction force. Grey lines represent muscles that did not meaningfully contribute to the anteroposterior joint reaction force.

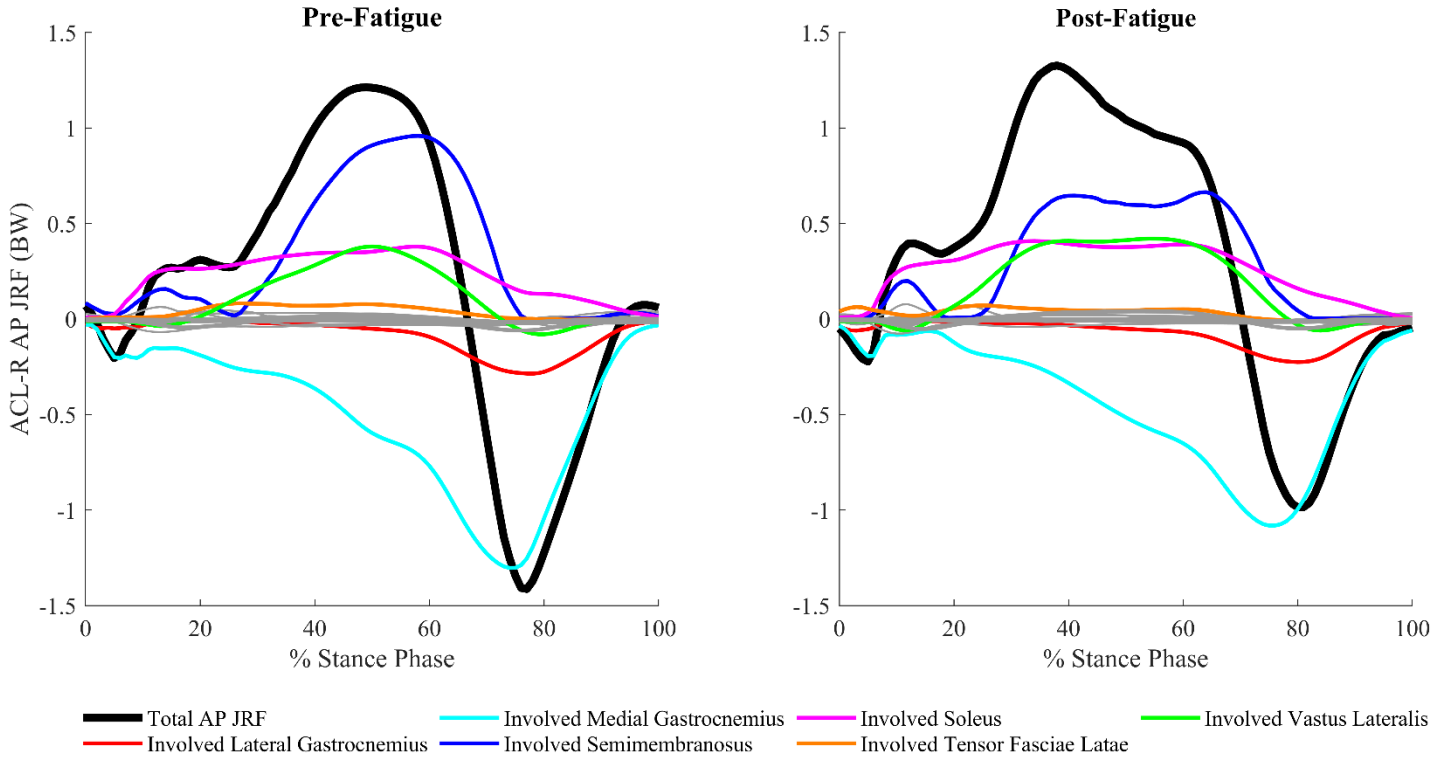


Figure 57: Subject 15 individual muscle contributions to the anteroposterior joint reaction force. Colored lines represent muscles that meaningfully contributed to the anteroposterior joint reaction force. Grey lines represent muscles that did not meaningfully contribute to the anteroposterior joint reaction force.

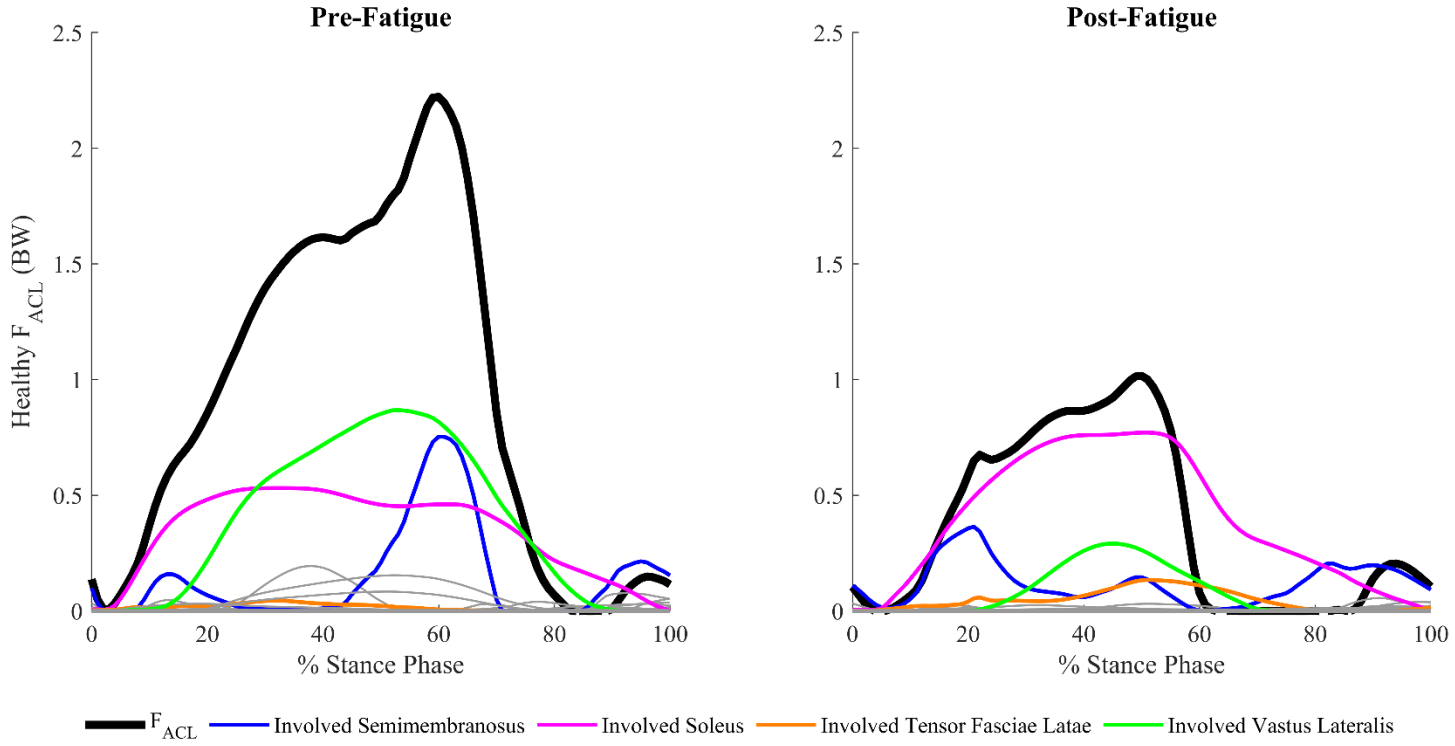


Figure 58: Subject 01 individual muscle contributions to F_{ACL}. Colored lines represent muscles that meaningfully contributed to F_{ACL}. Grey lines represent muscles that did not meaningfully contribute to F_{ACL}.

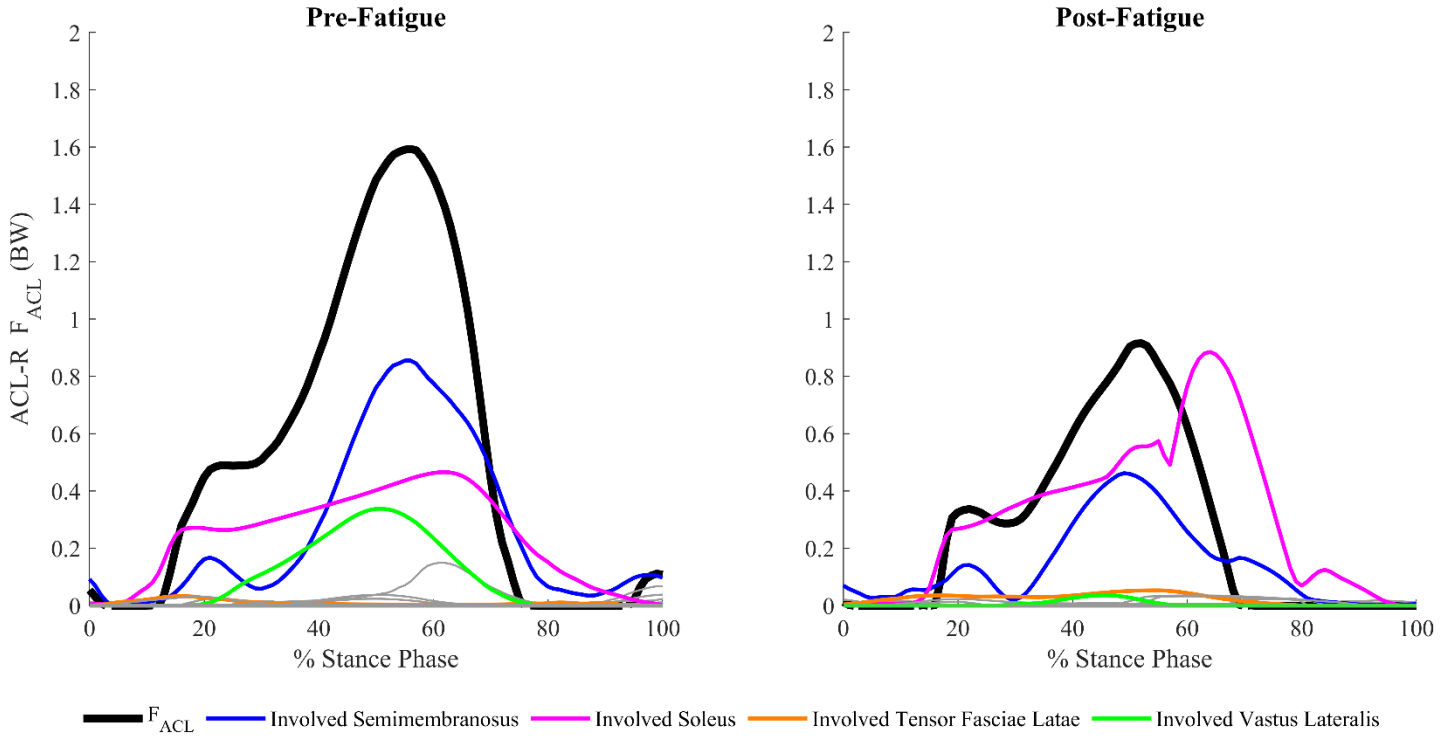


Figure 59: Subject 02 individual muscle contributions to F_{ACL}. Colored lines represent muscles that meaningfully contributed to F_{ACL}. Grey lines represent muscles that did not meaningfully contribute to F_{ACL}.

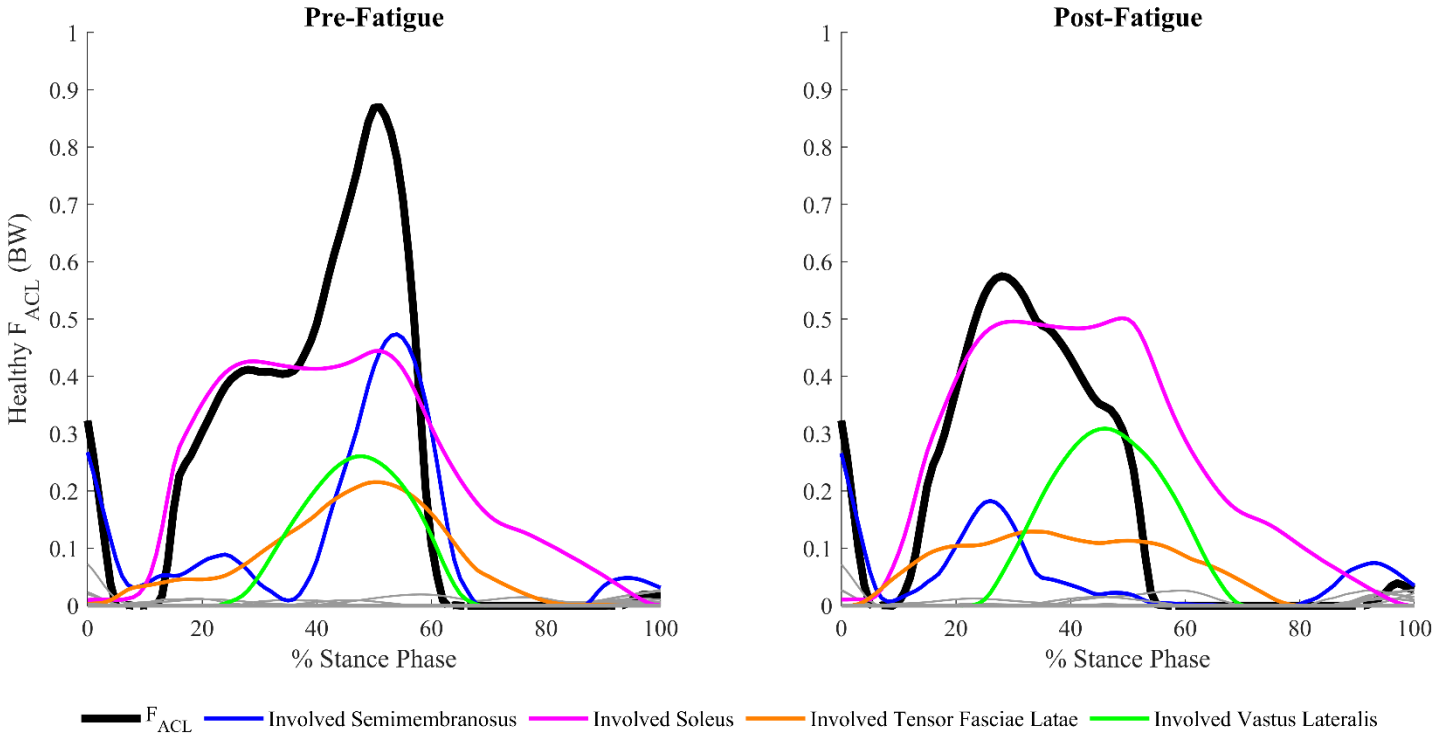


Figure 60: Subject 03 individual muscle contributions to F_{ACL}. Colored lines represent muscles that meaningfully contributed to F_{ACL}. Grey lines represent muscles that did not meaningfully contribute to F_{ACL}.

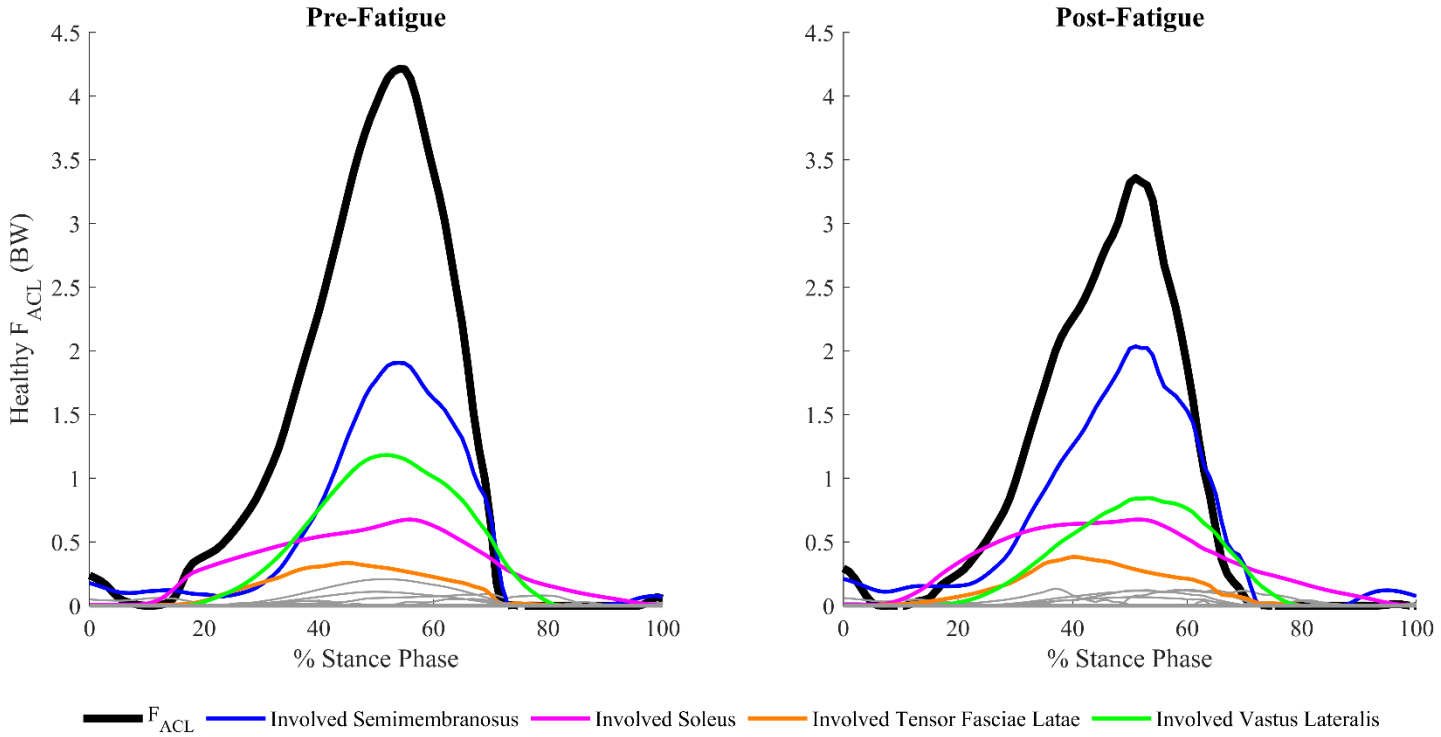


Figure 61: Subject 05 individual muscle contributions to F_{ACL}. Colored lines represent muscles that meaningfully contributed to F_{ACL}. Grey lines represent muscles that did not meaningfully contribute to F_{ACL}.

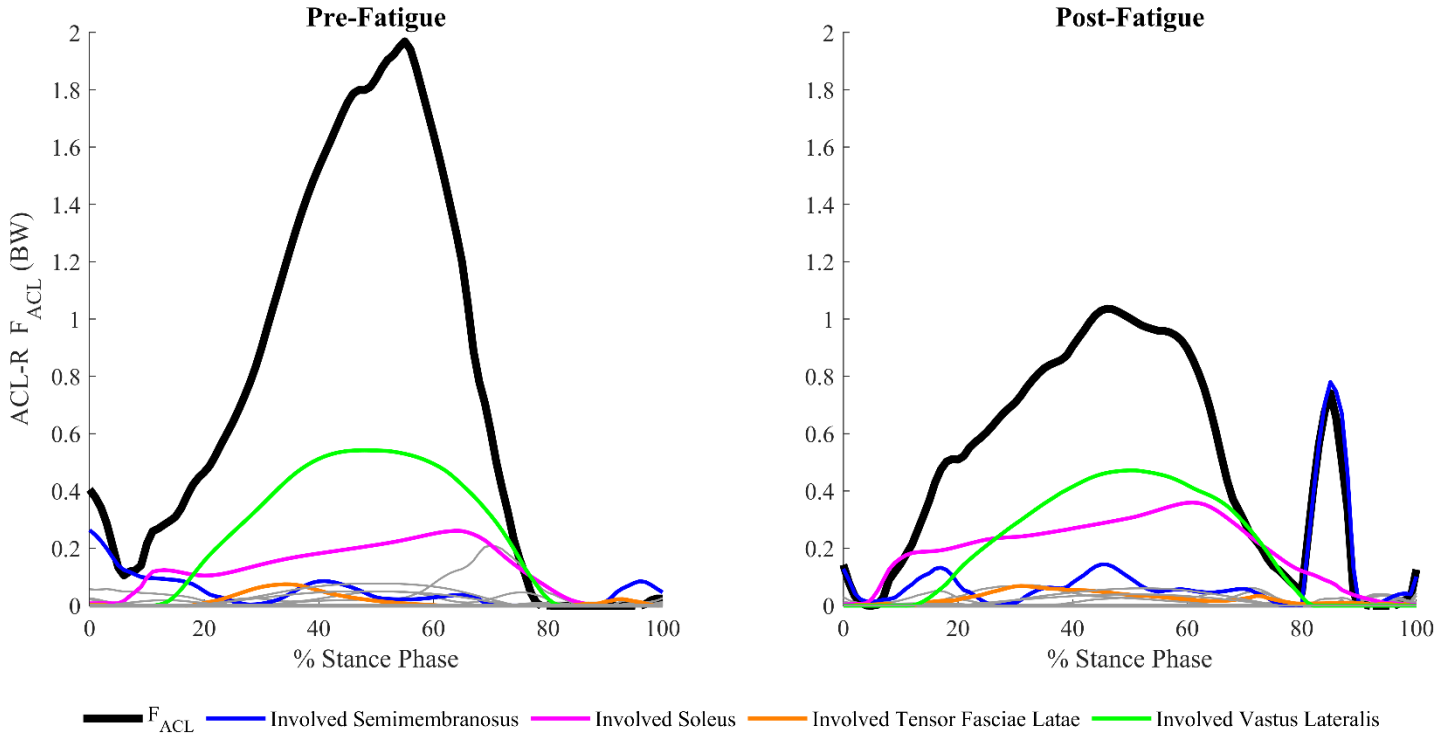


Figure 62: Subject 06 individual muscle contributions to F_{ACL}. Colored lines represent muscles that meaningfully contributed to F_{ACL}. Grey lines represent muscles that did not meaningfully contribute to F_{ACL}.

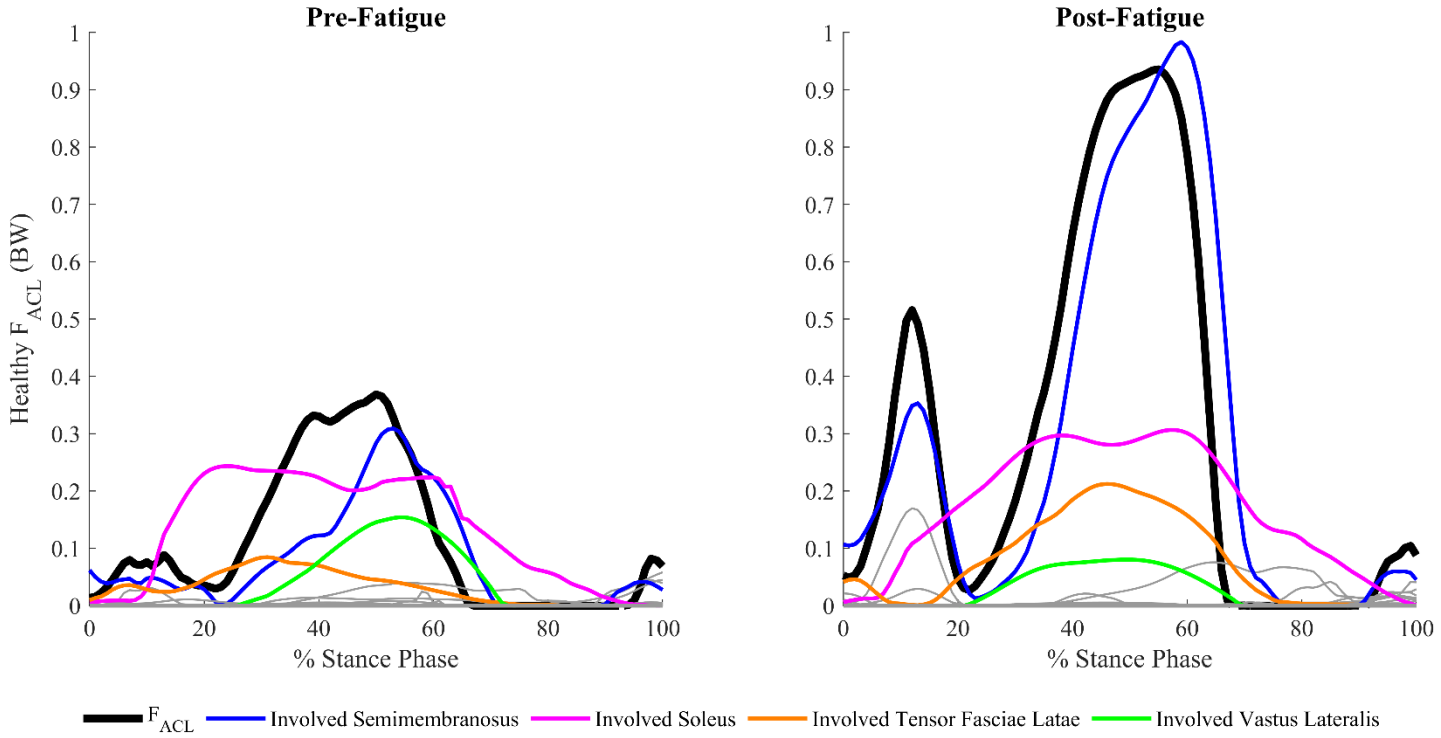


Figure 63: Subject 07 individual muscle contributions to F_{ACL}. Colored lines represent muscles that meaningfully contributed to F_{ACL}. Grey lines represent muscles that did not meaningfully contribute to F_{ACL}.

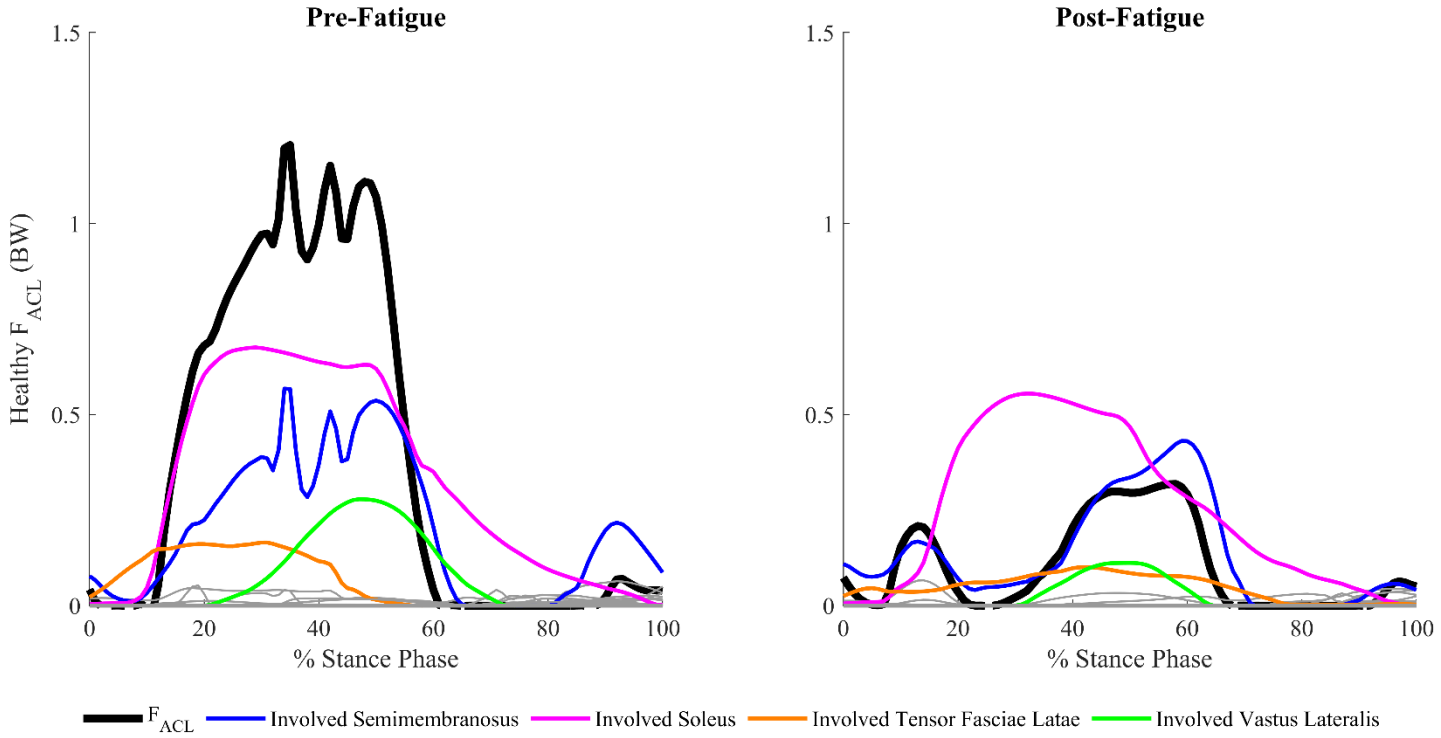


Figure 64: Subject 08 individual muscle contributions to F_{ACL}. Colored lines represent muscles that meaningfully contributed to F_{ACL}. Grey lines represent muscles that did not meaningfully contribute to F_{ACL}.

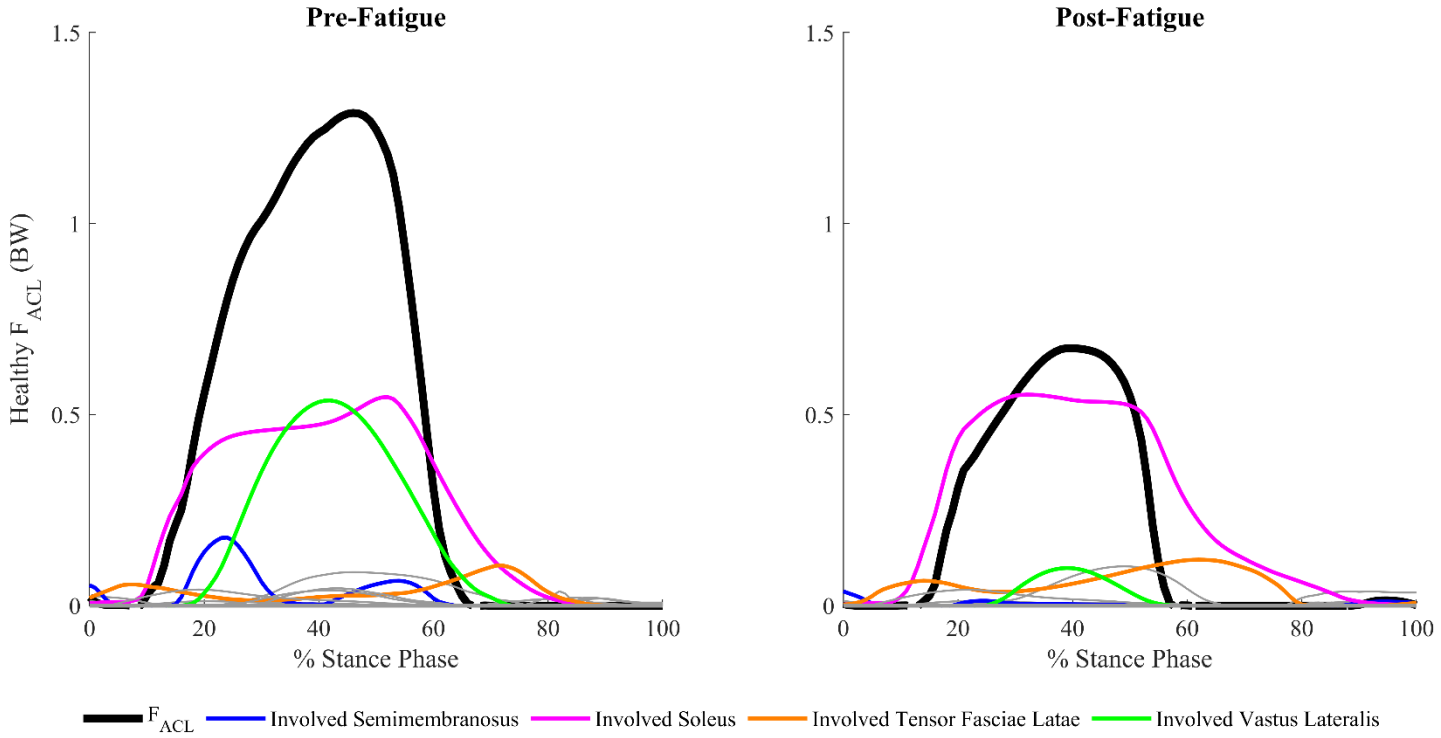


Figure 65: Subject 09 individual muscle contributions to F_{ACL}. Colored lines represent muscles that meaningfully contributed to F_{ACL}. Grey lines represent muscles that did not meaningfully contribute to F_{ACL}.

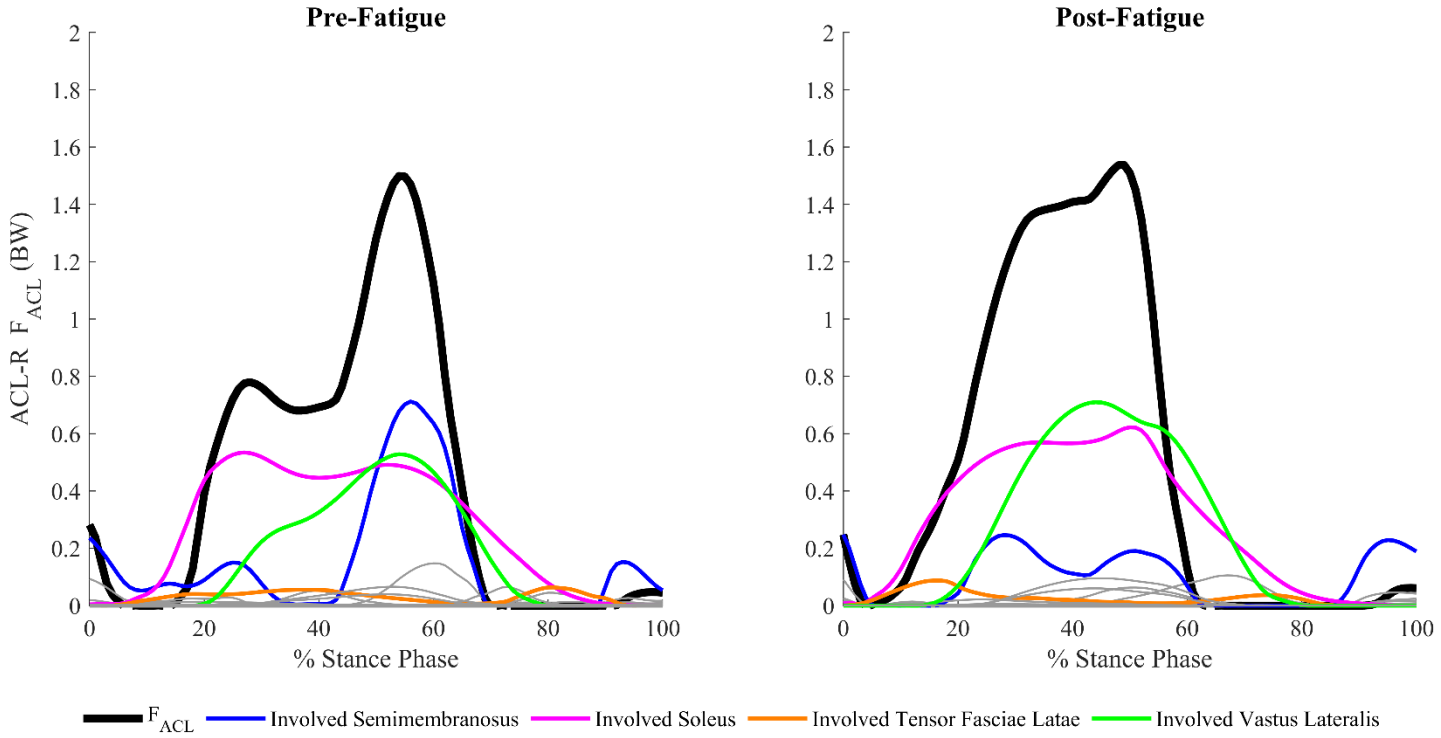


Figure 66: Subject 10 individual muscle contributions to F_{ACL}. Colored lines represent muscles that meaningfully contributed to F_{ACL}. Grey lines represent muscles that did not meaningfully contribute to F_{ACL}.

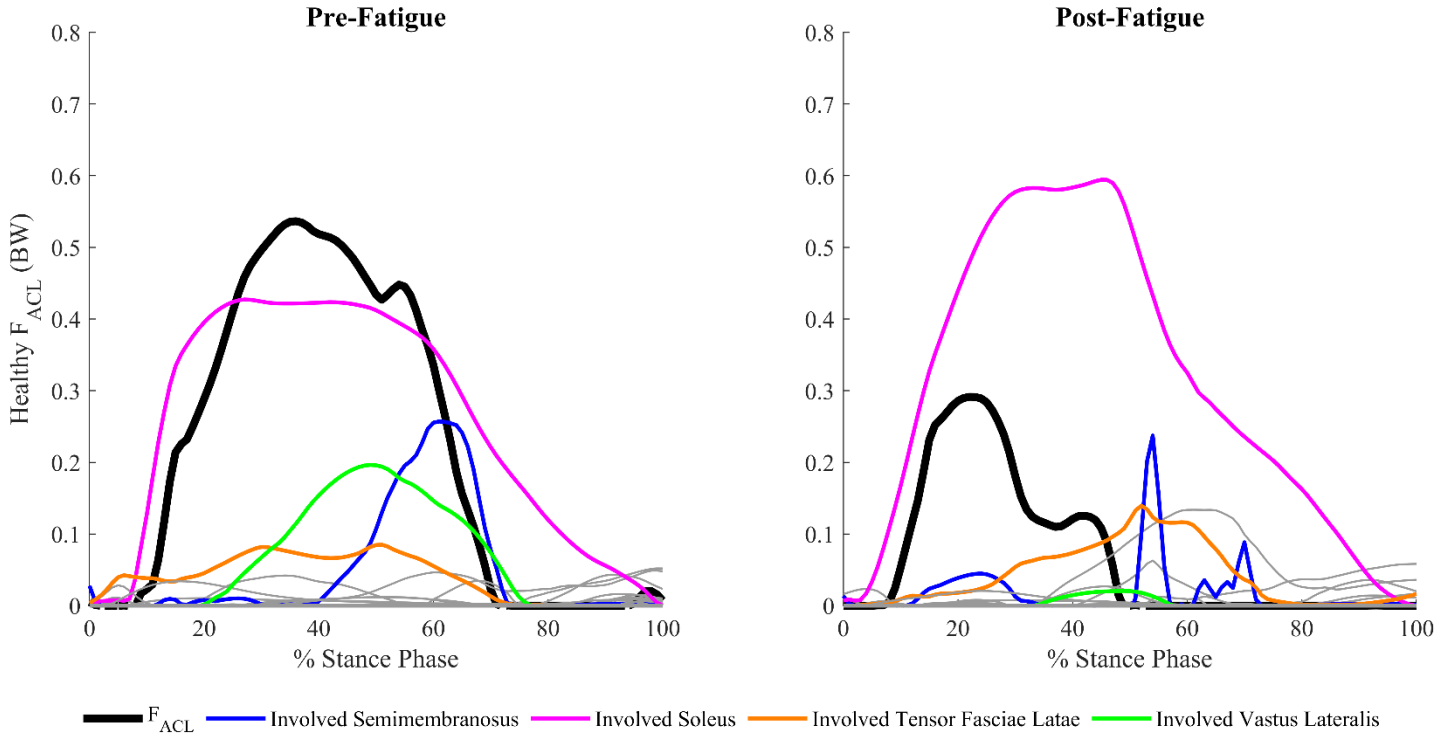


Figure 67: Subject 12 individual muscle contributions to F_{ACL}. Colored lines represent muscles that meaningfully contributed to F_{ACL}. Grey lines represent muscles that did not meaningfully contribute to F_{ACL}.

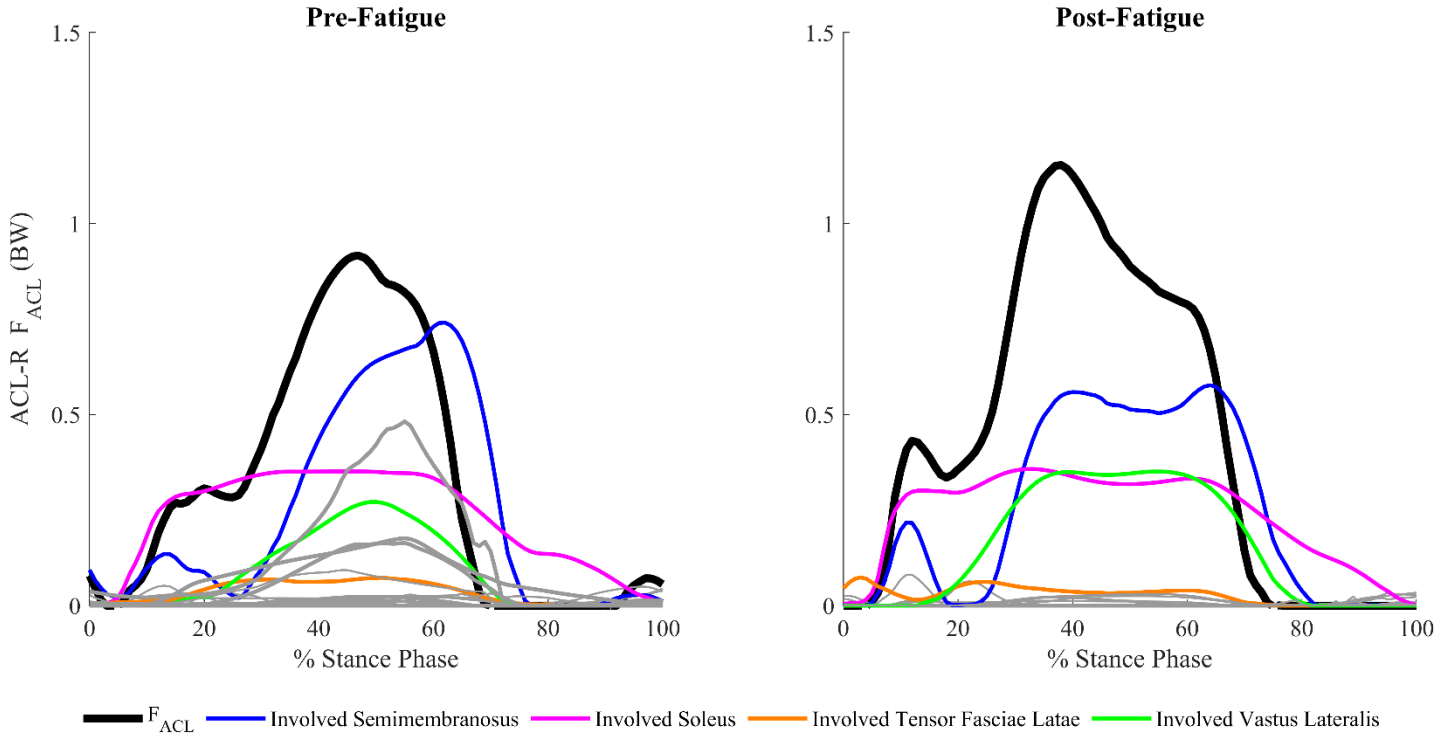


Figure 68: Subject 15 individual muscle contributions to F_{ACL}. Colored lines represent muscles that meaningfully contributed to F_{ACL}. Grey lines represent muscles that did not meaningfully contribute to F_{ACL}.

Appendix T. Comparing Hamner's IAA to Lin's IAA

Introduction

Muscles directly influence joints they cross, as well as indirectly influence joints they do not cross. This phenomenon is known as dynamic coupling (11). Dynamic coupling describes how an individual muscle force acts to accelerate instantaneously not only the joint it spans, but also other joints and segments that it has no direct relationship (11, 331). This means that individual muscles also contribute to the acceleration of the body's center of mass. Because the body is multisegmented, a muscle force acting at any joint in the body also instantaneously transfers force throughout the body due to joint intersegmental forces (11, 331, 332). Therefore, a single muscle can either directly or indirectly contribute to intersegmental forces, joint accelerations, and other components like joint moments, joint power, and joint work, for all joints in the body (11, 49, 331, 332).

In a perfectly linear system, the summation of all the individual forces that are contributing to the total body acceleration must equal the overall total body acceleration (49). When considering the human body, the summation of the internal forces of the body (i.e. muscle forces, ligamentous forces, etc.) must equal the GRF obtained from a force plate to produce the desired body's kinematics (49). However, a major problem that researchers encounter is that a force plate cannot measure the contribution of a single muscle's force to the overall GRF, which is necessary to evaluate the intersegmental forces and accelerations induced by that specific muscle (49). As such, an induced acceleration analysis (IAA) was developed to account for the dynamic coupling nature of the body during musculoskeletal modeling.

Various IAA methods for OpenSim are available for use. Two of the more common IAA methods were produced by Lin (333), which uses a five-point foot-ground contact model which

was later validated by Dorn, Lin and Pandy (334), and by Hamner, Seth and Delp (339), which uses a rolling constraint as the foot-ground contact model. Hamner, Seth and Delp (339)'s IAA method is now native to OpenSim while Dorn, Lin and Pandy (334) packaged the (333) IAA method into an OpenSim plugin. While both methods have been validated for use in musculoskeletal modeling, and have been utilized in previous research studying lower extremity muscle function during walking (336, 337, 366-369), running (335, 339), and most recently unanticipated sidestep cutting (338), there are subtle differences in how both IAA methods work.

Lin (333)'s IAA method calculates the contribution of each individual muscle force in the musculoskeletal model to the ground reaction force (GRF) by applying the muscle force in isolation and calculating the corresponding GRF using the equations of motion. Foot-ground contact was modeled by a five foot-contact points, four points which were located around the perimeter of the hind-foot segment, and one at the distal end of the toes. External GRFs exerted on the foot by the ground were transmitted through these foot-contact points from the ground to the rest of the body. A weighting matrix was used to constrain the foot contact with the ground in a way that would accurately represent realistic foot movement, thus becoming a more robust foot-ground contact model by accounting for all foot strike patterns, not just rearfoot strike patterned gait. Lin (333) decomposed the GRFs from these foot-contact points by solving an equality-constrained, least-squares problem. They solved this analytically by using the Moore-Penrose pseudo-inverse approach on the weighting matrix, which was repeated solved for all muscle forces in the body.

Hamner, Seth and Delp (339) created an IAA that quantifies the contribution of individual muscles within a musculoskeletal model to three-dimensional center of mass accelerations. In their IAA, the foot-ground interaction was modeled as a combination of non-

penetrating unilateral constraint (i.e. no foot penetration in the ground, but the foot can be lifted off the ground) and a pure rolling constraint (i.e. no foot slipping or twisting). Briefly, Hamner, Seth and Delp (339) modified the generic equations of motion and replaced the contribution of contact forces with a constraint matrix and constraint forces. This was done to accommodate the kinematic constraints placed on the foot-ground interaction during stance phase of any movement. Equations for the kinematic constraints included a non-penetrating constraint, a fore-aft no-slip constraint, a mediolateral no-slip constraint, and a no-twist constraint. These four equations were differentiated so that the results could be expressed in terms of conditions on the coordinate accelerations, which were then used in formulating the total system constraints needed to solve for the modified equations of motion. Muscle contribution to center of mass acceleration then was calculated for each muscle in isolation by solving for the accelerations caused by that specific muscle in the modified equations of motion. The results of this IAA give the potential for each muscle's ability to accelerate the center of mass. Individual muscle contributions to three-dimensional GRFs can then be calculated by 1) calculating the potentials via the dot product of the subject-specific model mass and the induced acceleration analysis results, and 2) taking the dot product of the potentials and the individual muscle forces obtained from static optimization.

Because individual muscle contributions to overall ACL loading is dependent on accurate individual muscle contributions to the GRFs, it is vital to use the appropriate IAA method for this data set. Therefore, the purpose of this communication was to compare the Hamner, Seth and Delp (339) and the Lin (333) IAA methods and calculate the superposition error between the experimental three-dimensional GRFs and the summed muscle contributions to the three-dimensional GRFs.

Methods and Materials

The average of five pre-fatigue trials from a representative healthy female participant (S01; age: 27; height: 171.5 cm; weight: 74.5 kg) was used as the experimental data. A generic musculoskeletal model (359) was scaled to match the participant's anthropometry based on experimentally measured anatomical landmarks. Individual muscle contributions to the three-dimensional GRFs were calculated directly by using the Lin (333) IAA methods, while muscle contributions to the three-dimensional center of mass accelerations were calculated by the Hamner, Seth and Delp (339), which were then in turn used to calculate individual muscle contributions to the three-dimensional GRFs. To verify the accuracy of the summed muscle GRFs to the experimental GRFs, normalized root mean square error (nRMSE) and coefficients of correlation (R^2) were calculated (12). To qualitatively verify the summed muscle GRFs, three-dimensional superposition plots for the experimental and summed muscle GRFs were created (Figure 69).

Results

Overall, the Hamner, Seth and Delp (339) IAA method (anteroposterior GRF: nRMSE = 5.2% ± 1.2%; R^2 = 0.99 ± 0.01; vertical GRF: nRMSE = 2.3% ± 0.2%; R^2 = 1.0 ± 0.0; mediolateral GRF: nRMSE = 1.4% ± 0.4%; R^2 = 1.0 ± 0.0) outperformed the Lin (333) IAA method (anteroposterior GRF: nRMSE = 13.0% ± 6.9%; R^2 = 0.88 ± 0.11; vertical GRF: nRMSE = 7.7% ± 1.6%; R^2 = 0.99 ± 0.0; mediolateral GRF: nRMSE = 11.9% ± 1.1%; R^2 =0.97 ± 0.01) in all three directions, both quantitatively and qualitatively.

Discussion and Conclusion

Due to the performance of the Hamner, Seth and Delp (339) IAA method compared to the Lin (333) IAA method, it was determined that the Hamner, Seth and Delp (339) IAA method

would be the best IAA method to use in the current studies. Differences between the two methods can most likely be attributed to the kinematic constraints set within the different foot-ground contact model used in each IAA method. These differences would change the equations of motion, thus impacting the calculations of individual muscle contributions.

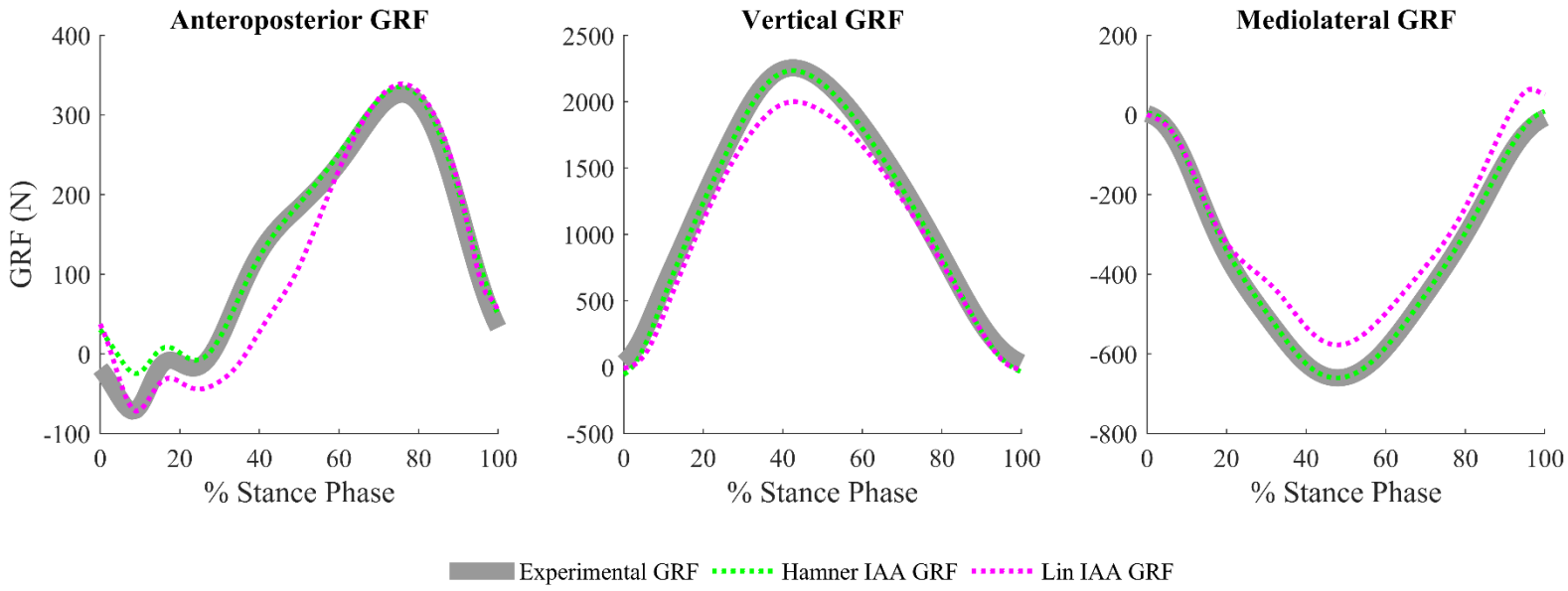


Figure 69: Comparison of the Hamner IAA and the Lin IAA summed muscle contributions to the three-dimensional GRFs and the experimental three-dimensional GRFs from one representative healthy participant (S01) during a pre-fatigue anticipated box-land-and-cut.

Appendix U. The Hopper Model

Introduction

Knee joint reaction forces (JRF) represent the sum of contact forces between the tibia and femur as well as all ligaments crossing the knee joint. Understanding resultant JRFs transmitted across the knee joint can be extremely useful in understanding certain types of knee injuries, such as ACL injuries. Specifically, anteroposterior knee JRF is a vital component in calculating the load placed upon the ACL during any given motion, and is commonly used in well-established ACL loading models (54, 137, 358). OpenSim allows for easy computation of JRFs via the JointAnalysis tool. A full description of how OpenSim calculates JRF can be found in Steele, Demers, Schwartz and Delp (363)'s supplemental material. Briefly, the JointAnalysis tool utilizes a recursive process that starts with the most distal segment and works upwards to calculate the JRFs. To calculate knee JRFs, the segment distal to the knee (i.e. the ankle) is treated as an independent body. Then, the sum of the external ground reaction forces, the sum of all muscle forces, and the calculated JRF from the distal segment are added together, and then subtracted from the sum of the segment mass, generalized coordinates, accelerations, and any constraint forces applied to the body.

Because the interest of this dissertation is to quantify individual muscle contribution to overall ACL loading, it is necessary to quantify individual muscle contributions to the anteroposterior JRF. Recent papers have created methods to calculating individual muscle contributions to three-dimensional ground reaction forces during various tasks (335-339, 366-369). As the ground reaction forces are used within the JointReaction analysis in OpenSim, individual muscle contributions to the anteroposterior JRF can easily be calculated by solving for

the dynamical equations of motion by using each muscle's contribution to the ground reaction forces and their respective muscle force from static optimization in isolation.

To validate that the muscle contributions to ground reaction forces are accurate, the theoretical principle of 'superposition' has been used to gain confidence in the simulated ground reaction forces compared to the experimental ground reaction forces. The principle of superposition states that the sum of all forces (e.g. muscle, gravity, velocity, Coriolis) acting on the body must equal the experimental ground reaction forces (334). If this principle is true, and if ground reaction forces are used in the JointReaction analysis, then the principle of superposition should theoretically apply as a way to validate that muscle contributions to the anteroposterior JRF compared to the overall anteroposterior JRF are accurate. If the muscle contributions to the ground reaction forces and the anteroposterior JRF are agreeable, then it could be confidently said that the muscle contributions to the overall ACL loading would also be accurate. However, it is unknown how model complexity (i.e. increased number of muscles, joints, degrees-of-freedom (*dof*)), would affect the principle of superposition.

Therefore, the purpose of this communication was to calculate individual muscle contributions to the anteroposterior JRF and compute superposition error between the experimental and simulated anteroposterior JRFs from a simplistic pendulum model as well as a representative trial from a healthy representative participant from the current dissertation.

Methods and Materials

OpenSim (v3.2, http://simtk.org) was used to simulate a single drop landing. A custom made pendulum model (i.e. Hopper model) was created to simplistically model the pelvis, femur, and tibia during the landing simulation. More specifically, this model was a three segment, eight degree-of-freedom (*dof*) actuated by 2 musculotendon actuators. A 20 kg block containing a 6-

dof custom joint was used to define the pelvis. To define the femur and tibia, two 5 kg links containing a 1-*dof* custom joint to model the hip and the knee were implemented. The patella was represented by a wrapping object within the knee joint. The model contained two muscles, vastus 1 and vasuts 2, both utilizing the Millard 2012 equilibrium muscle model (374). Landing motion and ground reaction forces during the simulated landing were obtained via forward dynamics. Inverse dynamics was used to obtain lower extremity joint moments. These joint moments were then decomposed into individual muscle forces via a static optimization algorithm (374), accomplished by minimizing the sum of muscle activations squared (362).

Anteroposterior knee JRF using the muscle forces obtained from static optimization were computed using the JointReaction Analysis in OpenSim and were applied and expressed in the tibial reference frame. The potential of the two musculotendon actuators to accelerate the Hopper center of mass were calculated using a previously established induced acceleration analysis which included a rolling constraint foot-ground contact model (339, 371). Then, individual muscle contributions to three-dimensional GRFs were calculated by 1) calculating the potentials via the dot product of the Hopper model mass and the induced acceleration analysis results, and 2) taking the dot product of the potentials and the individual muscle forces obtained from static optimization. Finally, each muscle's contribution to the anteroposterior JRF were computed by applying each muscle's contribution to the GRF in isolation and solving for the dynamical equations of motion.

Overall anteroposterior JRF as well as the individual contributions to the anteroposterior JRF was also calculated for one representative trial box-land-and-cut trial from a representative healthy female participant (S01; age: 27; height: 171.5 cm; weight: 74.5 kg). A generic musculoskeletal model (i.e. Lai model) consisting of 14 segments, 23 degrees of freedom (*dof),*

and 80 musculotendon actuators (40 right leg, 40 left leg) (359) was scaled to match the representative participant's anthropometry based on experimentally measured anatomical landmarks. Each hip was modeled as a 3-*dof* ball-and-socket joint. Each knee was modeled as a 1-*dof* hinge joint with abduction-adduction and internal-external rotations as well as anteroposterior and superior-inferior translations constrained to change as a function of knee flexion angle (360). The ankles were modeled as a 1-*dof* pin joint. The same methods for calculating overall anteroposterior JRF as well as the individual components to the JRF in the Hopper model were used to in the JRF calculations for the representative participant.

To verify the accuracy of the summed muscle contributions to the JRF as well as the summed contributions of all components (i.e. muscles, gravity, velocity, residuals, reserves) to the experimental JRF for the Hopper and the Lai models, normalized root mean square error (nRMSE) and coefficients of correlation (R^2) were calculated (12). To qualitatively verify the summed muscle JRF and the summed total component JRF for the Hopper model (Figure 70) and Lai model (Figure 71), a superposition plots for the experimental and summed JRFs was created. Hopper model muscle only JRF consisted of the summation of both muscles in the model (i.e. vastus 1 and vastus 2). The Lai model muscle only JRF was produced by the summation of all 80 muscles within the model (i.e. all 40 right leg and all 40 left leg muscles).

Results

When examining the Hopper model JRFs, the contributions to the anteroposterior JRF by the muscles only (nRMSE = 0.2%; R^2 = 1.0) outperformed the contributions to the anteroposterior JRF by all components within then model (i.e. sum of muscles, gravity, velocity, residuals, and reserves; nRMSE = 4.6%; R^2 = 0.99). When model complexity increased, both the nRMSE and R^2 increased. The Lai model contributions to the anteroposterior JRF by the muscles

only nRMSE = 24.7%; R^2 = 0.95) marginally outperformed the contributions to the anteroposterior JRF by all components within then model (i.e. sum of muscles, gravity, velocity, residuals, and reserves; nRMSE = 27.9%; R^2 = 0.93).

Discussion and Conclusion

The theory of superposition was partially supported in the current study. We did find that when using a simplistic pendulum model, the summation of the contributions to the anteroposterior JRF by the muscles only were agreeable to the experimental JRF. With the addition of other components, such as gravity, velocity, residuals, and reserves, we saw that both the nRMSE and R^2 increased. The residuals and reserves do not contribute to the GRFs, therefore would not contribute to the JRFs and would be inappropriate to include in the contributions summation. For the Hopper model specifically, it appears that gravity was the biggest influencer in the differences between the muscle only JRF and the all components JRF. When model complexity was increased with the addition of several muscles and *dof*s, both nRMSE and R^2 increased considerably. When examining the muscles only JRF for the Lai model, superposition error quantitatively and qualitatively vastly increased compared to the Hopper model. The addition of gravity, velocity, residuals, and reserves only minimally increased these errors. This would suggest that in a simplistic pendulum model, gravity is the largest influencer in superposition error, while in a complex model, the issue of superposition error seems to mostly lie in the summation of the muscles.

The theoretical principle of superposition states the net variable is a summation of individual components related to that variable. Dorn, Lin and Pandy (334) defined the principle of superposition as the sum of all forces (e.g. muscle, gravity, velocity, Coriolis) acting on the body must equal the experimental GRFs. We have determined that the principle of superposition

verifies that the summation of all individual muscle contributions to the GRF agree with the experimental GRFs observed in the current study (Appendix P; Appendix Q). However, for other variables such as anteroposterior JRF, the principle of superposition may not remain true as the principle of superposition only holds true when a linear relationship exists between the net variable and the corresponding individual contributions to that variable.

Tijs, van Dieën, Baan and Maas (375) investigated the principle of superposition in the contributions of the soleus and gastrocnemius to the net ankle joint moment in rats at different ranges of ankle angles. They found that the sum of the soleus and gastrocnemius contributions to the net ankle joint moment did not equal the actual net ankle joint moment at each ankle angle they tested in the sagittal, frontal, and transverse plane (375). The authors hypothesized that this was the result of different mechanisms, such as stretch of common elastic components shared between muscles, transfer of muscle forces between epimuscular myofascial connections between adjacent muscles, and increases in tendon moment arms attached to shared muscles, can affect the mechanical interaction between the gastrocnemius and soleus muscles. Therefore, it is possible that the same concepts described in the Tijs, van Dieën, Baan and Maas (375) paper could hold true for the nonlinear summation for individual muscle contributions to anteroposterior JRF when a more complex musculoskeletal model (i.e. increased number of muscles, increased number of *dof*s) is used. However, it is important to note that the importance of superposition between experimental JRFs and individual muscle contributions to the experimental JRFs is unknown. Further work is needed to investigate the principle of superposition and muscle contribution to JRFs.

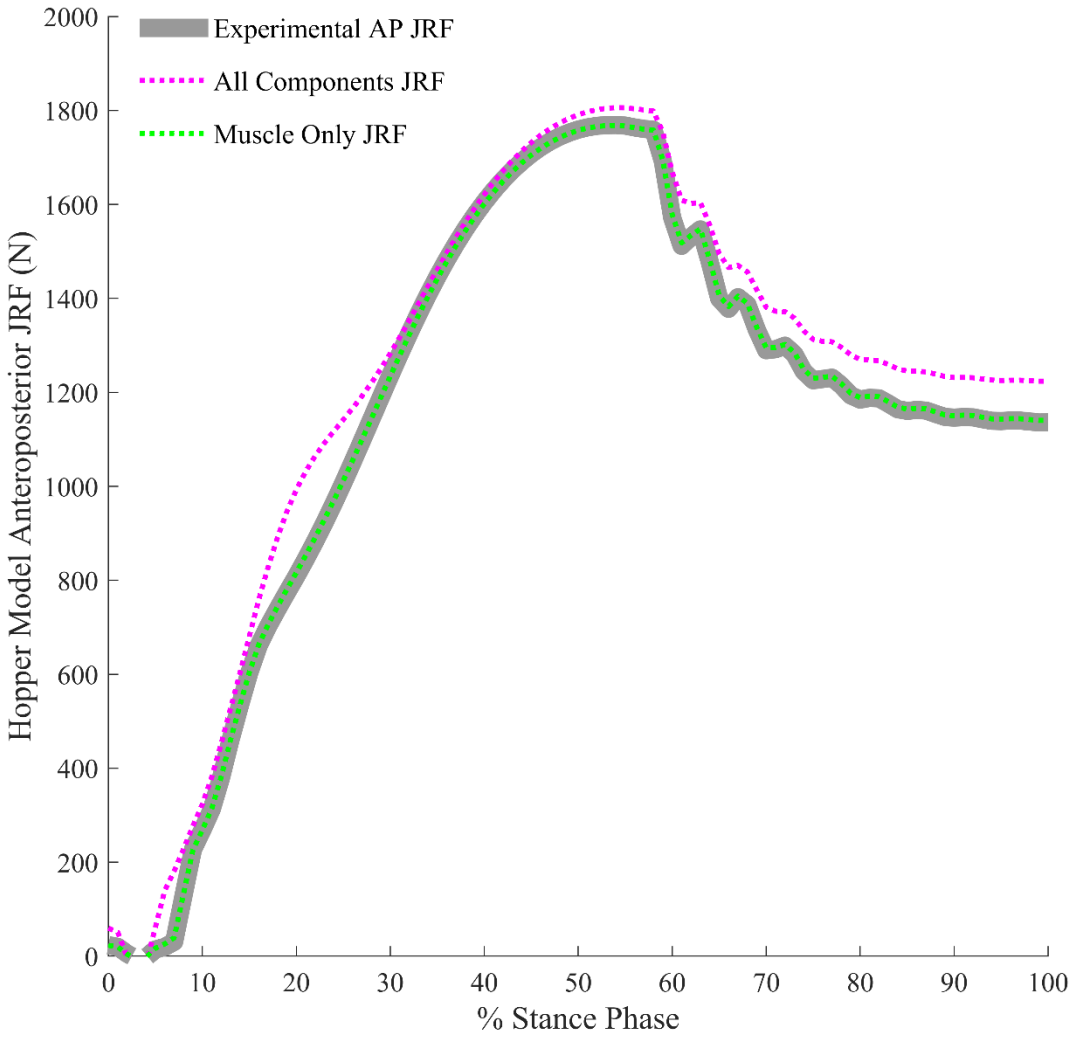


Figure 70: Comparison of the Hopper model summed muscle JRF and the Hopper model summed total component JRF to the Hopper model experimental anteroposterior JRF.

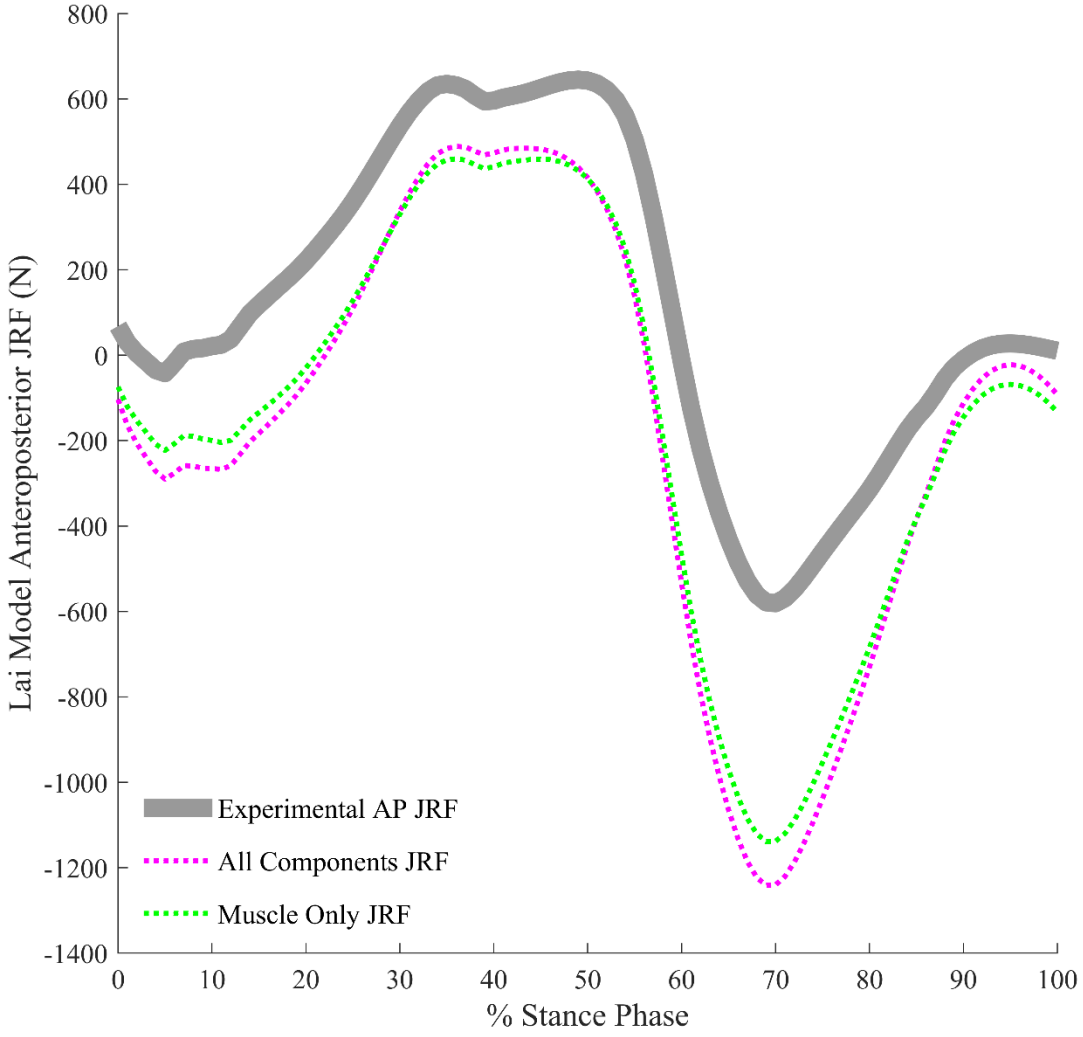


Figure 71: Comparison of the Lai model summed muscle JRF and the Lai model summed total component JRF to the Lai model experimental anteroposterior JRF from one representative trial box-land-and-cut trial from a representative healthy female participant (S01).

Vita

Shelby Peel was born in Port Charlotte, Florida in 1991 and is the daughter of Jack Peel. She is the oldest of two children, with one younger brother, Rhett Peel. Shelby graduated from Liberty Technology Magnet High School in Jackson, Tennessee in 2009. After high school, Shelby played softball at Jackson State Community College where she graduated with an Associate of Science degree in General Studies in 2011. She then transferred to the University of Memphis, where she earned her Bachelor of Science degree in Health and Human Performance with a concentration in Exercise and Sports Science in 2014. Shelby earned he Master of Science degree in Health and Human Performance with a concentration in Exercise and Sports Science at the University of Memphis in 2016. Shelby earned a second Master's degree in Statistics degree during her time at the University of Tennessee, Knoxville in 2020. She completed her education at the University of Tennessee, Knoxville, earning a Doctor of Philosophy in Kinesiology and Sports Studies with a concentration in Biomechanics in 2020. Shelby has accepted a post-doctoral position with the Geneva Foundation, working jointly with High Point University, in High Point, North Carolina and the Womack Army Medical Center in Fort Bragg, North Carolina.